

# **ANNUAL PUBLICATIONS**

**2 0 1 6**



**Graduate School of  
Medical and Dental Sciences  
Tokyo Medical and Dental University**

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## Graduate School of Medical and Dental Sciences

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# Oral Pathology

Professor  
Tohru Ikeda

Junior Associate Professor  
Kei Sakamoto

Assistant Professor  
Kou Kayamori

Technical Staff  
Miwako Hamagaki

Graduate Students  
Akane Yukimori  
Sawangarun Wanlada  
Yae Ohata  
Yuko Ymagata (Oral and Maxillofacial Surgery)  
Akane Wada  
Shoko Ishida  
Maiko Tsuchiya

## ( 1 ) Research

- 1) Pathology and biology associated with bone
- 2) Pathological and biological studies on oral cancers, odontogenic tumors and oral premalignant lesions
- 3) Pathological and biological studies on microenvironment associated with invasion and metastasis of cancers
- 4) Clinicopathological and diagnostic histopathological studies on oral and maxillofacial lesions

## ( 2 ) Education

Lectures and microscope practice in the module “Pathology” to 3rd grade students. The Pathology module comprises two sections; General pathology and Oral pathology. Main objective of General pathology is to provide students knowledge on various diseases, which is essential to work in dental, medical and biological fields. Oral pathology provides detailed knowledge on oral diseases, which is indispensable for a dentist.

## ( 3 ) Clinical Services & Other Works

Our staffs and graduate students participate in diagnostic pathology practice in the Dental Hospital, where nearly 3,000 specimens are annually submitted to laboratory investigation. Our staffs and graduate students also participate in autopsy in the Medical Hospital in cooperation with the staffs and graduate students at the Faculty of Medicine.

( 4 ) **Publications**

**[Original Articles]**

1. Kou Kayamori, Ken-Ichi Katsube, Kei Sakamoto, Yoshio Ohyama, Hideaki Hirai, Akane Yukimori, Yae Ohata, Takumi Akashi, Masao Saitoh, Kiyoshi Harada, Hiroyuki Harada, Akira Yamaguchi. NOTCH3 Is Induced in Cancer-Associated Fibroblasts and Promotes Angiogenesis in Oral Squamous Cell Carcinoma. PLoS ONE. 2016; 11(4); e0154112
2. Masita Mandasari, Wanlada Sawangarun, Ken-Ichi Katsube, Kou Kayamori, Akira Yamaguchi, Kei Sakamoto. A facile one-step strategy for the generation of conditional knockout mice to explore the role of Notch1 in oroesophageal tumorigenesis. Biochem. Biophys. Res. Commun.. 2016.01; 469(3); 761-767

# Bacterial Pathogenesis

Professor SUZUKI Toshihiko

Assistant Professor

SUZUKI Shiho

## ( 1 ) Research

Research Subjects

- 1) Molecular mechanisms of infection by pathogenic bacteria
- 2) Mechanisms of activation and regulation of inflammasomes via Nod-like receptors and caspase activation
- 3) Study of virulent genes based on comparative genomics
- 4) Relationship between persistent bacterial infection and chronic inflammatory diseases such as adipose or diabetes

## ( 2 ) Lectures & Courses

Purpose of Education

The aim of our laboratory in the graduate course is to understand molecular mechanism of pathogen infection and host immune responses. Students also learn planning of research, experiments and methods for evaluating.

## ( 3 ) Publications

### [Original Articles]

1. Ayumi Saeki, Toshihiko Suzuki, Akira Hasebe, Ryousuke Kamezaki, Mari Fujita, Futoshi Nakazawa, Ken-Ichiro Shibata. Activation of nucleotide-binding domain-like receptor containing protein 3 inflammasome in dendritic cells and macrophages by *Streptococcus sanguinis*. *Cell. Microbiol.* 2016.09; Epub;
2. Yohei Yamaguchi, Tomoko Kurita-Ochiai, Ryoki Kobayashi, Toshihiko Suzuki, Tomohiro Ando. Regulation of the NLRP3 inflammasome in *Porphyromonas gingivalis*-accelerated periodontal disease. *Inflamm. Res.* 2016.09; 66(1); 59-65

### [Books etc]

1. Toshihiko Suzuki etc.. Antibiotics and Chemotherapy. *Iyaku Journal-sha*, 2016.02
2. Shiho Suzuki, Toshihiko Suzuki. Antibiotics and Chemotherapy . *Iyaku Journal-sha* , 2016.09

### [Conference Activities & Talks]

1. Shiho Suzuki, Toshihiko Suzuki, Hitomi Mimuro, Chihiro Sasakawa. GLMN is novel negative regulator of inflammasome in response to bacterial infection. The 89th Annual Meeting of Japanese Society for Bacteriology 2016.03.23 Osaka



2. Ayumi Saeki, Akira Hasebe, Toshihiko Suzuki, Ken-ichiro Shibata. IL-1alpha-inducing activity of *Streptococcus sanguinis* in murine dendritic cells and macrophages. The 89th Annual Meeting of Japanese Society for Bacteriology 2016.03.25 Osaka
3. Ryosuke Kamezaki, Ayumi Saeki, Akira Hasebe, Yoshimasa Kitagawa, Toshihiko Suzuki, Ken-ichiro Shibata. Activation of inflammasome by *Aggregatibacter actinomycetemcomitans*. The 58th Annual Meeting of Japanese Association for Oral Biology 2016.08.24 Sapporo
4. Ayumi Saeki, Akira Hasebe, Ryosuke Kamezaki, Toshihiko Suzuki, Ken-ichiro Shibata. Involvement of inflammasome in IL-1alpha-inducing activity of *Streptococcus sanguinis*. The 58th Annual Meeting of Japanese Association for Oral Biology 2016.08.24 Sapporo
5. Shiho Suzuki, Toshihiko Suzuki, Hitomi Mimuro, Chihiro Sasakawa. GLMN is functionally involved in inflammasome activation. The 45th Annual Meeting of The Japanese Society for Immunology 2016.12.07 Okinawa

# Molecular Immunology

Professor	Miyuki Azuma
Associate Professor	Shigenori Nagai
Assistant Professor	Tatsukuni Ohno
Adjunct instructor	Hiroshi Kiyono
	Takeshi Azuma
Graduate Students (Doctor)	
	Siwen Kang(~Sept.)
	Yuta Kondo(~Mar.)
	Hirunwidchayarat Worawalun
	Nadya Niken Adiba
	Naoto Nishii
	Xia Yulong
	Katou Hiroshi(Apr.~)
	Furusawa Emi(Apr.~)
	Yang Yue(Apr.~)
	Tachinami Hidetake(Apr.~)
Research Student	Jin Xin

## ( 1 ) Research

Research Subjects

- 1) Mechanisms of immune responses in oral diseases
- 2) Studies on lymphocyte functional molecules
- 3) Immunotherapy by molecular targetting

## ( 2 ) Lectures & Courses

Purpose of Education

Main objective of Molecular Immunology in the graduate course is to understand and study how the immune system works for biological defense. Students also learn immunopathology and immunophysiology of systemic and organ-specific immune diseases and how the immune diseases control and regulate.

## ( 3 ) Publications

### [Original Articles]

1. Kondo Y, Ohno T, Nishii N, Harada K, Yagita H, Azuma M. Differential contribution of three immune checkpoint (VISTA, CTLA-4, PD-1) pathways to antitumor responses against squamous cell carcinoma. Oral Oncology. 2016; 57; 54-60

2. Kurebayashi Y, Baba Y, Minowa A, Nadya NA, Azuma M, Yoshimura A, Koyasu S, Nagai S. TGF- $\beta$ -induced phosphorylation of Akt and Foxo transcription factors negatively regulates the differentiation of induced regulatory T cells. *Biochem Biophys Res Commun.* 2016; 480; 114-119
3. Shiono Y, Ishii K, Nagai S, Kakinuma H, Sasaki A, Tsuji T, Okada Y, Koyasu S, Nakamura M, Toyama Y, Aizawa M, Matsumoto M. Delayed *Propionibacterium acnes* surgical site infections occur only in the presence of an implant. *Sci Rep.* 2016; 6; 32758
4. Yamazumi Y, Sasaki O, Imamura M, Oda T, Ohno Y, Shiozaki-Sato Y, Nagai S, Suyama S, Kamoshida Y, Funato K, Yasui T, Kikutani H, Yamamoto K, Koyasu S, Akiyama T. The RNA-binding protein Mex-3B is required for IL-33 induction in the development of allergic airway inflammation. *Cell Rep.* 2016; 16; 2456-2471
5. Funao H, Nagai S, Sasaki A, Hoshikawa T, Tsuji T, Okada Y, Koyasu S, Toyama Y, Nakamura M, Aizawa M, Matsumoto M, Ishii K. A novel hydroxyapatite film coated with ionic silver via inositol hexaphosphate chelation prevents implant-associated infection. *Sci Rep.* 2016; 6; 23238
6. Vo M, Holz LE, Wong YC, English K, Benseler V, McGuffog C, Azuma M, McGaughan GW, Bowen DG, Bertolino P. Effector T cell function rather than survival determines extent and duration of hepatitis in mice. *J Hepatol.* 2016; 64; 1327-1338
7. Kang S, Zhang C, Ohno T, Azuma M. Unique B7-H1 expression on masticatory mucosae in the oral cavity and trans-coinhibition by B7-H1-expressing keratinocytes regulating CD4<sup>+</sup> T-cell-mediated mucosal tissue inflammation. *Mucosal Immunol*; in press. 2016;

#### **[Conference Activities & Talks]**

1. Azuma M. Immune regulation in the oral cavity. Tokyo medical and Dental University-Taipei Medical University Joint Symposium 2016.11.12 Taiwan

# Advanced Biomaterials

Professor UO Motohiro  
Associate Professor HONGO Toshio  
Assistant Professor NAKAMURA Hideo  
Assistant Professor WADA Takahiro  
Graduate Student CHAIAMORNSUP Patcharanun

## ( 1 ) Research

1. Analysis of Dental and biomedical materials and biological tissue using the synchrotron radiation.  
Research is aimed to apply the new analysis method using synchrotron radiation for the estimation of various properties of the dental and biomedical materials.
2. Development of the functional dental and biomedical materials using glass and ceramics.  
Research is aimed to develop and evaluate the new glass and ceramics based materials as the dental and biomedical materials, e.g. composite resins, glass ionomer cements, dental porcelains and zirconia ceramics.

## ( 2 ) Education

1. Lecture of unit “Biomaterials and Dental Materials”  
A series of lectures on the “science on biomaterials”, “properties of dental and biomedical materials”, “application of dental materials” will be taught through the lecture and practice.
2. Lecture of unit “Advanced Biomaterials” (graduate school)  
Evaluation methods of various dental and biomedical materials will be taught.

## ( 3 ) Publications

### [Original Articles]

1. Motohiro Uo. Distribution analyses of trace metallic elements in oral mucosal tissues using high-energy SR-XRF SPring-8 Research Frontiers 2015. 2016;
2. Takahiro Wada, Naoyoshi Murata, Hiromitsu Uehara, Takuya Suzuki, Hiroaki Nitani, Yasuhiro Niwa, Motohiro Uo, Kiyotaka Asakura. Degradation mechanism of a high-performance real micro gas sensor, as determined by spatially resolved XAFS Physical Chemistry Chemical Physics. 2016.02; 18; 7374-7380
3. Satoru Takakusagi, Akitoshi Kunimoto, Natee Sirisit, Hiromitsu Uehara, Tadashi Ohba, Yohei Uemura, Takahiro Wada, Hiroko Ariga, Wang-Jae Chun, Yasuhiro Iwasawa, Kiyotaka Asakura. A New Indicator for Single Metal Dispersion on a TiO<sub>2</sub>(110) Surface Premodified with a Mercapto Compound Journal of Physical chemistry C. 2016.03;
4. Kitano R., Ishii M., Uo M., Morita K. Thermodynamic Properties of the CaO–AlO<sub>1.5</sub>–CeO<sub>1.5</sub> System ISIJ International. 2016.10;

5. Takahiro Wada, Hiroshi Churei, Toshiaki Ueno, Motohiro Uo. High shock absorbing faceguard using fiber-reinforced plastic (FRP) and elastomer The Journal of the Japanese Society for Dental Materials and Devices. 2016.11; 35(6); 325-328
6. WeiJen Lai, Yoshiyuki Midorikawa, Zusei Kanno, Hiroshi Takemura, Kazuhiro Suga, Kohei Soga, Takashi Ono, Motohiro Uo. Development and modification of a device for three-dimensional measurement of orthodontic force system: The V-bend system re-visited. Dent Mater J. 2016.12; 35(6); 908-917

#### [Misc]

1. Takahiro WADA, Naoyoshi MURATA, Hiromitsu UEHARA, Takuya SUZUKI, Hiroaki NITANI, Yasuhiro NIWA, Motohiro UO, Kiyotaka ASAKURA. XAFS Analysis of Pt-SnO<sub>2</sub> and Pd/Al<sub>2</sub>O<sub>3</sub> catalysts in the world's first battery driven gas sensor PF News. 2016.02; 33(4); 13-19
2. Motohiro Uo. Distribution analyses of trace metallic elements in oral mucosal tissues using high-energy SR-XRF SPring-8 Research Frontiers 2015. 2016.08; 19-20

#### [Conference Activities & Talks]

1. Rui Guan, Tomohiro Takagaki, Toru Nikaido, Takahiro Wada, Motohiro Uo, Junji Tagami. Adsorption behavior of phosphoric functional monomers to 3Y-TZP surface.. 45th Annual meeting of American Association for Dental Research 2016.03.17
2. Takahiro Wada, Hiroshi Churei, Shintaro Fukasawa, Takahiro Shirako, Toshiaki Ueno, Motohiro Uo. Shock-absorbing property of face guard by incorporating a glass-fiber reinforced plastic and space. 2016.06.12
3. M. YAMAMOTO, K. MOTOMURA, H. NAKAMURA, T. YOSHIOKA, F. YOSHIKAWA, S. TANAKA. Optimum conditions for resistance-heat-bending of NiTi arch wire. 94rd General Session & Exhibition of the IADR, 3rd Meeting of the Asia Pacific Region, 35th Annual Meeting of the IADR Korean Division 2016.06.23 Seoul
4. F.YOSHIKAWA, K.MOTOMURA, H.NAKAMURA, T.YOSHIOKA, M.YAMAMOTO, S.TANAKA. Improving adhesion of zirconia by surface modification. 94rd General Session & Exhibition of the IADR, 3rd Meeting of the Asia Pacific Region, 35th Annual Meeting of the IADR Korean Division 2016.06.24 Seoul
5. Midorikawa Y, Takemura H, Mizoguchi H, Soga K, Kamimura M, Suga K, Lai WJ, Kanno Z, Uo M. Six-axis orthodontic force and moment sensing system for dentist technique training. IEEE 38th Annual International Conference 2016.08.16
6. Qiuyi Yuan, Satoru Takakusagi, Yohei Uemura, Takahiro Wada, Kiyotaka Asakura. A XAFS Investigation of Pt Monolayer on Au(111) Obtained from Displacement Reaction. PRiME 2016/230th ECS Meeting 2016.10.03
7. Uo M, Wada T, Maekawa M, Kanno Z, Ono T, Hanawa T. Development of super engineering plastic V (PEEK) made orthodontic wires. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan
8. Takahiro Wada, Hiroshi Churei, Haruka Takayanagi, Mako Yokose, Shintaro Fukasawa, Takahiro Shirako, Toshiaki Ueno, Naohiko Iwasaki, Hidekazu Takahashi, Motohiro Uo. Development of a faceguard using a glass-fiber reinforced thermoplastic (GFRTTP) and shock escape space. Visual-JW 2016 2016.10.17 Suita, Osaka, Japan
9. Donghoon Kang, Takahiro Wada, Motohiro Uo, Takashi Okiji. Evaluation of mechanical properties of an experimental synthetic tricalcium silicate cement. 2016.10.22 Seoul, Korea
10. Takahiro Wada, Hiroshi Churei, Shintaro Fukasawa, Takahiro Shirako, Toshio Hongo, Toshiaki Ueno, Motohiro Uo. Analysis of shock absorption ability of a faceguard by incorporating a glass-fiber reinforced thermoplastic and space. International Dental Materials Congress 2016 2016.11.05 Bali, Indonesia
11. Tanabe G, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Effect of the use of commercial cleaning liquid in thermoforming process of mouthguard materials. International Dental Materials Congress 2016 2016.11.05 Bali, Indonesia

12. Toshio Hongo, Takahiro Wada, Motohiro Uo. Development of a quantitative method of residual substances in the autopolymerizing acrylic resin. International Dental Materials Congress 2016 2016.11.05 Bali, Indonesia

## Diagnostic Oral Pathology

Associate Professor: Toshiyuki IZUMO

Visiting Lecturer: Yasuo YAGISHITA, Yasumasa MORI

Hospital Staff: Rei TOHYAMA,  
Yuuichi YAMADA, Kiyoko NAGUMO,  
Kana NANBA, Akiko ASANO,  
Mayuko MINAMI, Yukiko Kuroki,  
Kou YANAI, Yuuta TAKAHASHI

### (1) Outline

Diagnostic oral pathology is a branch of pathology which studies human pathology, and aims at practice and development of the oral science as clinical medicine. The main object is to bring up graduate students and post-doctoral residents for pathology specialist to the great oral pathologists through the lecture of surgical pathology and pathology diagnosis and research instruction of oral and general diseases for the time being.

### (2) Research

Research Subjects

- 1) Surgical pathology of oral cancer.
- 2) New diagnostic approach and reconstruction of oral diseases.

### (3) Clinical Services & Other Works

Diagnostic oral pathology is playing three roles, pathological diagnosis (3,400 cases in a year), clinical laboratory (215,000 tests in a year) which consist of hematological, biochemical, bacteriological, physiological and pathological parts, and blood transfusion (100 cases in a year) in the dental hospital.

### (4) Publications

#### [Original Articles]

1. Nguyen CT, Okamura T, Morita K, Yamaguchi S, Harada H, Miki Y, Izumo T, Kayamori K, Yamaguchi A, Sakamoto K. LAMC2 is a predictive marker for the malignant progression of leukoplakia Journal of Oral Pathology and Medicine. 2016;
2. Okamura T, Izumo T, Yagishita H, Mori T, Sakamoto K, Harada K.. Disordered arrangements of basal cells as a prognostic factor for oral epithelial dysplasia: a morphometric study of 96 cases. Oral Surg Oral Med Oral Pathol Oral Radiol. . 2016; 122(3); 355-361
3. Morita T, Uzawa N, Mogushi K, Sumino J, Michikawa C, Takahashi KI, Myo K, Izumo T, Harada K.. Characterizing Genetic Transitions of Copy Number Alterations and Allelic Imbalances in Oral Tongue Carcinoma Metastasis. Genes Chromosomes Cancer. 2016; 55(12); 975-986

4. Morita T, Yamashiro M, Kayamori K, Mizutani M, Nakakuki K, Michi Y, Uzawa N, Izumo T, Harada K. Primary intraosseous squamous cell carcinoma derived from a maxillary cyst: A case report and literature review. *Molecular and Clinical Oncology*. 2016; 4; 553-558
5. Wake S, Yoshitake H, Kayamori K, Izumo T, Harada K. Expression of CD90 decreases with progression of synovial chondromatosis in the temporomandibular joint. *Cranio*. 2016; 34(4); 250-256



## Oral Radiation Oncology

Professor	Masahiko MIURA
Assistant Professor	Atsushi KAIDA
Clinical Fellow	Satoshi SATO
	Tatuaki GOTOU
Graduate Students	Kouhei OKUYAMA
	Hiroyuki ONOZATO
	Nisha GOWRI MANILA
	Sirimanas JIARANUCHART
	Hisao HONMA
Special Research Student	Taito ASAHINA

### ( 1 ) Outline

Main objective of this branch is to provide opportunities to study radiation oncology for oral cancer and translational research for radiosensitization of oral cancer.

### ( 2 ) Research

- 1) Visualization of tumor radioresponse by molecular imaging
- 2) Mechanism of DNA damage response
- 3) Radioresistant signal transduction pathways
- 4) Radiotherapy for oral cancer

### ( 3 ) Education

Oral Radiation Oncology is a branch of radiation oncology dealing with basic radiobiology, translational research, and radiotherapy for oral cancer. Main objective of this branch in the graduate course is to provide opportunities to study biological strategies for radiosensitization, development of radiosensitizers, molecular mechanism of tumor radioresistance, the state of the art technology of radiotherapy, and basis of individualized radiotherapy depending on each student's research projects.

### ( 4 ) Lectures & Courses

The educational policy is to cultivate researchers to be able to extract problems and to work out solutions to them.

### ( 5 ) Clinical Services & Other Works

Oral Radiation Oncology clinic provides radiotherapeutic treatment for head and neck cancer patients, especially brachytherapy for oral cancer, in cooperation with Diagnostic and Therapeutic Radiology clinic in the Medical Hospital.

**( 6 ) Clinical Performances**

We are performing brachytherapy for oral cancer, which is now the only treatment modality without surgical excision, as a center institution in Japan.

**( 7 ) Publications****[Original Articles]**

1. Taito Asahina, Atsushi Kaida, Tatsuaki Goto, Ryo-Ichi Yoshimura, Keisuke Sasai, Masahiko Miura. Temporo-spatial cell-cycle kinetics in HeLa cells irradiated by Ir-192 high dose-rate remote afterloading system (HDR-RALS). *Radiat Oncol.* 2016.07; 11; 99
2. Nisha Gowri Manila, Atsushi Kaida, Masahiko Miura. Kinetic analysis of radiation-induced cell-cycle alterations in HeLa cells expressing fluorescent ubiquitination-based cell cycle indicator (Fucci). *Radiat Environ Med.* 2016.08; 5(2); 16-21
3. Atsushi Kaida, Hiroshi Watanabe, Kazuma Toda, Keiko Yuasa-Nakagawa, Ryoichi Yoshimura, Masahiko Miura. Effects of dose rate on early and late complications in low dose rate brachytherapy for mobile tongue carcinoma using Ir-192 sources. *Oral Radiol.* 2016.12; published online;

**[Conference Activities & Talks]**

1. Watanabe H, Ozaki Y, Miura M, Yoshimura R, Sumi Y, Kurabayashi T. Estimation of whole body radiation exposure induced by oral cancer brachytherapy using Monte Carlo simulation. The 11th Asian Congress of Oral and Maxillofacial Radiology 2016.11.12 Chiang Mai, Thailand
2. Yusuke Onozato, Atsushi Kaida, Hiroyuki Harada, Masahiko Miura. Radiosensitivity of proliferating or quiescent human tongue carcinoma cells grown in multicellular spheroids. The 61th congress of the Japanese Society of Oral and Maxillofacial Surgeons 2016.11.25 Chiba city
3. Masahiko Miura. Cell cycle kinetics and radiosensitivity. The 29th Annual Meeting of JASTRO 2016.11.27 Kyoto city
4. Nisha Gowri Manila, Atsushi Kaida, Masahiko Miura. IGF-IR, but not EGFR, regulates DNA damage response (DDR) in HeLa cells following irradiation. ESMO Asia 2016 Congress 2016.12.17 Singapore

## Oral and Maxillofacial Surgery

Professor Hiroyuki HARADA

Junior Associate Professor Yuji KABASAWA, Eriko MARUKAWA

Assistant Professor Hiroaki SHIMAMOTO, Fumihiko TSUSHIMA, Hirofumi TOMIOKA, Hideaki HIRAI,  
Kae TANAKA

Graduate Student

Yu OIKAWA, Yusuke ONOZATO, Toru TAKEMOTO, Yuko YAMAGATA,

Naoto NISHII, JIARANUCHART Sirimanas, Shuhei FUKUDA,

Ruri KOMIYA, Yoshihisa KASHIMA, Hitomi NOJIMA,

Misaki YOKOKAWA, Naoya KINOSHITA, Yuuki TAKAGAWA,

Aoi KANEKO

### (1) Outline

#### Purpose of Education

The program is designed for acquiring the broad knowledge and basic skills of oral and maxillofacial surgery, mainly concerning the diagnostic procedure, treatment technique and the perioperative patient care. Also throughout the professional education, we promote the system in which each graduate student can select his or her special field in the full scope of oral and maxillofacial surgery in the future.

#### Research Subjects

- 1) Development of multidisciplinary treatment of oral cancer.
- 2) Clinical study on sentinel node navigation surgery for oral cancer.
- 3) Study on molecular markers for lymph node metastasis of oral cancer.
- 4) Clinical study on skeletal and dental changes after distraction osteogenesis in patients with cleft lip and palate.
- 5) Clinical study on maxillomandibular skeletal and dental changes after orthognatic surgery.
- 6) Study on neurosensory disturbances using the heat flux technique.
- 7) Clinical study on pre-surgical nasopalveolar molding in patients with cleft lip and palate.
- 8) Clinical study on alveolar bone grafting with platelet rich plasma.
- 9) Multidisciplinary treatment of temporomandibular disorders.
- 10) Clinical and experimental studies on bone regeneration using  $\beta$ -TCP and/or platelet rich plasma.
- 11) Development of multidisciplinary treatment of oral mucosal diseases.

#### Clinical Services

The Oral and Maxillofacial Surgery Clinic examines yearly more than 6,200 new patients with various diseases arising in oral and maxillofacial regions. The clinic has diplomat of the Japanese Society of Oral and Maxillofacial Surgeons and accepts many referrals from dentists and medical doctors. We provide a full range of services including extractions, removal of wisdom teeth and management of facial trauma, jawbone defect, facial deformity, temporomandibular joint disease, cleft lip and palate, oral mucosal disease, and benign and malignant tumors. The special outpatient clinics are organized by the specialists to offer the best service, especially for patients with malignant tumor, temporomandibular joint disease, cleft lip and palate, facial deformity and oral mucosal disease which need high degree of specialty and long term follow up. We also prepare some groups for inpatients with an emphasis on specialties, to provide the recent and advanced treatment.

**(2) Publications****[Original Articles]**

1. Tomohiro Kohmoto, Atsumi Tsuji, Kei-Ichi Morita, Takuya Naruto, Kiyoshi Masuda, Kenichi Kashimada, Keisuke Enomoto, Tomohiro Morio, Hiroyuki Harada, Issei Imoto. A novel COL11A1 missense mutation in siblings with non-ocular Stickler syndrome. *Hum Genome Var.* 2016; 3; 16003
2. Kou Kayamori, Ken-Ichi Katsube, Kei Sakamoto, Yoshio Ohyama, Hideaki Hirai, Akane Yukimori, Yae Ohata, Takumi Akashi, Masao Saitoh, Kiyoshi Harada, Hiroyuki Harada, Akira Yamaguchi. NOTCH3 Is Induced in Cancer-Associated Fibroblasts and Promotes Angiogenesis in Oral Squamous Cell Carcinoma. *PLoS ONE.* 2016; 11(4); e0154112
3. Kondo Y, Ohno T, Nishii N, Harada K, Yagita H, Azuma M. Differential contribution of three immune checkpoint (VISTA, CTLA-4, PD-1) pathways to antitumor responses against squamous cell carcinoma. *Oral Oncology.* 2016; 57; 54-60
4. Kondo Y, Ohno T, Nishii N, Harada K, Yagita H, Azuma M. Differential contribution of three immune checkpoint (VISTA, CTLA-4, PD-1) pathways to antitumor responses against squamous cell carcinoma *Oral Oncology.* 2016; 57; 54-60
5. Masaru S, Morita K, Kabasawa Y, Harada H. Bilateral nasolabial cysts: a case report *Journal of Medical case Reports.* 2016; 10; 246
6. Mochizuki Y, Tomioka H, Tsushima F, Shimamoto H, Oikawa Y, Harada H. Clinical evaluation of the coverage of open wounds in the oral surgical field with a polyglycolic acid sheet and a fibrin glue spray and coverage with split thickness skin grafting *Annals Maxillofacial Surgery.* 2016; 6(2); 228-234
7. Kato Y, Ogasawara S, Oki H, Honma R, Takagi M, Fujii Y, Nakamura T, Saidoh N, Kanno H, Umetsu M, Kamata S, Kubo H, Yamada M, Sawa Y, Morita K, Harada H, Suzuki H, Kaneko MK. Novel Monoclonal Antibody LpMab-17 Developed by CasMab Technology Distinguishes Human Podoplanin from Monkey Podoplanin Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2016; 2(35); 109-116
8. Masanori Kudoh, Ken Omura, Arata Satsukawa, Koshi Matsumoto, Takahide Taguchi, Hiroyuki Harada, Yoshimasa Ishii. Symmetric Lipomatosis Arising in the Tongue Presenting as Macroglossia and Articulatory Disorder Case Reports in Otolaryngology. 2016; (2016);
9. Nguyen CT, Okamura T, Morita K, Yamaguchi S, Harada H, Miki Y, Izumo T, Kayamori K, Yamaguchi A, Sakamoto K. LAMC2 is a predictive marker for the malignant progression of leukoplakia *Journal of Oral Pathology and Medicine.* 2016;
10. Ohata Y, Tohyama R, Kayamori K, Shimamoto H, Hirota Y, Harada H, Izumo T, Sakamoto K. A rare cancer of the tongue that demonstrated unusual histology and immunohistochemical phenotype: case report *International Dentistry Scientific Meeting 2016/UI Proceedings on Health and Medicine.* 2016; 1(1); 172-175
11. Oda S, Nozawa T, Nozawa-Minowa A, Tanaka M, Aikawa C, Harada H, Nakagawa I. Golgi-Resident GTPase Rab30 Promotes the Biogenesis of Pathogen-Containing Autophagosomes *PLoS One.* 2016.01; 11(1); e0147061
12. Shirakawa J, Harada H, Noda M, Ezura Y. PTH-Induced Osteoblast Proliferation Requires Upregulation of the Ubiquitin-Specific Peptidase 2 (Usp2) Expression *Calcified Tissue International.* 2016.03; 98(3); 306-315
13. Tohyama R, Kayamori K, Sato K, Hamagaki M, Sakamoto K, Yasuda H, Yamaguchi A. Establishment of a xenograft model to explore the mechanism of bone destruction by human oral cancers and its application to analysis of role of RANKL *Journal of Oral Pathology & Medicine.* 2016.05; 45(5); 356-364
14. Macedo R, Rochefort J, Guillot-Delost M, Tanaka K, Le Moignic A, Noizat C, Baillou C, Mateo V, Carpentier AF, Tartour E, Bertolus C, Bellier B, Lescaille G, Lemoine FM. Intra-cheek immunization as a novel vaccination route for therapeutic vaccines of head and neck squamous cell carcinomas using plasmid virus-like particles *Oncoimmunology.* 2016.07; 5(7); e1164363

15. Marukawa E, Tamai M, Takahashi Y, Hatakeyama I, Sato M, Higuchi Y, Kakidachi H, Taniguchi H, Sakamoto T, Honda J, Omura K, Harada H. Comparison of magnesium alloys and poly-l-lactide screws as degradable implants in a canine fracture model *Journal of Biomedical Materials Research Part B: Applied Biomaterials*. 2016.10; 104(7); 1282-1289

#### [Conference Activities & Talks]

1. Marukawa E, Harada H, Sasaki Y, Akiyoshi K. Osteoinduction using  $\beta$ -TCP with Nanogel-crosslinking hydrogel as Nobel scaffold for BMP-2. Academy of Osseointegration's 31st Annual Meeting, February 17-20 2016. 2016.02.17 San Diego
2. Marukawa E, Stricker A, Fleiner J, Flugge TV, Harada H, Schmelzeisen R, Nelson K. The difference in bone resorption between mandibular ramus bone block graft and bone splitting for alveolar ridge augmentation. Academy of Osseointegration's 31st Annual Meeting, February 17-20 2016. 2016.02.17 San Diego
3. Morita K, Naruto T, Tanimoto K, Yasukawa C, Oikawa Y, Masuda K, Imoto I, Inazawa J, Omura K, Harada H. Simultaneous detection of both single nucleotide variations and copy number alterations by next-generation sequencing in gorlin syndrome. The 13th International Congress of Human Genetics, April 3-7 2016 2016.04.03 Kyoto
4. Nishii N, Kondo Y, Li L, Lau W, Hi, Harada H, Azuma M. Combined treatment with PD-L1 blockade and a TLR7/8 agonist dramatically enhances antitumor immunity. AACR2016 2016.04.16 New Orleans, LA, USA Ernest N. Morial Convention Center
5. Takahara N, Kabasawa Y, Tetsumura A, Kurabayashi T, Harada H. Dynamic MR imaging of the temporomandibular joint: a preliminary study. Advanced Digital Technology (ADT) North America & Japan Regional Leadership Groups Conference, June 16-20 2016. 2016.06.16 San Diego
6. Kabasawa Y, Tsuchida Y, Takahara N, Kamiyo S, Suzuki T. :Accuracy of a 3D Model for Surgical Support in Orthognathic Surgery- Efficacy of Data Synthesis with Computed Tomography and Dental Model Scan. Advanced Digital Technology (ADT) North America & Japan Regional Leadership Groups Conference, June 16-20 2016. 2016.06.16 San Diego
7. Miyazaki H, Romeo U, Wada Y, Kato J, Tanaka K, Alessandro DV, Maruoka Y, Watanabe H, Harada H, Asamura S. Treatment strategies for large oral vascular anomalies using intralesional laser photocoagulation. The 15th Congress of the World Federation for Laser Dentistry, July 17-19 2016. 2016.07.17 Aichi

## Oral and Maxillofacial Radiology

Professor: Tohru KURABAYASHI

Associate Professor: Hiroshi WATANABE

Junior Associate Professor: Naoto OHBAYASHI, Norio YOSHINO

Assistant Professor: Akemi TETSUMURA, Shin NAKAMURA, Ami KURIBAYASHI, Junichiro SAKAMOTO

Hospital Staff: Yoshikazu NOMURA, Mamiko FUJIKURA

Graduate Student: Shinya KOTAKI, Ngamsom SUPAK, Hiroko ISHII, Noriko SUZUKI,  
Chutamas DEEPHO, Tran Thi Xuan LAN, Sakurako ASAI, Wamasing PEERAPONG

Research Student: Sakurako ASAI, Shintarou TAKADA

Secretary: Izumi MOTOHASHI

### ( 1 ) Research

- 1) Diagnosis of maxillofacial diseases by CT, MRI and PET imaging
- 2) Advantages of cone-beam CT for clinical dentistry
- 3) Development of high resolution MRI technology.
- 4) Novel MRI techniques for TMJ disorders.
- 5) Factors determining radioresistance of oral and maxillofacial cancers.

### ( 2 ) Lectures & Courses

Oral and maxillofacial radiology is a branch of dental science which deals with the effective application of radiation energy to the diagnosis and treatment of oral and maxillofacial diseases. Main objective of oral and maxillofacial radiology in the graduate course is to provide students opportunity to study advanced imaging modalities including digital imaging, cone-beam CT, multi-detector row CT and MRI, and also to study image processing and image analysis technology. Students are also taught on basic radiation oncology and its related laboratory technology depending on their research project.

### ( 3 ) Clinical Services & Other Works

Oral and maxillofacial radiology clinic provides a full spectrum of imaging examinations and diagnosis, including CT and MRI. Non-invasive, interventional radiology for patients with salivary gland stone is also performed in the clinic.

### ( 4 ) Publications

#### [Original Articles]

1. Yoshi S, Sumita Y, Hattori M, Ohbayashi N, Kurabayashi T, Taniguchi H. The morphological evaluation of denture space in glossectomy patients. *Maxillofacial Prothetics*. 2016; 39; 60-67
2. Sakamoto J, Kuribayashi A, Kotaki S, Fujikura M, Nakamura S, Kurabayashi T. Application of Diffusion Kurtosis Imaging to Odontogenic Lesions: Analysis of the Cystic Component *J Magn Reson Imaging*. 2016.12; 44(6); 1565-1571

3. Kotaki S, Sakamoto J, Kretapirom K, Supak N, Sumi Y, Kurabayashi T. Diffusion tensor imaging of the inferior alveolar nerve using 3T MRI: a study for quantitative evaluation and fibre tracking. *Dentomaxillofac Radiol.* 2016.12; 45(8); 20160200
4. Atsushi Kaida, Hiroshi Watanabe, Kazuma Toda, Keiko Yuasa-Nakagawa, Ryoichi Yoshimura, Masahiko Miura. Effects of dose rate on early and late complications in low dose rate brachytherapy for mobile tongue carcinoma using Ir-192 sources. *Oral Radiol.* 2016.12; published online;
5. Uraba S, Ebihara A, Komatsu K, Ohbayashi N, Okiji T. Ability of cone-beam computed tomography to detect periapical lesions that were not detected by periapical radiography: A retrospective assessment according to tooth group *Journal of Endodontics.*

### [Conference Activities & Talks]

1. Nakamura S. Imaging diagnosis of malignant lymphoma. The 38th Annual Scientific Conference on Dental Research 2016.04 Ho-Chi-Minh City, Vietnam
2. Kotaki S, Sakamoto J, Kurabayashi T. MRI findings of the inferior alveolar nerve. The 38th Annual Scientific Conference on Dental Research. April 5th, 2016, Ho-Chi-Minh City, Vietnam 2016.04.05
3. Ngamsom S, Nakamura S, Sakamoto J, Kotaki S, Kurabayashi T. Quantitative evaluation of lateral pterygoid muscles in patients with temporomandibular joint disorders by intravoxel incoherent motion MRI. *Swiss Congress of Radiology* 2016 2016.05 Davos, Switzerland
4. Ozawa E, Honda E, Ohmori H, Shimazaki K, Kurabayashi T, Ono M. Influence of orthodontic appliance-derived artifacts on 3-T MRI movies. *IADR/APR 94th General Session* 2016.06.22 Seoul
5. Watanabe C, Wada J, Mizutani K, Watanabe H, Wakabayashi N. The effect of removable partial denture placement on periodontal structures of abutment teeth in patients of periodontitis: A digital subtraction analysis. *The 125th Scientific Meeting of Japan Prosthodontic Society* 2016.07.10 Kanazawa
6. Nguyen Ho Q, Yamazaki Y, Imura H, Yoshino N, Kurabayashi T, Taira M, Shimada M. Peripheral injuries may lead to grey matter volume reduction in post traumatic trigeminal neuropathic pain. *16th World Congress of Pain* 2016.09.26 Yokohoma
7. Nakajima Y, Iwasaki N, Takahashi H, Yoshida M, Honda E, Kurabayashi T. MRI artifacts and radiopacity of CAD/CAM composite resin blocks. *The 2016 Academy of Dental Materials Annual Meeting* 2016.10.12 Chicago
8. Nakamura S, Sakamoto J, Yoshino N, Kurabayashi T. Imaging of lingual lymph node metastasis in patients with squamous cell carcinoma of the tongue. *The 11th Asian Congress of Maxillofacial Radiology* 2016.11 Chiang Mai, Thailand
9. Watanabe H, Ozaki Y, Miura M, Yoshimura R, Sumi Y, Kurabayashi T. Estimation of whole body radiation exposure induced by oral cancer brachytherapy using Monte Carlo simulation. *The 11th Asian Congress of Oral and Maxillofacial Radiology* 2016.11.12 Chiang Mai, Thailand
10. Deepho C, Watanabe H, Kotaki K, Sakamoto J, Sumi Y, Kurabayashi T. Utility of CT/MRI fusion volumetric images for localizing the mandibular canal. *The 11th Asian Congress of Oral and Maxillofacial Radiology* 2016.11.12 Chiang Mai, Thailand
11. Kotaki S, Sakamoto J, Kretapirom K, Ngamsom S, Kurabayashi T. Diffusion Tensor Imaging of the Inferior Alveolar Nerve Using 3T MRI. *The 11th Asian Congress of Oral and Maxillofacial Radiology.* November 12th, 2016, Chiang Mai, Thailand 2016.11.12
12. Toriihara A, Sakamoto J, Nakamura S, Oyama J, Kurabayashi T, Tateishi U. All about the mandible: chewing and absorbing key points for evaluating morphological and functional images. *Radiological Society of North America 2016 Annual Meeting* 2016.11.27 Chicago

### [Patents]

1. Method of Predicting Metastasis of Oral Cavity Cancer into Cervical Lymph Node and Diagnostic Kit to be used in the Prediction, Patent Number : 8129122 United States Patent

# Anesthesiology and Clinical Physiology

Professor  
 Haruhisa Fukayama  
 Associate Professor  
 Ryo Wakita  
 Junior Associate Professor  
 Keiko Abe  
 Assistant Professors  
 Tomoyuki Miyamoto, Tomoka Matsumura, Kazumasa Kubota,  
 Hospital Staffs  
 Yukiko Baba (Jan~), Kanako Saji (Apr~), Toru Yamamoto (Apr~),  
 Keiko Abe (Apr~), Kanji Doushita (Apr~), Sayumi Abe (Apr~)  
 Graduate Students  
 Takutoshi Inoue, Kaeko Araki, Asami Izumida, Chihiro Suzuki,  
 Takaya Itou (Apr~), Yuu Satou (Apr~), Tamae Hasegawa (Apr~)  
 Research Students  
 Tsunataka Abo (Apr~), Hiroyuki Tojo (Apr~),  
 Akira Oshima (Apr~), Yosuke Yamada (Apr~)  
 Advanced Clinical Training  
 Feng Yu Pin (Jun~)  
 Secretary  
 Natsu Sato

## ( 1 ) Outline

For safety and comfortable dentistry for both patients and dentists, educations, researches and clinical practices are performed in the department. Education includes basics and practices of local and general anesthesia, sedation, monitoring (monitored anesthesia care, MAC) in addition to cardio-pulmonary resuscitation, or, basic life support during dental treatment. Our researches are consisted of basic and clinical trials for the purposes. Many cases give us many chances to keep the patients safe and comfortable during local and general anesthesia. Local groups, such as dental associations, are welcomed to promote safe and comfortable dental treatments.

## ( 2 ) Research

- 1 ) Non-invasive drug delivery system
- 2 ) New methods for local anesthesia in dentistry
- 3 ) Neuropathic pain in oral and maxillofacial regions
- 4 ) Diffuse noxious inhibitory control or controlled pain modulation
- 5 ) Sedation for dentistry

## ( 3 ) Education

Anesthesia and anesthesiology for dentistry, which are not only local anesthesia but also general anesthesia are given to the both under and post graduate students. Lectures and trainings are consisted of local and



general anesthesia, sedation and cardio-pulmonary-resuscitation (CPR), or, basic life support (BLS). For local anesthesia, the students learn mechanism of local anesthesia, local anesthetics, techniques and local and systemic complications due to local anesthesia. Physiology, biochemistry and pharmacology are also provided for general anesthesia which includes possible mechanism of general anesthesia, anesthetics, muscle relaxants and what are used for general anesthesia. They also acquire the techniques of topical, infiltration and conduction anesthesia, nitrous oxide inhalation sedation and basic life support.

#### **( 4 ) Lectures & Courses**

Anesthesia and anesthesiology for dentistry, which are not only local anesthesia but also general anesthesia are given to the both under and post graduate students. Lectures and trainings are consisted of local and general anesthesia, sedation and cardio-pulmonary-resuscitation (CPR), or, basic life support (BLS). For local anesthesia, the students learn mechanism of local anesthesia, local anesthetics, techniques and local and systemic complications due to local anesthesia. Physiology, biochemistry and pharmacology are also provided for general anesthesia which includes possible mechanism of general anesthesia, anesthetics, muscle relaxants and what are used for general anesthesia. They also acquire the techniques of topical, infiltration and conduction anesthesia, nitrous oxide inhalation sedation and basic life support.

#### **( 5 ) Clinical Services & Other Works**

Safe medical and perioperative managements are given to the patients of our ambulatory anesthesia service which has more than 2,000 cases per year and the central operation rooms which has 750 cases per year. Some difficult cases are referred to our hospital because of many clinical experiences.

Several cases that need emergency care are also supported by our department. ER members are sometimes called in the medical hospital.

Local groups like dental associations often ask us to hold some lectures, trainings, workshops for safe dental treatment. These proposals are welcomed by our staffs. When intravenous sedation cases are introduced, some responsible staff is sent to their own clinic.

#### **( 6 ) Clinical Performances**

Any patient is welcomed, especially patients of oral surgery and implant operation who need special care using general anesthesia and sedation.

Referred patients from open practitioners are also accepted for safe and comfortable dental treatment.

#### **( 7 ) Publications**

##### **[Original Articles]**

1. Inoue T, Sugiyama T, Ikoma T, Shimazu H, Wakita R, Fukayama H. Drug delivery and transmission of lidocaine using iontophoresis in combination with direct and alternating currents *Journal of Medical and Dental Sciences*. 2016; 63(4); 71-77
2. Sasaki Y, Kato S, Miura M, Fukayama H. Correlation between body movements and salivary secretion during sedation *Anesthesia Progress*. 2016; 63; 185-191
3. Fjii-Abe K, Kawahara H, Fukayama H. An analysis of green discoloration of urine caused by propofol infusion *Journal of Clinical Anesthesia*. 2016; 35; 358-360
4. Matsumura T, Kubota K, Sakamoto K, Fukayama H. NGF is induced by lidocaine in human skin fibroblast cell in vitro *Masui*. 2016.03; 65; 288-290

##### **[Books etc]**

1. Kazuhiro Shimoyama, Haruhisa Fukayama. *Dictionary of Gerodontology*. Ishiyaku Publishers, INC., 2016.03 (ISBN : 978-4-263-45793-1)

### **[Conference Activities & Talks]**

1. Ryo Wakita and Haruhisa Fukayama. . Waveform of End-tidal Carbon Dioxide is useful to detect hypopnea during intravenous sedation. 36th Myanmar Dental Conference 2016.01 Yangon
2. Haruhisa Fukayama. Education of anesthesia in dentistry. 36th Myanmar Dental Conference & 17th FDI-MDA joint Educational Meeting 2016.01.28 Yangon, Myanmar
3. Haruhisa Fukayama. Safe Management of Medically Compromised Patients - How can we manage the patients ? -. The 38th Annual Scientific Conference on Dental Research 2016.04.05 Ho Chi Minh City, Vietnam
4. Ryo Wakita and Haruhisa Fukayama.. Emergency response in Tokyo Medical and Dental University Dental Hospital. -Two years statistical reports-. 7th Mandalay Dental Conference and Mid-year Meeting of Myanmar Dental association, 2016.07 Mandalay
5. Haruhisa Fukayama. Sedation for persons with disabilities. The 20th General Assembly, the 39th Annual Scientific Meeting and Dental Exhibition of the Association for Dental Sciences of the Republic of China 2016.09.02 Taipei, Taiwan
6. Transient ST-segment elevation and decreased blood pressure in a patient under sedation after an oral surgery: A case report.. 2016.10.29
7. Medical emergencies in 14,671 invasive dental treatment cases of medically compromised elderly patients. 2016.10.29

### **[Social Contribution]**

1. BLS training course in MDA conference, Myanmar Dental Association, Yangon, 2016.01.30

## Orofacial Pain Management

Professor	Masahiko SHIMADA
Junior Associate Professor	Akira NISHIYAMA
Assistant Professor	Yoko YAMAZAKI
Hospital Staff	Hiroko KIMURA, Daisuke TOMIZAWA, Hiroko IMURA, Masako TOBE, Hiroyuki ISHIYAMA, Maya SAKAMOTO
Graduate Student	Akitoshi HOSODA, Kaori TUKAGOSHI, Rena NAKAYAMA, Nguyen Ho QUYNH ANH Ngan Nguyen, Liang Shanshan

### ( 1 ) Outline

Main research subjects of orofacial pain management is to establish the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders , in particular, is to elucidate the mechanism of pain, neuropathic pain, temporomandibular disorders.

### ( 2 ) Research

Main research subjects of orofacial pain management is to establish the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders , in particular, is to elucidate the mechanism of pain, neuropathic pain, temporomandibular disorders.

- 1)New Treatment methods for neuropathic pain
- 2)Analyses of abnormal orofacial pain
- 3)Study on Biological Response to Dental Interventions
- 4)Analyses and new treatment of dysgeusia
- 5)Development of multidimensional evaluation system for etiological factors of TMD
- 6)Influence of patients' psychosomatic factors for TMD
- 7)Sleep bruxism: its etiology, influence and treatment
- 8)Effectiveness of physiological therapy for TMD
- 9)Mechanisms of occlusal discomfort

### ( 3 ) Education

Purpose of education for students and residents in this course is to provide an opportunity to learn basic knowledge on diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders in the orofacial area. In special course for graduate students, main objective of orofacial pain management is to learn the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders in the orofacial area, in particular, mechanism of pain, neuropathic pain, temporomandibular disorders, and we instruct statistical techniques especially with the multi variate analysis by using clinical data acquired from patients with temporomandibular disorders (TMD).

**( 4 ) Clinical Services & Other Works**

Orofacial Pain Clinic is concerned with the the pain, abnormal sensation, sensory paralysis, abnormal movement, and motor paralysis in the orofacial area and management of orofacial pain clinic is pharmacotherapy, nerve block, stimulation of the pheripheral nerves including acupuncture and psychotherapies. Temporomandibular joint clinic provides diagnosis and treatment for diseases and disfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

**( 5 ) Clinical Performances**

Orofacial Pain Clinic is concerned with the the pain, abnormal sensation, sensory paralysis, abnormal movement, and motor paralysis in the orofacial area and management of orofacial pain clinic is pharmacotherapy, nerve block, stimulation of the pheripheral nerves including acupuncture and psychotherapies. Temporomandibular joint clinic provides diagnosis and treatment for diseases and disfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

**( 6 ) Publications****[Original Articles]**

1. Imura Hiroko, Shimada Masahiko, Yamazaki Yoko, Sugimoto Kumiko. Characteristic changes of saliva and taste in burning mouth syndrome patients Jouranal of Oral Pathology and Medicine. 2016.03; 45(3); 231-236
2. Nishiyama A, Tsuchida E. Relationship Between Wind Instrument Playing Habits and Symptoms of Temporomandibular Disorders in Non-Professional Musicians The Open Dentistry Journal. 2016.08; 10; 411-416

**[Conference Activities & Talks]**

1. Ayako Kubota, Yoko Kono, Hiroko Imura, Hiroji Shimomura, Kiyoko Kanamori, Yasuko Kawakami, Shiro Mataka, Kumiko Sugimoto. Oral health status and behavior of Japanese university students. International Symposium on Dental Hygiene 2016 2016.06 Basel, Switzerland
2. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Chisato Ida, Yuko Mitsuma, Shota Hayashi, Akihito Uesato, Toshihide Fujie, Meiyo Tamaoka, Yasunari Miyazaki, Masahiko Shimada, Noriyuki Wakabayashi . Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy and compliance in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial.. Japanese Society of Sleep Research the 41th Annual Meeting 2016.07.07 Tokyo
3. Tomoko Niimi, Yoko Yamazaki, Masato Kawashima, Daisuke Tomizawa, HIroko Imura, Akitoshi Hosoda, Masahiko Shimada. Effectiveness of Rikkosan for Intraoral Intractable Pain. IASP 2016.09.27 Yokohama
4. Nguyen Ho Quynh Anh, Yamazaki Yoko, Imura Hiroko, Taira Masato, Kurabayashi Tohru, Shimada Masahiko. ERIPHERAL INJURIES MAY LEAD TO GREY MATTER VOLUME REDUCTION IN POST TRAUMATIC TRIGEMINAL NEUROPATHIC PAIN. IASP 2016.09.28 Yokohama
5. Nguyen Ho Quynh Anh, Yamazaki Yoko, Imura Hiroko, Norio Yoshino ,Taira Masato, Kurabayashi Tohru, Shimada Masahiko. TRIGEMINAL NEURALGIA AND THE BRAIN PLASTICITY. The 81th Annual Meeting of The Stomatological Society 2016.11.26 Tokyo

## Pediatric Dentistry

Associate Professor  
Michiyo MIYASHIN

Assistant Professor  
Yoshiaki HASHIMOTO, Haruko FUJITA(~Mar.), Mizuho MOTEGI,  
Satoko KAKINO, Tomoki UEHARA(Aug.~)

Clinical Professor  
Keiichi TAKEI

Adjunct Lecturer  
Hitoyata SHIMOKAWA, Mitsuko INOUE, Masayo ONO(Apr.~),  
Hiroaki NAGAI, Nobutaka ISOGAWA,  
Asuri jayawarudeina(Apr.~)  
Yuki IMAMURA(~Mar.), Naoko UEHARA, Makiko TAKASHI,  
Natsumi TSUCHIHASHI(Apr.~), Sachiko ITOH(Apr.~)  
Syuko MURATA(~Mar.)

Hospital staff  
Yukie Nakajima, Atsushi OISHI, Sachi GOTOH,  
Taki KEKIYA, Kanae WADA, Sachiko ITOH(~Mar.),  
Tomoki UEHARA(Apr.~Jul.)

Graduate Student  
Tomoki UEHARA(~Mar.), Kuniomi NAKAMURA,  
SHEN Dong He, GANBOLD Khongorzul, Erika KUBOTA,  
IJBARA Manhal M.A., ZUMULAITI Shaokelati,  
WIT Yee Wint(Oct.~), Satomi FURUSAWA,  
Shigeki NAGAHIRO(Apr.~)

Research Student  
Mami AOKI(~Mar.), Miki IIDA(~Mar.), Anri OHTA(~Mar.),  
Chikako SATOH(~Mar.), Aoi AKAIKE, Chika INOHARA,  
Maya KATAOKA(~Sep.), Kenichi MIURA(Apr.~)

Enrolled dentist  
Ayako TOKUDA, Gaku SHIMADA(Sep.~), Tomoko KAWAMURA(May.~)  
Yui SEKIDO(Aug.~), Mana KATAOKA(Nov.~)

### ( 1 ) Outline

The Department of Pediatric Dentistry was founded in 1955, as the first in Japan. Pediatric dentistry is a subject of clinical dentistry that deal with education and research of not only developmental oral health sciences but also

prevention and treatment methods of the diseases which disturb oro-facial growth and development of children.

## **( 2 ) Research**

Research Subjects

- 1) Physiological and biological studies on the stomatognathic function of children
- 2) Studies on the development and developmental disturbance of the teeth
- 3) Studies on the growth and development of the maxillofacial cranium and the dentition
- 4) Development of new Endodontics and Traumatology for deciduous and immature permanent teeth
- 5) Basic research on clinical pediatric dentistry

## **( 3 ) Education**

Lecture subjects

Pediatric dentistry, Oral pediatrics

## **( 4 ) Lectures & Courses**

The main objective of pediatric dentistry in this graduate course is to provide students an opportunity to study the theory and the method for the guidance of the oro-facial growth and development and for the diagnosis, prevention and treatment of diseases and malfunctions which disturb the oro-facial growth and development during the period of childhood.

Oral pediatrics is a subject of clinical dentistry that deal with education and research of not only maintenance and promotion of the oral health for growing children but also prevention and treatment methods of diseases and malfunctions which disturb oral health of growing children. The main objective of oral pediatrics in this graduate course is to provide students an opportunity to understand that a child is a living body with mental, physical, and physiological characteristics which are different from those of adults and to study the pathogenesis, prevention, and treatment of the particular oral diseases in childhood. Students are also taught the theory and the method of ongoing health care that is necessary for maintaining and promoting oral health from infant to adult. In addition, they are taught the clinical significance and importance of the behavioral management of child patients and the necessity and importance of understanding and cooperation of the parents to it.

## **( 5 ) Clinical Services & Other Works**

The pediatric dentistry clinic in the department of oro-facial development and function provides the comprehensive dental treatment for a child while growing.

## **( 6 ) Clinical Performances**

The examination, diagnosis, and treatment of the oral diseases and the oral abnormalities are performed in the clinic. In addition, health guidance, preventive measures, and the long-term oral health management by the periodical checking system are carried out, in order to keep and promote oral health from infant to adult.

## **( 7 ) Publications**

### **[Original Articles]**

1. Wada K, Ikeda E, Wada J, Inoue G, Miyasaka M, Miyashin M. Wear characteristics of trimethylolpropane trimethacrylate filler-containing resins for the full crown restoration of primary molars. *Dental Materials Journal*. 2016; 35(4); 585-593
2. Yamada A, Kakino S, Matsuura Y. Photoacoustic detection of blood in dental pulp by using short-time Fourier transform. *Proceeding of SPIE*. 2016.02; 9708-102
3. Tanaka S, Uehara N, Tsuchihashi N, Sugimoto K. Emotional relationships between child patients and their mothers during dental treatments. *Journal of Dental Sciences*. 2016.04; 11; 287-292

4. Sasagawa I, Oka S, Mikami M, Yokosuka H, Ishiyama M, Imai A, Shimokawa H and Uchida U. Immunohistochemical and Western blot analyses of ganoine in the ganoid scales of *Lepisosteus oculatus*, an actinopterygian fish. *J. Exp. Zool (Mol. Dev. Evol)*. 2016.05; 326B(3); 193-209
5. Uehara T, Mise-Omata S, Matsui M, Tabata Y, Murali R, Miyashin M, Aoki K. Delivery of RANKL-Binding Peptide OP3-4 Promotes BMP-2-Induced Maxillary Bone Regeneration. *J. Dent. Res.* 2016.06; 95(6); 665-672
6. Ito S, Shimada Y, Sadr A, Nakajima Y, Miyashin M, Tagami J, Sumi Y. Assessment of occlusal fissure depth and sealant penetration using optical coherence tomography. *Dental Materials Journal.* 2016.06; 35(3); 432-433
7. Seko Y, Azuma N, Yokoi T, Kami D, Ishii R, Nishina S, Toyoda M, Shimokawa H, Umezawa A. Antero-posterior Patterning of Gene Expression in the Human Infant Sclera: Chondrogenic Potential and Wnt Signaling. *Curr Eye Res.* 2016.06; 1-10
8. Yamada A, Kakino S, Matsuura Y. Detection of Photoacoustic Signals from Blood in Dental Pulp. *Optics and Photonics Journal.* 2016.09; 6; 229-236
9. Taki Sekiya, Hiroko Imura, Sachiko Ito, Michiyo Miyashin, Kumiko Sugimoto. Development of real-time stress monitoring system in pediatric dentistry: Assessment from autonomic nerve and brain activities 2016.11; 54(4); 443-449

#### [Conference Activities & Talks]

1. Tamura Y, Mise S, Sugamori Y, Bhuyan MZH, Takahashi M, Uehara T, Arai Y, Miyashin M, Wakabayashi N, Aoki K. A pharmacological role of metallothionein in zinc-treated cartilage-progenitor cells. The 13th Asia Pacific Federation of Pharmacologists Meeting 2016.02.01 Bangkok
2. Yamada A, Kakino S, Matsuura Y. Photoacoustic detection of blood in dental pulp by using short-time Fourier transform. Biomedical Optics Conference (BiOS), SPIE 2016.02.16 San Francisco, USA
3. Sugawara Y, Kashimada A, Moriyama K, Baba S, Imai K, Nishikomori R, Motegi M, Takeuchi Y, Morio T. Aicardi-Goutieres and Singleton-Merten overlapping phenotype due to IFIH1 mutation.. The 13th International Congress of Human Genetics 2016.04.06 Kyoto, Japan
4. Oishi A, Shimokawa H, Wit Yee Wint, Arakawa S, Miyashin M. Effects of Nanobubble water on human cells derived from impacted supernumerary teeth. 10th Biennial Conference of the Pediatric Dentistry Association of Asia in conjunction with 54th Annual Conference of the Japanese Society of Pediatric Dentistry 2016.05.27 Tokyo, Japan
5. Gotoh S, Fujita H, Shimokawa H, Miyashin M. A Case of Hyper-IgE Syndrome, Dental Treatment and Histologic Examinations of a Deciduous Tooth. 10th Biennial Conference of the Pediatric Dentistry Association of Asia 2016.05.27 Tokyo, Japan
6. Ganbold K, Kakino S, Matsuura Y, Matoba K, Miyashin M. Relevance of pulpal blood flow and root development of young permanent teeth measured by Transmitted-light Plethysmography (TLP). 10th Biennial Conference of the Pediatric Dentistry Association of Asia 2016.05.27 Tokyo
7. Ijbara M, Wada K, Miyashin K. Simulated Occlusal Wear In Immature Teeth: 3D Analysis. 10th Biennial Conference of the Pediatric Dentistry Association of Asia 2016.05.28 Tokyo, Japan
8. Kakino S, Ganbold K, Miyashin M. Pulpal circulation in developing healthy and traumatized teeth using TLP. 19th World Congress on Dental Traumatology and 5th Trans-Tasman Endodontic Conference 2016.08.11 Brisbane, Australia
9. Nakamura K, Oishi A, Nakajima Y, Shibata S, Miyashin M. Longer-term follow-up data of experimental traumatic dislocations and root fractures. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10.21 Fukuoka

#### [Awards & Honors]

1. Poster Presentation, Second Place Award, International Association for Dental Traumatology, 2016.08

## Orthodontic Science

Professor	Takashi ONO
Associate Professor	
Junior Associate Professor	Yoshiro MATSUMOTO, Zusei KANNO, Jun HOSOMICHI
Assistant Professor	Kazuo SHIMAZAKI, Ippei WATARI, Satoshi KOKAI, Ikuo YONEMITSU Takayoshi ISHIDA
Project Assistant Professor (International Exchange Center)	Yuji ISHIDA
Dental Resident	Naoki SHIBUTANI (Apr-), Hiroko OMORI (-Mar), Yasuhiro SHIMIZU, Risa USUMI Chiho KATO, Hidemasa OKIHARA, Yuhei IKEDA (Apr-)
Graduate Students	Shuji OISHI (-Mar), Soma KITA (-Mar) Yoichiro KUMA (-Mar), Tomomi SAKAGUCHI (-Mar), Mio MAKIGUCHI (-Mar) Hiroyuki YAMAGUCHI (-Mar), Jin-Gyu AN, Wei-Jen LAI (-Sep) Yasunori ABE, Yukano FUKUSHIMA, Yuki KASAHARA Takuya OGAWA, Iku SHIBATA, Karin Harumi UCHIMA KOECKLIN Akemi KANAGUCHI, Velusamy PAVETHY NATH, Eri SAITO Kayo KIMURA, Yuta NAKAI, Kenzo WATAKABE Erusu NIN, Huan TANG, Roody BEAUBOEUF Edward CHO, Masamu INOUE, Erika OZAWA Moe SATO, Kasumi HATANO, Keiko FUKINO Shin-Sheng Yang, Lu ZAHO, Thi kim Uyen DONG Meshari Faleh H ALRESHIDI, Misaki AOYAGI (Apr-) Yuta UCHIKAWA (Apr-), Akihiro KOYAMA (Apr-), Kim Sun-min (Oct-) Phyo Thura Aung (Oct-)
Graduate School Research Students	Hiroko OMORI (Apr-), Yukiha FUNAKI (-Mar), Ayako KAWABE (-Mar), Rieko ONO (-Mar), Arisa SAWADA (-Mar), Emina WAKASUGI (-Mar), Yuhei IKEDA (-Mar), Toshihiro IMAMURA Minami MIYASAKA, Mutsumi MIYAZAKI, Asuka OKITO Ayako KIRII, Syusuke UESUGI, Shuji OISHI (Apr-), Soma KITA (Apr-) Yoichiro KUMA (Apr-), Tomomi SAKAGUCHI (Apr-) Mio MAKIGUCHI (Apr-), Hiroyuki YAMAGUCHI (Apr-) Tomonari MATSUMURA, Junpei SUZUKI, Kyohei YAMADA Misako KOKETSU, Takahiro SHIMAMINE, Katsuhiko SUZUKI Mirei HAGIWARA, Chiho SATOKAWA, Asuka MANABE Shuntaro SAWAZAKI, Makiko OKUZAWA, Preska KEO (-Mar) Xiyuan GUO (-Mar), Wu YANG (-Mar), Sun-min KIM (-Sep) Masako KAWADA (Apr-), Takashi TANAKA (Apr-) Shunya HORIUCHI (Apr-), Shams SHAHRIAR MOHD (Apr-) Haixin HONG (Oct-)
Visiting Research Scholars	Jui-Chin HSU, Wei-Jen LAI (Oct-)

### (1) Outline

Orthodontic Science is one of the dental sciences which propose to control the craniofacial growth and development in equilibrium with the whole body, and also deals with the prevention and/or treatment of malocclusion



and related disorders, by which the alteration of maxillofacial function with aging could be kept to the most suitable condition.

## **( 2 ) Research**

Research Subjects

- 1) Biomechanical study of occlusion
- 2) Studies on biological response and functional adaptation followed by orthodontic and occlusal stimulation
- 3) Clinical application of autotransplantation in orthodontic treatment
- 4) Studies on interrelation between malocclusion and temporomandibular joint
- 5) Studies on occlusion and age-related changes in cranio-maxillofacial morphology and function
- 6) Studies on interrelation between cranio-maxillofacial complex and whole body
- 7) Development of mechanics and materials for orthodontic treatment
- 8) Pathophysiological studies on sleep and breathing disorders
- 9) Studies on interrelation between breathing and body function

## **( 3 ) Education**

Subjects of Education:

Orthodontic Science, Pathophysiology for Malocclusion, Biology for Functional Adaptation

## **( 4 ) Lectures & Courses**

Orthodontic Science

- 1) To explain the unhealthy physiological condition of malocclusion and deepen the scientific basis for orthodontic treatment.
- 2) To understand the biological reaction and adaptation of occlusal tissues to mechanical stresses such as occlusal force or orthodontic force, and also the changes with aging.
- 3) To explain the art for controlling the morphologic and functional problems of occlusion in orthodontic treatment, from the view points of biomaterials and biomechanics.
- 4) To enlighten the social dentistry for the needs and demands of orthodontic treatment.

Pathophysiology for Malocclusion

To understand the alteration of occlusal function and morphology with aging, and to explain the pathological condition of malocclusion from the viewpoint of physiology, biomechanics, biology and sociology.

Biology for Functional Adaptation

To understand the procedure of biological reaction and adaptation of occlusal system to the orthodontic stimuli, including the influence of aging, and to provide the control of the surroundings of the occlusal system.

## **( 5 ) Clinical Services & Other Works**

Clinical Services

In the field of practical orthodontic, with the development of materials and treatment techniques, we have taken initiatives in two big turning points at all time. Namely, one is the Direct Bonding System which has made it possible to attach brackets directly to the teeth surface without orthodontic metal bands. Another is the development of Super-Elastic Ti-Ni Alloy Wire, and following Improved Super-Elastic Ti-Ni Alloy Wire. With these new wires, we have provided an epoch-making orthodontic technique, where teeth could be moved more efficiently and safely with light continuous forces, and in consequences, the limits for teeth movement are expanded and the treatment outcomes are also improved. On the other hand, in order to determine the scientific basis for the needs of orthodontic treatment, we are engaging in the study of pathophysiology of malocclusion, and these research results are getting feedback to the orthodontic practices as soon as possible to stimulate the development of new treatment protocols.

Students in the graduate course not only pursue their scientific researches but also being educated in accordance with our curriculum for the post-graduated clinical program. In this program, we aim to bring up the leading

persons of next generation who have highly specialized knowledge and skills of orthodontics as well as prominent minds of clinical researches.

## (6) Clinical Performances

### Highlights of Clinical Services

- 1) Orthodontic treatments by using Improved Super-Elastic Ti-Ni Alloy Wire
- 2) Comprehensive Orthodontic Treatments

With the cooperation of related field, we provide comprehensive treatments for those patients with cleft lips and palates and other congenital anomalies, jaw deformities, maxillofacial functional disorders, periodontal diseases, impacted teeth, autotransplantation combined cases, and usages of implant anchorages.

## (7) Publications

### [Original Articles]

1. Oishi S, Shimizu Y, Hosomichi J, Kuma Y, Nagai H, Maeda H, Usumi-Fujita R, Kaneko S, Shitano C, Suzuki J, Yoshida K, Ono T. Intermittent hypoxia induces disturbances in craniofacial growth and defects in craniofacial morphology. *Arch Oral Biol.* 2016.01; 61; 115-124
2. Uesugi S, Yonemitsu I, Kokai S, Takei M, Omura S, Ono T. Features in subjects with the frontal occlusal plane inclined toward the contralateral side of the mandibular deviation. *Am J Orthod Dentofacial Orthop.* 2016.01; 149(1); 46-54
3. Miyazaki M, Yonemitsu I, Takei M, Kure-Hattori I, Ono T. The imbalance of masticatory muscle activity affects the asymmetric growth of condylar cartilage and subchondral bone in rats. *Arch Oral Biol.* 2016.03; 63; 22-31
4. Abbassy MA, Watari I, Bakry AS, Ono T, Hassan A. Calcitonin and vitamin D3 have high therapeutic potential for improving diabetic mandibular growth. *Int J Oral Sci.* 2016.03; 8(1); 39-44
5. Yamada K, Ohmori H, Kirimoto H, Shimazaki H, Ono T. Relation between condylar morphology and temporomandibular joint sounds in patients with mandibular laterodeviation. *Orthod Waves-Jpn Ed.* 2016.03; 75(1); 1-7
6. Arai Y, Aoki K, Shimizu Y, Tabata Y, Ono T, Murali R, Mise-Omata S, Wakabayashi N. Peptide-induced de novo bone formation after tooth extraction prevents alveolar bone loss in a murine tooth extraction model. *Eur J Pharmacol.* 2016.04;
7. Tomomi Sakaguchi-Kuma, Nao Hayashi, Hitomi Fujishiro, Kumiko Yamaguchi, Kazuo Shimazaki, Takashi Ono, Keiichi Akita. An anatomic study of the attachments on the condylar process of the mandible: muscle bundles from the temporalis *Surg Radiol Anat.* 2016.05; 38(4); 461-467
8. Maekawa M, Kanno Z, Ono T, Uo M. Development of the all-plastic orthodontic wires. 2016.05; 35(3); 189-192
9. Honda K, Omura S, Fujita K, Shibutani N, Yonemitsu I, Shimazaki K, Murata S, Takasu H, Yamashita Y, Iwai T, Ono T, Tohnai I. A survey of treatment for dentofacial deformities in the past 16 years in oral and maxillofacial surgery/orthodontics, Yokohama city university medical center. *The Japanese Journal of Jaw Deformities.* 2016.08; 26(3); 195-201
10. Oishi S, Shimizu Y, Hosomichi J, Kuma Y, Nagai H, Maeda H, Usumi-Fujita R, Kaneko S, Shibutani N, Suzuki J, Yoshida K, Ono T. Intermittent hypoxia Influences alveolar bone proper microstructure via hypoxia-inducible factor and VEGF expression in periodontal ligaments of growing rats. *Front physiol.* 2016.09; 7; Article 416
11. Dei A, Miyamoto JJ, Takada JJ, Ono T, Moriyama K. Evaluation of blood flow and electromyographic activity in the perioral muscles. *Eur J Orthod.* 2016.10;

12. Kita S, Oshima M, Shimazaki K, Iwai T, Omura S, Ono T. Computational fluid dynamic study of nasal respiratory function before and after bimaxillary orthognathic surgery with bone trimming at the inferior edge of the pyriform aperture. *J Oral Maxillofac Surg.* 2016.11; 74(11); 2241-2251
13. Lai WJ, Midorikawa Y, Kanno Z, Takemura H, Suga K, Soga K, Ono T, Uo M. Development and modification of a device for three-dimensional measurement of orthodontic force system: The V-bend system re-visited. *Dent Mater J.* 2016.12; 35(6); 908-917
14. Makiguchi M, Funaki Y, Kato C, Okihara H, Ishida T, Yabushita T, Kokai S, Ono T. Effects of increased occlusal vertical dimension on the jaw-opening reflex in adult rats. *Arch Oral Biol.* 2016.12; 72; 39-46
15. Honda K, Omura S, Fujita K, Shibutani N, Yonemitsu I, Shimazaki K, Murata S, Takasu H, Yamashita Y, Iwai T, Ono T, Tohnai I. A case of mandibular protrusion with excessive vertical maxillary deficiency treated with simultaneous maxillo-mandibular distraction osteogenesis. *The Japanese Journal of Jaw Deformities.* 2016.12; 26(4); 275-283
16. Koji Honda, Susumu Omura, Koichi Fujita, Naoki Shibutani, Ikuo Yonemitsu, Kazuo Shimazaki, Shogo Murata, Hikaru Takasu, Yosuke Yamashita, Toshinori Iwai, Takashi Ono, Iwai Tohnai . A Case of Mandibular Protrusion with Excessive Vertical Maxillary Deficiency Treated with Simultaneous Maxillo-mandibular Distraction Osteogenesis 2016.12; 26(4); 275-283

### [Conference Activities & Talks]

1. Kasahara Y, Usumi-Fujita R, Hosomichi J, Kaneko S, Ishida Y, Shibutani N, Shimizu Y, Okito A, Oishi S, Kuma Y, Ono T. Effect of low-intensity pulsed ultrasound on periodontal tissues in occlusal hypofunctional teeth. The 38th Annual Scientific Conference on Dental Research 2016.04.04 Ho Chi Minh city, Vietnam
2. Velusamy P, Matin K, Shimada Y, Kanno Z, Ono T, Tagami J. Detection of Hidden Enamel Demineralization beneath Orthodontic Brackets using Optical Coherence Tomography. The 116 th Annual session - American Association of Orthodontists 2016.04.29 Florida, USA
3. Ozawa E, Honda E, Ohmori H, Shimazaki K, Kurabayashi T, Ono T. Influence of orthodontic appliance-derived artifacts on 3-T MRI movies. The 94th General Session & Exhibition of the International Association for Dental Research 2016.05.26 Seoul, Korea
4. Hsu J, Watari I, Ono R, Mizumachi-Kubono M, Funaki Y, Kokai S, Ono T. Degeneration of fungiform and circumvallate papillae following molar extraction and unilateral nasal obstruction in rats.. The 17th International Symposium on Olfaction and Taste 2016.06.07 Kanagawa
5. Beauboeuf R, Watari I, Hsu J, Mizumachi-Kubono M, Inoue K , Watabe T, Ono T. Expression of GLP-1 and GLP-1 receptor in rat circumvallate papilla during growth period . The 17th International Symposium on Olfaction and Taste 2016.06.07 Kanagawa
6. Ren E, Watari I, Hsu J, Mizumachi-Kubono M, Inoue K, Watabe T, Ono T. Unilateral nasal obstruction effects taste cell in circumvallate papillae in rats. The 17th International Symposium on Olfaction and Taste 2016.06.07 Kanagawa
7. Abe Y, Uchima Koecklin KH, Kato C, Kokai S, Ono . Effects of nasal obstruction on development of the motor representation within the facial primary motor cortex in growing rats.. The 92nd Congress of the European Orthodontic Society 2016.06.11 Stockholm, Sweden
8. Kimura K, Shimazaki K, Sugimoto K, Ono T. Influence of Habitual Mouth-breathing on Taste Sensation. The 35th Annual Meeting of the International Association for Dental Research Korean Division 2016.06.23 Seoul, Korea
9. Satokawa C, Nishiyama A, Suzuki K, Uesugi S, Kokai S, Ono T. Changes in tissue oxygen saturation during various continuous clenching tasks. The 94th General Session & Exhibition of the International Association for Dental Research 2016.06.24 Seoul, Korea
10. Kita S, Shimazaki K, Yajima Y, Iwai T, Omura S, Ono T. Computational fluid dynamics study on the respiratory function before/after orthognathic surgery with pyriform aperture trimming. 2016.06.24 Tokyo

11. Ohmori H, Kirimoto H, Ono T. Associations among TMDs, craniofacial morphologies, premature contact, and occlusal force in female children patients with malocclusion. The 29th Annual Meeting of the Japanese Society for the Temporomandibular Joint 2016.07.17 Kanagawa
12. Fukushima Y, Inoue M, Ono Take, Wake H, Nakashima T, Ono T. Reduced mastication impairs mandibular growth and memory. The 58th Annual Meeting of Japanese Association for Oral Biology 2016.08.25 Sapporo
13. Ono T. Myths and facts in the Japanese Ni-Ti archwire. The 10th Asia Pacific Orthodontic Conference 2016.09.01 Bali, Indonesia
14. Imamura T, Kanno Z, Wada T, Honda E, Uo M, Ono T. Infiltration of trace metal ions in the oral mucosa analyzed using SR-XRF, XAFS, and ICP-MS. The 10th Asia Pacific Orthodontic Conference 2016.09.01 Bali, Indonesia
15. Fukino K, Sakaguchi-Kuma T, Shimazaki K, Ono T, Akita K. An anatomical study concerning superior region of the superior constrictor of the pharynx. The 8th international Symposium of Clinical and Applied Anatomy 2016.09.01 Budapest, Hungary
16. Oishi S, Shimizu Y, Hosomichi J, Kuma Y, Usumi-Fujita R, Maeda H, Nagai H, Kaneko S, Shibutani N, Suzuki J, Yoshida K, Ono T. Intermittent hypoxia influences bone microstructure via hypoxia inducible factor and VEGF in growing rats. The 10th Asia Pacific Orthodontic Conference 2016.09.01 Bali, Indonesia
17. Sakaguchi-Kuma T, Fukino K, Shimazaki K, Yamaguchi K, Okuda I, Ono T, Akita K. An anatomic study of the functional relationships between the temporalis with reference to the anterolateral muscle bundle and the facial muscle layer. The 8th International Symposium of Clinical and Applied Anatomy 2016.09.01 Budapest, Hungary
18. Yamaguchi H, Ishida Y, Hosomichi J, Watanabe R, Suzuki J, Ono T. Transfection of NF- $\kappa$ B decoy into the periodontium using ultrasound-microbubble technique can suppress alveolar bone resorption in periodontal model rats. The 59th Autumn Meeting of The Japanese Society of Periodontology 2016.10.07 Niigata
19. Matsumoto Y. For the better development of occlusion: Oral myofunctional therapy and orthodontic treatment. The 27th Annual Meeting of the Japanese Society of Clinical Sports Medicine 2016.11.05 Chiba
20. Shimamine T, Yonemitsu I, Shibutani N, Koketsu M, Imai H, Fujita K, Omura S, Ono T. Changes in upper airway morphology after Le Fort I and horse-shoe osteotomies in maxillary protrusion. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
21. Tang H, Yonemitsu I, Ikeda Y, Miyazaki M, Shibata S, Ono T. Effect of unilateral nasal obstruction on morphology of jaw-closing muscles in growing rat. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
22. Imai H, Omura S, Fujita K, Honda K, Shibutani N, Yonemitsu I, Shimazaki K, Tohna I, Ono T. Accuracy of maxillary repositioning by using SLM technique: verification by digitalization of model surgery. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
23. Abe Y, Kato C, Uchima Koecklin KH, Okihara H, Ishida T, Yabushita T, Kokai S, Ono T. Nasal obstruction affects development of the representation within the orofacial primary motor cortex in rats. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
24. Hatano K, Ishida Y, Yamaguchi H, Jun Hosomichi J, Suzuki J, Kasahara Y, Oishi S, Kuma Y, Okito A, Usumi-Fujita R, Shimizu Y, Shibutani N, Kaneko S, Ono T. The inhibition of SDF-1/CXCR4 signaling interrupts experimental tooth movement in rats. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
25. Uchima Koecklin KH, Kato C, Kataguchi T, Okihara H, Ishida T, Fujita K, Yabushita T, Kokai S, Ono T. Force changes of the tongue-protruding muscles after nasal obstruction during the growth period in rats. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima

26. Yonemitsu I, Fujita K, Imai H, Manabe A, Fukuyama E, Shibutani N, Shimazaki K, Omura S, Tohnai I, Ono T. Retreatment of a subject with hemi-mandibular hyperplasia by orthognathic surgery and condylec-tomy. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
27. Kato C, Kokai S, Ono T. An adult case of orthodontic movement with a contralateral maxillary incisor through the midpalatal suture. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
28. Koketsu M, Yonemitsu I, Shibutani N, Shimamine T, Imai H, Fujita K, Omura S, Ono T. Changes in upper airway morphology after Le Fort I and horse-shoe osteotomies in mandibular prognathism. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
29. Honda K, Fujita K, Imai H, Shibutani N, Yonemitsu I, Shimazaki K, Yamashita Y, Takasu H, Murata S, Iwai T, Hirota M, Omura S, Tohnai I, Ono T. Orthognathic surgery and implant-supported bridge in a jaw-deformity patient caused by traffic accidental injury. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
30. Watakabe K, Yonemitsu I, Ikeda Y, Miyazaki M, Ono T. Decrease in blood oxygen saturation associated with nasal obstruction influences mandibular morphology in growing rats. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
31. Kuma Y, Usumi-Fujita R, Hosomichi J, Oishi S, Yamaguchi H, Okito A, Shimizu Y, Shibutani N, Ishida Y, Kaneko S, Suzuki J, Yoshida K, Ono T. Intermittent hypoxia alters the growth of rat nasal cavity via the inflammatory pathway activation. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
32. Shimizu Y, Aoki K, Kato G, Ono T. Occlusal disharmony-induced stress causes osteopenia of the lum-bar vertebrae and long bones in mice. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
33. Kasahara Y, Usumi-Fujita R, Kuma Y, Oishi S, Okito A, Shimizu Y, Shibutani N, Ishida Y, Kaneko S, Hosomichi J, Ono T. Low-intensity pulsed ultrasound recovers the periodontal tissues in occlusal hypo-functional teeth. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
34. Sakaguchi-Kuma T, Ishida Y, Kawabe A, Imamura T, Ikeda Y, Oishi S, Matsumura T, Ono T. Three dimensional analyses of relationship between skeletal pattern and shape of mandibular alveolar bone. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
35. Kanaguchi Arita A, Yonemitsu I, Ikeda Y, Miyazaki M, Ono T. Effects of low-intensity pulsed ultrasound stimulation on the mandibular condyle for osteoarthritis lesions. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.09 Tokushima
36. Usumi-Fujita R, Nakakuki K, Fujita K, Yonemitsu I, Fukuyama E, Ono T. A case with condylar hyper-plastic facial asymmetry treated by unilateral alveolar segmental osteotomy. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.09 Tokushima
37. Uchima Koecklin KH, Hiranuma M, Kato C, Funaki Y, Kataguchi T, Yabushita T, Kokai S, Ono T. Unilateral nasal obstruction during later growth periods affects craniofacial function in rats. The 81th Annual Meeting of The Stomatological Society, Japan 2016.11.26 Tokyo
38. Ono T. Myths and facts in Japanese Ni-Ti archwire. The 29th TAO Annual Meeting 2016.12.02 Taipei, Taiwan
39. Lai WJ, Midorikawa Y, Kanno Z, Ono T. Development of a device for three-dimensional measurement of orthodontic force systems requiring high operability.. The 29th TAO Annual Meeting 2016.12.02 Taipei, Taiwan

#### [Awards & Honors]

1. Yamaguchi H. The 75th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2016.11
2. Kato C. The 75th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2016.11

3. Usumi-Fujita R. The 75th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2016.11
4. Fukushima Y. The 75th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2016.11

## Cariology and Operative Dentistry

Professor: Junji Tagami

Associate Professor: Masayuki Otsuki

Junior Associate Professor: Toru Nikaido, Masatoshi Nakajima

Assistant Professor: Takako Yoshikawa, Yasushi Shimada, Yuichi Kitasako (～ March) , Go Inoue, Keiichi Hosaka, Tomohiro Takagaki, Rena Takahashi

Hospital Staff: Masahiro Takahashi (～ March) , Oto Aramaki,

Naoko Matsui, Ikumi Wada (～ March) , Yukiko Tanno (～ March) , Ayaka Chiba (April ～) , Takaaki Sato (April ～) , Kento Sato (April ～)

Specially Appointed Assistant Professor: Noriko Hiraishi, NHM Khairul Matin

JSPS Research Fellowship Noriko Hiraishi(January ～)

Secretary: Shiori Ogi, Takako Nakagawa

Graduate Student: Shigeyuki Nagai (～ March) , Rena Oguro (～ March) , Takahide Ibusuki (～ March) ,

Asami Aida (～ March) , Ayaka Chiba (～ March) , Kei Horie (～ March) , Tomoka Ueno (～ March) ,

Hiroki Tezuka (～ March) , Kento Sato (～ March) ,

Takaaki Sato (～ March) , Masami Arai (～ March) ,

Maria Nakamura (～ March) , Ritsuko Mashiko (～ March) ,

Alaa Turkistani (～ March) , Kong Kalyan (～ March) ,

Baba Bista (～ March) ,

Maria Jacinta Rosario Hernandez Romero (～ March) ,

Zaher Bukhari (～ March) , Patrycja Zakilna Majkut (～ March) ,

Rui Guan (～ September) ,Ayaka Sto, Yuka Tsuda,

Nami Takashino, Takashi Hatayama,

Chihiro Matsuura, Yukinori Kano, Yuuki Naruse, Juri Hayashi,

Miho Sugiura, Yuta Sumitani, Atsuko Tagami, Keiki Nakamura, Yukari Noda, Mari Okada, Keita Taguchi,

Jorge Espigares, Junji Atomura, Thwe Zin Ei,

Hamed Atrgiran Yazdi, Tomoko Tabata, Ayako Nakamoto,

Narifumi Takahashi, Takuya Nakata,

Daisuke Araoka, Luong Dao Minh Nguyet, Khine Win Zan,

Khin Yupar Kyaw, Amr Abdelaziz Aly Aly SAAD,

Michelle Sunico SEGARRA, Wa Than Lin, Dhaifallah Abdullah ALQARNI,

Ali Guzan AL-GHAMDI, Sae Akehashi, Nao Takahashi,

Yuna Kanamori, Yukina Ochiai, Kurumi Ide, Yusuke Kuno,

Yuki Ito, Shigeki Uchinuma, Daiki Nagano, Yusuke Kakinuma,

Akira Nakane, RIMA ZAKZOUK, HALABI SOMAYAH ABDULRAHMAN A,

RUMMANI GHASSAN MAHMOOD S, ALQAHTANI ALI AWAD M,

ARAVETI SANDEEP KUMAR, Hosea Lalrin Muana, Sai Kham Lyann,

Aye Ko Ko, Meiken Hayashi (April ～) , Shou Obayashi (April ～) ,

Saori Muta (April ～) , Kazuhide Uonekura (April ～) , Satomi Mtsunaga (April ～) , Shin Rozan (April ～) ,

Yukiko Tanno (April ～) , HESHAM HASSAN OSMAN MOHAMMED (April ～) ,

AHMED MOHAMED ABDELRAHMAN ABDOL (October) ,

MAHMOUD MOHAMED SAYED ALSAADI, HANI BAKHEET S (October) ,

ALMASABI, WALEED ABDULQADER M (October) ,

WIJETUNGA CHAMARI LASINDRA (October) , AHMED (October) ,

Soe Yupaing (October) , Swe Zin Aung (October) ,

QUTAIBA Y A A ALSANDI (October) , San San Mayphyo Aung (October) )

Research Student: Shinji Ogura, Mineo Kijima,

Erick Luz Madrigal, San San May Phyto Aung ( September) ,

Khine Win Zan (April September) , Qutaiba Alsandi (April September) ,

Chamari Lasindra Wijetunga (April September) , Martina Vicheva (April September) ,

VICHEVA MARTINA GEORGIEVA (October) )



## (1) Outline

TMDU possesses the longest history as a national dental university in Japan. We have contributed to the progress of science and education through presenting a number of world leading graduates in the field of dentistry. Many of their achievements are now recognized as global standards in the field of dental research and clinical practice.

At Cariology and Operative Dentistry, we believe that the ultimate goal of the oral health care programs is to provide well-being of the patients. In order to achieve this goal, besides the clinical training that we offer to the licensed graduate students, high-caliber research projects are being carried out aimed at developing, enhancing and evaluation of the materials and techniques in dentistry; particularly for adhesives, caries prevention, diagnosis and treatment, and oral health maintenance.

Cariology and Operative Dentistry is a home to the late professor Takao Fusayama, who developed the “Caries Detector” for removal of the caries, and promoted “Total-etch technique” and other restorative techniques using adhesive resin composite for the minimally invasive caries treatment.

Our group, consisting of members of the faculty, staff and graduate students, is among the international leaders in the ongoing dental research. I would hereby like to extend an invitation to those fellows and prospect graduate students interested in perusing high-level research and gaining an insight into modern concepts to join our diverse international team of scientists.

## (2) Research

### 1) Evaluation of dentin bonding systems

Adhesion of bonding materials to enamel, dentin and cementum of tooth are evaluated using methods such as the microshear and the microtensile bond strength tests. Factors affecting adhesion such as the region and caries state of tooth substrate, light-curing irradiation, release of fluoride from material, tooth preparation methods, root canal treatment of the tooth, etc. have been investigated. We have also focused on the difference between various adhesives system in terms of their composition, performance and bonding durability.

### 2) Super Enamel and Super Dentin

Using various electron microscopy techniques, we have demonstrated that resistance of enamel and dentin to acid attack could be increased in an acid-base resistant zone which was formed following the application of some self-etching dental adhesives. We proposed that the diffusion of such acidic monomers beyond the classic hybrid layer (interfacial zone) and their ion-exchange interactions with the available hydroxyapatite could result in formation of stable organic-inorganic complexes, and that the structures should be termed “super tooth”, which includes the reinforced enamel and dentin.

### 3) Development of OCT for establishing its clinical application

Optical coherent tomography (OCT) is a noninvasive, cross-sectional imaging system that can visualize the internal structures nondestructively and without exposure to X-ray or ionizing radiation. Our research has aimed to further develop OCT and introduce a dental OCT system that can be used to diagnose dental defects and diseases such as tooth cracking and caries.

### 4) Non-destructive test of adhesive restorations

We are working to establish a method for non-destructive detection of gap and secondary caries beneath composite restorations using optical coherence tomography (OCT).

### 5) Evaluation of polymerization behavior of light-cured resin composites

Aim to establish clinical techniques to compensate polymerization shrinkage stress of resin composite, we evaluated effect of adhesives, resin composite composition, light curing methods and cavity configuration factor (C-factor) on polymerization shrinkage stress using micro-focus X-ray computed tomography (micro-CT) and 3D visualization method.

### 6) Resin coating technique

Resin coating using a bonding agent and flowable composite benefits the adaptation of indirect restorations to dentin surface which is a key interface within a restoration. We have proposed that this resin coating technique should be technique of choice for placement of indirect restorations.

### 7) Research on optical properties of the dental structure

As a part of the OCT development project, we work on characterization of the basic optical properties such as attenuation coefficient and refractive index of dentin and enamel, and their changes following demineralization



and remineralization.

8) Research on direct core build up materials

Adhesive performance to the root canal dentin by resin core build up systems has been evaluated. These materials can be used in combination with fiber posts.

9) Study on dental erosion

Erosive loss of enamel due to consumption of acidic beverages and some drugs has been evaluated using 3D focus-variation microscopy as well as profilometry.

10) Caries risk assessment

We have investigated caries risk based on the measurement of saliva buffering capacity in samples collected from patients. We have also probed the association between the pH of lesion surface and caries activity.

11) Adhesion of cariogenic bacteria to dentin surface

We have developed a model to experimentally evaluate factors affecting the ability of cariogenic bacteria such as *S.mutans* to attach to the tooth surface in the initial phase of biofilm formation.

12) Biocompatibility of resin-based dental adhesives

Immunohistochemical studies have been performed to evaluate the effects of various adhesive materials on dental pulp tissue.

13) The potential of fluoride- and/or Calcium containing materials on caries prevention

Inhibitory effects of CPP-ACP paste and fluoride on the enamel and dentin demineralization have been evaluated by the micro-focus X-ray computed tomography (micro-CT) non-destructively. We have also established a standard methodology for assessment of lesion parameters such as depth and mineral loss for micro-CT.

14) Evaluation of caries removal methods

We have evaluated the effect of caries removal method by the conventional rotary cutting instruments in comparison with new caries removal methods such as chemical removal agents, laser irradiation and abrasion on the adhesion performance and restoration success.

15) Development and evaluation of aesthetic dental materials

We have worked on optical properties and color match of the composite resins, in addition to clinical applications of tooth whitening materials .

16) Clinical research

We have created a protocol to evaluate the long-term and short-term performance of restorative materials in the patients who were admitted to the operative dentistry clinics at TMDU Dental Hospital.

### ( 3 ) Education

Cariology and Operative Dentistry section offers a four-year graduate program. First-year graduate students attend lectures and seminars given in the graduate school and are expected to gain an understanding of the fundamentals about methodology and the knowledge necessary for their research. The contents of the classes given in our section include topics related to cariology and operative dentistry: caries diagnosis, biocompatibility, caries treatment and restoration, prevention and control, dental materials, new instruments and equipment. In keeping with the internationally orientated philosophy of this section, lectures are conducted in English and are open to all foreign students. First-year graduate students also undergo clinical training the procedures of modern adhesive restorations. Laboratory work, which commences in the first year, is performed under the supervision of our faculty staff. During the four-year program, several papers are required to be presented in domestic and / or international conferences and submitted to journals. The minimum requirements are completing the prescribed courses, a supervised research project and a dissertation for the degree published in a top international journal.

### ( 4 ) Lectures & Courses

The ultimate goal of the oral health care programs is to provide well-being of the patients. In order to achieve this goal, besides the clinical training that we offer to the licensed graduate students, high-caliber research projects are being carried out aimed at developing, enhancing and evaluation of the materials and techniques in dentistry; particularly for adhesives, caries prevention, diagnosis and treatment, and oral health maintenance.

**( 5 ) Clinical Services & Other Works**

Full-time faculty see patients in Operative Dentistry and Endodontics, and provide restoration of teeth with fillings for dental cavities, trauma and tooth wear, and root canal treatments. The faculty members supervise both pre-and postdoctoral students in the clinic.

**( 6 ) Clinical Performances**

Our Operative Dentistry clinic provide restoration of teeth with fillings for dental cavities, trauma and tooth wear under Minimal intervention concept. The clinical services are based on accumulated scientific researches.

**( 7 ) Publications****[Original Articles]**

1. Takako Yoshikawa, Makoto Morigami, Alireza Sadr, Junji Tagami . Environmental SEM and dye penetration observation on resin-tooth interface using different light curing method *Dental Materials Journal*. 2016; 35(1); 89-96
2. Chiba A, Zhou J, Nakajima M, Tan J, Tagami J, Scheffel DLS, Hebling J, Agee KA, Breschi L, Grégoire G, Jang SS, Tay FR, Pashley DH. The effects of ethanol on the size-exclusion characteristics of type I collagen to adhesive resin monomers *Acta Biomaterialia*. 2016;
3. Sachiko Ito, Yasushi Shimada, Alireza Sadr, Yukie Nakajima, Michiyo Miyashin, Junji Tagami, Yasunori Sumi. Assessment of occlusal fissure depth and sealant penetration using optical coherence tomography. *Dent Mater J*. 2016; 35(3); 432-439
4. Hiroki Tezuka, Yasushi Shimada, Khairul Matin, Masaomi Ikeda, Alireza Sadr, Yasunori Sumi, Junji Tagami. Assessment of cervical demineralization induced by *Streptococcus mutans* using swept-source optical coherence tomography. *J Med Imaging (Bellingham)*. 2016.01; 3(1); 014504
5. A Chiba, J Zhou, M Nakajima, J Tan, J Tagami, D L S Scheffel, J Hebling, K A Agee, L Breschi, G Grégoire, S S Jang, F R Tay, D H Pashley. The effects of ethanol on the size-exclusion characteristics of type I dentin collagen to adhesive resin monomers. *Acta Biomater*. 2016.03; 33; 235-241
6. Maria Jacinta Rosario H Romero, Syozi Nakashima, Toru Nikaido, Alireza Sadr, Junji Tagami. In vitro dentine remineralization with a potential salivary phosphoprotein homologue. *Arch. Oral Biol.*. 2016.03; 68; 35-42
7. Baba Bista, Syozi Nakashima, Toru Nikaido, Alireza Sadr, Tomohiro Takagaki, Maria J R H Romero, Takaaki Sato, Junji Tagami. Adsorption behavior of methacryloyloxydecyl dihydrogen phosphate on an apatite surface at neutral pH. *Eur. J. Oral Sci.*. 2016.04; 124(2); 195-203
8. Md Sofiqul Islam, Sahar Jameel Khunkar, Syozi Nakashima, Alireza Sadr, Toru Nikaido, Junji Tagami. Comparative study of demineralized collagen degradation determined by hydroxyproline assay and microscopic depth measurement. *J Dent*. 2016.04; 47; 94-97
9. Takaaki Sato, Tomohiro Takagaki, Naoko Matsui, Hidenori Hamba, Alireza Sadr, Toru Nikaido, Junji Tagami. Morphological Evaluation of the Adhesive/Enamel interfaces of Two-step Self-etching Adhesives and Multimode One-bottle Self-etching Adhesives. *J Adhes Dent*. 2016.06; 18(3); 223-229
10. Rui Guan, Tomohiro Takagaki, Naoko Matsui, Takaaki Sato, Michael F Burrow, Joseph Palamara, Toru Nikaido, Junji Tagami. Dentin bonding performance using Weibull statistics and evaluation of acid-base resistant zone formation of recently introduced adhesives. *Dent Mater J*. 2016.06;
11. Junichi Shinagawa, Go Inoue, Toru Nikaido, Masaomi Ikeda, Alireza Sadr, Junji Tagami. Dentin bonding performance and interface observation of an MMA-based restorative material. *Dent Mater J*. 2016.06;
12. Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Masahiro Takahashi, Suppason Thittaweerat, Richard M Foxton, Shizuko Ichinose, Junji Tagami, Masatoshi Nakajima. Effect of Scrubbing Technique with Mild Self-etching Adhesives on Dentin Bond Strengths and Nanoleakage Expression. *J Adhes Dent*. 2016.06; 18(3); 197-204

13. Wataru Komada, Tasuku Inagaki, Yoji Ueda, Satoshi Omori, Keiichi Hosaka, Junji Tagami, Hiroyuki Miura. Influence of water immersion on the mechanical properties of fiber posts. *J Prosthodont Res.* 2016.06;
14. Kanae Wada, Eri Ikeda, Junichiro Wada, Go Inoue, Munenaga Miyasaka, Michiyo Miyashin. Wear characteristics of trimethylolpropane trimethacrylate filler-containing resins for the full crown restoration of primary molars. *Dent Mater J.* 2016.06; 35(4); 585-593
15. Ehab Z Alsayed, Ilnaz Hariri, Syozi Nakashima, Yasushi Shimada, Turki A Bakhsh, Junji Tagami, Alireza Sadr. Effects of coating materials on nanoindentation hardness of enamel and adjacent areas. *Dent Mater.* 2016.06; 32(6); 807-816
16. Takaaki Sato, Tomohiro Takagaki, Naoko Matsui, Hidenori Hamba, Alireza Sadr, Toru Nikaido, Junji Tagami. Morphological Evaluation of the Adhesive/Enamel interfaces of Two-step Self-etching Adhesives and Multimode One-bottle Self-etching Adhesives. *J Adhes Dent.* 2016.06; 18(3); 223-229
17. Minh Nguyet Dao Luong, Yasushi Shimada, Alaa Turkistani, Junji Tagami, Yasunori Sumi, Alireza Sadr. Fractography of interface after microtensile bond strength test using swept-source optical coherence tomography. *Dent Mater.* 2016.07; 32(7); 862-869
18. Tomoka Ueno, Yasushi Shimada, Khairul Matin, Yuan Zhou, Ikumi Wada, Alireza Sadr, Yasunori Sumi, Junji Tagami. Optical analysis of enamel and dentin caries in relation to mineral density using swept-source optical coherence tomography. *J Med Imaging (Bellingham).* 2016.07; 3(3); 035507
19. Rena Oguro, Masatoshi Nakajima, Naoko Seki, Alireza Sadr, Junji Tagami, Yasunori Sumi. The role of enamel thickness and refractive index on human tooth colour. *J Dent.* 2016.08; 51; 36-44
20. Asami Aida, Masatoshi Nakajima, Naoko Seki, Yukinori Kano, Richard M Foxton, Junji Tagami. Effect of enamel margin configuration on color change of resin composite restoration. *Dent Mater J.* 2016.08; 35(4); 675-683
21. Ornnicha Thanatvarakorn, Md Sofiqul Islam, Syozi Nakashima, Alireza Sadr, Toru Nikaido, Junji Tagami. Effects of zinc fluoride on inhibiting dentin demineralization and collagen degradation in vitro: A comparison of various topical fluoride agents. *Dent Mater J.* 2016.08;
22. Yuan Zhou, Yasushi Shimada, Khairul Matin, Alireza Sadr, Yasunori Sumi, Junji Tagami. Assessment of bacterial demineralization around composite restorations using swept-source optical coherence tomography (SS-OCT). *Dent Mater.* 2016.09; 32(9); 1177-1188
23. Kei Horie, Yasushi Shimada, Khairul Matin, Masaomi Ikeda, Alireza Sadr, Yasunori Sumi, Junji Tagami. Monitoring of cariogenic demineralization at the enamel-composite interface using swept-source optical coherence tomography. *Dent Mater.* 2016.09; 32(9); 1103-1112
24. Kalyan Kong, Noriko Hiraishi, Mohannad Nassar, Masayuki Otsuki, Cynthia K Y Yiu, Junji Tagami. Effect of phytic acid etchant on resin-dentin bonding: Monomer penetration and stability of dentin collagen. *J Prosthodont Res.* 2016.10;
25. Takako YOSHIKAWA, Alireza SADR, Makoto ARAKAWA, Junji TAGAMI. . Bond strength of resin composites to cavity floor and cavity wall dentin. *Asian Pacific Journal of Dentistry.* 2016.11; 16; 23-26
26. Miho Sugiura, Yuichi Kitasako, Alireza Sadr, Yasushi Shimada, Yasunori Sumi, Junji Tagami. White spot lesion remineralization by sugar-free chewing gum containing bio-available calcium and fluoride: A double-blind randomized controlled trial. *Journal of Dentistry.* 2016.11; 54; 86-91
27. Takako YOSHIKAWA, Alireza SADR, Junji TAGAMI. . Effects of C-factor on bond strength to floor and wall dentin. *Dental Materials Journal.* 2016.12; 35(6); 918-922
28. Iori Sugita, Syozi Nakashima, Masaomi Ikeda, Michael F Burrow, Toru Nikaido, Shisei Kubo, Junji Tagami, Yasunori Sumi. A pilot study to assess the morphology and progression of non-carious cervical lesions. *J Dent.* 2016.12;

**[Books etc]**

1. Junji Tagami. Quarterly dental care. First publication, 2016.04
2. ryo imai,ritu aoki,reiko kaduki,hiko hyakusoku. rehabilitation makeup-To be visible makeup therapy option-. kokuseidou publishing company, 2016.06
3. nico. Quintessence publishing, 2016.08

**[Misc]**

1. 3. Yasuko Momoi, Akihiko Shimizu, Mikako Hayashi, Satoshi Imazato, Masako Unemori, Yuichi Kitasako, Shisei Kubo, Rena Takahashi, Shoji Nakashima, Toru Nikaido, Masayoshi Fukushima, Morioki Fujitani, Chinami Yamaki, Kenichi Sugai. Root caries management: Evidence and consensus based report Curr Oral Health Rep. 2016.03; 30; 1-7

**[Conference Activities & Talks]**

1. Keiichi Hosaka. Direct Composite Restorations. Invited Lecture 2016.01.15 Trisakty University, Jakarta, Indonesia
2. Keiichi Hosaka. Lecture Direct Veneer & Class 3-4 Restorations. Sminar Sehari Tentang Estetik Veneer, Hukum, Kode Etik Dan Perpajakan 2016.01.16 Jakarta, Indonesia
3. Keiichi Hosaka. Hands On Direct Veneer & Class 3-4 Restorations. Sminar Sehari Tentang Estetik Veneer, Hukum, Kode Etik Dan Perpajakan 2016.01.16 Jakarta, Indonesia
4. Yasushi Shimada. Optical coherence tomography as a new tool for caries diagnosis and assessment of restoration. KPPIKG 2016 2016.02.27 Jakarta
5. Yuan Zhou, Khairul Matin. Evaluation of Resin Infiltration to Prevent Progression of Root Caries. American Association for Dental Research (AADR) Annual Meeting 2016.03.16 Los Angeles, Calif, USA
6. Yuki Naruse, Tomohiro Tkakagaki, Naoko Matsui, Takaaki Sato, Toru Nikaido, Masaomi Ikeda, Junji Tagami. Effects of alumina-blasting for a CAD/CAM resin block on adhesion. 45th Annual meeting of American Association for Dental Research 2016.03.17 Los Angeles
7. Tomoko TABATA, Yasushi SHIMADA, Alireza SADR, Junji TAGAMI, Yasunori SUMI. Assessment of Enamel Crack at Cavo-surface Margin Using 3D SS-OCT. 45th annual meeting of AADR 2016.03.17 Los Angeles
8. Chihiro MATSUURA, Yasushi SHIMADA, Alireza SADR, Junji TAGAMI, Yasunori SUMI . 3D assessment of dentin caries under composite restorations using SS-OCT . AADR 2016.03.17 Los Angeles
9. Rui Guan, Tomohiro Takagaki, Toru Nikaido, Takahiro Wada, Motohiro Uo, Junji Tagami. Adsorption behavior of phosphoric functional monomers to 3Y-TZP surface.. 45th Annual meeting of American Association for Dental Research 2016.03.17
10. Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Masahiro Takahashi, Suppason Thittaweerat, Junji Tagami, Masatoshi Nakajima. Scrubbing effect of one-step self-etch adhesives on dentin bonding. 45th AADR 2016.03.18 Los Angeles, Calif
11. Masatoshi Nakajima, Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Keiichi Hosaka, Junji Tagami. Effect of smear layer-deproteinizing on dentin bonding of self-etch adhesives. 45th AADR 2016.03.18 Los Angeles, Calif
12. Taweesak Prasansuttiorn, Ornnicha Thanatvarakorn, Junji Tagami, Masatoshi Nakajima. Bonding durability of dental adhesive to smear layer-deproteinized dentin. 45th AADR 2016.03.18 Los Angeles, Calif
13. David Pashley, Ayaka Chiba, Jianfeng Zou, Masatoshi Nakajima, Jianguo Tan, Junji Tagami, Debora Scheffel, Josimeri Heblingm, Kelli Agee, Lorenzo Breschi, Genevieve Gregorie, Seung Jang, Franklin Tay. Effect of ethanol on size-exclusion characteristics of dentin-collagen to monomer. 45th AADR 2016.03.18 Los Angeles, Calif.

14. Inoue G, Mashiko R, Nakashima S, Tagami J. Surface assessment on artificial caries-affected dentin with FCP-COMPLEX. 45th Annual Meeting of American Association for Dental Research 2016.03.19 Los Angeles, USA
15. Prof. Nairn H F Wilson. History and reasons behind current trends in dentistry in the UK. 2016.04.04 Tokyo medical and dental university
16. Junji Tagami. About composite resin restorations. 2016.05.18
17. Noriko Hiraishi, Fumiaki Hayashi, Tomohiro Takagaki, Masayuki Otsuki, Junji Tagami. Interaction of MDP-based adhesive with dentin studied by solid-state NMR. 2016.06 Seoul, Korea
18. Microtensile bond strength to dentin of a newly developed one-step self-etch system containing hydrophilic amide monomer. 2016.06.09
19. Sae AKEHASHI, Rena TAKAHASHI, Toru NIKAIDO, Junji TAGAMI. Enhancement of Dentin Bond Strength of Resin Cement using New Resin Coating Materials. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.10 Tochigi, Japan
20. Khin Yupar Kyaw, Masayuki Otsuki, Junji Tagami . Effect of application of sodium fluoride on in-office bleaching. 2016.06.10
21. Nagano Daiki. The effect of surface treatment on repairing procedure of aged resin composite in the different term of water immersion. 2016.06.10
22. Rainer Guggenburger. How innovation comes to live in dentistry - from idea to clinical success. Special lecture 2016.06.17 Tokyo medical and dental University Cariology and Operative Dentistry
23. Aramaki O, Kawashima N, Shimada Y, Okiji T, Tagami J . Three-dimensional analysis of Iba1+ macrophages in human dental pulp using whole mount immunostaining. 94th General Session & Exhibition of the IADR 2016.06.22 Seoul, Korea
24. Yasushi Shimada, Juri Hayashi, Ikumi Wada, Oto Aramaki, Alireza Sadr, Yasunori Sumi, Junji Tagami. 3D Assessment of Dental Caries Using Swept-source Optical Coherence Tomography in Vivo. 94th General session & exhibition of the IADR 2016.06.23 Seoul, Korea
25. Rena Takahashi, Yasushi Shimada, Yu-Chih Chiang, Ikumi Wada, Yasunori Sumi, Junji Tagami. Comparison of light-cured pit and fissure sealants on enamel demineralization using swept-source optical coherence tomography. 94th General Session & Exhibition of the IADR 2016.06.24 Seoul, Korea
26. Yu-Jung Lai, Ting-Chen Liu, Szu-Ying Huang, Rena Takahashi, Yasushi Shimada, Junji Tagami, Yu-Chih Chiang. Effects of S-PRG Fillers-containing Composite on Demineralization Inhibition of Enamel Surface: Optical Coherence Tomography (OCT) and Micro Computed Tomography (Micro CT) Approaches. 94th General Session & Exhibition of the IADR 2016.06.24 Seoul, Korea
27. Junji ATOMURA. Influence of FCP-COMPLEX on bond strength to caries-affected dentin. 2016 IADR/APR General Session in Seoul 2016.06.24 KOREA
28. Otsuki M, Sawada K, Arakawa S, Shiba A, Shioda G, Tagami J. Effect of ozone gel on tooth bleaching. 94th General Session of the IADR 2016.06.25 Seoul, Korea
29. Otsuki M, Nagai S, Alireza S, Shimada Y, Hayashi J, Tagami J, Sumi Y. Effect of Er:YAG laser preparation on resin-cavity interface evaluated by SS-OCT. 2016 International Conference on QLF 2016.06.26 Seoul, Korea
30. Noda S, Kawashima N, Hashimoto K, Aramaki O, Yamamoto M, Okiji T. Effects of confluent culture condition on dental pulp stem cell surface markers, proliferation, gene expression. IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.28 Nagoya
31. Akira Nakane, Masayuki Otsuki, Junji Tagami . Change of dentin surface by low-power irradiation of Er:YAG laser. 15th Congress of the World Federation for Laser Dentistry 2016.07.19 Nagoya
32. Yuki Ito, Masayuki Otsuki, Junji Tagami, Takao Asaki, Norika Okawara. Effect of pH conditioners on tooth bleaching. 2016.08.27

33. Effect of cavity depth on Ultimate Tensile Strength of bulk fill flowable resin. 2016.09.10
34. Yuan Zhou, Yasushi Shimada, Khairul Matin, Yasunori Sumi, Junji Tagami. . Assessment of Root Caries under Wet and Dry Conditions Using Swept-source Optical Coherence Tomography (SS-OCT).. The 145th Meeting of the Japanese Society of Conservative Dentistry (JSCD). 2016.10 Nagano, Japan.
35. Keiichi Hosaka. Adhesive Dentistry meets Direct Composite Restoration. Invited Lecture 2016.10.14 Chulalongkorn University, Bangkok, Thailand
36. Junji Tagami. Creating a future dentistry with the adhesive dentistry. Research Day with CU,UI,UMPandTMDU Dental Students 2016 2016.10.18 Akio Suzuki memorial Hall in TMDU
37. Yuna KANAMORI, Rena TAKAHASHI, Toru NIKAIDO, Junji TAGAMI. The effect of light irradiation on dentin bond strengths of dual-cure resin cements. The 145th Meeting of Japanese Society of Conservative Dentistry 2016.10.27 Nagano, Japan
38. Yukina Ochiai, Go Inoue, Junji Atomura, Toru Nikaido, Junji Tagami. The evaluation of bond strength of calcium containing adhesive system . 2016.10.27 Nagano
39. Junji Tagami. The top researcher talks "The best adhesion". 2016.11.13 Tokyo international forum
40. Junji Tagami. New trend of dental materials, adhesive resin and composite resin. 2016.11.23 Study medicine in Czech Republic
41. Zhou Yuan, Matin Khairul, Shimada Yasushi, Sumi Yasunori, Tagami Junji. . Evaluation of Resin Infiltration to Reduce Enamel Cracks by Swept-source Optical Coherence Tomography (SS-OCT).. The 35th Annual Meeting of Japan Society for Adhesive Dentistry 2016.12 Hokkaido, Japan
42. Sato Takaaki, Takagaki Tomohiro, Nikaido Toru, Tagami Junji. Observation of Acid-base Resistant Zone on adhesive/enamel interface using newly developed one step self-etching adhesive. The 35th Annual Meeting of Japan Society for Adhesive Dentistry 2016.12.03
43. Interfacial adaptation of composite restorations before and after light-curing .
44. Toothbrushing timing after acidic drinks affects enamel loss in-situ. Boston, USA
45. The evaluation of bond strength of calcium containing adhesive system to artificial demineralized dentin.

## Fixed Prosthodontics

Professor  
Hiroyuki MIURA

Associate Professor  
Kenichi YOSHIDA

Junior Associate Professor  
Daizo OKADA  
Wataru KOMADA

Assistant Professor  
Chiharu SHIN  
Shiho OTAKE  
Reiko OGURA  
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Attending Staff  
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Yoji UEDA  
Rie FUJITA  
Tazuko MAKIYAMA  
Hiroyuki OKAMOTO  
Miho SATO  
Kyoshi MATSUKAWA  
Fujino OSHIMA  
Yoko ISHIKAWA  
Natsuko IWATA  
Mariko KUBO  
Kazuhisa FUJITA  
Hideto MATSUI  
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### ( 1 ) Research

- 1)Occlusion and Mastication.(mandibular position, mandibular movement, articulator, masticatory efficiency)
- 2)Influence of mechanical stress caused by occlusal contact on stomatognathic system. (Tooth displacement, distortion of alveolar bone, occlusal contact, proximal contact etc.)



- 3) Relationship of main occluding area and occlusal contact
- 4) Research on post and core (materials, stress analysis etc.)
- 5) Clinical application of latest technology and development of new materials (CAD/CAM, Zirconia, optical impression etc.)
- 6) Influence of occlusal contact for an important prosthesis on the periodontal tissues of the antagonist.
- 7) Application of laser welding in crown and bridge restorations.
- 8) Influence of dental materials for periodontal tissues and biological body.
- 9) Functional analysis of abnormal stomatognathic function

## **( 2 ) Lectures & Courses**

The major subjects of the studies are occlusion of Cr-Co prostheses (fixed restoration such as crown and fixed partial denture), analysis of mandibular movement, influence of crown and periodontal tissue and its systemic affect, accuracy of manufacturing processes of crown (i.e. casting, soldering, luting and adjustment of occlusion), functional analysis of stomatognathic system and development of apatite ceramic implant. The research themes are investigated with measurement systems of mandibular movement, measuring instruments of tooth micro-displacement, electromyography, measurement apparatus of dimensional accuracy, EPMA (electron probe microanalyzer) for analyzing very small amount of dental alloy and histopathological methods. Clinical training and general lecture on prosthodontics are prepared for the graduate students in the first year. After the second year they will have special training for their research methods and experiments will be performed according to the research plan. In the last year the students will write the paper for thesis under the direction of the professor.

## **( 3 ) Clinical Services & Other Works**

### **1) Clinic for prosthodontics (Prosthodontics practice clinic)**

This clinic is organized by clinical teams, and 4 to 8 dentists compose 1 team working in cooperation between teams. Here offers a complete range of restorative, rehabilitative, and esthetic dentistry, treatment types include since simple one teeth to complete oral rehabilitation using the latest technologies.

### **2) Clinic for dental allergy (Dental allergy clinic)**

This clinic provides allergy tests test for dental alloys and dental materials on potential patients before dental treatment, besides, patients with skin and/or oral diseases histories induced by previous dental restorations. The causal allergen/s is/are identified by patch tests or if some metal restoration is allergy set on, is analyze by Electron Probe Micro Analyzer (EPMA), removing out only restoration such content allergens.

## **( 4 ) Publications**

### **[Original Articles]**

1. Oshima F, Okada D, Ogura R, Shin C, Ueda Y, Inagaki T, Fujita R, Miura H. A finite element analysis of stress distribution in roots with different types of post systems. *Asian Pacific Journal of Dentistry*. 2016; 16(1); 1-7
2. Kosuke Nozaki, Risa Yamada, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. Antibacterial activity of silver nanoparticles coating on zirconia against oral bacteria *Visual-JW* 2016. 2016; 41



3. Ana Milheiro, Kosuke Nozaki, Cornelis J Kleverlaan, Joris Muris, Hiroyuki Miura, Albert J Feilzer. In vitro cytotoxicity of metallic ions released from dental alloys. *Odontology*. 2016.05; 104(2); 136-142

### [Conference Activities & Talks]

1. Omori S, Takeuchi K, Inagaki T, Miura H. Relationship between framework thickness and fracture strength of Ce-TZP/Al crown. 45th Annual Meeting & Exhibition of the AADR 2016.03.16 Los Angeles, California
2. Ishikawa Y, Komada W, Inagaki T, Nemoto R, Omori S, and Miura H. Root Surface-strain of Bridge Using Different Post and Core Systems. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
3. Fujita R, Takita M, Otake S, Shirasaki A, Miura H. Bond strengths of cements to a new indirect resin composite. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
4. Iwata N, Nozaki K, Miura H, Yamashita K, Nagai A. Surface modification of Ti implant with controlled micro/nano-structured topography. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
5. Risa Yamada, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita and Akiko Nagai. Antimicrobial activity of silver nanoparticle-coated yttria-stabilized zirconia. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
6. Minamifuchi.M, Nemoto.R, Inagaki.T, Uraba.A, Nozaki.K and Miura.H. Influence of framework design on shear stress distribution . AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
7. Nemoto R, Shirasaki A , Otake S , Takita M, Miura H. Bond strengths of cements to a new CAD/CAM resin composite . AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
8. Otake S, Uraba A, Minamifuchi M, Miura H. Bond strengths of cements to a new polyetheretherketone material. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
9. Uraba A, Inagaki T, Nemoto R, Minamifuchi M, Nozaki K, Miura H. The shear stress distribution of two different cantilever RBFPDs. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
10. Kubo M, Komada W, Otake S, Inagaki T, Omori S, Miura H. Fracture strength of composite resin core with glass fiber ribbon.. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
11. Asano R, Okada D, Shin C, Rikitoku S, Shirasaki A, Takita M, Shibaguchi K, Uraba A, Minamifuchi M, Ishikawa Y, Iwata N, Kubo M, Fujita K, Matsui H, Yamada R, Matsukawa K and Miura H. Statistical Analysis of Prosthetic Restorations in year 2014-2015 at Tokyo Medical and Dental University — Single Restorations— . AADR/CADR Annual Meeting & Exhibition 2016.03.18 Los Angeles, CA, USA
12. Rikitoku S, Omori S, Okada D, Shin C, Asano R, Shirasaki A, Takita M, Shibaguchi K, Uraba A, Minamifuchi M, Ishikawa Y, Iwata N, Kubo M, Fujita K, Matsui H, Yamada R, Matsukawa K and Miura H. Statistical Analysis of Prosthetic Restorations in year 2014-2015 at Tokyo Medical and Dental University - Dental Prosthesis for Missing Teeth - . AADR/CADR Annual Meeting & Exhibition 2016.03.18 Los Angeles, CA, USA
13. Shibaguchi K, Okamoto H, Noda A, Matsui H, Fukumoto I, Hani H, Kitazaki H, Matsumura M, Miura H. Recent trends in Relationship between Pustulosis Palmoplantaris and Metal Allergy. 2016.03.19 AADR/CADR Annual Meeting & Exhibition Los Angeles, CA, USA
14. Fujita K, Nozaki K, Yamashita K, Miura H, and Nagai A. Differentiation of periodontal ligament cell on hydroxyl- and carbonated-apatites. AADR/CADR Annual Meeting & Exhibition 2016.03.19 Los Angeles, CA, USA
15. Nozaki K, Fujita K, Miura H, Yamashita K, Nagai A. Bone remodeling-optimization of carbonated apatite for guided bone regeneration. AADR/CADR Annual Meeting & Exhibition 2016.03.19 Los Angeles, CA, USA

16. Kosuke Nozaki, Kazuhisa Fujita, Naohiro Horiuchi, Miho Nakamura, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. In vivo evaluation of the role of carbonate ion in hydroxyapatite for bone remodeling. 10th World Biomaterials Congress 2016.05.20
17. Matukawa K, Nemoto R, Inagaki T, Kubo M, Oomori T, Yoshida K, Miura H. Tensile Bond Strengths of Resin Cements to Zirconia Fixed Partial Dentures. 2016.05.28 Sapporo, Japan
18. W. Komada, S. Otake, R. Nemoto, K. Yoshida, H. Miura . Pull-out strength of glass fiber post with composite resin. The 27th Annual Meeting of Japan Academy of Esthetic Dentistry 2016.08.27 Sapporo
19. Kosuke Nozaki, Risa Yamada, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. Antibacterial activity of silver nanoparticles coating on zirconia against oral bacteria. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development 2016.10.17

## Pulp Biology and Endodontics

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### ( 1 ) Outline

The Department of Pulp Biology and Endodontics deals with endodontics/endodontology, and is concerned with research and clinical practice on the prevention, diagnosis and treatment of dental pulp and periapical diseases. In order to preserve and well maintain the function of the teeth in the oral cavity, it is important to understand the structural and functional features of the dental pulp and protect it carefully from noxious stimuli. However, pulp diseases, if left untreated, may progress to develop pulp necrosis and apical periodontitis, where meticulous treatment is required to eliminate infection from the complex root canal system. The goal of endodontics is to achieve long term maintenance of tooth function by the prevention and treatment of pulpal and periapical diseases.

**( 2 ) Research**

- 1) Dental pulp tissue engineering
- 2) Cell biology of odontoblasts, pulp calls and dental pulp stem cells
- 3) Analysis of regulatory factors associated with pulp inflammation
- 4) Root canal irrigation regimens for pulp regeneration therapy
- 5) Laser-activated root canal irrigation
- 6) Bioactivity evaluation of newly developed pulp capping materials and root canal sealers
- 7) Mechanical property analysis of NiTi rotary instruments for safe and efficient root canal preparation
- 8) Evaluation of cone-beam computed tomography in the diagnosis of endodontic lesions
- 9) Application of optical coherence tomography to endodontic diagnosis

**( 3 ) Education**

The educational aim of the Department of Pulp Biology and Endodontics is to cultivate students so that they can obtain knowledge and skills required for leading scientists, researchers or practitioners of endodontics. Since recent progress of pulp biology and endodontics is remarkable, the students are educated to acquire the newest knowledge on modern endodontology and its related subjects, such as neuroscience, microbiology, molecular biology, immunology and biomaterial sciences, and are trained to master the newest technology of endodontics. All the students are asked to add new findings to the field of endodontics based on their own original research.

**( 4 ) Clinical Services & Other Works**

The Department of Pulp Biology and Endodontics is in charge of the Clinic of Operative Dentistry and Endodontics in our Dental Hospital, together with the Department of Cariology & Operative Dentistry, and offers the global standard of care in the treatment of pulpal and periapical diseases to our patients. We provide clinical care in the full spectrum of endodontics including;

- Vital pulp therapies,
- Nonsurgical root canal therapies,
- Root canal retreatments,
- Endodontic microsurgeries,
- Internal tooth bleaching, and
- Post-endodontic restorations

**( 5 ) Clinical Performances**

The latest development of endodontics is remarkable as seen in root canal instrumentation by super-elastic Ni-Ti rotary files, diagnosis by cone beam computed tomography, and microendodontics by using a surgical operating microscope. In particular, microendodontics has dramatically changed conventional “blind” endodontics into more predictable endodontics since it allows us to obtain accurate diagnostic information and provide precise procedures under an illuminated and magnified view. Also, we seek to provide evidence-based endodontic treatment based on our laboratory and clinical research.

**( 6 ) Publications****[Original Articles]**

1. Sakaue Y, Domon H, Oda M, Takenaka S, Kubo M, Fukuyama Y, Okiji T, Terao Y. Anti-biofilm and bactericidal effects of Magnolia bark-derived magnolol and honokiol on *Streptococcus mutans*. *Microbiology & Immunology*. 2016.01; 60(1); 10-16
2. Yamamoto S, Han L, Okiji T. S-PRG filler extract solutions induce dentinal tubule occlusion and elemental incorporation in ground human dentin *The Journal of Japan Endodontic Association*. 2016.01; 37(1); 31-37

3. Kawashima N, Saito M, Okiji T. Osr2 (odd-skipped related 2) induced differentiation of hard-tissue forming cells in mouse dental papilla cells The journal of Japan Endodontic Association. 2016.01; 37(1); 38-44
4. Edanami N, Shigetani Y, Yoshiba K, Hinata G, Yoshiba N, Okiji T. Evaluation of the biocompatibility of a 4-META containing resin-based root canal sealer in the rat subcutaneous tissue Japanese Journal of Conservative Dentistry. 2016.02; 59(1); 65-73
5. Ishizaki H, Nakajima T, Ito H, Okumura N, Kobayashi T, Uoshima K, Takagi R, Okiji T, Fujii N. Analysis and safety management of incidents in post-graduate clinical training The Journal of Japanese Dental Education. 2016.04; 32(1); 29-36
6. Han L, Okiji T. An ion extract obtained from mineral trioxide aggregate induced dentin remineralization and dentinal tubule occlusion in artificially demineralized bovine dentin. American Journal of Dentistry. 2016.06; 29(3); 166-170
7. Han L, Yamamoto S, Okiji T. Effect of a prototype S-PRG filler-containing endodontic paste on root canal dentin: dentinal tubule occlusion and incorporation of elements Japanese Journal of Conservative Dentistry. 2016.06; 59(3); 279-286
8. Shigetani Y, Ohkura N, Yoshiba K, Ohshima H, Hosoya A, Yoshiba N, Okiji T. GaAlAs laser-induced pulp mineralization involves dentin matrix protein 1 and osteopontin expression. Oral Diseases. 2016.07; 22(5); 399-405
9. Takafumi Ito, Tomoatsu Kaneko, Yukiko Sueyama, Reika Kaneko, Takashi Okiji. Dental pulp tissue engineering of pulpotomized rat molars with bone marrow mesenchymal stem cells. Odontology. 2016.11;
10. Komatsu K, Ebihara A, Okiji T. Differential diagnosis of vertical root fractures using a three-dimensional bone defect evaluation system Journal of Japan Association of Dental Traumatology. 2016.12; 12(1); 26-35
11. Y Sueyama, T Kaneko, T Ito, T Okiji. Effect of lipopolysaccharide stimulation on stem cell-associated marker-expressing cells. Int Endod J. 2016.12;
12. Yamamoto S, Han L, Noiri Y, Okiji T. Evaluation of the Ca ion release, pH and surface apatite formation of a prototype tricalcium silicate cement. International Endodontic Journal. 2016.12; Epub ahead of print
13. Uraba S, Ebihara A, Komatsu K, Ohbayashi N, Okiji T. Ability of cone-beam computed tomography to detect periapical lesions that were not detected by periapical radiography: A retrospective assessment according to tooth group Journal of Endodontics.

#### [Books etc]

1. Kaneko T, Sueyama Y, Okiji T, Nör JE. Understand Cancer - Research and Treatment. iConcept Press, 2016.03 (ISBN : 978-1-922227-386)
2. Okiji T. Case assessment and strategy for endodontics. 2016.05 (ISBN : 978-7-5381-9510-1)

#### [Misc]

1. Nishijo M, Watanabe S, Okiji T. Outcome of orthograde retreatment after failed apicoectomy: use of mineral trioxide aggregate apical plug 2016.03; 35(3); 203-205
2. Watanabe S, Okiji T. Application of laser to endodontics The Journal of Japan Society for Laser Surgery and Medicine. 2016.04; 37(1); 37-42
3. Noda S, Watanabe S, Okiji T. A prospective study of the incidence of asymptomatic pulp necrosis following crown preparation The Quintessence. 2016.06; 35(6); 226-228
4. Kawashima N, Okiji T. Odontoblasts: Specialized hard-tissue-forming cells in the dentin-pulp complex Congenital Anomalies (Kyoto). 2016.07; 56(4); 144-153
5. Okiji T. Mineral trioxide aggregate: current development and physicochemical properties The Journal of the Japanese Society for Dental Materials and Devices. 2016.07; 35(4, 5); 237-240

6. Hashimoto K, Watanabe S, Okiji T. Treatment outcome of repaired root perforation: a systematic review and meta-analysis the Quintessence. 2016.10; 35(10); 218-220
7. Sunakawa M. Infection Control in Deentistry Carlisle. 2016.12; 21(3); 1-3

### [Conference Activities & Talks]

1. Sueyama Y, Kaneko T, Ito T, Okiji T. Effects of lipopolysaccharide for three kinds of dental pulp related stem cells. Universitas Indonesia-Niigata University collaborative symposium 2016.01.09 Lombok, Indonesia
2. Komatsu K, Ebihara A, Okiji T. Differential diagnosis of vertical root fractures using a three-dimensional bone defect evaluation new system. The 6th conference of Japan Association of Dental Traumatology 2016.04.17 Tokyo
3. Ikeda H. Dentin hypersensitivity from the point of view of pulpal nerves and cells -Preconception and truth-. Federation of Endodontic Association (World Endodontic Congress) 2016.06.03 Cape Town, South Africa
4. TOKITA Daisuke, NISHIJO Miki, MIYARA Kana, EBIHARA Arata, OKIJI Takash. Analysis of stresses developed on the root during root canal shaping with different reciprocal motions. The 144th JSCD Meeting 2016.06.09 Utsunomiya, Tochigi
5. Watanabe S, Hongo T, Ide A, Satake K, Yao K, Ebihara A, Okiji T. Diode laser activation of sodium hypochlorite for lateral root canal soft tissue dissolution. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya
6. Nishijo M, Tokita D, Miyara K, Ebihara A, Okiji T. Evaluation of shaping ability and cyclic fatigue resistance during glide path preparation with prototype automatic root canal preparation system. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya
7. Yamamoto S, Han L, Okiji T. Evaluation of a prototype S-PRG filler-containing endodontic material: Dentinal tubule occlusion and element incorporation into the root canal dentin. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya, Tochigi
8. Ohkura N, Yoshida N, Yoshida K, Oda Y, Okiji T. Effect of prostaglandin EP4 receptor agonist on cultured human dental pulp tissue. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya, Tochigi
9. Tazawa K, Ikeda H, Kawashima N, Okiji T. Expression of TRPM8 in human odontoblasts. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya
10. Ikeda H, Aierken S, Tazawa K, Okiji T. Quantitative evaluation of the effects of etching/whitening materials on enamel permeability. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya
11. Fukumori Y, Nishijo M, Tokita D, Miyara K, Ebihara A, Okiji T. Comparative evaluation of mechanical properties with different tapered nickel-titanium files -cyclic fatigue and torsional load-. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya
12. Bakhit A, Kawashima N, Yamamoto M, Hashimoto K, Noda S, Nara K, Okiji T. Effects of strontium ranelate on the mouse dental papillae cells (MDPs). IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.22 Nagoya
13. Hongo T, Watanabe S, Ide A, Satake K, Yao K, Ebihara A, Kobayashi C, Okiji T. Kinetics of vaporized cavitation bubbles during root canal irrigation activated by diode laser. 94th General Session and Exhibition of the IADR 2016.06.22 Seoul, Korea
14. Sueyama Y, Kaneko T, Ito T, Okiji T. Lipopolysaccharide induces proliferation and CD146-upregulation of dental pulp stem cell. 94rd General Session and Exhibition of the IADR 2016.06.22 Seoul, Korea
15. Tazawa K, Ikeda H, Kawashima N, Ozawa M, Suda H, Okiji T. Expression of TRPM8 in freshly isolated human odontoblasts. 94th General Session and Exhibition of the IADR 2016.06.22 Seoul, Korea

16. Ikeda H, Suda H, Okiji T. Cold stimulus activates ionic channels in freshly isolated human odontoblasts. 94rd General Session and Exhibition of the IADR 2016.06.22 Seoul, Korea
17. Aramaki O, Kawashima N, Shimada Y, Okiji T, Tagami J. Three-dimensional analysis of Iba1+ macrophages in human dental pulp using whole mount immunostaining. 94th General Session & Exhibition of the IADR 2016.06.22 Seoul, Korea
18. Ikeda H, Aierken S, Tazawa K, Suda H, Okiji T. Quantitative analysis of changes in human enamel permeability after acid-etching/whitening procedures. IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.26 Nagoya
19. Kawashima N, Noda S, Hashimoto K, Yamamoto M, Okiji T. Properties of dental pulp derived-mesenchymal stem cells and effects of culture conditions. IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.26 Nagoya
20. Yoshiba N, Yoshiba K, Ohkura N, Edanami N, Takeuchi R, Tohma A, Oda Y, Hosoya A, Nakamura H, Okiji T. Fibrillin-1 microfibrils influence human dental pulp regeneration. IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.28 Nagoya
21. Hashimoto K, Kawashima N, Nara K, Noda S, Saito M, Okiji T. Recovery effects of EDTA treatment on the attachment and differentiation of mouse dental pulp cells cultured on NaOCl-treated dentin. IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.28 Nagoya
22. Noda S, Kawashima N, Hashimoto K, Aramaki O, Yamamoto M, Okiji T. Effects of confluent culture condition on dental pulp stem cell surface markers, proliferation, gene expression. IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.28 Nagoya
23. Nara K, Kawashima N, Noda S, Hashimoto K, Bakhit A, Okiji T. Increase of miR21 expression in dental pulp cells and tissues in response to LPS stimulation. IADR Pulp Biology and Regeneration Group Satellite Symposium 2016 2016.06.28 Nagoya
24. Ebihara A, Komatsu K, Kawamura J, Tsuruta J, Kinoshita A, Okiji T. Application of flip teaching to preclinical practice of endodontics. The 35th General and Scientific Meeting of the Japanese Dental Education Association 2016.07.02 Osaka
25. Kawamura J, Ebihara A, Suzuki N, Okiji T. Application of dental operating microscope to preclinical practice of endodontics. The 35th General and Scientific Meeting of the Japanese Dental Education Association 2016.07.02 Osaka
26. Kaneko T, Niwano K, Noiri Y, Maeda T, Okiji T. Introduction of the use of Ni-Ti rotary instruments in preliminary clinical practice of endodontics; root canal preparation using R-phase Ni-Ti rotary instruments. The 35th General and Scientific Meeting of the Japanese Dental Education Association 2016.07.02 Osaka
27. Komatsu K, Ebihara A, Okiji T. Differential diagnosis of vertical root fractures using a three-dimensional bone defect evaluation system: new indexes. The 16th conference of Japan Association of Dental Traumatology 2016.07.16 Kobe
28. Watanabe S, Ide A, Yao K, Satake K, Hongo T, Ebihara S, Kobayashi C, Okiji T. Pressure generated outside the apical foramen during root canal irrigation activated by diode laser. The 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya
29. Hongo T, Watanabe S, Ide A, Satake K, Yao K, Ebihara A, Okiji T. Kinetics of vaporized cavitation bubbles during root canal irrigation activated by diode laser. The 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya
30. Iino Y, Yoshioka T, Hanada T, Ebihara A, Sunakawa M, Sumi Y, Okiji T. Visualization of substructures of resected apical root surface by swept-source optical coherence tomography. The 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya
31. Rashed BA, Ebihara A, Iino Y, Yoshioka T, Hanada T, Sunakawa M, Sumi Y, Okiji T. Evaluation of root canal anatomy of maxillary premolars using swept source optical coherence tomography in comaparison with dental operating microscope and cone beam computed tomography. The 15th Congress of the World Federation for Laser Dentistry 2016.07.18 Nagoya



32. TOKITA Daisuke, NISHIJO Miki, MAKI Keiichiro, MIYARA Kana, EBIHARA Arata, OKIJI Takashi. Analysis of stresses during root canal shaping with TF Adaptive system. The 37th Annual Scientific Meeting of JEA 2016.07.23
33. Nakajima A, Yao K, Ide A, Hongo T, Satake K, Watanabe S, Okiji T. Efficacy of a new ultrasonic device in removing calcium hydroxide. The 37th Annual Scientific Meeting of Japan Endodontic Association 2016.07.23 Nagoya
34. Yamamoto S, Han L, Noiri Y, Okiji T. Evaluation of bioactivity on the prototype tricalcium silicate cement. The 37th Annual Scientific Meeting of Japan Endodontic Association 2016.07.23 Nagoya
35. Ikeda S, Kim S, Ide A, Satake K, Watanabe S, Okiji T. Cone-Beam Computed Tomography Analysis of Root Canal Configuration of Maxillary and Mandibular Molars. The 37th Annual Scientific Meeting of Japan Endodontic Association 2016.07.23 Nagoya
36. Maki K, Nishijo M, Tokita D, Ebihara A, Okiji T. Change of cyclic fatigue and cantilever bending properties of EndoWave instruments after clinical use. The 37th Annual Scientific Meeting of Japan Endodontic Association 2016.07.24 Nagoya
37. Kaneko T, Ito T, Sueyama Y, Okiji T. Immunohistochemical characterization of macrophage-like cells in mesenchymal stem cell-implanted engineered pulp tissues. The 37th Annual Scientific Meeting of Japan Endodontic Association 2016.07.24 Nagoya
38. Nishijo M, Maki K, Tokita D, Miyara K, Ebihara A, Okiji T. Shaping ability of ProTaper NEXT driven by a new automatic root canal preparation device in simulated root canals performed by undergraduate students. The 37th Annual Scientific Meeting of Japan Endodontic Association 2016.07.24 Nagoya
39. Fujii M, Kawashima N, Okiji T. Induction of HIF1  $\alpha$  in human dental pulp cells by lipopolysaccharide. The 58th Annual Meeting of Japanese Association of Oral Biology 2016.08.24 Sapporo
40. Sueyama Y, Kaneko T, Ito T, Okiji T. Implantation of stem cells with endothelial cells accelerates tissue regeneration. Japanese Association for Dental Research Hatton Award Competition 2016.09.02 Tokyo
41. Okiji T. Defense, repair and regeneration of the dentin/pulp complex: a biological basis for vital pulp therapy. Penn Endodontic Global Symposium in Japan: Endodontics in Implant Era 2016.09.10 Tokyo
42. Kagaya N, Sawa E, Kobayashi N, Hanaoka S, Kobayashi M, Matsumoto H, Suzuki H. Patient's attitude survey to "harmful rumor" of HIV/AIDS. The 33rd Annual Meeting of The Japan Society for Disability and Oral Health 2016.10.02 Omiya
43. Iino Y, Ebihara A, Yoshioka T, Hanada T, Sunakawa M, Sum Y, Okiji T. Application of optical coherence tomography in endodontics. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10.21 Fukuoka
44. Tazawa K, Ikeda H, Gu J, Okiji T. Human odontoblasts have a ability to detect cold stimulation. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10.21 Fukuoka
45. Okiji T. Vital pulp therapy: biological basis and current concepts. The 18th Joint Scientific Meeting of Korean Academy of Conservative Dentistry - Japanese Society of Conservative Dentistry 2016.10.23 Seoul, Korea
46. Nara K, Kawashima N, Noda S, Hashimoto K, Okiji T. MicroRNA21 down-regulates the expression of inflammatory mediators in LPS-stimulated human dental pulp cells via an NF- $\kappa$ B dependent mechanism. The 18th Joint Scientific Meeting of Korean Academy of Conservative Dentistry - Japanese Society of Conservative Dentistry 2016.10.23 Seoul, Korea
47. Kang D, Wada T, Uo M, Okiji T. Evaluation of mechanical properties of an experimental synthetic tricalcium silicate cement. The 18th Joint Scientific Meeting of Korean Academy of Conservative Dentistry - Japanese Society of Conservative Dentistry 2016.10.23 Seoul, Korea
48. XU Jing, TOKITA Daisuke, KIMURA Shunsuke, MAKI Keiichirou, NISHIJO Miki, MIYARA Kana, EBIHARA Arata, OKIJI Takashi. Evaluation of mechanical properties of ProTaper Gold and ProTaper NEXT instruments. 2016.10.26



49. Kuramoto M, Kawashima N, Bakhit A, Nara K, Fujii M, Noda S, Hashimoto K, Saitoh M, Okiji T. Effects of mineral trioxide aggregate on mouse dental papillae cells treated with lipopolysaccharide. The 145th Meeting of the Japanese Society of Conservative Dentistry 2016.10.27 Matsumoto
50. Yasumiko Wakabayashi, Nobuyuki Kawashima, Alamuddin Yassin Bakhit, Kentaro Hashimoto, Sonoko Noda, Keisuke Nara, Takashi Okiji. Cytotoxicity and osteoblast-differentiation induction of a prototype S-PRG filler-containing endodontic sealer. The Japanese Society of Conservative Dentistry 2016.10.28 Matsumoto City, Nagano Prefecture
51. Sunakawa M. Sterilization and disinfection methods of the used instruments in the dental clinic -actuals at the dental hospital, Tokyo Medical and Dental University-. Instrument Management & Infection Prevention Symposium 2016.10.30 Tokyo
52. Watanabe S. 30 Evidences quick update. Innovative Zahnmedizin 2016.11.06 Tokyo
53. Kawashima N, Hashimoto K, Okiji T. Rescue of mouse dental papillae cell-attachment to sodium hypochlorite-treated dentin disks by EDTA treatment. The 49th Scientific Meeting of Korean Academy of Endodontics 2016.11.19 Seoul, Korea
54. Gu B, Kaneko T, Sueyama Y, Sone PP, Okiji T. Immunohistochemical characterization of M2 macrophages in a rat experimental model of coronal pulp tissue engineering. The 59th Symposium of The Japanese Society of Microscopy 2016.11.19 Tokyo
55. Ikeda H. Microcirculation of the dental pulp. Symposium on Pulp Biology in Taiwan 2016.12.27 Taipei, Taiwan

#### **[Awards & Honors]**

1. Best oral presentation award 2nd prize (Evaluation of root canal anatomy of maxillary premolars using swept source optical coherence tomography in comparison with dental operating microscope and cone beam computed tomography, Rashed BA), The 15th Congress of the World Federation for Laser Dentistry, 2016.07
2. Best poster award (Rescue of mouse dental papillae cell-attachment to sodium hypochlorite-treated dentin disks by EDTA treatment, Nobuyuki Kawashima), The 49th Scientific Meeting of Korean Academy of Endodontics, 2016.11

# Removable Partial Prosthodontics

Professor - Noriyuki Wakabayashi

Associate professor - Kenji Fueki

Junior associate professor - Takeshi Ueno

Assistant professors

- Ichiro Minami, Juro Wadachi, Shusuke Inukai, Eiko Kohno, Junnichi Wada, Natsuko Murakami

Hospital staff

- Atsushi Takaichi, Natsuki Suzuki, Maho Shiozawa, Yuki Arai, Yuka Kajima, Chiaki Tsutsumi, Yasuha Nogawa

Graduate students

- Keigo Isoshima, Hideaki Inagawa, Yuka Inamochi, Keiichiro Uchikura, Hisami Okawara, Kittikundecha Nuttaphon, Hiroki Saito, Yuya Satokawa, Erina Seki, Kensuke Takakusaki, Tenhaku Tan, Kazutoshi Nakamura, Tomiharu Nagayama, Gen Nabeshima, Yoko Hayashi, Hironari Hayama, Masahiro Hirasawa, Toshiki Yamazaki, Chie Yoshihara, Chie Watanabe

## ( 1 ) Outline

The Department of Removable Partial Prosthodontics specializes in removable partial denture treatment, which is one of the major disciplines of clinical dentistry. The department has taken the baton from the First Department of Prosthodontics and the Department of Masticatory Function Rehabilitation.

Our objectives are to enhance the art and science of removable prosthodontics for the management of various oral conditions associated with tooth loss, from a single missing tooth to a single remaining tooth, in the maxillary and/or mandibular arch.

## ( 2 ) Research

1. Function and Physiology in Partial Denture Wearers
2. Optimization of Partial Denture Design based on Stress Analysis
3. Development and Applications of New Prosthodontic Biomaterials
4. Biology of Oral Tissues in Denture Wearers
5. Epidemiology and Education for Removable Partial Prosthodontics

## ( 3 ) Education

School of Dentistry

Year 1

Introduction to Dentistry

Year 3

Tooth Carving

Introduction to Clinical Dentistry

Observation and assistance at clinic term I and II

Basic Occlusal Reconstruction

Introduction to Research article writing and Patent acquisition

Year 4

Research Project

Removable Partial Prosthodontics

Advanced knowledge and skill with occlusion

Experience learning of dental practice

Years 5 and 6

Case study

Dental Practice and Clinical Practicum for Comprehensive Patient Care (Clinical Internship)

School of Oral Health Care Sciences, School of Oral Health Care Sciences

Year 2 Prosthodontics

Years 3 and 4 Practice for Dental Hygiene Care

School of Oral Health Care Sciences, Course for Oral Health Engineering

Year 2 Removable Prosthodontics Technology

#### ( 4 ) Lectures & Courses

The Department of Removable Partial Prosthodontics offers a variety of educational courses pertaining to the specialized clinical management of tooth loss, primarily for undergraduate students at the School of Dentistry. The courses include lectures, tutorials, hands-on sessions, clinical simulations, and clinical internship instructions.

The ability to perform clinical operations on patients with tooth loss, including the skills required for medical interviews, oral examinations, diagnosis, decision making, impression making, bite registration, denture design and technology, and denture delivery and maintenance, is essential for clinical dental professionals. The objectives of our courses are to provide learning and training in contemporary removable prosthodontics and enhance the knowledge and skills of students to help them develop and flourish in their future career as dental and oral health professionals.

#### ( 5 ) Clinical Services & Other Works

All faculty members of the Department of Removable Partial Prosthodontics are assigned to treat patients at the Prosthodontics department in the Dental Hospital of the Tokyo Medical and Dental University. While the rate of tooth retention has increased in comparison with previously reported rates, the number of patients in need of a removable partial denture has increased. Our specialists primarily work on advanced cases that are referred from other departments and outside the hospital. The departmental mission also includes the development and application of new prosthodontic materials, their clinical trial, and the spread of novel and inventive knowledge to the community.

#### ( 6 ) Clinical Performances

The department specializes in removable partial prosthodontics and aims to restore missing teeth and associated oral tissues; improve physiological functions such as occlusion, mastication, swallowing, and speech; maintain normal oral sensation; and restore the original appearance of individual patients.

Treatment modalities, materials, and denture design are all based on the case history and chief complaint of the patients. The ultimate goal is to improve the oral health-related quality of life of patients.

## (7) Publications

### [Original Articles]

1. Wada K, Ikeda E, Wada J, Inoue G, Miyasaka M, Miyashin M. Wear characteristics of trimethylolpropane trimethacrylate filler-containing resins for the full crown restoration of primary molars. *Dental Materials Journal*. 2016; 35(4); 585-593
2. Matsuura H, Yamamoto T, Wada J, Inukai S, Hideshima M. A detection method using phonetic segments for the influence of fatigue on speech 2016; J99-A(9); 351-360
3. Kajima Y, Takaichi A, Yasue T, Doi H, Takahashi H, Hanawa T, Wakabayashi N.. Evaluation of the shear bond strength of dental porcelain and the low magnetic susceptibility Zr-14Nb alloy. *Journal of the Mechanical Behavior of Biomedical Materials*. 2016.01; 53; 131-141
4. Yuk Kajima, AtsushiTakaichi, Takayuki Nakamoto, Takahiro Kimura, Yoshiaki Yogo, Maki Ashida, Hisashi Doi, Naoyuki Nomura, Hidekazu Takahashie, Takao Hanawa, Noriyuki Wakabayashi. Fatigue strength of Co-Cr-Mo alloy clasps prepared by selective laser melting. *Journal of the mechanical behavior of biomedical materials*. 2016.06; 59; 446-458
5. Tsunglin James Lee, Takeshi Ueno, Naoyuki Nomura, Noriyuki Wakabayashi, Takao Hanawa. Titanium-Zirconium Binary Alloy as Dental Implant Material: Analysis of the Influence of Compositional Change on Mechanical Properties and In Vitro Biologic Response. *Int J Oral Maxillofac Implants*. 2016.06; 31(3); 547-554
6. K Fueki, Y Igarashi, Y Maeda, K Baba, K Koyano, K Sasaki, Y Akagawa, T Kuboki, S Kasugai, N R Garrett. Effect of prosthetic restoration on masticatory function in patients with shortened dental arches: a multicentre study. *J Oral Rehabil*. 2016.07; 43(7); 534-542
7. Yuki Arai, Kazuhiro Aoki, Yasuhiro Shimizu, Yasuhiko Tabata, Takashi Ono, Ramachandran Murali, Setsuko Mise-Omata, Noriyuki Wakabayashi. Peptide-induced de novo bone formation after tooth extraction prevents alveolar bone loss in a murine tooth extraction model. *Eur. J. Pharmacol.*. 2016.07; 782; 89-97
8. Kohji Nagata, Sufyan K. Garoushi, Pekka K. Vallittu, Noriyuki Wakabayashi, Hidekazu Takahashi, Lippo V. J. Lassila. Fracture behavior of single-structure fiber-reinforced composite restorations *Acta Biomaterialia Odontologica Scandinavica*. 2016.07; 2(1); 118-124
9. Hiroshi Matsuura, Yuji Hojo, Koichi Sawasaki, Junichiro Wada, Shusuke Inukai, Masayuki Hideshima. An E-Learning System of Phrase Accent and Intonation for Learners of Japanese, Based on Phonetic Segment Labels and Fundamental Frequency 2016.08; 16; 29-39
10. H Kumagai, K Fueki, E Yoshida-Kohno, N Wakabayashi. Factors associated with mucosal pain in patients with partial removable dental prostheses. *J Oral Rehabil*. 2016.09; 43(9); 683-691
11. Takeshi Ueno, Takayuki Ikeda, Naoki Tsukimura, Manabu Ishijima, Hajime Minamikawa, Yoshihiko Sugita, Masahiro Yamada, Noriyuki Wakabayashi, Takahiro Ogawa. Novel antioxidant capability of titanium induced by UV light treatment. *Biomaterials*. 2016.11; 108; 177-186
12. Teisuke Akimoto, Takeshi Ueno, Yusuke Tsutsumi, Hisashi Doi, Takao Hanawa, Noriyuki Wakabayashi. Evaluation of corrosion resistance of implant-use Ti-Zr binary alloys with a range of compositions. *J. Biomed. Mater. Res. Part B Appl. Biomater.*. 2016.11;
13. Yasuha Ikawa, Ayako Mochizuki, Keisuke Katayama, Takafumi Kato, Minako Ikeda, Yuka Abe, Shiro Nakamura, Kiyomi Nakayama, Noriyuki Wakabayashi, Kazuyoshi Baba, Tomio Inoue. Effects of citalo-pram on jaw-closing muscle activity during sleep and wakefulness in mice. *Neurosci. Res.*. 2016.12; 113; 48-55

## [Books etc]

1. Standard Partial Denture. 2016.01 (ISBN : 978-4-7624-2656-8)
2. Wada J, Takaichi A, Wakabayashi N. Partial Denture Decision Making. Ishiyaku Publishing, 2016.02 (ISBN : 978-4-263-44460-3)
3. Masaru Yatabe, Kaori Maehata. Denture Q&A. 2016.09 (ISBN : 978-4-88510-358-2)

## [Misc]

1. Hisatomo Kondo, Shogo Ozawa, Takashi Sawase, Atsuro Yokoyama, Hideshi Sekine, Takeo Maida, Yasunori Ayukawa, Tamaki Nakano, Takayasu Kubo, Ryuji Hosokawa, Yoritoki Tomotake, Hirofumi Kido, Morio Ochi, Makoto Shiota, Masahiko Ozeki, Masahiro Nishimura, Yoshinobu Maeda, Hideki Aita, Katsushi Tamaki, Kenji Fueki, Hiroaki Tsukasaki, Takahiro Ono, Yasuyuki Matsushita, Yoshizo Matsuka, Hajime Minakuchi, Rika Kuwatsuru, Shuichiro Yamashita, Tomoaki Iizuka, Kazuyoshi Baba, Masanori Fujisawa, Kiyoshi Koyano, Hirofumi Yatani. Occlusal consideration for fixed implant prosthesis in mandibular posterior region Ann Jpn Prosthodont Soc. 2016.01; 8(1); 1-8
2. Katsushi Tamaki, Shoichi Ishigaki, Takumi Ogawa, Hitoshi Oguchi, Takafumi Kato, Takeshi Suganuma, Atsushi Shimada, Shinsuke Sadamori, Yoshihiro Tsukiyama, Youji Nishikawa, Shin-Ichi Masumi, Taihiko Yamaguchi, Hideki Aita, Takahiro Ono, Hisatomo Kondo, Hiroaki Tsukasaki, Kenji Fueki, Masanori Fujisawa, Yoshizo Matsuka, Kazuyoshi Baba, Kiyoshi Koyano. Japan Prosthodontic Society position paper on "occlusal discomfort syndrome". J Prosthodont Res. 2016.07; 60(3); 156-166
3. Natsuko Murakami, Junichiro Wada, Noriyuki Wakabayashi. Q11\_Why is tooth preparation necessary when making a partial denture? DHstyle Special issue Denture Q&A. 2016.09; 10(10); 34-35
4. Natsuko Murakami, Junichiro Wada, Noriyuki Wakabayashi. Q12\_What is a snap impression? DHstyle Special issue Denture Q&A. 2016.09; 10(10); 36-37
5. Natsuko Murakami, Junichiro Wada, Noriyuki Wakabayashi. Q13\_What is a study model? DHstyle Special issue Denture Q&A. 2016.09; 10(10); 38-39
6. Natsuko Murakami, Junichiro Wada, Noriyuki Wakabayashi. Q14\_What are the points of taking denture impression? DHstyle Special issue Denture Q&A. 2016.09; 10(10); 40-41
7. Natsuko Murakami, Junichiro Wada, Noriyuki Wakabayashi. Q15\_How to care for gag reflex patients DHstyle Special issue Denture Q&A. 2016.09; 10(10); 42-43
8. Natsuko Murakami, Junichiro Wada, Noriyuki Wakabayashi. Q16\_How to pour dental plaster models? DHstyle Special issue Denture Q&A. 2016.09; 10(10); 44-45
9. Junichiro Wada, Natsuko Murakami, Noriyuki Wakabayashi. Q17\_What should we check when bite taking? 2016.09; 10(10); 46-47
10. Junichiro Wada, Natsuko Murakami, Noriyuki Wakabayashi. Q18\_What should we check when we try-in the RPD? 2016.09; 10(10); 48-49
11. Junichiro Wada, Natsuko Murakami, Noriyuki Wakabayashi. Q19\_What should we do at the day of RPD placement? 2016.09; 10(10); 50-51
12. Fueki K. Non-metal clasp dentures: More evidence is needed for optimal clinical application. J Prosthodont Res. 2016.10; 60(4); 227-228
13. Akihito Uezato, Mitsuhiro Enomoto, Meiyo Tamaoka, Mizue Hobo, Shusuke Inukai, Masayuki Hideshima, Yasunari Miyazaki, Toru Nishikawa and Kazuyoshi Yagishita. Shorter sleep onset latency in patients undergoing hyperbaric oxygen treatment Psychiatry and Clinical Neurosciences. 2016.12; 71(1); 73-74

**[Conference Activities & Talks]**

1. Yukihiro Tamura, Setsuko Mise, Yasutaka Sugamori, Md. Zahirul Haq Bhuyan, Mariko Takahashi, Tomoki Uehara, Yuki Arai, Michiyo Miyashin, Noriyuki Wakabayashi, Kazuhiro Aoki. A pharmacological role of metallothionein in zinc-treated cartilage-progenitor cells. APFP 2016(The 13th Asia Pacific Federation of Pharmacologists Meeting) 2016.02.01 The Berkeley Hotel Pratunam,Bangkok (Thailand)
2. Masuru Yatabe. Non-metal clasp denture 2016. 2016.02.07
3. Wakabayashi N. Future Perspectives of Dental Education and Research in Globalized Society. Programme for visit from Tokyo Medical and Dental University (TMDU) 16-18 March 2016 2016.03.15 Gothenburg, Sweden
4. Yogo Y,Kajima Y,Takaichi A,Nakamoto T,Doi H,Takahashi H,Nomura N,Wakabayashi N. The effect of heat treatment on microstructure and mechanical properties of Co-Cr-Mo alloys fabricated by selective laser melting process. The 67th General Session of the Japanese Society for Dental Materials and Devices 2016.04.17 Fukuoka
5. Mochizuki A, Ikawa Y, Kato T, Katayama K, Nakamura S, Nakayama K, Baba K, Inoue T. The effects of Citalopram on the modulation of masseter muscle activity during non-REM sleep . 57th Scientific Meeting of the Japanese Society of Stomatognathic Function 2016.04.23 Saitama
6. Yoshihara C, Ueno T, Chen P, Tsutsumi Y, Hanawa T, Wakabayashi N. Inverse behavior between osteoblasts and fibroblasts on carbon-coated titanium surfaces. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
7. Akimoto T, Ueno T, Tsutsumi Y, Doi H, Hanawa T, Wakabayashi N. The Corrosion Resistance of Ti-Zr Binary Alloy with Compositional Change. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
8. Ueno T, Wakabayashi N, Ogawa T. . An anti-oxidant property of titanium induced by ultraviolet photoactivation. . The 10th World Biomaterials Congress (WBC) 2016.05.22 Montreal, Canada
9. Masaru Yatabe. Non-metal clasp denture: from designing to maintenance. 2016.05.22
10. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Chisato Ida, Yuko Mitsuma, Shota Hayashi, Akihito Uesato, Toshihide Fujie, Meiyo Tamaoka, Yasunari Miyazaki, Masahiko Shimada, Noriyuki Wakabayashi . Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy and compliance in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial.. Japanese Society of Sleep Research the 41th Annual Meeting 2016.07.07 Tokyo
11. Current status of CPAP therapy for OSAS in late stage elderly at our hospital. 2016.07.07
12. Practice and practical experience of OA therapy for dental clinic for sleep disorders. 2016.07.07
13. Wada J,Hideshima M, Inukai S, Matsuura H, Wakabayashi N. Influence of shape of dental arch and palate on the accuracy of speech production disturbed by major connector of maxillary removable partial denture. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07.09 Kanazawa
14. In vitro analysis of two body wear of CAD/CAM machinable ceramics . 2016.07.09
15. Kumagai H, Fueki K, Kohno E, Wakabayashi N. A structural equation model relating mucosal pain and subjective masticatory function in patients with removable partial dentures. . The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07.09 Kanazawa
16. Fueki K, Kohno E, Yatabe M, Wakabayashi N. Efficacy of Non-metal Clasp Dentures with Metal Framework: A Randomized Cross-over Trial. 125th JPS general meeting 2016.07.10 Kanazawa
17. Takaichi A,Kajima Y,Yogo Y, Takahashi H, Wakabayashi N. The heat treatment of Co-Cr-Mo alloys fabricated by selective laser melting process. The 125th annual meeting of the japan prosthodontic society 2016.07.10 Kanazawa
18. Watanabe C, Wada J, Mizutani K, Watanabe H, Wakabayashi N. The effect of removable partial denture placement on periodontal structures of abutment teeth in patients of periodontitis: A digital subtraction analysis. The 125th Scientific Meeting of Japan Prosthodontic Society 2016.07.10 Kanazawa

19. C Tsutsumi, K Takakusaki, M Hirasawa, N Wakabayashi. Reduction of Candida biofilm adhesion by incorporation of prereacted glass ionomer filler in denture base resin. 2016.07.10
20. Kajima Y, Takaichi A, Wakabayashi N. The change of magnetic susceptibility and density in dental alloy affect the range of artifact. The 125th annual meeting of the Japan prosthodontic society 2016.07.10 Kanazawa
21. Wakabayashi N.. Education and Research in Tokyo Medical and Dental University. 2016.08.02 Boston University School of Dental Medicine, 7th Floor, Room G-718
22. Ikawa Y, Mochizuki A, Kato T, Katayama K, Abe Y, Nakamura S, Nakayama K, Baba K, Wakabayashi N, Inoue T. The effects of Citalopram on the modulation of masseter muscle activity during non-REM sleep. The 58th Annual Meeting of Japanese Association for Oral Biology 2016.08.26 Sapporo
23. K.takakusaki, C.tsutsumi, M.hirasawa, K.takakuda, K.fueki, N.wakabayashi. Effect of S-PRG filler content on C.albicans adherence and mechanical properties of tissue conditioner. Japanese society for bacteriology 2016.10.06 Tokyo
24. A.Wirianski, R.Harakawa, CC.Peck, GM.Murray, I.Minami. Jaw Muscle Electromyographic Activity During Chewing is Altered by Isometric Resistance Jaw Exercises.. 23rd General Meeting of the Japanese Association for Dental Science. 2016.10.22 Hakata, Fukuoka.
25. Yuki Arai, Kazuhiro Aoki, Noriyuki Wakabayashi. Peptide-induced de novo bone formation after tooth extraction prevents alveolar bone loss. The 5th Tri-University Consortium on Oral Science and Education 2016.10.27 Peking University
26. Ogawa M, Koyanagi T, Takeuchi Y, Katagiri S, Ikawa T, Takeuchi S, Sekiuchi T, Arai Y, Kazama R, Wakabayashi N, Izumi Y. Evaluation of palatal mucosal thickness measurements using CBCT. 145th Meeting of the Japanese Society of Conservative Dentistry 2016.10.28 Matsumoto
27. Ogawa M, Koyanagi T, Takeuchi T, Katagiri S, Ikawa T, Takeuchi S, Sekiuchi T, Arai Y, Kazama R, Wakabayashi N, Izumi Y. Evaluation of palatal mucosal thickness measurements using CBCT. 145th Meeting of the Japanese Society of Conservative Dentistry 2016.10.28 Matsumoto
28. Kajima Y, Takaichi A, Kittikundecha N, Nakamoto T, Doi H, Takahashi H, Nomura N, Hanawa T, Wakabayashi N. Effects of heat treatment on the microstructure and mechanical property of selective laser melted Co–Cr–Mo alloys. . International Dental Materials Congress 2016 (IDMC 2016) 2016.11.05 Bali (Indonesia)
29. Takaichi A, Kajima Y, Kittikundecha N, Nakamoto T, Nomura N, Takahashi H, Hanawa T, and Wakabayashi N . Effects of support structure on the fatigue strength of selective laser melted Co-Cr-Mo clasps. International Dental Materials Congress 2016 (IDMC2016) 2016.11.06 Bali, Indonesia
30. Inagawa H, Suzuki N, Hachikawa M, Wakabayashi N. Conversion to bone Young's modulus from CT values: Validity assessment in mouse maxilla.. Scientific Meeting of the Kanetsu Branch of Japan Prosthodontic Society Niigata, Japan 2016.11.06 Niigata
31. Yuka Inamochi, Kenji Fueki, Masato Taira, Noriyuki Wakabayashi . Adaptive change in chewing-related brain activity while wearing a palatal plate: An fMRI study. The 81th Annual Meeting of The Stomatological Society, Japan 2016.11.26 Tokyo Medical and Dental University
32. Kenji Fueki. Clinical evidence for non-metal clasp denture. Prosthodont'16 2016.12.10 Tokyo

#### [Awards & Honors]

1. DENTSPLY Merit Award, Japan Prosthodontic Society , 2016.07
2. International Poster Award Presentation, The Japanese Association for Dental Science., 2016.10



## Oral Implantology and Regenerative Dental Medicine

Professor and Chair        Shohei KASUGAI  
Associate Professor       Makoto SHIOTA  
Assistant Professor(Lecturer) Noriko TACHIKAWA, Shinji KURODA  
Assistant Professor       Hidemi NAKATA

### Medical Staffs:

Kazuhiro KON, Masaki FUJII, Takayuki MIYAHARA, Tokuo AKINO,  
Masahiro SHIMOGISHI, Masahiro ISHIWATA, Chiharu IMAKITA, Maiko Yamamoto

### Graduate Students:

Yu YAMASHITA, Taiji HAMADA, Masaki SHIBASAKI, Emi OKADA, DING Lin, NGUYEN Vo Ngoc Trang, BOOSAN

### Graduate Research Students:

Shuichi KOYAMA, Tadamasa YOSHIDA, Toshimitsu SHIGEMATSU, Toshihiko MORIKAWA,  
Kazuhiko INOUE, Takeshi WATANABE, Arihiro IWATA, Narumi SATO,  
Gou INOUE, Seiji OHARA, Junya HAMAGUCHI,  
Dotetsu TAKONAI, Yoshitaka TANABE, Maho AKATSUKA,  
Munemitsu MIYASAKA, Akihiro Takahashi, Kento TAIRA, You-kyoung KIM, Mizuki SATO, Yoko Oba, Chang Kuangs

### Resident:

Kaho TAMURA

### Registered Residents:

Toshifumi KOJIMA, Kensuke FUKUTOMI, Reina SHIBUYA, Aoi SAKUYAMA, Kazuhisa TSURUMI, Ai KOBAYASHI

Clinical Professor (Faculty of Dentistry)       Hideaki KATSUYAMA  
Clinical Visiting Associate Professor       Koji HAGINO  
Clinical Visiting Associate Professor       Tsuneji OKADA

### Adjunct Assistant Professor (Faculty of Dentistry):

Maho KON, Yuki DATE, Akiko FURUICHI, Hiroshi KOBAYASHI,  
Daisuke SATO, Shang GAO

### Adjunct Assistant Professor (Dental Hospital):

Hisatomo KONDO, Hidemichi KIHARA, Toru KANAI

## ( 1 ) Research

Materials and structures of dental implant prostheses  
Implant design and surface modification of dental implant  
Dental implant and its surrounding tissues  
Regeneration of soft tissues  
Regeneration of bone



Adipose-derived stem cells for osteogenesis

## ( 2 ) Lectures & Courses

Currently, oral rehabilitation with dental implant is very effective and predictable. It is absolutely important for the dental student to understand dental implant treatment compared to other modalities. Nine hours lectures for the 5th year dental students are the introduction part. Each of these students has a chance to see patient examination process and several steps of treatment planning for half a day in the dental implant clinic. Furthermore, each of the 6th year students have a chance to see surgical procedures, prosthodontic treatments and maintenance procedures. In the residential program, we accepted 9 dentists and teach them more advanced contents of dental implant treatment.

In the doctoral course of Implantology Biomaterial sciences, structural engineering, anatomical structures, diagnosis and technical innovations are overviewed. In the doctoral course of Regenerative Dental Medicine, tissue engineering concept, regeneration of soft tissue and bone and recent technological advancements in these field are overviewed.

## ( 3 ) Clinical Services & Other Works

In Dental Implant Clinic in the dental hospital, we treat partially or fully edentulous patients with dental implants. If soft tissue management and/or bone augmentation procedures are required, we also do these surgeries. Number of patients in Dental Implant Clinic is increasing every year and approximately 120 patients per day are treated, which is extremely over our capacities. Approximately 2,000 implants were installed in 2012. Patients with some clinical problems, who are treated in other clinics, are increasing and this is a great concern.

## ( 4 ) Publications

### [Original Articles]

1. You-kyoung KIM, Hidemi NAKATA, Maiko YAMAMOTO, Munemitsu MIYASAKA, Shohei KASUGAI, \*Shinji KURODA. Osteogenic Potential of Mouse Periosteum-derived Cell Sorted for CD90 in vitro and in vivo STEM CELLS Translational Medicine. 2016; 5; 1-8
2. Hidemi Nakata, Maiko Yamamoto, Emi Okada, Tomoko Nagayama, Shohei Kasugai, \*Shinji Kuroda. Osteogenic potential of adipose-derived macrospheroids cocultured with CD11b+ monocytes International Journal of Oral and Maxillofacial Implant. 2016;
3. Hidemi Nakata, \*Shinji Kuroda, Noriko Tachikawa, Emi Okada, Maho Akatsuka, Shohei Kasugai, Hisatomo Kondo. Histological and micro-computed tomographic observations after maxillary sinus augmentation with porous hydroxyapatite alloplasts: a clinical case series SpringerPlus. 2016;
4. Madi M, Zakaria O, Ichinose S, Kasugai S. Effect of induced periimplantitis on dental implants with and without ultrathin hydroxyapatite coating. Implant Dentistry. 2016; 25(1); 39-46
5. Hidemi Nakata, Shinji Kuroda, Noriko Tachikawa, Munemitsu Miyasaka, Kenya Yoneda, Hisatomo Kondo, Shohei Kasugai. Clinical outcomes of aesthetic and functional rehabilitation with dental implants in patients with alveolar cleft Journal of Tissue Science & Engineering. 2016; 6(160);
6. Yu Yamashita, Kang Chen, Shinji Kuroda, Shohei Kasugai. Stability of Platelet-rich Fibrin in vivo: Histological Study in Rats Journal of Oral Tissue Engineering. 2016; 14(2); 83-90
7. Sato D, Kanazawa M, Kim YK, Yokoyama S, Omura Y, Ozeki M, Minakuchi S, Kasugai S, Baba K. Immediate loading of two freestanding implants placed by computer-guided flapless surgery supporting a mandibular overdenture with magnetic attachments. J Prosthodont Res. 2016.01; 60(1); 54-62
8. Trang N Nguyen Vo, Jia Hao, Josh Chou, Masamitsu Oshima, Kazuhiro Aoki, Shinji Kuroda, Boosana Kaboosaya, Shohei Kasugai. Ligature induced peri-implantitis: tissue destruction and inflammatory progression in a murine model. Clin Oral Implants Res. 2016.01;

9. Kei Fuchigami, Motohiro Munakata, Takaaki Kitazume, Noriko Tachikawa, Shohei Kasugai, Shinji Kuroda. A diversity of peri-implant mucosal thickness by site Clinical Oral Implants Research. 2016.02;
10. Omura Y, Kanazawa M, Sato D, Kasugai S, Minakuchi S. Comparison of patient-reported outcomes between immediately and conventionally loaded mandibular two-implant overdentures: A preliminary study. J Prosthodont Res. 2016.07; 60(3); 185-192
11. Sato M, Chen P, Tsutsumi Y, Shiota M, Hanawa T, Kasugai S . Effect of strontium ions on calcification of preosteoblasts cultured on porous calcium- and phosphate-containing titanium oxide layers formed by micro-arc oxidation Dent. Mater. J.. 2016.07; 35(4); 627-634
12. Kazuhiro Kon, Makoto Shiota, Maho Ozeki, Shohei Kasugai. The effect of graft bone particle size on bone augmentation in a rabbit cranial vertical augmentation model: a microcomputed tomography study. Int J Oral Maxillofac Implants. 29(2); 402-406

#### [Conference Activities & Talks]

1. Emi Okada, Hidemi Nakata, Shohei Kasugai, Shinji Kuroda. Short-term exposure of bisphosphonates may enhance osteoblast differentiation through osteoclasts. The Annual Meeting of the Academy of Osseointegration 2016.02.18 San Diego, CA, USA
2. M. Kanazawa, M. Iwaki, D. Sato, Y. Omura, A. Miyayasu, S. Kasugai, S. Minakuchi.. Immediate Loading of two-implants mandibular overdentures: 4-years prospective study.. 94th General Session & Exhibition of the IADR 2016.06 Seoul, Republic of Korea
3. Asami Mari,Miyayasu Anna,Kanazawa Manabu,Takeshita Shin,Tanoue Mariko,Sato Daisuke,Oda Ken,Shimizu Haruki,Morisawa Masayuki,Kasugai Shohei,Minakuchi Shunsuke. Cost-effectiveness analysis of mandibular single-implant overdentures and conventional complete dentures Study protocol for a randomized controlled clinical trial . The 125th Scientific Meeting of Japan Prosthodontic Society 2016.07.09 Kanazawa
4. Shimada Ryo, Kanazawa Manabu, Miyayasu Annna, Tanoue Mariko, Sato Daisuke, Kusumoto Yuriko, Abe Yuka, Yokowama Sawako, Baba Kazemi, Minakuchi Syunnsuke. Prospective clinical trial of IARPD with short implants -research protocol- . 2016.11.06 gihu

## Plastic and Reconstructive Surgery

Professor: Mutsumi Okazaki

Junior Associate Professor: Hiroki Mori

Assistant Professor (Hospital Staff): Noriko Uemura

Project Assistant Professor (Hospital Staff) : Kentaro Tanaka

Graduate Student: Aki Takada, Takuya Higashino, Tsutomu Homma, Satoshi Usami,  
Mayuko Hamanaga, Nobuko Suesada

### ( 1 ) Research

Basic research

1. A mechanism and prophylaxis of the post-inflammatory pigmentation
2. A scarless wound healing
3. The blood circulation study of the flap using indocyanine green
4. Donor specificity on various flaps or full thickness skin

Clinical research

1. Sensory recovery and contour prediction in the breast reconstruction
2. The algorithmic development and the evaluation of various reconstructions in the skull base reconstruction
3. The development of reconstructive method after an oral cavity / pharyngeal cancer resection - Aiming at the functional preservation
4. The classification of the symptom and static and dynamic reconstruction of the facial paralysis
5. A classification and the algorithmic development in blepharoptosis surgery
6. The objective evaluation for the ischemic limb and therapeutic strategy utilizing wound healing mechanism
7. The prospective studies about the color reproducibility of the medical tattoo in the nipple areola reconstruction

### ( 2 ) Education

Plastic surgery is a specialized branch of surgery concerned with the repair of deformities and the correction of functional deficits. The specialty of plastic surgery covers a wide range of procedures, and unlike other medical specialties which concentrate on one particular area of the body, plastic surgeons are involved in the reconstruction and remodeling of nearly all external body structures.

### ( 3 ) Clinical Performances

We cover the whole field of plastic surgery. In particular, we deal with the following field; congenital anomaly (cleft lip and palate, microtia blepharoptosis or polydactyly etc), LASERs, cutaneous malignant tumor, skin ulcer, breast reconstruction, head and neck reconstruction, facial palsy, axillary osmidrosis.

**(4) Publications****[Original Articles]**

1. Mori H, Uemura N, Okazaki M, Nakagawa T, Sato T. Nipple malposition after nipple-sparing mastectomy and expander-implant reconstruction *Breast Cancer*. 2016; 23; 740-744
2. Uemura N, Okazaki M, Mori H. Anatomical and histological study to determine the border of sole skin *Surgical and Radiologic Anatomy*. 2016; 38(7); 767-773
3. Tanaka K, Okazaki M, Homma T, Yano T, Mori H. Bilateral inferior alveolar nerve reconstruction with a vascularized sural nerve graft included in a free fibular osteocutaneous flap after segmental mandibulectomy *Head & Neck*. 2016; 38(5); E111-E114
4. Usami S, Yamamoto M, Okazaki M. Intraoperative ultrasound-assisted repair of zone III flexor tendon rupture with a minimal incision *The Journal of Hand Surgery*. 2016; 41(9); 1003-1004
5. Usami S, Kodaira S, Okazaki M. Primary On-top Plasty for Treatment of Short-type Postaxial Polydactyly of the Foot *Annals of Plastic Surgery*. 2016; 77(2); 223-225
6. Usami S, Ohkubo A, Okazaki M. Vascularized Nerve Bypass Graft: A Case Report of an Additional Treatment for Poor Sensory Recovery PRS *Global Open*. 2016; 4(4); e686-e689
7. Yano T, Okazaki M, Tanaka K, Iida H. The Flap Sandwich Technique for a Safe and Aesthetic Skull Base Reconstruction *Annals of Plastic Surgery*. 2016; 76(2); 193-197
8. Yano T, Okazaki M, Tanaka K, Tsunoda A, Aoyagi M, Kishimoto S. Use of Intraoperative Fluorescent Indocyanine Green Angiography for Real-Time Vascular Evaluation of Pericranial Flaps *Annals of Plastic Surgery*. 2016; 76(2); 198-204
9. Yano T, Okazaki M, Tanaka K, Tsunoda A, Aoyagi M, Kishimoto S. Feasibility and Advantage of a Muscle-Sparing Laterally Based Pericranial Flap *The Journal of Craniofacial Surgery*. 2016; 27(3); 552-557
10. Yano T, Suesada N, Usami S. Esthetic Craniofacial Bony and Skull Base Reconstruction Using Flap Wrapping Technique *The Journal of Craniofacial Surgery*. 2016; 27(5); 1234-1238
11. Sakisaka M, Kurita M, Okazaki M, Kagaya Y, Takushima A, Harii K. Drug-Induced Atrial Fibrillation Aggravates the Results of Flap Surgery in a Rat Model *Annals of Plastic Surgery*. 2016; 76; 244-248
12. Namiki T, Miura K, Ueno M, Tanaka K, Yokozeki H. Case of basal cell carcinoma with myoepithelial differentiation: Its characteristic clinical and histopathological features *The Journal of Dermatology*. 2016; 43(9); 1109-1110

**[Conference Activities & Talks]**

1. Mori H, Uemura N, Okazaki M. Orbital myectomy using brow lift approach in blepharospasm. The 13th Japan-Korea Congress of Plastic and Reconstructive Surgery 2016.05.17 Kanazawa
2. Usami S, Kawahara S, Shibahara H, Abe K, Yamaguchi T, Minamikawa Y. Surface replacement arthroplasty using Self Locking Finger Joint implant for the painful proximal interphalangeal joint osteoarthritis. The 13th Japan-Korea Congress of Plastic and Reconstructive Surgery 2016.05.17 Kanazawa
3. Homma T, Okazaki M, Tanaka K, Uemura N. Simultaneous surgical treatment for smile dysfunction and lagophthalmos involving a dual latissimus dorsi neuromuscular flap transfer combined with fascia lata grafting. The 3rd meeting of Asian Pacific Federation of Societies 2016.06.04 Beijing
4. Tanaka K, Suesada N, Yano T, Okazaki M. Indication of Reconstructive Surgery for Middle Skull Base Defects. The 7th International Congress of the World Federation of Skull Base Societies 2016.06.15 Osaka
5. Imai K, Tanaka K, Suesada N, Homma T, Okazaki M, Kishimoto S. One-stage reconstruction of the extensive defects involving middle skull base and orbital floor with the combination of temporalis muscle flap and free ALT flap. The 7th International Congress of the World Federation of Skull Base Societies 2016.06.17 Osaka

6. Mori H, Mihara R, Okazaki M. Nipple reconstruction with dorsal skin provides better projection than reconstruction with abdominal or breast skin with cartilage grafting. Plastic Surgery The Meeting 2016 2016.09.24 Los Angeles
7. Tanaka K, Igari K, Kishino M, Usami S, Homma T, Toyofuku T, Inoue Y, Okazaki M. The possibility of free tissue transfer to be the nutrient flap for critical ischemic foot based on the postoperative angiography findings. World Union of Wound Healing Societies 2016.09.25 Florence
8. Haraguchi M, Tanaka K, Sumita YI, Okazaki M, Taniguchi H. Prosthetic rehabilitation for a patient with extensive vascular malformation in the head and neck region. The 63rd Annual Meeting of the American Academy of Maxillofacial Prosthetics 2016.10.01 San Diego

## Head and Neck Surgery

Professor: Takahiro Asagkage  
Project professor: Seiji Kishimoto  
Junior associate professor: Takuro Sumi, Yosuke Ariizumi  
Assistant professor: Yusuke Kiyokawa, Fuminori Nomura  
Senior Resident: Fuminori Nomura, Akihisa Tasaki, Ryuhei Okada  
Student: Hirofumi Fukushima, Takao Tokumaru, Masaharu Kishikawa

### ( 1 ) Outline

Our department is responsible for clinical management, education and research in the field of head and neck surgery. Clinically, the Department of Head and Neck Surgery manages the tumor of extensive area of head and neck, except brain, eye and vertebra. Surgical and medical treatment of the head and neck tumors are mainly employed in our department.

### ( 2 ) Research

Surgical approaches to the skull base and deep area of the face.  
Surgical anatomy of the skull base.  
Establishment of the standard neck dissection.  
Treatment of pediatric head and neck tumors.  
Chemoradiotherapy for head and neck cancers.  
Clinical application of navigation system and 3D entity model surgery for skull base surgery.  
Diagnosis and treatment for superficial squamous cell carcinoma of head and neck region.  
Human papilloma virus infection and head and neck cancer.  
Polymorphisms in alcohol metabolism genes and Head and Neck Cancers.

### ( 3 ) Education

Education: Undergraduate Course

In the classes at the 3th grade of medical school, head and neck oncology are systematically lectured. Clinical practice is experienced at the 4th to 6th grade in the out-patient clinic, the ward, and operating theater.

Education :Graduate Course

Education and researches at the graduate school are focused on (1)surgery of the head and neck tumor, (2)clinical management of the patients with head and neck tumor, and (3)clinical anatomy of head and neck region.

#### (4) Publications

##### [Original Articles]

1. Hirofumi Fukushima, Takeharu Kanazawa, Kazuyoshi Kawabata, et al. Indwelling Voice Prosthesis insertion after Total Pharyngolaryngectomy with Free Jejunal Reconstruction. *Laryngoscope Investigative Otolaryngology*. 2016;
2. Kondo T, Sato Y, Tanaka H, Fukushima H, et al. Two Cases of Ectopic Hamartomatous Thymoma Masquerading as Sarcoma. *Case Rep Otolaryngol.* 2016;
3. K Ichikura, A Yamashita, S Kishimoto, et al. Persistence of psychological distress and correlated factors among patients with head and neck cancer Palliative and Supportive Care. 2016.02; 14(1); 42-51
4. Ichikura Kanako, Yamashita Aya, Sugimoto Taro, Kishimoto Seiji, Matsushima Eisuke. Persistence of psychological distress and correlated factors among patients with head and neck cancer. *Palliat Support Care*. 2016.02; 14(1); 42-51
5. Nakano K, Sato Y, Toshiyasu T, Fukushima H, et al. Predictive factors of head and neck squamous cell carcinoma patient tolerance to high-dose cisplatin in concurrent chemoradiotherapy. *Mol Clin Oncol*. 2016.02; 4(2); 303-309
6. T Yano, M Okazaki, K Tanaka, A Tsunoda, M Aoyagi, S Kishimoto. Use of Intraoperative Fluorescent Indocyanine Green Angiography for Real-Time Vascular Evaluation of Pericranial Flaps *Annals of plastic surgery*. 2016.02; 76(2); 198-204
7. T Yano, M Okazaki, K Tanaka, S Kishimoto, et al. Feasibility and Advantage of a Muscle-Sparing Laterally Based Pericranial Flap. *Journal of Craniofacial Surgery*. 2016.05; 27(3); 552-557
8. Nakano K, Sato Y, Sasaki T, Shimbashi W, Fukushima H, et al. Combination chemotherapy of carboplatin and paclitaxel for advanced/metastatic salivary gland carcinoma patients: differences in responses by different pathological diagnoses *Acta Otolaryngol.* 2016.09; 136(9); 948-951
9. K. Nakagawa, R Yoshimura, S Kishimoto, etc. Tongue reconstruction with minimal donor site morbidity using a deep inferior epigastric perforator (DIEP) free flap in a 6-year-old girl *Microsurgery*. 33(6); 487-490

##### [Conference Activities & Talks]

1. M Kishimoto, T Nomura, S Kishimoto, et al. A case report of advanced infantile fibromatosis involving masseter muscle and mandible. 16th Japan-Korea joint meeting of ORL-HNS, 2016.03.29 東京
2. Sugimoto T. ELPS for the patients with laryngo-pharyngeal cancer. A Collaborative Laboratory Investigation by Stanford Head and Neck Surgery and Intuitive Surgical, Inc.. Transoral Endoscopic Head & Neck Surgery for the Hypopharynx and Cervical Esophagus, 2016.05.24 California, USA
3. Sugimoto T. How I do it? ELPS using a small diameter upper GI endoscope. 2016 International Symposium of Transoral Head & Neck Surgery 2016.05.28 Seoul, Korea
4. Sugimoto T. How to Maintain Quality and Standards of Transoral Head and Neck Surgery Oncological Outcomes in transoral head and neck surgery including ELPS. 2016 International Symposium of Transoral Head & Neck Surgery 2016.05.28 Seoul, Korea
5. Okada R, Sugimoto T, Sumi, et al. The successful performance of two transoral partial hypopharyngectomy operations after chemotherapy for local metachronous recurrence following chemoradiotherapy for advanced hypopharyngeal cancer: A case report. ANHS 9th international conference on head and neck cancer. 2016.06 washington
6. Asakage T. Chairman. Breakfast Seminar 2-3 Ultimate Management of Orbital and Frontal Sinus Tumor.. 7th International congress of the world federation of skull base societies 2016.06.14 Osaka
7. Asakage T. Surgical treatment of frontal sinus carcinoma. Breakfast Seminar 2-3 Ultimate Management of Orbital and Frontal Sinus Tumor. 7th International congress of the world federation of skull base societies. 2016.06.15 Osaka

8. K Imai, K Tanaka, N Suesada, S Kishimoto, et al. One-stage reconstruction of the extensive defects involving middle skull base and orbital floor with the combination of temporalis muscle flap and free ALT flap.. 7th International congress of the world federation of skull base societies 2016.06.15 osaka
9. Y Kawano, M Aoyagi, T Asakage, S Kishimoto. Multidisciplinary surgical approach for advanced juvenile nasopharyngeal angiofibroma with skull base and cavernous sinus extension. . 7th International Congress of the World Federation of Skull Base Societies 2016.06.15 Osaka
10. T Sugawara, M Aoyagi, S Kishimoto, et al. Extended orbital exenteration for sinonasal malignancy w/ orbital apex extension. 7th International Congress of the World Federation of Skull Base Societies 2016.06.15 Osaka
11. S Kishimoto, A Tsunoda, et al. Craniofacial surgery for advanced juvenile nasopharyngeal angiofibromas with intracranial extension. 7th International Congress of the World Federation of Skull Base Societies 2016.06.15 Osaka
12. S Kishimoto, A Tsunoda, et al. Surgical treatment of pediatric sarcomas in the skull base. . 7th International Congress of the World Federation of Skull Base Societies 2016.06.15 Osaka
13. Ryuhei Okada, Taro Sugimoto, Takuro Sumi, Taro Fujikawa, Yusuke Kiyokawa, Fuminori Nomura, Akihisa Tasaki, Tomoaki Asamori, Seiji Kishimoto, Takahiro Asakage. Chemotherapy and followed endoscopic laryngo-pharyngeal surgery (ELPS) is useful for recurrence of pharyngeal carcinoma: a case report. AHNS 9TH International Conference on Head and Neck Cancer 2016.07.16 Washington
14. S Kishimoto. Surgical treatment for pediatric head and neck sarcomas with skull base invasion . 2016 Annual Meeting of Taiwan Head and Neck Society in conjunction with International Head and Neck Cancer Conference & Cross-Straits HNS Forum( 2016.10.15 Taipei
15. S Kishimoto. Lecture "Craniofacial approach to the skull base", . Morning Lecture in Tainan Cheng Gung University 2016.10.17 Tainan
16. Asakage T. Year in review from Japan. International session 16 head and neck cancer . 54th Japan Society Clinical Oncology annual meeting 2016.10.20 Yokohama
17. R Okada, T Sugimoto, T Sumi, T Fujikawa, S Kishimoto, et al. The successful performance of two transoral partial hypopharyngectomy operations after chemotherapy for local metachronous recurrence following chemoradiotherapy for advanced hypopharyngeal cancer A case report.. AHNS 9th International Conference on Head and Neck Cancer Seattle USA



## Radiation Therapeutics and Oncology

**Professor** Ryoichi Yoshimura

**Lecturers** Kazuma Toda

**Research Associates** Keiko Nakagawa, Mio Kojima

**Hospital Staff members** Hirohumi Kuwabara(∼Mar), Takuya Nagano(Apr∼)

**Resident** Takuya Nagano(∼Mar)

### ( 1 ) Outline

At the Department of Radiation Therapeutics and Oncology, clinical services, research, and education related to radiotherapy for all cancers are undertaken.

### ( 2 ) Research

Mainly clinical research related to radiotherapy is performed.

### ( 3 ) Education

Lectures are given to medical students or graduate students, and clinical clerkship is organized. After the students enter our department, comprehensive training is provided at both our department and the Department of Diagnostic Radiology and Nuclear Medicine for 3 years, since the certified radiologist exam is common.

Our department holds a radiation oncology seminar for students and residents with the Department of Radiation Oncology of Juntendo University and Showa University.

Lectures for medical students or graduate students, and clinical clerkship are performed.

### ( 4 ) Lectures & Courses

Our department teaches students and residents about cancer therapy from the radiation oncologist's perspective.

Every student/resident of this department aims to be a certified radiation oncologist.

### ( 5 ) Clinical Services & Other Works

All the staff members are engaged in performing external beam radiation therapy or high-dose-rate or low-dose-rate brachytherapy in the hospital.

A total of 596 patients, including 132 head and neck cancer patients, 126 urological cancer patients, 90 breast cancer patients, 64 lung cancer patients, and 53 esophageal cancer patients, were treated by external beam radiotherapy at our hospital in 2015. Moreover, high-dose-rate brachytherapy was performed in 51 patients with uterine cancer, and low-dose-rate brachytherapy in 58 patients with oral cancer, and in 19 patients with prostate cancer.

**( 6 ) Clinical Performances**

Our department specializes in low-dose-rate brachytherapy for oral cancer patients.

**( 7 ) Publications****[Original Articles]**

1. Taito Asahina, Atsushi Kaida, Tatsuaki Goto, Ryo-Ichi Yoshimura, Keisuke Sasai, Masahiko Miura. Temporo-spatial cell-cycle kinetics in HeLa cells irradiated by Ir-192 high dose-rate remote afterloading system (HDR-RALS). *Radiat Oncol.* 2016.07; 11; 99
2. Murakami N, Kato S, Nakano T, Yamanaka T, Sakurai H, Yoshimura R, Hiratsuka J, Kuroda Y, Yoshioka K, Itami J. A phase I/II clinical trial for the hybrid of intracavitary and interstitial brachytherapy for locally advanced cervical cancer. *Bio Med Central Cancer.* 2016.08; 16(640);

**[Conference Activities & Talks]**

1. Ryoichi Yoshimura. Multi-institutional joint research of brachytherapy Head and Neck/Breast. Japanese Group of Brachytherapy/Japanese Society for Therapeutic Radiology and Oncology 2016.05.28 Osaka
2. Hirofumi Kuwabara, Akira Toriihara, Keiko Nakagawa, Kazuma Toda, Ukihide Tateishi, Ryoichi Yoshimura. Utility of metabolic tumor burden calculated from dual-time-point FDG positron emission tomography/computed tomography to evaluate prognostic value of oropharyngeal or hypopharyngeal cancer.. ASTRO 2016 Annual Meeting 2016.09.25
3. Ryoichi Yoshimura. Brachytherapy techniques: intracavitary implants. The 4th Congress of the Japan Oncoplastic Breast Surgery Society 2016.10.06 Chiba
4. Watanabe H, Ozaki Y, Miura M, Yoshimura R, Sumi Y, Kurabayashi T. Estimation of whole body radiation exposure induced by oral cancer brachytherapy using Monte Carlo simulation. The 11th Asian Congress of Oral and Maxillofacial Radiology 2016.11.12 Chiang Mai, Thailand
5. Retrospective review of POEMS syndrome initially treated with radiotherapy in our institute. The 29th annual meeting of the japanese society for radiation oncology 2016.11.27
6. Yuasa-Nakagawa K, Yoshimura R, Toda K, Kojima M, Shibuya H. The therapeutic changes influence on the treatment results of the hypopharyngeal cancer. ESMO-ASIA 2016 2016.12.17 Singapore

## Maxillofacial Anatomy

Professor	Shunichi SHIBATA
Assistant Professor	Shun-ichi SHIKANO
Graduate Student	Masato Takahashi
Graduate Student	Maki Hasegawa
Graduate Student	Shota Kusaka
Lecturer	Rei Sato
PD	Chiho Watanabe

### (1) Outline

Maxillofacial anatomy section is engaged in lecture and practical course of gross anatomy and dental anatomy in undergraduate school. In graduate school, this section is engaged in morphological studies of hard tissues such as tooth, bone and cartilage.

### (2) Research

Research Subjects

- 1) Structural features of mandibular condylar cartilage.
- 2) Mechanism of epithelial attachment of junctional epithelium in human gingiva.
- 3) Comparative histology and embryology of teeth.
- 4) Observation on the structural features of oral mucous
- 5) Anatomical names of the structures of human skeletal system.
- 6) Hyaluronan synthesis in tooth germ.
- 7) Studies on regeneration of jaw bone.
- 8) Structural features of dental pulp and extracellular matrix

### (3) Education

In Undergraduate school

Lecture for 2nd degree students: Human structure I, II, Dental anatomy, Neuroanatomy,

Practical course for 2nd degree students: Gross Anatomy, Neuroanatomy, Dental Anatomy

Lecture and practical course for 5th degree students: Clinical craniofacial anatomy

In Graduate school

Lecture, seminar and practical course to understand the function of various oral organs in a morphological viewpoint, and to evaluate various vital phenomenon encountered in medical practice.

### (4) Lectures & Courses

The main purpose of education in undergraduate school is to understand human structure and function from the viewpoints of gross anatomy. In line with this purpose, we execute lectures of systematic anatomy (osteology, myology, neurology, angiology, splanchnology) and topographic anatomy (craniofacial anatomy). To understand three-dimensional structures of human body, we execute practical course of human gross anatomy

after completing lectures. In the practical course, we make an effort to make students understand ethics as dental students to be bright future dentist.

The main purpose of education in graduate school is to understand various vital phenomenon, which we encounter in research fields of basic and clinical sciences, from the viewpoints of morphology. In lectures, we teach various techniques to investigate structural features from the standpoints of light and electron microscopy, organ and tissue culture, and molecular biology.

## ( 5 ) Publications

### [Original Articles]

1. Sato R, Fukuoka H, Yokohama-Tamaki T, Kaku M, Shibata S. Immunohistochemical localization of tenascin-C in rat periodontal ligament with references to alveolar bone remodeling *Anatomical Science International*. 2016.02; 91(2); 196-206
2. Hirano-Kawamoto A, Honkura Y, Shibata S, Abe S, Murakami G, Katori Y. Cricoarytenoid articulation in elderly Japanese with special reference to morphology of the synovial and capsular tissues *Annals of Otolaryngology, Rhinology, and Laryngology*. 2016.03; 125(3); 219-227
3. Hayashi K, Takahashi T, Ikegawa M, Horie M, Oyaizu T, Enomoto M, Shibata S, Yagishita K, Ueno T. The facilitatory effects of hyperbaric oxygen treatment on membrane bone wound healing in a rat calvarial defect model. *Undersea Hyperbaric Medicine*. 2016.03; 43(2); 135-142
4. Cho KH, Jin ZW, Abe H, Shibata S, Murakami G, Rodríguez-Vázquez JF. Neural-dural transition at the thoracic and lumbar spinal nerve roots: a histological study of human late-stage fetuses *BioMed Research International*. 2016.05; 2016(8163519);
5. Morita T, Fujikawa K, Baba O, Shibata S. An in situ hybridization study of Hyaluronan synthase (Has) mRNA in developing mouse molar and incisor tooth germs *Gene Expression Patterns*. 2016.05; 21(1); 28-40
6. Noda M, Aoki A, Mizutani K, Lin T, Komaki M, Shibata S, Izumi Y. High-frequency pulsed low-level diode laser therapy accelerates wound healing of tooth extraction socket: An in vivo study. *Lasers in Surgery and Medicine*. 2016.07; 48(10); 955-964
7. Jin ZW, Abe H, Jin Y, Shibata S, Murakami G, Rodríguez-Vázquez JF. Positional changes in tendon insertions from bone to fascia: development of the pes anserinus and semimembranosus muscle insertion in human fetuses *Folia Morphologica*. 2016.11; 75(4); 503-511

### [Conference Activities & Talks]

1. Shibata S. Expression of Hyaluronan Synthase (Has) in Developing Mouse Molar and Incisor Tooth Germ. 2015 Frontier meeting in Hong Kong 2016.02.12 The University of Hong Kong, Hong Kong, China.
2. Ito Y, Takahashi Y, Hikita R, Watanabe C, Akiyama S, Higashihori N, Moriyama K. Long-term changes in clinical crown height after surgical orthodontic treatment for mandibular prognathism. The 10th Asia Pacific orthodontic Conference and 11th Annual Meeting of the Indonesian Association of Orthodontists 2016.09.03 Bali, Indonesia
3. Masahiro Noda, Akira Aoki, Koji Mizutani, Taichen Lin, Motohiro Komaki, Shunichi Shibata, Yuichi Izumi. Effect of low level laser irradiation on early stage of wound healing of tooth extraction socket. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10 Fukuoka

## Cognitive Neurobiology

Professor Masato Taira  
Junior Associate Professor Hisayuki Ojima  
Assistant Professor Narumi Katsuyama  
Assistant Professor Nobuo Usui  
Research fellow Rui Watanabe  
Graduate Student Eriko Kikuchi(Tachi)  
Yuko Imai  
Kono Youko  
Maki Okada  
Hiroaki Tanaka  
Adjunct instructor Saneyuki Mizutani

### ( 1 ) Outline

Higher brain functions have been studied in this laboratory. To explore the individual functions listed below, functional MRI, psychological or psychophysical approach, and traditional electrophysiological recordings together with animal training are applied to animal models such as non-human primates and rodents as well as to human. Our goal is to clarify how perceptual mechanisms underlying higher brain functions are described by the neuronal activity pattern and how cortical wide connectivity is interacted while brain is judging, decision making, extracting biological meanings of sounds including languages.

### ( 2 ) Research

1. Neural Mechanisms of control of motor behavior.  
Research is aimed at understanding the brain mechanisms of execution and control of the motion and behavior of animals and human.
2. Neuronal mechanisms for perception and cognition.  
Research is aimed at understanding the brain mechanisms of perception and cognition of objects through vision and tactile senses of animals and human.
3. Processing of natural sounds in auditory cortex  
Research is aimed at understanding the brain mechanisms of hearing and vocalization of animals.

### ( 3 ) Education

1. Lectures of unit "Functions of Nervous Systems I (Introduction to Neurophysiology, Motor Functions)"  
Basic knowledge of neurophysiology will be lectured as an introduction together with the motor functions.
2. Lectures of unit "Functions of Nervous Systems II (Perception, Emotion, Instinct, Sleep, Higher functions)".  
A series of lectures will be taught on functions of the sensation, perception, and motion as well as the neural mechanisms of higher brain functions.
3. Lectures of unit "Homeostatic Functions for Life Support".  
Lectures will be taught on the structure of the autonomic nervous system and its regulatory mechanisms in the circulation, respiration, digestion/absorption, humor/body temperature, metabolism, excretion, and internal secretion/reproduction.

#### 4. Lectures of unit "Oral Physiology"

Lectures will be taught on the structure and function of various somatosensory organs in the oral cavity. Neural regulations of mastication and deglutition as well as the secretion mechanism of saliva will also be learned.

#### 5. Unit of "Practice in Physiological Functions"

The purpose of the practice is to learn about the physiological mechanisms underlying the normal functions of human body through experiments. The goal is to master the basic experimental procedures, and to experience how to capture and analyze the data in order to draw conclusions.

### (4) Lectures & Courses

Students are expected to be voluntarily involved in research activity. Brain is an extremely complicated organ in terms of its morphology and functions. Learning of textbook knowledge is mandatory and is followed by capturing up-to-date scientific information through reading published articles. Once the overview of the field in which graduates/undergraduate students are interested in is completed, they will start to be engaged in on-going research topics under the tutelage of laboratory staff. Through this process, students are encouraged to associate their own research interests with the on-going research topics and will learn practically how data can be captured, rearranged and analyzed through real experiments.

### (5) Publications

#### [Original Articles]

1. Hisayuki Ojima and Junsei Horikawa. Recognition of modified conditioning sounds by competitively trained guinea pigs *Frontiers in Behavioral Neuroscience*. 2016.01; 26(9); 373
2. Yasuhiro Mochizuki, Tomokatsu Onaga, Hideaki Shimazaki, Takeaki Shimokawa, Yasuhiro Tsubo, Rie Kimura, Akiko Saiki, Yutaka Sakai, Yoshikazu Isomura, Shigeyoshi Fujisawa, Ken-Ichi Shibata, Daichi Hirai, Takahiro Furuta, Takeshi Kaneko, Susumu Takahashi, Tomoaki Nakazono, Seiya Ishino, Yoshio Sakurai, Takashi Kitsukawa, Jong Won Lee, Hyunjung Lee, Min Whan Jung, Cecilia Babul, Pedro E Maldonado, Kazutaka Takahashi, Fritzie I Arce-McShane, Callum F Ross, Barry J Sessle, Nicholas G Hatsopoulos, Thomas Brochier, Alexa Riehle, Paul Chorley, Sonja Grün, Hisao Nishijo, Satoe Ichihara-Takeda, Shintaro Funahashi, Keisetsu Shima, Hajime Mushiake, Yukako Yamane, Hiroshi Tamura, Ichiro Fujita, Naoko Inaba, Kenji Kawano, Sergei Kurkin, Kikuro Fukushima, Kiyoshi Kurata, Masato Taira, Ken-Ichiro Tsutsui, Tadashi Ogawa, Hidehiko Komatsu, Kowa Koida, Keisuke Toyama, Barry J Richmond, Shigeru Shinomoto. Similarity in Neuronal Firing Regimes across Mammalian Species. *J. Neurosci.* 2016.05; 36(21); 5736-5747
3. Rui Watanabe, Takahiro Higuchi. Behavioral advantages of the first-person perspective model for imitation. *Frontiers in Psychology*. 2016.05; 7(701);
4. Chiharu Matsuda, Toshio Shimizu, Yuki Nakayama, Michiko Haraguchi, Yoko Mochizuki, Chiyoko Hakuta, Masato Taira, Takaya Numayama, Masanobu Kinoshita. Analysis of resting salivation rate in patients with amyotrophic lateral sclerosis using tracheostomy invasive ventilation. *Rinsho Shinkeigaku*. 2016.07; 56(7); 465-471
5. T Shinozaki, Y Imamura, R Kohashi, K Dezawa, Y Nakaya, Y Sato, K Watanabe, Y Morimoto, T Shizukuishi, O Abe, T Haji, K Tabei, M Taira. Spatial and Temporal Brain Responses to Noxious Heat Thermal Stimuli in Burning Mouth Syndrome. *J. Dent. Res.* 2016.09; 95(10); 1138-1146
6. Narumi Katsuyama, Nobuo Usui, Masato Taira. Activation of the Human MT Complex by Motion in Depth Induced by a Moving Cast Shadow *PLoS One*. 2016.09; 11(9); e0162555
7. Chiharu Matsuda, Toshio Shimizu, Yuki Nakayama, Michiko Haraguchi, Chiyoko Hakuta, Yumi Itagaki, Akiko Ogura, Kanako Murata, Masato Taira, Takaya Numayama, Masanobu Kinoshita. Macroglossia in advanced amyotrophic lateral sclerosis. *Muscle Nerve*. 2016.09; 54(3); 386-390

**[Books etc]**

1. Fukushima M, Ojima H. Information Processing in the Auditory Ventral Stream Brain and Nerve 68(11);1371-1378. 2016.11

**[Misc]**

1. Makoto Fukushima, Hisayuki Ojima. [ Information Processing in the Auditory Ventral Stream] . Brain Nerve. 2016.11; 68(11); 1371-1378

**[Conference Activities & Talks]**

1. Hayashi K, Ojima H, Horikawa J . Changes in temporal pattern of AI activity after interval discrimination of repetitive sounds in guinea pigs. 39th Annual Midwinter Meeting of ARO 2016.02.20 San Diego, CA, USA
2. Eriko Kikuchi, Hisayuki Ojima, Akiko Yamashita, Narumi Katsuyama, Masato Taira. Effects of stimulus intensity on the induced jaw movement patterns in guinea pigs. 8th CBIR Inspive Symposium 2016.02.20
3. Ayako Kubota, Yoko Kono, Hiroko Imura, Hiroji Shimomura, Kiyoko Kanamori, Yasuko Kawakami, Shiro Mataka, Kumiko Sugimoto. Oral health status and behavior of Japanese university students. International Symposium on Dental Hygiene 2016 2016.06 Basel, Switzerland
4. Ikeda A, Miyamoto J, Usui N, Taira M, Moriyama K.. Effect of mastication on satiety using an attentional bias task.. 94th General Session & Exhibition of the International Association for Dental Research 2016.06.24
5. Akitsu Ikeda, Jun Miyamoto, Nobuo Usui, Masato Taira, Keiji Moriyama. Effect of Mastication on Satiety Using an Attentional Bias Task. 94th General Session&Exhibition of the IADR 2016.06.24
6. Sawada A, Usui N, Shimazaki K, Taira M, Ono T.. Neural mechanisms underlying time-dependent changes in orthodontic pain.. 94th General Session & Exhibition of the International Association for Dental Research 2016.06.25
7. Alisa Sawada, Nobuo Usui, Kazuo Shimazaki, Masato Taira, Takashi Ono. Neural Mechanisms Underlying Time-dependent Changes in Orthodontic Pain. 2016.06.25
8. Rui Watanabe et al.. Effects of perspective and motion of body parts on imitation behavior: investigation from neural aspects by fMRI. 10TH FENS FORUM OF NEUROSCIENCE 2016.07.04
9. Hisayuki Ojima, Koki Hayashi, Masato Taira, Junsei Horikawa. Changes in Temporal Activation Pattern of the Guinea Pig's AI after Interval Discrimination. The 39th Annual Meeting of the Japanese Neuroscience Society 2016.07.21 Yokohama, Japan
10. Fujiwara J, Tsutsui K-I, Taira M, Ugawa Y, Eifuku S. Neural mechanism of self-consistency in social behavior . The 39th Annual Meeting of the Japan Neuroscience Society 2016.07.21
11. Effects of stimulus intensities on the induced jaw movement patterns in guinea pigs. 2016.07.21
12. Eriko Kikuchi, Hisayuki Ojima, Akiko Yamashita, Narumi Katsuyama, Masato Taira. Effects of stimulus intensities on the induced jaw movement patterns in guinea pigs. The 39th Annual Meeting of the Japan Neuroscience Society 2016.07.22
13. J. Fujiwara. P.N. Tobler. K.I. Tsutsui. M. Taira. Y. Ugawa. S. Eifuku. Neural mechanisms underlying self-consistency in social behavior. 46th Annual Meeting of the Society for Neuroscience 2016.11.15

## Molecular Craniofacial Embryology

### Staffs and Students

#### Professor

Sachiko Iseki

#### Associate Professor

Masa-Aki Ikeda

#### Tenure Track Assistant Professor

Masaki Takechi

#### Part-time lecturers

Hirofumi Doi, Shumpei Yamada,  
Shigeru Okuhara

#### Visiting Researcher

Yoichiro Ninomiya

#### Graduate Students

Toshiko Furutera, Mya Nandar,  
Charoenlarp Ponkawee,  
Norisuke Yokoyama,  
Erika Kubota (Pedodontics),  
Tian Xiaohui (Oral Implantology  
and Regenerative Dental  
Medicine),  
Rajendran Arun Kumar,  
Takahiko Yamada (Maxillofacial Surgery), Vou Hoang Tri (Oct-)

### ( 1 ) Research

- 1) Molecular mechanisms of mammalian craniofacial development
- 2) Application of developmental mechanisms to regenerative medicine
- 3) Identification of tissue stem cells in craniofacial region and molecular mechanism of their stemness
- 4) Regulation of gene expression in cell growth and stress response
- 5) Nuclear architecture and function in regulating gene expression

### ( 2 ) Publications

#### [Original Articles]

1. Otsuki Y., Ueda K., Satoh C., Maekawa R., Yoshiura K., Iseki S.. Intermediate phenotype between ADULT syndrome and EEC syndrome caused by R243Q mutation in TP63 Plastic and Reconstructive Surgery-Global Open. 2016.12; 4(12); e1185

#### [Misc]

1. Takechi, M., Kitazawa, T., Hirasawa, T., Hirai, T., Iseki, S., Kurihara, H., Kuratani, S.. Developmental mechanisms of the tympanic membrane in mammals and non-mammalian amniotes. Congenit Anom (Kyoto). 2016.01; 56(1); 12-17

#### [Conference Activities & Talks]

1. Ikeda MA. Novel Candidates of Therapeutic Targets for Head and Neck Squamous Cell Carcinomas Defined by Recent Comprehensive Mutation Analysis . The 17th Scientific and Refresher Course in Dentistry (KPPIKG 2016) 2016.02.27 Jakarta, Indonesia



2. Yuki Otsuki, Koichi Ueda, Chisei Sato, Koichiro Yoshiura, Sachiko Iseki. A intermediate phenotype between ADULT syndrome and EE syndrome caused by R243Q mutation in TP63.. The 13th Japan Korea Congress of Plastic and Reconstructive Surgery 2016.05.15

# Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama  
Assistant Professor Yasuhiro Yoshimatsu  
Junior Associate Professor Hiroshi Fujita, Yasuki Ishizaki, Masao Saito

Research Student: Mizuki Nagata,  
:Syun Nishihara  
:Hiroki Kuwahara  
:Syuhei Fukuda

:Asuka Okito

## ( 1 ) Outline

In our Lab, we study the role of cell-communication in bone remodeling, cancer and vascular calcification using various techniques, for example, cell culture, molecular biology and mutant mice.

## ( 2 ) Research

Research Subjects

- 1, Cell-cell communication and cell functions
- 2, Bone remodeling and cell communications
- 3, Cancer and cell communications
- 4, Mechanism of vascular calcification

## ( 3 ) Education

For undergraduate students. We have some class in biological chemistry for the second grader.

For graduate students. These students can choose the one of themes in our lab. They have to attend meetings and seminars in our Lab.

## ( 4 ) Lectures & Courses

Undergraduate students should understand basic biochemistry and physiology under healthy/diseased conditions.

Graduate students are expected to solve the problems by themselves. However, appropriate suggestions will be given by at least three supervisors whenever you want.

( 5 ) Publications

**[Original Articles]**

1. Tsuyoshi Matsuura, Shizuko Ichinose, Masako Akiyama, Yuki Kasahara, Noriko Tachikawa, Ken-Ichi Nakahama. Involvement of CX3CL1 in the Migration of Osteoclast Precursors Across Osteoblast Layer Stimulated by Interleukin-1 $\beta$ . J. Cell. Physiol.. 2016.08;

**[Misc]**

1. Yasuhiro Yoshimatsu, Hideki Miyazaki, Tetsuro Watabe. Roles of signaling and transcriptional networks in pathological lymphangiogenesis. Adv. Drug Deliv. Rev.. 2016.04; 99(Pt B); 161-171
2. Yasuhiro Yoshimatsu. Roles of Transcription Factors in the Formation of Lymphatic Vessels Inflammation and Immunity. 2016.08; 24(5); 372-378

**[Conference Activities & Talks]**

1. Ken-ichi Nakahama, Tsuyoshi Matsuura, Takako Tachikawa. Involvement of CX3CL1 in the migration of osteoclast precursors across osteoblast layer stimulated by interleukin-1 $\beta$ .. The 2nd annual meeting of Japanese Society of Osteoimmunology 2016.07.07
2. Asuka Okito, Masako Akiyama, Jun Hosomichi, Takashi Ono, Ken-ichi Nakahama. Transcriptional regulation of osteopontin in osteoblasts.. The 2nd annual meeting of Japanese Society of Osteoimmunology 2016.07.07
3. Masahiro Shinohara, Ken-ichi Nakahama, Hiroshi Asahara. Regulation of osteoblastic bone formation by class IA PI3K in osteocytes. The 2nd annual meeting of Japanese Society of Osteoimmunology 2016.07.07
4. Kazuki Takahashi, Katarzyna Anna Inoue, Yasuhiro Yoshimatsu. Hironori Harada and Tetsuro Watabe. Role of TGF- $\beta$  in the invasiveness of oral cancer cell lines. The 88th Annual Meeting of Molecular Biology Society of Japan 2016.12 Yokohama
5. Yasuhiro Yoshimatsu. Roles of signaling and transcriptional networks in the formation and maintenance of lymphatic vasculature. The 24th Annual Meeting of the Japanese Vascular Biology and Medicine Organization/ The 14th Korea-Japan Joint Symposium on Vascular Biology 2016.12.10 Nagasaki

# Biodesign

Professor Kazuo TAKAKUDA  
 Assistant Professor Hisashi DOI  
 Mari YUASA  
 Research Assistants Shukan OKANO  
 Hiroyuki MASUNO  
 Noriko NAKAISHI  
 Graduate Students (Doctoral coarse)  
 Hiroki IKEDA, Hiroyuki KUSABA,  
 Hisaya NOMATA, Eiko MARUKAWA

## ( 1 ) Outline

Biodesign division started in 1951 at establishment of the dental materials research institute as one of the constituting department. Since then, the division changed its name from the department of machinery, the department of precision machinery, the division of mechanics, and the division of biodesign as the institute continued reorganization till the present form of the Institute of Biomaterials and Bioengineering. Although our research work was originally concentrated to cutting tool for dentistry, we are now investigating mechanics of living tissues and biomaterials, biomechanical compatibility of tissues and artificial materials, and the development of artificial organs bearing the mechanical functions in living bodies.

## ( 2 ) Education

Basic-Clinical Borderless Education

## ( 3 ) Publications

### [Original Articles]

1. Wei Wang, Soichiro Itoh, Kazuo Takakuda. Comparative study of the efficacy of decellularization treatment of allogenic and xenogeneic nerves as nerve conduits. J Biomed Mater Res A. 2016.02; 104(2); 445-454
2. Yagihara A, Kawasaki R, Mita A, Takakuda K.. Impact of Dynamic and Static Load on Bone Around Implants: An Experimental Study in a Rat Model Int J Oral Maxillofac Implants. 2016.05; 31(3); 49-56
3. Kusaba H, Terada-Nakaishi M, Wang W, Itoh S, Nozaki K, Nagai A, Ichinose S, Takakuda K.. Comparison of nerve regenerative efficacy between decellularized nerve graft and nonwoven chitosan conduit Biomed Mater Eng. 2016.05; 27(1); 75-85
4. Suzuki R, Takakuda K.. Wound healing efficacy of a 660-nm diode laser in a rat incisional wound model Lasers Med Sci.. 2016.08; 31(8); 1683-1689

## Maxillofacial Surgery

Junior Associate Professor: Satoshi YAMAGUCHI, Narikazu UZAWA

Assistant Professor: Hiroyuki YOSHITAKE, Yasuyuki MICH, Kazuto KUROHARA, Kouichi NAKAKUKI,  
Yoshio OHYAMA  
(from April) Keiichi MORITA

Hospital Staff: Itaru SONODA, Kunihiro MYO, Nobuyoshi TOMOMATSU, Chie AKATSU, Tomomi SAKUMA,  
Ryousuke NAGAOKA, Yoshinori INABA, Jun SUMINO, Chika MIURA,

(from April) Yukihiro HASHIDA, Masahiko TERAUCHI, Machiko KOSUGI

Graduate Student: Reiko HOSHI, Sakie KATSUMURA, Tomoki KANEMARU, Uyannga ENKHBOLD,  
Syun NISHIHARA, Erina TONOUCHI, Takasuke INADA, Durugu-nn BATBO-RUDO,  
Eri SONE, Narumi OSIBE, Keiichiro NAKAZATO, Hiroshi KATO  
Takahiko YAMADA, Yusun KIMU

(from April) Katsuya HYOUDOU, Daisuke YAMAMOTO

Student: (from April) Mari SHIBATA, Kentarou SUGIYAMA, Natsuko HONDA, Mayuko MARUIWA,  
Tokiwa OOISHI, Mana TAKAGI

Emeritus Professor: Teruo AMAGASA

Clinical professor: Masashi YAMASHIRO

Part-time Lecturer: Kazuki HASEGAWA, Hitoshi MIYAOKA, Hiroyuki WAKE, Takahumi YAMADA,  
Fumiaki SATO, Junichi ISHII, Eizi FUZII, Junzi KOBAYASHI,  
Akiko KOBAYASHI, Yutaka SATO, Yasushi NIINAKA, Takao WATANABE  
Testuo SUZUKI, Masayuki YAMANE, Takashi MISHIMAGI,  
Shigehiro ABE, Miho MIZUTANI, Yasuhiro KURASAWA,  
Chieko MICHIKAWA, Erika OUE, Norihiro ENDO

### (1) Research

#### Research Subjects

- 1) Head and Neck Surgery: Innovation of management patients with benign and malignant tumors and cysts in oral and facial region.
- 2) Reconstructive Surgery: Developing method of correcting jaw, facial bone and facial soft tissue trouble left as the result of removal of disease or previous trauma.
- 3) Correction of Birth Defects: Improving surgically correction of birth defects of the face and skull, including cleft lip and palate.
- 4) Dentofacial Deformities and Orthognathic Surgery: Development of new surgical techniques to improving reconstruct and realign the upper and lower jaws.
- 5) Temporomandibular Joint Disorders: Renewing skills in the diagnosis and treatment due to temporomandibular joint problem.
- 6) Oral Mucosa Disease: Creation new method with light and color for diagnosis of oral mucosa disease, including leukoplakia and cancer.

**( 2 ) Lectures & Courses**

Oral and maxillofacial surgery is a surgical specialty involving the diagnosis, surgical treatment and management of defects and injuries related to the function and aesthetics of the face and jaws. In order to practice the full scope of the specialty, oral and maxillofacial surgeons are required education in dentistry, medicine and surgery for regional requirement.

**( 3 ) Clinical Services & Other Works**

Total number of new patients was 6312 of 2015.

**( 4 ) Clinical Performances**

Clinical Services

- 1) Diagnosis, removing and reconstruction of jaw, oral or facial tumor or cyst.
- 2) Diagnosis and treatment of cleft lip and palate.
- 3) Treatment of jaw aligned with orthognathic surgery.
- 4) Therapy of temporomandibular disorder with or without temporomandibular joint surgery.
- 5) Diagnosis and treatment of oral mucosa disease.
- 6) Treatment of inflammation in the region jaw and facial trauma.
- 7) Extraction tooth including wisdom tooth.

**( 5 ) Publications****[Original Articles]**

1. Okuyama K, Michi Y, Mizutani M, Yamashiro M, Kaida A, Harada K. Clinical study on mandibular fracture after marginal resection of the mandible. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2016;
2. Kato Y, Ogasawara S, Oki H, Honma R, Takagi M, Fujii Y, Nakamura T, Saidoh N, Kanno H, Umetsu M, Kamata S, Kubo H, Yamada M, Sawa Y, Morita K, Harada H, Suzuki H, Kaneko MK. Novel Monoclonal Antibody LpMab-17 Developed by CasMab Technology Distinguishes Human Podoplanin from Monkey Podoplanin. *Monoclon Antib Immunodiagn Immunother.* . 2016; 35(2); 109-116
3. Kohmoto T, Tsuji A, Morita K, Naruto T, Masuda K, Kashimada K, Enomoto K, Morio T, Harada H, Imoto I. A novel COL11A1 missense mutation in siblings with non-ocular Stickler syndrome. *Hum Genome Var.* 2016; 7(3); 16003
4. Khanom R, Nguyen CT, Kayamori K, Zhao X, Morita K, Miki Y, Katsube K, Yamaguchi A, Sakamoto K. Keratin 17 Is Induced in Oral Cancer and Facilitates Tumor Growth. *PLoS One.* . 2016; 11(8); e0161163
5. Pal SK, Nguyen CT, Morita KI, Miki Y, Kayamori K, Yamaguchi A, Sakamoto K. THBS1 is induced by TGFB1 in the cancer stroma and promotes invasion of oral squamous cell carcinoma. *J Oral Pathol Med.* 2016; 45(10); 730-739
6. Sato M, Morita K, Kabasawa Y, Harada H. Bilateral nasolabial cysts: a case report. *J Med Case Rep.* 2016; 10(1); 246
7. Kondo Y, Ohno T, Nishii N, Harada K, Yagita H, Azuma M. Differential contribution of three immune checkpoint (VISTA, CTLA-4, PD-1) pathways to antitumor responses against squamous cell carcinoma. *Oral Oncology.* 2016; 57; 54-60
8. Matsushita Y, Nakakuki K, Kosugi M, Kurohara K, Harada K. Does Intraoral miniplate fixation have a good postoperative stability after sagittal splitting ramus osteotomy?: Comparison with intraoral bicortical screw fixation. *Journal of Oral and Maxillofacial Surgery.* 2016.01; 74; 181-189

9. Nakajima K, Kho DH, Yanagawa T, Harazono Y, Hogan V, Chen W, Ali-Fehmi R, Mehra R, Raz A. Galectin-3 cleavage alters bone remodeling: Different outcomes in breast and prostate cancer skeletal metastasis. *Cancer Res.* 2016.03; 76(6); 1391-1402
10. Morita T, Yamashiro M, Kayamori K, Mizutani M, Nakakuki K, Michi Y, Uzawa N, Izumo T, Harada K. Primary intraosseous squamous cell carcinoma derived from a maxillary cyst: A case report and literature review. *Mol Clin Oncol.* 2016.04; 4(4); 553-558
11. Kayamori K, Katsube K, Sakamoto K, Ohyama Y, Hirai H, Yukimori A, Ohata Y, Akashi T, Saitoh M, Harada K, Harada H, Yamaguchi A. NOTCH3 Is Induced in Cancer-Associated Fibroblasts and Promotes Angiogenesis in Oral Squamous Cell Carcinoma. *PLoS One.* 2016.04; 11(4); e0154112
12. Suzuki M, Deno M, Myers M, Asakage T, Takahashi K, Saito K, Mori Y, Saito H, Ichikawa Y, Yamamoto-Mitani N, Miyashita M. Anxiety and depression in patients after surgery for head and neck cancer in Japan. *Palliat Support Care.* 2016.05; 299(8); 1110-1120
13. Okuyama K, Michi Y, Mizutani M, Yamashiro M, Kaida A, Harada K. Clinical study on mandibular fracture after marginal resection of the mandible. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2016.05; 121(5); 461-467
14. Badri MK, Zhang H, Ohyama Y, Venkitapathi S, Kamiya N, Takeda H, Ray M, Scott G, Tsuji T, Kunieda T, Mishina Y, Mochida Y. Ellis van Creveld2 is required for postnatal craniofacial bone development. *Anat Rec (Hoboken).* 2016.05; 299(8); 1110-1120
15. Yoshitake H, Kayamori K, Wake S, Sato F, Kino K, Harada K. Synovial chondromatosis of the right side temporomandibular joint extending to the middle cranial fossa: A case report with 7-year postoperative follow up and expression of a biomarker of cell proliferative activity. *Anat Rec (Hoboken).* 2016.06; 20; 133-137
16. Kondo Y, Ohno T, Nishii N, Harada K, Yagita H, Azuma M. Differential contribution of three immune checkpoint (VISTA, CTLA-4, PD-1) pathways to antitumor responses against squamous cell carcinoma. *Oral Oncol.* 2016.06; 57; 54-60
17. Ohyama Y, Lin JH, Govitvattana N, Lin IP, Venkitapathi S, Alamoudi A, Husein D, An C, Hotta H, Kaku M, Mochida Y. FAM20A binds to and regulates FAM20C localization. *Sci Rep.* 2016.06; 6; 27784
18. Wake S, Yoshitake H, Kayamori K, Izumo T, Harada K. Expression of CD90 decreases with progression of synovial chondromatosis in the temporomandibular joint. *Cranio.* 2016.07; 34(4); 250-256
19. Jaha H, Husein D, Ohyama Y, Xu D, Suzuki S, Huang GT, Mochida Y. N-terminal Dentin Sialoprotein fragment induces type I collagen production and upregulates dentinogenesis marker expression in osteoblasts. *Biochemistry and Biophysics Reports.* 2016.07; 6; 190-196
20. Shuji Hibiya, Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Nobukatsu Horita, Sho Watanabe, Tomoaki Shirasaki, Ryu Nishimura, Natsuko Kimura, Tatsunori Nishimura, Noriko Gotoh, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Long-term inflammation transforms intestinal epithelial cells of colonic organoids. *J Crohns Colitis.* 2016.10;
21. Masanori Kobayashi, Shigeru Oshima, Chiaki Maeyashiki, Yoichi Nibe, Kana Otsubo, Yu Matsuzawa, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. The ubiquitin hybrid gene UBA52 regulates ubiquitination of ribosome and sustains embryonic development. *Sci Rep.* 2016.11; 6; 36780
22. Morita T, Uzawa N, Mogushi K, Sumino J, Michikawa C, Takahashi KI, Myo K, Izumo T, Harada K. Characterizing Genetic Transitions of Copy Number Alterations and Allelic Imbalances in Oral Tongue Carcinoma Metastasis. *Genes Chromosomes Cancer.* 2016.12; 55; 975-986
23. Terauchi M, Inada T, Tonegawa A, Tamura A, Yamaguchi S, Harada K, Yui N. Supramolecular inclusion complexation of simvastatin with methylated  $\beta$ -cyclodextrins for promoting osteogenic differentiation. *Int. J. Biol. Macromol.* 2016.12; 93(PtB); 1492-1498

**[Conference Activities & Talks]**

1. Morita K, Naruto T, Tanimoto K, Yasukawa C, Oikawa Y, Masuda K, Imoto I, Inazawa J, Omura K, Harada H. Simultaneous detection of both single nucleotide variations and copy number alterations by next-generation sequencing in gorlin syndrome. . The 13th International Congress of Human Genetics 2016.04.03 Kyoto
2. Uezono M, Takakuda K, Hiratsuka T, Ogasawara T, Oshima S, Sato T, Kikuchi M, Suzuki S, Harada K, Moriyama K. Mechanical properties of newly formed bone around subperiosteal devices evaluated with micro-indentation test.. 10th World Biomaterials Congress (WBC) 2016.05.17 Montreal, Canada.
3. Masahiko Terauchi, Takasuke Inada, Atsushi Tamura, Satoshi Yamaguchi, Nobuhiko Yui. Osteoregeneration by supramolecular sulfonated polurotaxane/BMP-2 polyelectrolyte complexes in mouse calvarial defect model.. 11th International Conference Medical Applications of Novel Biomaterials and Nanotechnology, 5th International Conference Smart and Multifunctional Materials Structures & Systems. Centro Congressi 2016.06.05 Italy
4. Uezono M, Takakuda K, Hiratsuka T, Ogasawara T, Kikuchi M, Harada K, Suzuki S, Moriyama K.. Yield Strength of Newly Formed Bone Around Subperiosteal Anchorage Devices. 94th General Session & Exhibition of International Association for Dental Research. 2016.06.22 Seoul, Korea
5. Kondo Y, Ohno T, Azuma M. Combined VISTA and CTLA-4 immune-checkpoint blockade enhances antitumor immunity. 94th Annual Meeting of the International Association for Dental Research (IADR 2016) 2016.06.22 Seoul, Korea
6. Horita N, Demitrack ES, Gifford GB, Keeley TM, Siebel CW, Samuelson LC. Notch1 and Notch2 regulate epithelial cell proliferation in mouse and human gastric corpus. The 2016 Gordon Research Conference on Notch Signaling in Development, Regeneration & Disease 2016.08.01 Lewiston (USA)
7. Yoshitake H. Development of the new instrument for measurement of mouth opening and mouth-opening pathway. 23rd Congress of the European Association for Cranio Maxillo-Facial Surgery 2016.09.13 London, UK
8. Yoshitake H. Development of the new TMJ rehabilitation device that induces a protrusive sliding movement of the mandibular condyle. 23rd Congress of the European Association for Cranio Maxillo-Facial Surgery 2016.09.13 London, UK
9. Masahiko Terauchi, Atsushi Tamura, Nobuhiko Yui.. Supramolecular Sulfonated Polyrotaxanes complexed with Bone Morphogenetic Protein-2 for Bone Tissue Engineering. International Dental Materials Congress 2016 2016.11.04 Indonesia
10. Ogasawara T, Uezono M, Takakuda K, Kikuchi M, Hiratsuka T, Suzuki S, Moriyama K. Finite element analysis of bone bonding strength for the orthodontic subperiosteal devices. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.07 Tokushima

**[Patents]**

1. MEDICAL DEVICE, DEVICE STRUCTURE FOR DENTAL, HEAD AND NECK SURGICAL AND ORTHOPEDIC USE, AND METHOD FOR JOINING MEDICAL DEVICE TO BONE , Announcement Number : WO 2016136913



## Maxillofacial Orthognathics

Professor	Keiji MORIYAMA
Associate Professor	Shoichi SUZUKI
Junior Associate Professor	Takuya OGAWA
Assistant Professor	Michiko TSUJI, Norihisa HIGASHIHORI, Jun MIYAMOTO, Yukiho KOBAYASHI, Yosuke ITO
Clinical Fellow	Rina HIKITA, Yuko KOMAZAKI, Kenji OGURA, Yuki TAKAHASHI, Naoki KOUDA, Sakiko AKIYAMA, Takuya ASAMI
Post-doctoral Fellow	Chiho KADOTA, Masayoshi UEZONO
Graduate Student	Keiko MURAMOTO, Akitsu IKEDA, Kouhei YAHIRO, Ayumi SHOJI, Taizo HIRATSUKA, Entei RIN, Miyu ARAKI, Takeshi OGASAWARA, Yoshihiro YAMAGATA, Aung Bhone Myat, Hiroyuki KAMIMOTO, Kyoko HIRABAYASHI, Kenta FUNAHASHI, Hideyuki YOSHIZAWA, Wu Yu Yun, Kaori KADOWAKI, Soonhwa KANG, Sayuri SAITO, Hidekazu MATSUMOTO, Takayuki MIYAZAKI, Teramoto Iida Airy, Phyo Thiha, Nay Myo Min Swe
Graduate International Research Student	Naomi YAMAMOTO, Rie KINOSHITA, Ruriko NAKAMURA, Misato HANDA, Syuhei AKIYAMA, Megumi ARIMURA, Asuka TAMURA, Cheng Shih-wei Eric, Kenjiro MATSUMURA, Yuri BABA, Yukiko KINOSHITA, Chisato TOMINAGA, Daichi HAYAKA, Thili HLA Myint, Yuki NAKAZAWA, Sahori MATSUNO
Visiting Research Scholar	Tsasan Tumurkhuu, Lisa R. Amir
Part-time Lecturer	Tatsuo KAWAMOTO, Naoto SUDA, Takafumi SUSAMI, Tamiko TERASHIMA, Yoshiyuki KATO, Yasuo ISHIWATA, Yoshiyuki BABA, Toshimoto TENGAN, Masahiko YOKOZEKI, Shigetoshi HIYAMA, Shigeki TAKAHASHI, Momotoshi SHIGA, Hiroki FUKUOKA, Junichi TAKADA, Maristela Sayuri INOUE, Keiichi KATAOKA, Hiroyuki SUZUKI, Ryo MARUOKA

**(1) Research**

- 1) Basic and clinical studies of cleft lip and/or palate and other congenital craniofacial conditions
- 2) Morphological and physiological studies of facial deformity
- 3) Physiological study about control mechanism of stomatognathic function
- 4) Functional MRI study in the craniofacial region
- 5) Clarify the factors of malocclusion with epidemiological technique

**(2) Education**

The goal of the program of Maxillofacial Orthognathics is to provide information related to craniofacial growth and development, and stomatognathic function in order to develop basic knowledge and skills for the treatment of the patients with a wide variety of malocclusion. It also provides valuable information of diagnosis and treatment planning for orthodontic and orthognathic therapies of the patients with jaw deformities and congenital craniofacial anomalies.

Comprehensive care by a team of specialists including maxillofacial surgeons, orthodontists, speech therapists etc. is needed for the treatment of the patients with cleft lip and palate and other craniofacial anomalies. The Graduate Program provides the clinical education of orthodontics as a part of the multi-disciplinary approach for such patients.

**(3) Clinical Performances**

In the Clinic, we treat a large number of patients presenting a variety of malocclusions to be assigned to group practice in order to gain valuable experience in diagnosis, treatment planning, orthodontic therapy, and patient management. Especially for patients born with cleft lip and/or palate and who need craniofacial and orthognathic surgery, we have clinical meetings and conferences for the comprehensive care through a team approach with maxillofacial surgeons, maxillofacial prosthodontists and speech therapists. We also provide supportive counseling to families who have members with congenital anomalies before the treatment.

**(4) Publications****[Original Articles]**

1. Koda N, Sato T, Shinohara M, Ichinose S, Ito Y, Nakamichi R, Kayama T, Suzuki H, Moriyama K, Asahara H. The transcription factor mohawk homeobox regulates homeostasis of the periodontal ligament. *Development*. 2016;
2. Lin W, Ezura Y, Izu Y, Aryal SA, Kawasaki M, Chantida PN, Moriyama K, Noda M. Profilin Expression Is Regulated by Bone Morphogenetic Protein (BMP) in Osteoblastic Cells. *Journal of Cellular Biochemistry*. 2016.03; 117(3); 621-628
3. Morishita M, Muramatsu T, Suto Y, Hirai M, Konishi T, Hayashi S, Shigemizu D, Tsunoda T, Moriyama K, Inazawa J. Chromothripsis-like chromosomal rearrangements induced by ionizing radiation using proton microbeam irradiation system. *Oncotarget*. 2016.03; 7(9); 10182-10192
4. Duarte C, Kobayashi Y, Morita J, Kawamoto T, Moriyama K. A preliminary investigation of the effect of relaxin on bone remodelling in suture expansion. *The European Journal of Orthodontics*. 2016.05;
5. Sato M, Baba Y, Haruyama N, Higashihori N, Tsuji M, Suzuki S, Moriyama K. Clinicostatistical analysis of congenitally missing permanent teeth in Japanese patients with cleft lip and/or palate *Orthodontic Waves*. 2016.06; 75(2); 41-45
6. Suzuki H, Ito Y, Shinohara M, Yamashita S, Ichinose S, Kishida A, Oyaizu T, Kayama T, Nakamichi R, Koda N, Yagishita K, Lotz MK, Okawa A, Asahara H.. Gene targeting of the transcription factor Mohawk in rats causes heterotopic ossification of Achilles tendon via failed tenogenesis. *Proceedings of the National Academy of Sciences of the United States of America*. 2016.07; 113(28); 7840-7845

7. Sato C, Ogawa T, Tsuge R, Shiga M, Tsuji M, Baba Y, Kosaki K, Moriyama K. Systemic and maxillofacial characteristics of 11 Japanese children with Russell-Silver syndrome. *Congenit Anom (Kyoto)*. 2016.09; 56(5); 217-225
8. Dei A, Miyamoto JJ, Takada J, Ono T, Moriyama K. Evaluation of blood flow and electromyographic activity in the perioral muscles. *European Journal of Orthodontics*. 2016.10; 38(5); 525-531
9. Tumurkhuu T, Fujiwara T, Komazaki Y, Kawaguchi Y, Tanaka T, Inazawa J, Ganburged G, Bazar A, Ogawa T, Moriyama K. Association between maternal education and malocclusion in Mongolian adolescents: a cross-sectional study. *BMJ Open*. 2016.11; 6(11);
10. Ogura K, Iimura T, Makino Y, Sugie-Oya A, Takakura A, Takao-Kawabata R, Ishizuya T, Moriyama K, Yamaguchi A. Short-term intermittent administration of parathyroid hormone facilitates osteogenesis by different mechanisms in cancellous and cortical bone. *Bone Reports*. 2016.12; 5; 7-14

#### [Books etc]

1. Kobayashi Y, Duarte C, Moriyama K.. *Biomarkers in Bone Disease. Part of the series Biomarkers in Disease: Methods, Discoveries and Applications*. 2016.07 (ISBN : 978-94-007-7745-3)

#### [Conference Activities & Talks]

1. Koda N, Shinohara M, Nakamichi R, Ito Y, Ichinose S, Moriyama K, Asahara H. Roles of Transcriptional Factor Mohawk in Periodontal Ligament. *IBMS Herbert Fleisch Workshop* 2016.02.28 Brugge,Belgium
2. Hikita R, Matsuno S, Asami T, Ogawa T, Baba Y, Tsuji M, Moriyama K. Systemic and cranimaxillofacial characteristics of patients with Williams syndrome. *International Congress of Human Genetics* 2016. 2016.04.03 Kyoto
3. Tsuji M, Ogura K, Hikita R, Kobayashi Y, Moriyama K. Maxillofacial morphological characteristics of two Japanese patients with chromosome 18p deletion syndrome. *International Congress of Human Genetics* 2016. 2016.04.03 Kyoto
4. Uezono M, Takakuda K, Hiratsuka T, Ogasawara T, Oshima S, Sato T, Kikuchi M, Suzuki S, Harada K, Moriyama K. Mechanical properties of newly formed bone around subperiosteal devices evaluated with micro-indentation test.. *10th World Biomaterials Congress (WBC)* 2016.05.17 Montreal, Canada.
5. Ikeda A, Miyamoto JJ, Usui N, Taira M, Moriyama K.. Effect of mastication on satiety using an attentional bias task. . *94th General Session & Exhibition of International Association for Dental Research*. 2016.06.22 Seoul,Korea
6. Uezono M, Takakuda K, Hiratsuka T, Ogasawara T, Kikuchi M, Harada K, Suzuki S, Moriyama K.. Yield Strength of Newly Formed Bone Around Subperiosteal Anchorage Devices. *94th General Session & Exhibition of International Association for Dental Research*. 2016.06.22 Seoul,Korea
7. Koda N, Shinohara M, Nakamichi R, Ito Y, Ichinose S, Asahara H, Moriyama K. Roles of Transcriptional Factor Mohawk in Periodontal Ligament. *94th General Session & Exhibition of International Association for Dental Research*. 2016.06.22 Seoul,Korea
8. Lin W, Ezura Y, Izu Y, Moriyama K, Noda M.. Role of Profilin1 in BMP-induced Activities in Skeletal Cells. *94th General Session & Exhibition of International Association for Dental Research*. 2016.06.22 Seoul,Korea
9. The Dental Education Consortium to promote healthy longevity -Second report- Agendas after the second year. 2016.07.02
10. Moriyama K. Dental Equilibrium Revisited : Soft Tissue Considerations in Treatment of Dentofacial Deformity. *The 10th Asia Pacific orthodontic Conference and 11th Annual Meeting of the Indonesian Association of Orthodontists* 2016.09.03 Bali,Indonesia
11. Ito Y, Takahashi Y, Hikita R, Watanabe C, Akiyama S, Higashihori N, Moriyama K. Long-term changes in clinical crown height after surgical orthodontic treatment for mandibular prognathism. *The 10th Asia Pacific orthodontic Conference and 11th Annual Meeting of the Indonesian Association of Orthodontists* 2016.09.03 Bali,Indonesia

12. Higashihori N, Hikita R, Moriyama K. Surgical-orthodontic treatment for facial asymmetry patient whose occlusal plane canted opposite to the mandibular deviation. The 10th Asia Pacific orthodontic Conference and 11th Annual Meeting of the Indonesian Association of Orthodontists 2016.09.03 Bali,Indonesia
13. Akiyama S, Ogura K, Miyamoto JJ, Komazaki Y, Takada J, Moriyama K. Clinical study of Marfan syndrome patients: intraoral characteristics.. The 49th Annual Scientific Congress,Korean Association of Orthodontists 2016.10.07 Seoul,Korea
14. Baba Y, Komazaki Y, Miyamoto J, Ogura K, Ahiko N, Baba Y, Tuji M, Moriyama K. Maxillofacial morphology of 4 cases of Marfan-related disorders in mixed dentition stage. The 49th Annual Scientific Congress,Korean Association of Orthodontists 2016.10.07 Seoul,Korea
15. Arimura M, Komazaki Y, Miyamoto JJ, Ogura K, Kobayashi Y, Moriyama K. Clinical study of Japanese Marfan syndrome patients: craniofacial morphology. The 49th Annual Scientific Congress,Korean Association of Orthodontists 2016.10.07 Seoul,Korea
16. Lin W. Role of Profilin1 in Skeletal Cells. Tri-University Consortiune 5th Tri-University Consortium 2016.10.27 Peking,China
17. Ogawa T, Muramoto K, Moriyama K. Long-tern observation of maxillofacial growth in a Klippel-Trenaunay-Weber syndrome patienr. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07
18. Shoji A, Ono T, Nakashima T, Moriyama K. Elucidation of the mechanism on alveolar bone remodeling during orthodontic tooth movement. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07
19. Asami T, Ito Y, Akiyama S, Hirabasyshi K, Ogasawara T, Kurohara K, Moriyama K. A case report of surgical orthodontic treatment fot monozygotic twins with mandibular prognathism. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
20. Ogura K, Iimura T, Yamagushi A, Moriyama K. Effect of intermittent administration of parathyroid hormone on osteogenesis. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
21. Yahiro K, Higashiori N, Moriyama K. The roles of histone methyltransferase Setdb1 during craniofacial development. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
22. Ogasawara T, Uezono M, Takakuda K, Kikuchi M, Hiratsuka T, Suzuki S, Moriyama K. Finite element analysis of bone bonding strength for the orthodontic subperiosteal devices. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
23. Kobayashi Y, Tsuji M, Hikita R, Ogura K, Moriyama K. Analysis of maxillofacial morphology of craniosynostosis patients: comparison between Apert syndrome and Crouzon syndrome. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
24. Tamura A, Ogura K, Miyamoto J, Komazaki Y, Takada J, Yoshizawa H, Go I, Tsuji M, Moriyama K. Clinical study of Marfan syndrome patients: medical symptoms. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
25. Takahashi Y, Higashihori N, Moriyama K. treatment of a high-angle class II malocclusion with condylar resorption using an orthodontic anchor plate. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
26. Kobayashi Y, Moriyama K. Identification of micro RNA responsible for the onest of craniosynostosis and cranial sutural development. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
27. Arimura M, Komazaki Y, Miyamoyo J, Ogura K, Takada J, Cheng E, Baba Y, Teramoto A, Funahashi K, Kobayashi Y, Moriyama K. Clinical study of Marfan syndrome patients:Craniofacial morphology. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima
28. Akiyama S, Ogura K, Miyamoto J, Komazaki Y, Takada J, Go I, Tsuji M, Moriyama K. Clinical study of Marfan syndrome patients: Intraoral characteristics. The 75th Annual Meeting of the Japanese Orthodontic Sciety 2016.11.07 Tokushima

29. Baba Y, Komazaki Y, Miyamoto J, Ogura K, Takada J, Hirabayashi K, Ahiko N, Baba Y, Kobayashi Y, Tsuji M, Moriyama K. Maxillofacial morphology of 4 cases of Marfan-related disorders in mixed dentition stage. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.07 Tokushima
30. Hikita R, Tsuji M, Kobayashi Y, Ogura K, Moriyama K. Craniofacial characteristics of two Seathre-Chozen syndrome cases. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.07 Tokushima
31. Matsumura K, Ogura K, Miyamoto J, Komazaki Y, Takada J, Kaminoto H, Hikita R, Moriyama K. Clinical study of Marfan syndrome patients: Morphological characteristics of pharyngeal airway and intraoral soft tissue. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.07 Tokushima
32. Araki M, Komazaki Y, Ogawa T, Tumurkhuu T, Ganburged G, Bazar A, Fujiwara T, Moriyama K. Association between malocclusion and oral health-related quality of life in Mongolian adolescents. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.07 Tokushima
33. Asami T, Ito Y, Moriyama K. Surgical orthodontic treatment of high-angle Class II malocclusion. The 29th Taiwan Association of Orthodontists Annual Meeting 2016.12.02 Taipei, Taiwan

#### **[Patents]**

1. MEDICAL DEVICE, DEVICE STRUCTURE FOR DENTAL, HEAD AND NECK SURGICAL AND ORTHOPEDIC USE, AND METHOD FOR JOINING MEDICAL DEVICE TO BONE , Announcement Number : WO 2016136913

## Maxillofacial Prosthetics

2016 April

Professor  
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Junior Associate Professor  
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HATTORI Mariko  
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Clinical Staff  
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ASWEHLEE Amel Mohamed  
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KAMIYANAGI Ayuko  
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HATANO Noriko  
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ZHANG Manjin  
LIU Rongguang

Speech-Language-Hearing Therapist  
MIBU Michiko

### (1) Outline

Department of Maxillofacial Prosthetic is the special unit of the prosthodontic and/or prosthetic treatment for patients with defects in oral and/or maxillofacial regions. The main objective of this course is to provide students with opportunity to gain sound understanding of the restoration of functional and esthetic disorders of oral and/or maxillofacial areas that are caused by congenital developmental or acquired diseases by means of the high-advanced dental and medical cares.

### (2) Research

Our department is the special unit for the prosthodontic treatment for patients with congenital or acquired defects in head and neck regions. The main goal of the research is to establish a novel theory and feedback it to the clinic to improve the quality of life of each patient. In this respect, we are focusing on several projects.

Diagnosis of functional impairment in patients with a maxillofacial defect

Treatments for functional rehabilitation of patients with a maxillofacial defect

Masticatory evaluation in patients with a maxillofacial defect

Speech evaluation in patients with a maxillofacial defect

Development of new materials for facial prosthesis

### (3) Publications

#### [Original Articles]

1. Aimaijiang Y, Otomaru T, Taniguchi H. Relationships between perceived chewing ability, objective masticatory function and oral health-related quality of life in mandibulectomy or glossectomy patients with a dento-maxillary prosthesis. *Journal of Prosthodontic Research*. 2016.04; 60(2); 92-97
2. Haraguchi M, Michi Y, Tanaka K, Harada H, Sumita YI, Harada K, Okazaki M, Taniguchi H. Appliances aimed improvement of oral form in postoperative oral cancer patients - Two modified oral stent cases -. 2016.05; 42(1); 13-20
3. Otomaru T, Sumita YI, Aimaijiang Y, Munakata Y, Tachikawa N, Kasugai S, Taniguchi H. Rehabilitation of a bilateral maxillectomy patient with a free fibula osteocutaneous flap and with an implant-retained obturator: a clinical report. *Journal of Prosthodontics*. 2016.06; 25(4); 341-348
4. Nomura K, Otomaru T, Kosaka M, Yoshi S, Said M, Taniguchi H. Prosthodontic rehabilitation of an adolescent patient with maxillary resection up to 7 years -a case report- *Maxillofacial Prosthetics*. 2016.06; 39(1); 15-20
5. Elbashti ME, Hattori M, Sumita YI, Aswehlee A, Yoshi S, Taniguchi H. Creating a digitized database of maxillofacial prostheses (obturators): A pilot study. *Journal of Advanced Prosthodontics*. 2016.06; 8(3); 219-223
6. Li N, Otomaru T, Said M, Munakata M, Tachikawa N, Kasugai S, Taniguchi H. Prosthodontic rehabilitation in a maxillectomy patient with an implant-supported overdenture: a clinical report. *Cresco Journal of Clinical Case Reports*. 2016.08; 1(1); 1-7
7. Hattori M, Sumita YI, Elbashti ME, Kurtz KS, Taniguchi H. Effect of Experimental Palatal Prosthesis on Voice Onset Time. *J Prosthodont*. 2016.08;
8. Oki M, Kanazaki A, Taniguchi H. Osteoradionecrosis following carbon ion radiotherapy: Case history report of a soft palate defect. *International Journal of Prosthodontics*. 2016.09; 29(5); 448-450
9. Elbashti ME, Sumita YI, Aswehlee AM, Haraguchi M, Otomaru T, Hattori M, Taniguchi H. Preschool and School Phases of Postmaxillectomy Prosthetic Rehabilitation in a Child: A Clinical Report. *J Prosthodont*. 2016.10;
10. Said M, Otomaru T, Aimaijiang Y, Li N, Taniguchi H. Association between masticatory function and oral health-related quality of life in partial maxillectomy patients. *International Journal of Prosthodontics*. 2016.11; 29(6); 561-564



11. Elbashti ME, Aswehlee A, Hattori M, Sumita YI, Taniguchi H. The role of digitization in the rapid reproduction of an obturator in a frail elderly patient. *International Journal of Prosthodontics*. 2016.11; 29(6); 592-594
12. Sumita YI, Hattori M, Shigen Y, Taniguchi H. Facial prosthesis using an acrylic base for a patient with a large facial defect. *JSM Dental Surgery*. 2016.11; 1(1); 1006
13. Kanazaki A, Otomaru, Said M, Li N, Taniguchi H. Effect of chewing on body sway in patients wearing dento-maxillary prosthesis after head and neck tumor resection. *Maxillofacial Prosthetics*. 2016.12; 39(2); 53-59
14. Sumita YI. Consideration point for the morphological change in a long-term follow up Maxillofacial Prosthetics. 2016.12; 39(2); 68-71
15. Yoshi S, Sumita YI, Hattori M, Ohbayashi N, Kurabayashi T, Taniguchi H. The morphological evaluation of denture space in glossectomy patients Maxillofacial Prosthetics. 2016.12; 39(2); 60-67

### [Conference Activities & Talks]

1. Sakata T, Matsumoto Y, Haraguchi M, Watanabe H, Nanba Y, Adachi T, Kaida A, Miura M, Yoshimura R, Taniguchi H. A clinical report of perioperative oral care by a dental hygienist in brachytherapy for a tongue cancer patient. The 34th Annual Meeting of Japanese Society of Oral Oncology 2016.01.22 Kanagawa
2. Kamiyanagi A, Sumita YI, Taniguchi H, Chikai M, Kimura K, Seki Y, Ino S. Evaluation of the acoustic characteristics of swallowing and expiratory sounds using throat microphone with AE sensor . Tsukuba BME Collaboration Forum 2016 2016.01.22
3. Nagai H, Haraguchi M, Sumita YI, Taniguchi H. Satisfaction improvement with a stent in postoperative edentulous mandibulectomy patient. 88th Annual Scientific Meeting of American Prosthodontic Society 2016.02 Chicago, USA
4. Said M, Otomaru T, Yeerken Y, Taniguchi H. Prosthetic treatment outcomes in partial maxillectomy patients with and without oronasal communication. 88th Annual Scientific Meeting of American Prosthodontic Society 2016.02 Chicago, USA
5. Elbashti ME, Aswehlee AM, Hattori M, Sumita YI, Taniguchi H. The role of digital technologies in maxillofacial prosthetic 3D presentations. 11th Biennial Meeting of the International Society for Maxillofacial Rehabilitation 2016.05.04 Belgrade, Serbia
6. Elbashti ME, Hattori M, Patzelt SBM, Schulze D, Sumita YI, Taniguchi H. Evaluating the feasibility and accuracy of digitizing edentulous maxillectomy defects: A comparative study. 11th Biennial Meeting of the International Society for Maxillofacial Rehabilitation 2016.05.04 Belgrade, Serbia
7. Elbashti ME, Said M, Aswehlee AM, Hattori M, Sumita YI, Taniguchi H. Maxillofacial prosthetic literature in prosthodontic journals: A 10-year observation. 11th Biennial Meeting of the International Society for Maxillofacial Rehabilitation 2016.05.04 Belgrade, Serbia
8. Elbashti ME. Application of digital technology in prosthetic rehabilitation of head and neck cancer patients. 52nd Tokyo International Exchange Center-TIEC Research and Presentation 2016.05.14 Tokyo, Japan
9. Otomaru T, Oki M, Yoshi S, Suzuki T, Taniguchi H. Consideration of a trial method to fabricate an individual lead shield in radiotherapy of eyelid tumor using three dimensional digital technology. 33rd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2016.06 Niigata
10. Kamiyanagi A, Sumita YI, Nagai H, Murase M, Haraguchi M, Hattori M, Otomaru T, Taniguchi H. A study of changes in the number of maxillectomy patients fabricated immediate surgical obturator at our department. 33rd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2016.06 Niigata
11. Li N, Otomaru T, Said M, Kamiyanagi A, Yeerken Y, Taniguchi H. Factors affecting sleep quality in maxillectomy patients with dento-maxillary prosthesis. 33rd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2016.06 Niigata



12. Elbashti ME, Hattori M, Aswehlee AM, Sumita YI, Taniguchi H. Adoption and use of digital technologies in maxillofacial prosthetics in Japan. 33rd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2016.06 Niigata
13. Sumita YI. Consideration point for the morphological change in a long-term follow-up. 21st JAMP 2016.06.04 Niigata
14. Haraguchi M, Sumita YI, Taniguchi H. Immediate surgical obturator treatment for maxillectomy patients. The 40th Annual Meeting of Japan Society for Head and Neck Cance 2016.06.09 Saitama
15. Hattori M, Sumita YI, Elbashti ME, Kelimu S, Aswehlee A, Taniguchi H. New powder-free palatogram method using sandblast: In vitro examination. 2016 meeting of the International Association of Dental Research - General Session 2016.06.25 Seoul, Korea
16. Churei H, Shrestha A, Sumita YI, Suzuki T, Matsubara H, Taniguchi H, Ueno T. Evaluation of an obturator type of sports mouthguard for a maxillectomy sports-active patient. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07 Ishikawa
17. Murase M, Yanagi A, Sumita YI, Taniguchi H. Nutrition assessment for a maxillectomy patient from preoperative period to insertion of definitive obturator period. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07 Ishikawa
18. Yanagi A, Murase M, Sumita YI, Taniguchi H. Investigation of Nutritional Status using Mini Nutritional Assessment-Short Form and Analysis of the Relevant Factors in Head and Neck Tumor/Cancer Patients. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07 Ishikawa
19. Sumita YI. Consideration of the soft tissue can brush up the dental examination. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07.10 Ishikawa
20. Hattori M. Prosthodontic treatment after maxillectomy and the spontaneously closed perforation. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07.10
21. Hattori M, Elbashti ME, Sumita YI, Taniguchi H. Visualization of voice sound in a patient after head-and-neck cancer surgery. 12th International Voice Symposium Salzburg 2016.08.28 Salzburg, Austria
22. Elbashti ME, Aswehlee A, Hattori M, Sumita YI, Taniguchi H. Geometrical evaluation of prosthetic rehabilitation effect on facial appearance of mandibulectomy patients. 2nd Annual Meeting of the International Academy for Digital Dental Medicine 2016.09.04 Busan, Korea
23. Elbashti ME, Hattori M, Patzelt SBM, Schulze D, Aswehlee A, Sumita YI, Taniguchi H. Precision and trueness of computerized optical impressions in maxillectomy defects: An in vitro 3D comparison. 2nd Annual Meeting of the International Academy for Digital Dental Medicine 2016.09.04 Busan, Korea
24. Aswehlee A, Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Feasibility and accuracy of non-contact 3D digitizers in facial defect: An in vitro 3D comparison. 2nd Annual Meeting of the International Academy for Digital Dental Medicine 2016.09.04 Busan, Korea
25. Hattori M, Aggarwal H, Kelimu S, Namba T, Nagai H, Sumita YI, Taniguchi H. Effect of palatal prosthesis on consonant duration of affricate sounds. 40th European Prosthodontic Association and 65th German Society for Prosthetic Dentistry and Biomaterials 2016.09.17 Halle, Germany
26. Sumita YI, Haraguchi M, Murase M, Yoshi S, Hattori M, Otomaru T, Taniguchi H. Prostheses for brachytherapy in TMDU. The 23rd General Meeting of the Japanese for Dental Science 2016.10 Fukuoka
27. Sumita YI, Haraguchi M, Murase M, Yoshi S, Hattori M, Otomaru T, Taniguchi H. Immediate surgical obturator in TMDU. The 23rd General Meeting of the Japanese for Dental Science 2016.10 Fukuoka
28. Haraguchi M, Tanaka K, Sumita YI, Okazaki M, Taniguchi H. Prosthetic rehabilitation for a patient with extensive vascular malformation in the head and neck region. The 63rd Annual Meeting of the American Academy of Maxillofacial Prosthetics 2016.10 San Diego, USA
29. Hatano N, Sumita YI, Otomaru T, Takano T, Taniguchi H. An application of maxillofacial prosthesis in a maxillectomy patient with edentulous maxillae and the flap. The 63rd Annual Meeting of the American Academy of Maxillofacial Prosthetics 2016.10 San Diego, USA

30. Li N, Otomaru T, Taniguchi H. Sleep survey in long-term head and neck cancer survivors with dento-maxillary prostheses. The 63rd Annual Meeting of the American Academy of Maxillofacial Prosthetics 2016.10 San Diego, USA
31. Murase M, Sumita YI, Taniguchi H. A case of mandibular retrognathia with neurofibromatosis type 1 and medication-related osteonecrosis of the jaw. The 63rd Annual Meeting of the American Academy of Maxillofacial Prosthetics 2016.10 San Diego, USA
32. Nagai H, Haraguchi M, Hattori M, Sumita YI, Taniguchi H. Speech assessment in mandibulectomy patients with stents. The 63rd Annual Meeting of the American Academy of Maxillofacial Prosthetics 2016.10 San Diego, USA
33. Hattori M, Patzelt SBM, Sumita YI, Taniguchi H. Lateral embouchure impression in the dental treatment of a saxophonist. 15.Symposium der Deutschen Gesellschaft für Musikphysiologie und Musikermmedizin 2016.10.07 Berlin, Germany
34. Yagihara K, Ishii J, Katsurano M, Tsuchida E, Okamura T, Haraguchi M, Ishikawa A, Yagishita H, Izumo T, Okabe S. Prognosis of tongue cancer patients treated with local resection plus skin graft -part 2-. 54th Annual Meeting of Japan Society of Clinical Oncology 2016.10.22 Kanagawa
35. Suzuki A, Otomaru T, Taniguchi H, Nakata H, KAsugai S, Kuroda S. A modal analysis of fixed implant supported prosthetic devices of the six abutments embedded in edentulous maxillae. 20th Annual Meeting of Japanese Academy of Maxillofacial Implants 2016.12.03 Tokyo
36. Sumita YI. Functional improvements with maxillofacial prostheses. The 2nd Scientific Meeting of Japan Prosthodontic Society "Prosthodontics '16" 2016.12.11 Tokyo

#### [Awards & Honors]

1. International Collage of Prosthodontists research grant award (Mahmoud Elbashti), International Collage of Prosthodontists, 2016.04
2. 3rd place prize winner of poster presentation award of the 11th Biennial Meeting of the International Society for Maxillofacial Rehabilitation-ISMIR (Mahmoud Elbashti), International Society for Maxillofacial Rehabilitation-ISMIR, 2016.05
3. 2nd prize of best poster award of the 2nd Annual Meeting of the International Academy for Digital Dental Medicine (Mahmoud Elbashti), International Academy for Digital Dental Medicine, 2016.09
4. First Place in the poster competition of the 63rd Annual Meeting of the American Academy of Maxillofacial Prosthetics (Li Na) , 2016.10

# Cell Biology

Professor : Takao Nakata  
Associate Professor : Akihiro Inoue  
Junior Associate Professor : Tomohiro Ishii  
Assistant Professor : Toshifumi Asano  
Technical Staff : Satoko Nakamura

## ( 1 ) Outline

We started a new laboratory from April 2009. We are interested in the cellular responses to spatio-temporal activation of signaling molecules. For this purpose, we took synthetic approaches combined with optogenetics. We introduce the photo switches into cells, and analyze signaling systems quantitatively. Research will be conducted by using molecular biology, molecular genetics, cell biology, theoretical biology, and live-imaging techniques.

## ( 2 ) Research

We are studying cell signaling using optogenetics. We made photo-switch of various signaling proteins and introduced them into cells. Parts of the cells were stimulated by blue lasers. The photo-switches were activated locally within the cells and we observe the cell phenotypes by time-lapse microscope using these techniques. We can understand molecular mechanisms of cell signaling in spatio-temporal fashion and also can manipulate cellular conditions using these switches.

## ( 3 ) Education

We teach histology and cell biology to 2nd year medical students. The courses are composed of sets of lecture and laboratory study of tissues and organs. Our goal in undergraduate course is to provide students with fundamental knowledge and skill to analyze microscopic samples of normal human body.

In new curriculum in lecture provide students information on fine structure and hints on laboratory work. This helps the students to sketch the tissue in their laboratory work. We aimed our lecture provide fundamental knowledge of human tissues and organ to learn clinical lectures. In laboratory work we adopt classical sketch of tissues because we believe it shows ability of students to search the place representative of area and extract essential structure. Evaluation depends on paper test, sketch and laboratory test.

In cell biology course we start a little bit advanced lectures such as cell death, cell cycle because we avoid to teach the same contents they have learned in past year biology course. We also provide more stimulative lectures in later half of the course such as autophagy zebrafish genetics and mathematical model.

## ( 4 ) Publications

### [Misc]

1. Tomohiro Ishii, Takao Nakata. Light manipulation of intracellular  $\text{Ca}^{2+}$  signals by a genetically encoded protein Experimental Medicine. 2016.03; 34(4); 601-606

**[Conference Activities & Talks]**

1. Shiori Seki, Tomohiro Ishii, Takao Nakata. Optical control of intracellular  $\text{Ca}^{2+}$  signals and simultaneous imaging of  $\text{Ca}^{2+}$  fluctuation and cellular events. The 121st Annual Meeting of the Japanese Association of Anatomists 2016.03.28
2. Tomohiro Ishii, Takao Nakata. BACCS, a novel optogenetic tool controlling intracellular  $\text{Ca}^{2+}$  signals. The 121st Annual Meeting of the Japanese Association of Anatomists 2016.03.28
3. Tomohiro Ishii, Takao Nakata. Optical control of  $\text{Ca}^{2+}$  signaling by a synthetic protein BACCS. International and Interdisciplinary Symposium 2016 "Towards a New Era of Cardiovascular Research" 2016.07.13 Tokyo Medical and Dental University, Tokyo
4. Tomohiro Ishii, Koji Sato, Toshiyuki Kakumoto, Shigenori Miura, Kazushige Touhara, Shoji Takeuchi, Takao Nakata. Light control of intracellular  $\text{Ca}^{2+}$  signals by a genetically encoded protein, BACCS. The 39th Annual Meeting of the Japan Neuroscience Society 2016.07.21 Pacifico Yokohama, Yokohama
5. Tomohiro Ishii, Koji Sato, Takao Nakata. A novel optogenetic tool controlling intracellular  $\text{Ca}^{2+}$  signals. 8th Symposium on Optogenetics 2016.09.29 Keio University, Mita, Tokyo

# Medical Biochemistry

Professor Yutaka Hata

Assistant Professor Hiroaki Iwasa

Assistant Professor Kyoko Arimoto-Matsuzaki

Assistant Professor Junichi Maruyama

Other two staffs

## ( 1 ) Research

- 1) The biological and chemical approach to study the Hippo pathway that controls cell proliferation, cell differentiation, and cell death.
- 2) Versatile roles of the tumor suppressive RASSF proteins
- 3) Discovery and development of chemical compounds that suppress cancer stemness and metastasis
- 4) Discovery and development of chemical compounds that facilitate myogenesis and prevent muscle atrophy
- 5) Physiological meanings of the formation of the stress granules in mammalian cells.

## ( 2 ) Education

1 : Undergraduate course

We organized the course of Biochemistry for the undergraduate students.

2 : Master course

We organized the course of Biochemistry for the master students.

3 : Others

We gave a lecture about metabolism of cancer cells.

We gave a lecture entitled "How is the life of human maintained?" for the students of Tokyo University of Foreign Studies.

## ( 3 ) Lectures & Courses

1) Undergraduate

We organize the course, "Medical Biochemistry". The students are requested through these courses to obtain a comprehensive integrated knowledge of human biochemistry, which is important to understand how health is maintained and which molecular and biochemical events cause human diseases and underlie the rational treatments.

2) Graduate and others

We are studying the signaling pathway that regulates cell proliferation, cell differentiation, cell polarity, and cell death. This pathway is well conserved from fly to human. The mutations of the components lead to oncogenesis and organ malformation. Several recent studies suggest that this pathway is implicated in inflammation and cell differentiation such as adipogenesis, osteogenesis, and keratinocyte differentiation. The pathway plays an important role in various human diseases and could be a new therapeutic target. We give lectures about

our current studies to graduate students and others, and provide graduate students with the opportunity to participate in them.

#### (4) Publications

##### [Original Articles]

1. Maruyama J, Kobayashi Y, Umeda T, Vandewalle A, Takeda K, Ichijo H, Naguro I. Osmotic stress induces the phosphorylation of WNK4 Ser575 via the p38MAPK-MK pathway. *Scientific Report*. 2016.01; 6; 18710
2. Arimoto-Matsuzaki K, Saito H, Takekawa M.. TIA1 oxidation inhibits stress granule assembly and sensitizes cells to stress-induced apoptosis. *Nature Communications*. 2016.01;
3. Nagashima S, Maruyama J, Kawano S, Iwasa H, Nakagawa K, Ishigami-Yuasa M, Kagechika H, Nishina H, Hata Y. . Validation of chemical compound library screening for transcriptional co-activator with PDZ-binding motif inhibitors using GFP-fused transcriptional co-activator with PDZ-binding motif. *Cancer Science*. 2016.07; 107(6); 791-802
4. Katano T, Fukuda M, Furue H, Yamazaki M, Abe M, Watanabe M, Nishida K, Yao I, Yamada A, Hata Y, Okumura N, Nakazawa T, Yamamoto T, Sakimura K, Takao T, Ito S. Involvement of Brain-Enriched Guanylate Kinase-Associated Protein (BEGAIN) in Chronic Pain after Peripheral Nerve Injury. *eNeuro*. 2016.10; 3(5); 110-116
5. Nagashima S, Bao Y, Hata Y.. The Hippo pathway as drug targets in cancer therapy and regenerative medicine. *Current Drug Targets*. 2016.11;

##### [Books etc]

1. Iwasa H, Shimizu T, Hata Y.. *Encyclopedia of Signaling Molecules RASSF6*. Springer, (ISBN : 978-1-4419-0460-7)
2. Xu X, Kodaka M, Iwasa H, Hata Y. *Encyclopedia of Signaling Molecules MAGI2/S-SCAM*. Springer,
3. Kodaka M, Xu X, Yang X, Maruyama J, Hata Y. *Springer Protocol Application of split-GFP reassembly assay to the study of the in vitro myogenesis and myofusion..* Springer,

##### [Misc]

1. Yutaka Hata, Takeru Sawada. Hippo tumor suppressor pathway *Journal of Molecular Targeted Therapy for Cancer*. 14(4); 10-16

## Joint Surgery and Sports Medicine

Takeshi Muneta  
Hideyuki Koga  
Kazumasa Miyatake, Mio Udo

Department of Joint Reconstruction  
Tomoyuki Mochizuki

Department of Cartilage Regeneration  
Kunikazu Tsuji  
Toshifumi Watanabe  
Hiroki Katagiri

Yoshie Seki, Enichi Nakatsuru, Arata Yuki  
Akimasa Kimura, Mikio Shioda, Kanehiro Hiyama  
Mari Uomizu, Kim Minde, Etsuko Matsumura  
Kei Inomata, Hiroko Ueki, Mai Katakura, Takashi Kondo, Shinji Hagio, Takashi Hoshino  
Masaki Amemiya, Naoko Araya, Hiroaki Onuma

Miyoko Ojima, Kahaer Abula  
Aiko Ymada, Risa Tada, Haruno Kuroda

### ( 1 ) Research

1. Development and establishment of isolation and expansion of mesenchymal stem cells
2. Research of biological characteristics of mesenchymal stem cells
3. Development and improvement of treatment method of articular cartilage defect with mesenchymal stem cells
4. Development of treatment strategy to joint structure injuries with mesenchymal stem cells
5. Development of artificial cartilage and bone
6. Development of novel agents related to bone and cartilage metabolism
7. Genetical approach to bone and cartilage metabolism
8. Clarifying mechanism and control of post-injury and postoperative inflammation with tissue fibrosis
9. Clarifying mechanism of joint pain with novel treatment strategy
10. Novel treatment strategy for cufftear

### ( 2 ) Lectures & Courses

We are working with the Orthopaedic and Spinal Surgery as a Department of Orthopaedic Surgery of University Hospital. The doctors start to have education of orthopedic surgery as a member of the department from the staffs of the department of Orthopaedic Surgery according to the orthopaedic education and training program after completing the two-year fundamental education and training program as a junior resident. They experience a lot of traumatic patients and deepen their basic orthopaedic skills for two-year junior orthopaedic training in one of the branch hospitals every year. They expand their skills and obtain orthopaedic specialty educations in the advanced two-year education and training program. After completing a six-year educational program of the

orthopaedic surgery, they are recommended to apply to the orthopedic specialist form the Japanese Orthopaedic Association. They usually apply to enter the graduate school program after 4 or 5 years of clinical experience.

We encourage not only orthopedic doctors but doctors of other specialty, veterinarian doctors and physical therapists, etc to work with us.

### ( 3 ) Clinical Services & Other Works

Treatment for sports injuries

Prevention, conservative treatment and rehabilitation for sports injuries

Anatomic double-bundle anterior cruciate ligament (ACL) reconstruction for ACL injuries

Surgical treatment for knee multiple ligament injuries

Surgical treatment for meniscal injuries to restore meniscal function

Regenerative medicine for unrepairable meniscus and cartilage injuries

Treatment for osteoarthritis (OA)

Conservative approaches to early OA

Joint-sparing surgeries such as osteotomies for moderate OA

Total arthroplasties for severe OA

Clinical researches and clinical results for above-mentioned approaches have been presented at both domestic and international congresses, as well as reported in Japanese and English articles.

### ( 4 ) Clinical Performances

Sports injuries

We have been performing double-bundle ACL reconstruction since 1994 as a pioneer, and reported good clinical outcomes regarding knee stability, ratio of return to sports and patients' satisfaction. As for meniscal surgeries, we have been trying to repair as much as possible to restore meniscal function. In addition, we have developed a novel surgical procedure to restore meniscal function for patients with post-menisectomy and discoid meniscus. We have also analyzed mechanisms and preventive methods for ACL injuries, and first in the world clarified a detailed ACL injury mechanism. Based on the findings, various approaches to ACL injury prevention and rehabilitation after ACL reconstruction is being conducted.

Arthroplasties

We have developed a new total knee system called Actiyas, named after the combination of active and healed ("iyas" in Japanese), which is specifically designed for Japanese. In order to develop this, we analyzed Japanese bone morphology, and this system is designed for more functional and "active" motion without knee pain, and eventually patients to be "healed". Ceramic is used for the femoral implant, by which we can expect lesser implant wear, resulting in better long-term results. We perform simultaneous bilateral arthroplasties for Bilateral OA patients, helping them earlier return to daily life.

Regenerative medicine for cartilage and meniscus injuries using synovial stem cells

Based on numerous basic researches performed in our laboratory, we started stem cell therapy for cartilage injuries using synovial stem cells since April 2008. In this therapy, we take synovium from patients at day surgery, culture synovial stem cells at the cell processing center in our university, and transplant them arthroscopically. The safety and effectiveness had been already confirmed. In addition, we also started a clinical trial of synovial stem cell transplantation for unrepairable meniscal tear since August 2014.

### ( 5 ) Publications

#### [Original Articles]

1. Takashi Ikeda, Junya Aizawa, Hiroshi Nagasawa, Ikuko Gomi, Hiroyuki Kugota, Keigo Nanjo, Tetsuya Jinno, Tadashi Masuda, Sadao Morita. Effects and feasibility of exercise therapy combined with branched



- chain amino acid supplementation on muscle strengthening in frail and pre-frail elderly people requiring long-term care: A crossover trial *Applied Physiology, Nutrition, and Metabolism*. 2016; 41(4); 438-445
2. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Yuki Yamauchi, Yoshinori Asou, Takeshi Muneta, Atsushi Okawa. Limited significance of screening computed tomography after cementless total hip arthroplasty with highly cross-linked polyethylene at 7 to 10 years of follow-up *Mod Rheumatol*. 2016; 26(5); 757-760
3. Tsuyoshi Yamada, Toshitaka Yoshii, Satoru Egawa, Ryohei Takada, Takashi Hirai, Hiroyuki Inose, Tsuyoshi Kato, Tetsuya Jinno, Atsushi Okawa. Drain tip culture is not prognostic for surgical site infection in spinal surgery under prophylactic use of antibiotics *Spine (Phila Pa 1976)*. 2016; 41(14); 1179-1184
4. Takanori Kokubun, Naohiko Kanemura, Kenji Murata, Hideki Moriyama, Sadao Morita, Tetsuya Jinno, Hidetoshi Ihara, Kiyomi Takayanagi. Effect of changing the joint kinematics of knees with a ruptured anterior cruciate ligament on the molecular biological responses in a spontaneous healing in a rat model *Am J Sports Med*. 2016; 44(11); 2900-2910
5. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Masanobu Hirao, Takeshi Muneta, Atsushi Okawa. Comparison of wear rate and osteolysis between annealed and remelted highly cross-linked polyethylene in total hip arthroplasty. A 7 to 10 year follow-up *Orthop Traumatol Surg Res*. 2016; 102(6); 707-721
6. Yusuke Nakagawa, Ichiro Sekiya, Shimpei Kondo, Takashi Tabuchi, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Takeshi Muneta. Relationship between MRI T1 rho value and histological findings of intact and radially incised menisci in microminipigs. *J Magn Reson Imaging*. 2016.02; 43(2); 434-445
7. Yusuke Nakagawa, Takeshi Muneta, Koji Otabe, Nobutake Ozeki, Mitsuru Mizuno, Mio Udo, Ryusuke Saito, Katsuaki Yanagisawa, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Cartilage Derived from Bone Marrow Mesenchymal Stem Cells Expresses Lubricin In Vitro and In Vivo. *PLoS ONE*. 2016.02; 11(2); e0148777
8. Toshifumi Watanabe, Takeshi Muneta, Kazuyoshi Yagishita, Kenji Hara, Hideyuki Koga, Ichiro Sekiya. Closed Suction Drainage Is Not Necessary for Total Knee Arthroplasty: A Prospective Study on Simultaneous Bilateral Surgeries of a Mean Follow-Up of 5.5 Years. *J Arthroplasty*. 2016.03; 31(3); 641-645
9. Katsuaki Yanagisawa, Takeshi Muneta, Nobutake Ozeki, Yusuke Nakagawa, Mio Udo, Ryusuke Saito, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Weekly injections of Hylan G-F 20 delay cartilage degeneration in partial meniscectomized rat knees. *BMC Musculoskelet Disord*. 2016.04; 17(1); 188
10. Kazumasa Miyatake, Takeshi Muneta, Miyoko Ojima, Jun Yamada, Yu Matsukura, Kahaer Abula, Ichiro Sekiya, Kunikazu Tsuji. Coordinate and synergistic effects of extensive treadmill exercise and ovariectomy on articular cartilage degeneration. *BMC Musculoskelet Disord*. 2016.05; 17(1); 238
11. Nobutake Ozeki, Takeshi Muneta, Hideyuki Koga, Yusuke Nakagawa, Mitsuru Mizuno, Kunikazu Tsuji, Y Mabuchi, C Akazawa, E Kobayashi, K Matsumoto, K Futamura, T Saito, Ichiro Sekiya. Not single but periodic injections of synovial mesenchymal stem cells maintain viable cells in knees and inhibit osteoarthritis progression in rats. *Osteoarthr. Cartil.*. 2016.06; 24(6); 1061-1070
12. Hideyuki Koga, Takeshi Muneta. Graft impingement ACL Injury and Its Treatment. 2016.06; 267-278
13. Hideyuki Koga, Takeshi Muneta. ACL injury mechanisms ACL Injury and Its Treatment. 2016.06; 113-128
14. Takeshi Muneta, Hideyuki Koga. Part X Revision ACL Reconstruction. 36 Double-Bundle Technique. ACL Injury and Its Treatment, Ochi M, Shino K, Yasuda K, Kurosaka M, Eds.. 2016.06; 453-468
15. Mio Udo, Takeshi Muneta, Kunikazu Tsuji, Nobutake Ozeki, Yusuke Nakagawa, Toshiyuki Ohara, Ryusuke Saito, Katsuaki Yanagisawa, Hideyuki Koga, Ichiro Sekiya. Monoiodoacetic acid induces arthritis and synovitis in rats in a dose- and time-dependent manner: proposed model-specific scoring systems. *Osteoarthr. Cartil.*. 2016.07; 24(7); 1284-1291
16. Takeshi Muneta, Hideyuki Koga, Tomomasa Nakamura, Masafumi Horie, Toshifumi Watanabe, Ichiro Sekiya. Behind-remnant arthroscopic observation and scoring of femoral attachment of injured anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc*. 2016.09; 24(9); 2906-2914

17. Hideyuki Koga, Takeshi Muneta, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Yusuke Nakagawa, Ichiro Sekiya. Two-Year Outcomes After Arthroscopic Lateral Meniscus Centralization. *Arthroscopy*. 2016.10; 32(10); 2000-2008
18. Arata Yuuki, Takeshi Muneta, Toshiyuki Ohara, Ichiro Sekiya, Hideyuki Koga. Associated lateral/medial knee instability and its relevant factors in anterior cruciate ligament-injured knees. *J Orthop Sci*. 2016.11;
19. Toshifumi Watanabe, Takeshi Muneta, Hideyuki Koga, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Yusuke Nakagawa, Mai Katakura, Ichiro Sekiya. In-vivo kinematics of high-flex posterior-stabilized total knee prosthesis designed for Asian populations. *Int Orthop*. 2016.11; 40(11); 2295-2302
20. Kaori Nakamura, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Takeshi Muneta. Dynamic Evaluation of Pivot-Shift Phenomenon in Double-Bundle Anterior Cruciate Ligament Reconstruction Using Triaxial Accelerometer. *Arthroscopy*. 2016.12; 32(12); 2532-2538
21. Toshiyuki Ohara, Takeshi Muneta, Yusuke Nakagawa, Yu Matsukura, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. < Original Article> Hypoxia enhances proliferation through increase of colony formation rate with chondrogenic potential in primary synovial mesenchymal stem cells. *J. Med. Dent. Sci.*. 2016.12; 63(4); 61-70

### [Conference Activities & Talks]

1. Gaku Koyano, Tetsuya Jinno, Daisuke Koga, Takeshi Muneta, Atsushi Okawa. Bilateral Comparison of Hip Joint Morphology between the Hips with and without Herniation Pit. *Orthopaedic Research Society* 2016.03
2. Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Clinical Outcomes after Arthroscopic Centralization of an Extruded Lateral Meniscus. *AAOS* 2016.03.02
3. Toshiyuki Ohara, Takeshi Muneta, Yusuke Nakagawa, Yu Matsukura, Kunikazu Tsuji, Ichiro Sekiya. Hypoxia enhances proliferation with chondrogenic potential in primary synovial MSCs. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05
4. Yusuke Nakagawa, Hideyuki Koga, Takeshi Muneta, Kiuchi S, Ono H, Nagata T, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Hisako Katano, Ichiro Sekiya. Three-dimensional Reconstructed MRI Evaluation of Arthroscopic Centralization Technique for Extruded Lateral Meniscus. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05
5. Toshifumi Watanabe, Takeshi Muneta, Ichiro Sekiya, Hideyuki Koga, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Scott Banks. In-vivo Kinematics of Posterior-stabilized Total Knee Prosthesis Designed for Asian. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05
6. Kaori Nakamura, Kunikazu Tsuji, Hiroki Katagiri, Makiko Inoue, Miyoko Ojima, Ichiro Sekiya, Takeshi Muneta. Dynamic analysis of inflammatory cells in synovial fluid after index anterior cruciate ligament reconstruction surgery. *Osteoarthritis Research Society 2016 Annual Meeting* 2016.03.05
7. Etsuko Matsumura, Takeshi Muneta, Kunikazu Tsuji, Keiichiro Komori, Ichiro Sekiya. IL-1  $\beta$  Enhances Proliferation And Chondrogenic Potential Of Synovial MSCs. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05 Orlando, USA
8. Nobutake Ozeki, Junpei Matsuda, Takeshi Muneta, Hideyuki Koga, Kunikazu Tsuji, Kenta Katagiri, Mitsuru Mizuno, T Saito, Ichiro Sekiya. Biomechanical analysis of centralization with an anchor for meniscus extrusion in a porcine model. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05 Orlando, USA
9. Yuji Kohno, Mitsuru Mizuno, Kenta Katagiri, Koji Otabe, Nobutake Ozeki, Masafumi Horie, Hideyuki Koga, Kunikazu Tsuji, Mikio Matsumoto, Haruka Kaneko, Yuji Takazawa, Takeshi Muneta, Ichiro Sekiya. Yields and chondrogenic potential of synovial MSCs are comparable between RA and OA patients who undergo TKA. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05

10. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Nobutake Ozeki, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya. PDGF-AA/AB In Human Serum Are Potential Indicators Of The Proliferative Capacity Of Human Synovial Mesenchymal Stem Cells. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
11. Mitsuru Mizuno, Hisako Katano, Yo Mabuchi, Yusuke Ogata, Shizuko Ichinose, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Nobutake Ozeki, Kunikazu Tsuji, Chihiro Akazawa, Takeshi Muneta, Ichiro Sekiya. Properties of MSCs Derived From Surface, Stroma, and Perivascular Synovium Of Oa Patients. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
12. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya. Interleukin-1  $\beta$  Promotes In Vitro Chondrogenesis Of Synovial Mesenchymal Stem Cells. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
13. Hideyuki Koga, Kaori Nakamura, Ichiro Sekiya, Takeshi Muneta. Minimum required tension in double-bundle anterior cruciate ligament reconstruction based on objective evaluation of pivot shift phenomenon using triaxial accelerometer. ACL Study Group Meeting 2016.03.13
14. Miyoko Ojima, Kunikazu Tsuji, Koji Otabe, Masafumi Horie, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Different methods of detaching adherent cells significantly affect the detection of stem cell antigens in synovial mesenchymal stem cells.. OARSI 2016 World Congress on Osteoarthritis 2016.03.31
15. Hideyuki Koga. Keynote lecture: ACL injury - video analysis. 17th ESSKA 2016.05.04 Barcelona, Spain
16. Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Clinical and Radiographic Outcomes after Arthroscopic Centralization of Lateral Meniscus Extrusion. 17th ESSKA 2016.05.04 Barcelona, Spain
17. Toshifumi Watanabe, Takeshi Muneta, Kenji Hara, Hideyuki Koga, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Yusuke Nakagawa, Mai Katakura, Atsushi Okawa, Ichiro Sekiya. Is Closed Suction Drainage Necessary for Total Knee Arthroplasty? :A Prospective Study of a Mean Follow-up of 5.5 Years. 89th Annual Meeting of JOA 2016.05.12 Yokohama, Japan
18. Hideyuki Koga, Takeshi Muneta, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Yusuke Nakagawa, Mai Katakura, Atsushi Okawa, Ichiro Sekiya. Two-year results of remnant-preserved double-bundle anterior cruciate ligament reconstruction: Frontside approach versus behind-remnant approach. 89th JOA 2016.05.12 Yokohama, Japan
19. Hideyuki Koga, Takeshi Muneta, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Yusuke Nakagawa, Mai Katakura, Atsushi Okawa, Ichiro Sekiya. Clinical outcomes after arthroscopic centralization of lateral meniscus extrusion. 89th JOA 2016.05.12 Yokohama, Japan
20. Mari Uomizu, Hideya Yoshimura, Akimoto Nimura, Takashi Miyamoto, Tomoyuki Mochizuki. Return to Sports Activity after Arthroscopic Rotator Cuff Repair on the Middle-aged and Senior Patients. The 13th International Congress of Shoulder and Elbow Surgery 2016.05.18 Korea
21. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Masanobu Hirao, Takeshi Muneta, Atsushi Okawa. Comparison of wear rate and osteolysis between annealed and remelted highly cross-linked polyethylene in total hip arthroplasty. 17th EFORT 2016.06
22. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Masanobu Hirao, Takeshi Muneta, Atsushi Okawa. Limited significance of screening computed tomography after cementless total hip arthroplasty with highly cross-linked polyethylene. 17th EFORT 2016.06
23. Hideyuki Koga. Arthroscopic Centralization of an Extruded Lateral Meniscus. JOSKAS-SIGASCOT travelling fellowship 2016.09.20 Parma, Italy
24. Hideyuki Koga. Arthroscopic Centralization of an Extruded Lateral Meniscus. JOSKAS-SIGASCOT travelling fellowship 2016.09.22 Milan, Italy
25. Etsuko Matsumura, Kunikazu Tsuji, Keiichiro Komori, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Investigate the effects of pretreatment of IL-1  $\beta$  on proliferation and chondrogenic differentiation of synovial MSCs. ICRS 2016 2016.09.24

26. Miyoko Ojima, Kunikazu Tstuji, Koji Otabe, Masafumi Horie, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Analyses of biologically active substances in synovial fluid which support proliferation of synovial mesenchymal stem cells. International Cartilage Repair Society 2016 Annual Meeting 2016.09.24
27. Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Two-year outcomes after arthroscopic centralization of an extruded lateral meniscus. 6th SIGASCOT 2016.09.28 Florence, Italy
28. Hideyuki Koga. Arthroscopic Centralization of an Extruded Lateral Meniscus. JOSKAS-SIGASCOT travelling fellowship 2016.10.03 Rome, Italy
29. Hideyuki Koga. Minimum required tension in double-bundle ACL reconstruction based on objective evaluation of pivot shift phenomenon using triaxial accelerometer. JOSKAS-SIGASCOT travelling fellowship 2016.10.03 Rome, Italy
30. Hideyuki Koga. Minimum required tension in double-bundle ACL reconstruction based on objective evaluation of pivot shift phenomenon using triaxial accelerometer. JOSKAS-SIGASCOT travelling fellowship 2016.10.05 Rome, Italy

## Biostructural Science

Associate Professor: Makoto TABATA  
Technician: Makoto SUGIURA  
Secretary: Tomoko YAMAMOTO  
Graduate Student: Takafumi NAKANO

### ( 1 ) Outline

Section of biostructural science is the inheritor of the laboratory of Oral Anatomy II, then our focus is understanding of the mechanism and histology of tooth formation. And also we study the tooth evolution using fish scale and tooth.

### ( 2 ) Research

The study of the mechanisms of dental formation and their evolution is the central focus of our research. Followings are rough description of current research subjects in our laboratory.

- 1) Study of the mechanism in tooth development
- 2) Study of the mechanism in ameloblast differentiation
- 3) Histological and developmental study of fish scales and teeth
- 4) Space experiments for the bone biology using fish

### ( 3 ) Lectures & Courses

We are inheritor of the laboratory of Oral Anatomy II, then we involved in the education of histology, embryology, and oral histology.

In the first place, anatomy and histology is the study to learn the structure, the name, and the function of "HUMAN BODY". Then the subject histology is not able to separate from subject anatomy, relate to physiology, pathology, and embryology and further become to be the fundamentals of clinical subjects. So we carry out of our subjects, with an awareness of the relationships between histology and other subjects.

On the curriculum of the 2nd grade of dental students, lectures of histology contains practical histology using tissue sections and microscopy. This skills work is a good opportunity to know the variation and the finesse of the human body in histology.

# Pharmacology

Staffs and Students(April, 2016)

Associate Professor Kazuhiro AOKI  
Assistant Professor Yukihiro TAMURA  
Technologist Mariko TAKAHASHI

Researchers  
Nobuyoshi TOMOMATSU (Maxillofacial Surgery)  
Yasuhiro SHIMIZU (Orthodontic Science)  
Tomoki UEHARA (Pediatric Dentistry)  
Yuki ARAI (Removable Prosthodontics)

Graduate Students  
Md. Haque Bhuyan ZAHIRUL  
Toru TAKEMOTO(Oral and Maxillofacial Surgery)  
Kenya YONEDA(Regenerative Dental Medicine)  
Hideaki INAGAWA(Removal Prosthodontics)  
Eri SONE(Maxillofacial Surgery)  
Hisami OKAWARA(Removable Prosthodontics)  
Michiko OZAWA

Lecturers  
Etsuko TAKAHASHI  
Akira NIFUJI  
Nozomi HASEGAWA  
Eiichi MURASE  
Yoshihiro WAKI  
Hiroyuki SETO  
Toshimi SATO  
Genki KATO  
Setsuko MISE  
Kiichi NONAKA

## ( 1 ) Research

Research subjects

- 1) Pharmacological analyses of formation and resorption on bones and teeth
- 2) Identification of a new therapeutic target for hard tissue-related diseases
- 3) Translational research for hard tissue regeneration
- 4) Interdisciplinary research toward the application of peptide drug
- 5) Analyses of drug side effects appeared at oral tissues

**( 2 ) Lectures & Courses**

## Purpose of Education

Pharmacology is situated between the basic and clinical sciences and is important for dental students. There is a growing demand on the dental clinicians to know huge knowledge of drugs and how to use them for patients. For these purpose, the first lecture is aimed to teach the scientific aspects of pharmacology and how drugs act on the various organ system. The second lecture deals with drugs of medical and dental fields and the last with drugs of special importance of dentistry. Dental students learn the principle of pharmacology through laboratory practice. Following these learning, they must acquire an adequate background for drug use in general practice.

**( 3 ) Publications****[Original Articles]**

1. Trang N Nguyen Vo, Jia Hao, Josh Chou, Masamitsu Oshima, Kazuhiro Aoki, Shinji Kuroda, Boosana Kaboosaya, Shohei Kasugai. Ligature induced peri-implantitis: tissue destruction and inflammatory progression in a murine model. *Clin Oral Implants Res.* 2016.01;
2. T Uehara, S Mise-Omata, M Matsui, Y Tabata, R Murali, M Miyashin, K Aoki. Delivery of RANKL-Binding Peptide OP3-4 Promotes BMP-2-Induced Maxillary Bone Regeneration. *J. Dent. Res.* 2016.03;
3. Moe Htet, Marwa Madi, Ossama Zakaria, Takayuki Miyahara, Wang Xin, Zayar Lin, Kazuhiro Aoki, Shohei Kasugai. Decontamination of Anodized Implant Surface with Different Modalities for Peri-Implantitis Treatment: Lasers and Mechanical Debridement with Citric Acid. *J. Periodontol.* 2016.03; 1-17
4. Yuki Arai, Kazuhiro Aoki, Yasuhiro Shimizu, Yasuhiko Tabata, Takashi Ono, Ramachandran Murali, Setsuko Mise-Omata, Noriyuki Wakabayashi. Peptide-induced de novo bone formation after tooth extraction prevents alveolar bone loss in a murine tooth extraction model. *Eur. J. Pharmacol.* 2016.07; 782; 89-97
5. Yasutaka Sugamori, Setsuko Mise-Omata, Chizuko Maeda, Shigeki Aoki, Yasuhiko Tabata, Ramachandran Murali, Hisataka Yasuda, Nobuyuki Udagawa, Hiroshi Suzuki, Masashi Honma, Kazuhiro Aoki. Peptide drugs accelerate BMP-2-induced calvarial bone regeneration and stimulate osteoblast differentiation through mTORC1 signaling. *Bioessays.* 2016.08; 38(8); 717-725

**[Conference Activities & Talks]**

1. Yukihiro Tamura, Setsuko Mise, Yasutaka Sugamori, Md. Zahirul Haq Bhuyan, Mariko Takahashi, Tomoki Uehara, Yuki Arai, Michiyo Miyashin, Noriyuki Wakabayashi, Kazuhiro Aoki. A pharmacological role of metallothionein in zinc-treated cartilage-progenitor cells. APFP 2016(The 13th Asia Pacific Federation of Pharmacologists Meeting) 2016.02.01 The Berkeley Hotel Pratunam, Bangkok (Thailand)
2. Mikami R, Aoki A, Mizutani K, Tamura Y, Aoki K, Izumi Y. Low-level laser irradiation using a high-frequency ultra-short pulsed blue laser enhances osteoblasts proliferation and differentiation. The 59th Spring Meeting of The Japanese Society of Periodontology 2016.05.20 Kagoshima
3. Md.Zahirul Haque Bhuyan, Chizuko Maeda, Yuki Yoshinari, Marin Kawasaki, Yasutaka Sugamori, Genki Kato, Mariko Takahashi, Yukihiro Tamura, Kazuhiro Aoki. The therapeutic effects of the RANKL-binding peptides on cartilage destruction.. 13th Bone Biology Forum 2016.08.20 Cross Wave Makuhari (Chiba)
4. Mikami R, Aoki A, Mizutani K, Tamura Y, Aoki K, Izumi Y. Low-level blue laser irradiation enhances osteoblast proliferation and differentiation. The 102nd Annual Meeting of the American Academy of Periodontology 2016.09.10 San Diego, USA
5. Mikami R, Aoki A, Mizutani K, Tamura Y, Aoki K, Izumi Y. Low-level blue laser irradiation enhances osteoblast proliferation and differentiation. The 102nd Annual Meeting of the American Academy of Periodontology 2016.09.10 San Diego Convention Center(USA)



# Connective Tissue Regeneration

Associate Professor Tamayuki SHINOMURA

## (1) Outline

Our group is interested in the restoration of damaged connective tissue. In general, connective tissue is characterized by the presence of abundant extracellular matrix, and its function is highly dependent on the properties of extracellular matrix. Therefore, to restore connective tissue normal, it is essential for us to understand the behavior of extracellular matrix molecules. So, we pursue research on the molecular mechanisms underlying the formation and maintenance of extracellular matrix in connective tissues.

## (2) Research

Currently, we are engaged in the following research subject.

1. Study on the mechanisms that regulate the expression of type II collagen and aggrecan in chondrocytes.
2. Study on transcription factors necessary for the maintenance of chondrogenic phenotype.
3. Study on the molecular dynamics of extracellular matrix in connective tissues.

## (3) Education

We give a lecture on molecular biology in general and laboratory exercise for undergraduate students. Also, in our graduate course, we offer lectures on the synthesis and formation of extracellular matrix focusing on cartilage tissue.

## (4) Lectures & Courses

We provide education based on the belief that an integrated and organized connection of various knowledge is important to understand life phenomena.

## (5) Publications

### [Original Articles]

1. K, Ito, T. Shinomura. Development and application of a new silent reporter system to quantitate the activity of enhancer elements in the type II collagen gene *Gene*. 2016.03; 585; 13-21
2. Tani, H., Sato, Y., Ueda, M., Miyazaki, Y., Suginami, K., Horie, A., Konishi, I., and Shinomura, T.. Role of Versican in the Pathogenesis of Peritoneal Endometriosis *The Journal of Clinical Endocrinology & Metabolism*. 2016.11; 101(11); 4349-4356



3. Nakayama Y, Kobayashi R, Matsui S, Matsumura H, Iwai Y, Noda K, Yamazaki M, Kurita-Ochiai T, Yoshimura A, Shinomura T, Ganss B, Ogata Y.. Localization and expression pattern of amelotin, odontogenic ameloblast-associated protein and follicular dendritic cell-secreted protein in the junctional epithelium of inflamed gingiva *Odontology*. 2016;11;

# Biochemistry

Professor Testuro Watabe  
 Associate Professor Miki Yokoyama  
 Junior Associate Professor Yasuhiro Kumei  
 Assistant Professor Katarzyna Anna Podyma-Inoue  
 Technical staff Kazue Terasawa  
 Part-time Lecturer Zeredo, Jorge Luis Lopes, Akira Asari  
 Graduate student Akihiko Inagawa, Takumi Matsuda  
 Postgraduate Rajapakshe Mudiyanseelage Anupama Rasadari Rajapakshe

## (1) Outline

Since cancer is the leading cause of death in Japan, we need to develop novel strategies to cure it. Tumor consists of not only cancer cells but also the non-cancerous cells including fibroblasts, immune cells and cells that comprise the blood and lymphatic vessels. We aim to elucidate the mechanisms how cancer cells become malignant by the various cytokines in cancer microenvironment in order to develop novel therapeutic strategies targeting multiple components of cancer microenvironment.

## (2) Research

### (1) Understanding the molecular mechanisms underlying endothelial-mesenchymal transition (EndMT)

Endothelial cells undergo differentiation into mesenchymal cells during not only various physiological processes including heart valve formation but also pathological processes including cancer progression, heart failure and diabetes. However, the molecular mechanisms that regulate such endothelial-mesenchymal transition (EndMT) remain to be elucidated. We aim to study the molecular mechanisms underlying EndMT in order to identify novel targets and attempt to develop therapeutic strategies for EndMT-related diseases.

### (2) Elucidation of the molecular mechanisms underlying tumor angio- and lymphangiogenesis

Tumor angiogenesis and lymphangiogenesis are key features of tumor progression and metastasis. While multiple signaling pathways have been implicated in the formation of blood and lymphatic vessels, the molecular mechanisms underlying these processes have not yet fully elucidated. Recent findings revealed that members of the transforming growth factor- $\beta$  (TGF- $\beta$ ) family play pivotal roles on in angiogenesis and lymphangiogenesis, and that abnormalities in TGF- $\beta$  family signaling lead to development of certain vascular disorders, including hereditary hemorrhagic telangiectasia (HHT), pulmonary arterial hypertension, Marfan syndrome and Loeys-Dietz syndrome. We attempt to elucidate the molecular mechanisms how TGF- $\beta$  family signals regulate angiogenesis and lymphangiogenesis in tumor microenvironment.

### (3) Understanding the molecular mechanisms underlying metastasis of cancer cells

Epithelial-mesenchymal transition (EMT) plays important roles in various physiological and pathological processes, and is regulated by signaling pathways mediated by cytokines including TGF- $\beta$ . Using various types of in vitro cultured oral carcinoma cells and in vivo systems, we aim to identify the molecules involved in the acquisition of invasive properties of cancer cells, in order to develop novel therapeutic strategies.

### (4) Structural and functional mapping of lysosomal membranes

Lysosomes are ubiquitous organelles rich in hydrolytic enzymes, responsible for the degradation of macro-

molecules derived from the extracellular space through endocytosis or phagocytosis, and from the cytoplasm through autophagy. These processes are vital to acquire energy source and essential materials, to defend against pathogen, and to clear unnecessary or potentially harmful intracellular obstacles. Furthermore, accumulating evidence has revealed that the lysosome surface is a crucial site for the activation of mammalian or mechanistic target of rapamycin complex 1 (mTORC1), a master regulator of cell growth and metabolism. mTORC1. Clinically, impairment of lysosome function gives rise to progressive and ultimately serious damages in widespread tissue and organ, particularly in brain, bones and connective tissues.

Lysosome-associated membrane proteins 1 and 2 (LAMP-1 and LAMP-2) have a large, heavily glycosylated luminal domain composed of the two subdomains, and are the most abundant protein components in lysosome membranes. LAMP-1 and LAMP-2 have distinct functions, and the presence of both proteins together is required for the vital essential regulation of autophagy to avoid embryonic lethality. However, the structural aspects of LAMP-1 and LAMP-2 have not been elucidated. Here, we demonstrated that the subdomains of LAMP-1 and LAMP-2 have adopted the unique  $\beta$ -prism fold. Furthermore, we found that the N-domain of the LAMP-1 is necessary, whereas that of LAMP-2 is repressive, for the organization of a multimeric assembly of the LAMPs. Accordingly, the present study suggests for the first time that the assembly modes of LAMP-1 and LAMP-2 are different, which may underlie their distinct functions [ *Biochemical and Biophysical Research Communications* 479, 489-495 (2016)] .

#### (5) Heparan sulfate proteoglycan-dependent cellular logistics

Heparan sulfate proteoglycans (HSPGs) are one of the basic constituents of plasma membranes and have ability to interact with a number of the extracellular ligands. HSPGs have been suggested to mediate the trafficking of various macromolecules from the cell surface. Growth factors, cytokines, lipoproteins, cell penetrating peptides, polycation-nucleic acid complexes, along with exosomes, and pathogens enter cells through HSPG-dependent endocytosis. HSPGs-dependent endocytic events have been involved in tumor progression, stressing the importance of the identification of HSPG species participating in a formation of various endocytic complexes. We have characterized the intracellular trafficking complexes formed in the presence of HSPGs in a rat C6 glioma cell line model. Successful isolation of HSPG-positive transport vesicles followed by detailed proteomic analysis allowed us the identification of over eighty proteins related to vesicular transport; i.e. endocytosis or recycling. Part of HSPGs in glioma cells found to be internalized through clathrin-dependent endocytosis and underwent recycling. Further characterization of HSPG-rich vesicular compartments will help us understand the nature of HSPG-ligand interactions and to design the tools for targeted delivery of ligands into the cells (reported in *Cancer Genomics & Proteomics*, 2016, 13, 443-452).

#### (6) Posture, behavior, and motion sickness of common marmosets in low gravities.

In planetary development projects such as manned Mars exploration that will take longer than 3 years, long-term biological adaptation to weightlessness and partial-gravity environments is a critical issue. Since rodents of short lifespan (rats and mice) cannot survive in such a long-term flight, other animals of longer lifespan must be used alternatively so as to conduct appropriate studies on posture and exploration as well as voice communication and social behaviors of animals that have some relevance to long-term manned spaceflight. Common marmoset belonging to the same anthropoid with humans has a lifespan of 15 years is characterized by unique social behavior resembling humans with abundant squealing. In parabolic flight experiment carried out in February 2016, we first examined the adaptation and social behavior of common marmoset under such conditions as Moon and Mars simulation or weightlessness. We have gained new knowledge on the response and behavior of primates in partial gravities.

### (3) Education

For the second-year undergraduate students, we are in charge of the unit, “Molecular aspect of cell biology” and “Laboratory course” under the module of “Molecular basis of biology” . The contents of “Molecular aspect of cell biology (lecture)” includes, topics related to the structure and function of membranes, transport across membranes, organization and function of intracellular organelles, intracellular trafficking, cytoskeleton, extracellular matrix, signal transduction, cell cycle and cell death. During the laboratory course, the purification and characterization of an enzyme (pH-dependency, effects of inhibitors, comparison of isozymes, kinetic analysis) were done.

For the graduate students, in order to demonstrate various research examples, we lectured on the following

subjects; (1) cell-surface assembly of proteins (CD38 as an example), (2) membrane domains (lipid rafts) and sphingosine-1-phosphate signaling, (3) structure and function of proteoglycans, (4) structure and role of extracellular matrix (5) analysis of the response to the gravity change at a cellular and individual levels and its clinical application. All the lectures were done in English. We also hold the special lectures "Tissue Myeloid Progenitors Differentiate into Pericytes in Developing Skin Vasculature" (October 14, 2016) and "New function of lysosomes in osteoclasts and osteoblasts" (December 22, 2016).

#### (4) Lectures & Courses

For the undergraduate students, our aim is to provide the students with the basic knowledge in biochemistry to help them to understand cellular function based on the structure and function of biomolecules. For the graduate students, we encourage them to acquire an ability and research skill to study the cellular responses at molecular levels.

#### (5) Publications

##### [Original Articles]

1. Masato Morikawa, Daizo Koinuma, Anna Mizutani, Natsumi Kawasaki, Katarina Holmborn, Anders Sundqvist, Shuichi Tsutsumi, Tetsuro Watabe, Hiroyuki Aburatani, Carl-Henrik Heldin, Kohei Miyazono. BMP Sustains Embryonic Stem Cell Self-Renewal through Distinct Functions of Different Krüppel-like Factors. *Stem Cell Reports*. 2016.01; 6(1); 64-73
2. Akihiro Katsura, Hiroshi I Suzuki, Toshihide Ueno, Hajime Mihira, Tomoko Yamazaki, Takahiko Yasuda, Tetsuro Watabe, Hiroyuki Mano, Yoshitsugu Yamada, Kohei Miyazono. MicroRNA-31 is a positive modulator of endothelial-mesenchymal transition and associated secretory phenotype induced by TGF- $\beta$ . *Genes Cells*. 2016.01; 21(1); 99-116
3. Fusa Ogata, Katsuhito Fujiu, Sahohime Matsumoto, Yukiteru Nakayama, Munehiko Shibata, Yuichi Oike, Isao Koshima, Tetsuro Watabe, Ryoza Nagai, Ichiro Manabe. Excess Lymphangiogenesis Cooperatively Induced by Macrophages and CD4(+) T Cells Drives the Pathogenesis of Lymphedema. *J. Invest. Dermatol.* 2016.03; 136(3); 706-714
4. Kyohei Muguruma, Fumika Yakushiji, Ryosuke Kawamata, Daichi Akiyama, Risako Arima, Takuya Shirasaka, Yamato Kikkawa, Akihiro Taguchi, Kentaro Takayama, Takeshi Fukuhara, Tetsuro Watabe, Yuji Ito, Yoshio Hayashi. Novel Hybrid Compound of a Plinabulin Prodrug with an IgG Binding Peptide for Generating a Tumor Selective Noncovalent-Type Antibody-Drug Conjugate. *Bioconjug. Chem.* 2016.07; 27(7); 1606-1613
5. Kazue Terasawa, Yuri Tomabechei, Mariko Ikeda, Haruhiko Ehara, Mutsuko Kukimoto-Niino, Motoaki Wakiyama, Katarzyna A Podyma-Inoue, Anupama R Rajapakshe, Tetsuro Watabe, Mikako Shirouzu, Miki Hara-Yokoyama. Lysosome-associated membrane proteins-1 and -2 (LAMP-1 and LAMP-2) assemble via distinct modes. *Biochem. Biophys. Res. Commun.* 2016.10; 479(3); 489-495
6. Katarzyna A Podyma-Inoue, Takuya Moriwaki, Anupama R Rajapakshe, Kazue Terasawa, Miki Hara-Yokoyama. Characterization of Heparan Sulfate Proteoglycan-positive Recycling Endosomes Isolated from Glioma Cells. *Cancer Genomics Proteomics*. 2016.12; 13(6); 443-452
7. Y Kumei, R Shimokawa, M Kimoto, Y Kawauchi, H Shimokawa, K Makita, K Ohya, K Toda. Gravity stress elevates the nociceptive threshold level with immunohistochemical changes in the rat brain. *Acta Astronaut.* 49(3-10); 381-390

##### [Misc]

1. Yasuhiro Yoshimatsu, Hideki Miyazaki, Tetsuro Watabe. Roles of signaling and transcriptional networks in pathological lymphangiogenesis. *Adv. Drug Deliv. Rev.* 2016.04; 99(Pt B); 161-171
2. Takenobu Katagiri, Tetsuro Watabe. Bone Morphogenetic Proteins. *Cold Spring Harb Perspect Biol.* 2016.06; 8(6);

3. Yasuhiro Yoshimatsu. Roles of Transcription Factors in the Formation of Lymphatic Vessels Inflammation and Immunity. 2016.08; 24(5); 372-378
4. Tetsuro Watabe. Towards understanding cancer microenvironment Journal of the Stomatological Society. 2016.11; 83(3); 103-106

#### [Conference Activities & Talks]

1. Tetsuro Watabe, Yuichi Akatsu, Yasuhiro Yoshimatsu, Kohei Miyazono. Dual targeting of vascular endothelial growth factor and bone morphogenetic protein-9/10 impairs tumor growth through inhibition of angiogenesis. 10th AACR-JCA Joint Conference 2016.02.17
2. Tetsuro Watabe. Roles of TGF- $\beta$  signals in endothelial-to-mesenchymal transition (EndMT) of lymphatic endothelial cells. Gordon Research Conference Lymphatics 2016.03.23 Ventura, USA
3. Ershu Ren, Ippei Watari, Jui-Chin Hsu, Rieko Ono, Emina Wakasugi-Aoyama, Mariko Mizumachi-Kubono, Katarzyna A. Podyma-Inoue, Tetsuro Watabe, Takashi Ono. Unilateral nasal obstruction affects taste cells in circumvallate papillae in rat. The 17th International symposium on olfaction and taste (ISOT2016) 2016.05 Yokohama, Japan
4. Beauboeuf Roody, Ippei Watari, Jui-Chin Hsu, Mariko Mizumachi-Kubono, Katarzyna A. Podyma-Inoue, Tetsuro Watabe, Takashi Ono. Expression of GLP-1 and GLP-1 receptor in rat circumvallate papillae during growth period. The 17th International symposium on olfaction and taste (ISOT2016) 2016.05 Yokohama, Japan
5. Anupama R. Rajapakshe, Katarzyna A. Podyma-Inoue, Kazue Terasawa, and Miki Hara-Yokoyama. Lysosome-associated membrane proteins (LAMPs) regulate intracellular positioning of mitochondria in MC3T3-E1 cells. The Pathobiology of the Lysosome and Lysosomal Diseases Conference 2016.07 Cambridge, England
6. Katarzyna A. Podyma-Inoue, Miki Yokoyama and Tetsuro Watabe. Characterization of extracellular vesicles isolated from osteoblastic cells lines. The 89th Annual Meeting of Japanese Biochemistry Society 2016.09 Sendai, Japan
7. Tetsuro Watabe. Roles of signaling networks during endothelial-to-mesenchymal transition (EndMT) in cancer microenvironment.. 2016.10.08
8. Yasuhiro Kumei, Jorge Zeredo, Ryota Watahiki, Machiko Hattori, Hitoshi Hibino, Kensuke Kagiya, Kazumasa Fukasawa, Hirofumi Hashimoto, Noriaki Ishioka, Yuko Inatomi . Motion Sickness of Common Marmosets in Lunar and Martian Gravity Environments by Parabolic Flight. American Society for Gravitational and Space Research 2016.10.27
9. Tetsuro Watabe. Dual targeting of vascular endothelial growth factor and bone morphogenetic protein-9/10 impairs tumor growth through inhibition of angiogenesis. 11th International BMP Conference 2016.10.28 Boston
10. Ryota Watahiki, Jorge Zeredo, Kensuke Kagiya, Hirofumi Hashimoto, Noriaki Ishioka, Yuko Inatomi, Otto Baba, Shuji Aou, Kiyohisa Natsume, Yasuhiro Kumei. Postural and Behavioral Response of Primates (Common Marmoset) to Martian, Lunar, and Zero Gravity Conditions. American Society for Gravitational and Space Research 2016.10.29
11. Kazuki Takahashi, Katarzyna Anna Inoue, Yasuhiro Yoshimatsu. Hironori Harada and Tetsuro Watabe. Role of TGF- $\beta$  in the invasiveness of oral cancer cell lines. The 39th Annual Meeting of Molecular Biology Society of Japan 2016.12 Yokohama
12. Yasuhiro Yoshimatsu. Roles of signaling and transcriptional networks in the formation and maintenance of lymphatic vasculature. The 24th Annual Meeting of the Japanese Vascular Biology and Medicine Organization/ The 14th Korea-Japan Joint Symposium on Vascular Biology 2016.12.10 Nagasaki

# Cell Signaling

Professor(Principal Investigator)Tomoki NAKASHIMA  
 Assistant Professor Mikihiro HAYASHI  
 Assistant Professor Takehito ONO

## ( 1 ) Research

Research Subjects

- 1)Regulation of bone remodeling by bone cells
- 2)Identification of bone-derived systemic regulatory factors (osteokines)
- 3)Mechanism of sensing and adapting to mechanical stress
- 4)Functional analysis of genes by gene manipulations and gene-disrupted mice
- 5)Development of clinical application by experimental animal disease models

## ( 2 ) Education

Purpose of Education

Organized signal networks in the body are crucial for the higher physiological functions and the tissue organization. To understand the regulation of signal events, we take on cell signaling course including the molecular mechanism of both the “intra” cellular and the “inter” cellular signal transduction. Especially, the course will be focused on the molecular networks of signal transduction in osteoclasts, osteoblasts and osteocytes which is a new integrated field of osteonetwork (systemic network between bone and other systems). Besides, to promote the practical and clinical understanding, the course will deal with the molecular mechanism of osteoporosis and inflammatory bone destructed diseases, such as periodontal disease and rheumatoid arthritis, in parallel with the basic molecular biology.

## ( 3 ) Publications

### [Original Articles]

1. Takehito Ono, Kazuo Okamoto, Tomoki Nakashima, Takeshi Nitta, Shohei Hori, Yoichiro Iwakura, Hiroshi Takayanagi. IL-17-producing  $\gamma \delta$  T cells enhance bone regeneration. Nat Commun. 2016.03; 7; 10928
2. Aritoshi Iida, Weirong Xing, Martine K F Docx, Tomoki Nakashima, Zheng Wang, Mamori Kimizuka, Wim Van Hul, Dietz Rating, Jürgen Spranger, Hirohumi Ohashi, Noriko Miyake, Naomichi Matsumoto, Subburaman Mohan, Gen Nishimura, Geert Mortier, Shiro Ikegawa. Identification of biallelic LRRK1 mutations in osteosclerotic metaphyseal dysplasia and evidence for locus heterogeneity. J. Med. Genet.. 2016.04;
3. Asuka Terashima, Kazuo Okamoto, Tomoki Nakashima, Shizuo Akira, Koichi Ikuta, Hiroshi Takayanagi. Sepsis-Induced Osteoblast Ablation Causes Immunodeficiency. Immunity. 2016.06; 44(6); 1434-1443

**[Misc]**

1. Semaphorin and osteoporosis 2016.10; 26(10); 1419-1427

# Periodontology

Professor Yuichi IZUMI  
 Associate Professor Hisashi WATANABE  
 Lecturer Akira AOKI  
 Research Associate  
 Yasuo TAKEUCHI, Tatuya AKIZUKI, Koji MIZUTANI, Sayaka KATAGIRI

## Graduate Students

Yasuo ITO, Takahiko SHIBA, Shogo MAEKAWA, Ayano UEKUBO,  
 Wataru ONO, Hiroki SATO, Takeaki SUDO, Mizuki NAGATA, Kiichi MARUYAMA, Kosei YANO,  
 Chantida Pawauputanon Na Mahasarakham  
 Ammar Shujaa Addin,  
 Tooru TAKAGI, Anri OHTSU, Eri IKEDA (TAZAKI), Sayuri UDAGAWA,  
 Risako MIKAMI, Rina KOMAZAKI, Daisuke KIDO, Takashi ODE,  
 Sophannary Kong, Thatawee Khemwong, Nay Aung,  
 Shinta SUZUKI (April~), Yuto OOSUGI, Kohei TAKEDA, Yosuke TUCHITANI, Shunsuke FUKUBA, Naho SUZUKI,  
 Kaori FUJIWARA, Naho SUZUKI,  
 Naoki SASAKI (April~), Munehiro OKADA (April~), Chihiro KANO (April~), Yuji KATO (April~), Rie KAWAMU

Hospital Staff: 7, Research Student: 20, Registered dentist: 41

## (1) Outline

Periodontology is a branch of dental sciences which deals with the research, prevention and treatment of periodontal diseases. Periodontal disease is a general disease name which occurred in the periodontal tissue: gingiva, periodontium, cementum and alveolar bone. At present, it is indicated mainly an acute or chronic inflammatory diseases. The mission of our department was to educate etiology of periodontal diseases, host response, oral bacteria, periodontal medicine, regenerative therapy and so on profoundly, and to find a solution through discussion research outcomes as to periodontal destructive process and to develop a novel periodontal treatment modalities.

## (2) Research

- 1) Periodontopathic bacteria and their pathogenicity
- 2) Inflammatory and immunological factors in periodontal diseases
- 3) Analyses of growth factors and bio materials in periodontal regeneration
- 4) Clinical applications of laser in periodontics
- 5) Influence of periodontal disease on general health

## (3) Lectures & Courses

Periodontology is a branch of dental science which deals with supporting structures of teeth, diseases and conditions affect them. Main objectives of periodontology in the graduate course is to provide students basic



knowledge of etiology of periodontal diseases, its treatment modality and prognosis, and also to study advanced regenerative therapy.

#### (4) Clinical Performances

Periodontal clinic provides diagnosis, treatment and prevention of periodontal disease. Periodontal surgery and regenerative therapy are also performed in the clinic.

#### (5) Publications

##### [Original Articles]

1. Thanakun S, Pornprasertsuk-Damrongsri S, Gokyu M, Kobayashi H, Izumi Y. Inverse Association of Plasma IgG Antibody to *Aggregatibacter actinomycetemcomitans* and High C-Reactive Protein Levels in Patients with Metabolic Syndrome and Periodontitis. *PLoS ONE*. 2016; 11(2); e0148638
2. Kobayashi N, Suzuki JI, Aoyama N, Sato H, Akimoto S, Wakayama K, Kumagai H, Ikeda Y, Akazawa H, Komuro I, Izumi Y, Isobe M. Toll-like receptor 4 signaling has a critical role in *Porphyromonas gingivalis*-accelerated neointimal formation after arterial injury in mice. *Hypertension Research*. 2016; 39(10); 717-722
3. Tsumanuma Y, Iwata T, Kinoshita A, Washio K, Yoshida T, Yamada A, Takagi R, Yamato M, Okano T, Izumi Y. Allogeneic Transplantation of Periodontal Ligament-Derived Multipotent Mesenchymal Stromal Cell Sheets in Canine Critical-Size Supra-Alveolar Periodontal Defect Model. *BioResearch Open Access*. 2016.01; 5(1); 22-36
4. Ikawa T, Akizuki T, Matsuura T, Hoshi S, Ammar S, Kinoshita A, Oda S, Izumi Y. Ridge Preservation After Tooth Extraction With Buccal Bone Plate Deficiency Using Tunnel Structured  $\beta$ -Tricalcium Phosphate Blocks: A 2-Month Histologic Pilot Study in Beagle Dogs. *J. Periodontol.*. 2016.02; 87(2); 175-183
5. Hoshi S, Akizuki T, Matsuura T, Ikawa T, Kinoshita A, Oda A, Tabata Y, Matsui M, Izumi Y. Ridge augmentation using recombinant human fibroblast growth factor-2 with biodegradable gelatin sponges incorporating  $\beta$ -tricalcium phosphate: a preclinical study in dogs. *J. Periodont. Res.*. 2016.02; 51(1); 77-85
6. Lin T, Kawamura R, Aoki A, Ichinose S, Mizutani K, Taniguchi Y, Eguro T, Saito N, Izumi Y. Energy output reduction and surface alteration of quartz tips following Er:YAG laser contact irradiation on soft and hard tissues in vitro. *Dental Materials Journal*. 2016.02; 35(1); 51-62
7. Khamaisi M, Katagiri S, Keenan H, Park K, Maeda Y, Li Q, Qi W, Thomou T, Eschuk D, Tellechea A, Veves A, Huang C, Orgill DP, Wagers A, King GL. PKC  $\delta$  inhibition normalizes the wound-healing capacity of diabetic human fibroblasts. *J. Clin. Invest.*. 2016.03; 126(3); 837-853
8. Kitamura M, Akamatsu M, Kawanami M, Furuichi Y, Fujii T, Mori M, Kunitatsu K, Shimauchi H, Ogata Y, Yamamoto M, Nakagawa T, Sato S, Ito K, Ogasawara T, Izumi Y, Gomi K, Yamazaki K, Yoshie H, Fukuda M, Noguchi T, Takashiba S, Kurihara H, Nagata T, Hamachi T, Maeda K, Yokota M, Sakagami R, Hara Y, Noguchi K, Furuuchi T, Sasano T, Imai E, Ohmae M, Koizumi H, Watanuki M, Murakami S. Randomized Placebo-Controlled and Controlled Non-Inferiority Phase III Trials Comparing Trafermin, a Recombinant Human Fibroblast Growth Factor 2, and Enamel Matrix Derivative in Periodontal Regeneration in Intrabony Defects. *J. Bone Miner. Res.*. 2016.04; 31(4); 806-814
9. Shiheido Y, Maejima Y, Suzuki J, Aoyama N, Kaneko M, Watanabe R, Sakamaki Y, Wakayama K, Ikeda Y, Akazawa H, Ichinose S, Komuro I, Izumi Y, Isobe M. *Porphyromonas gingivalis*, a periodontal pathogen, enhances myocardial vulnerability, thereby promoting post-infarct cardiac rupture. *J. Mol. Cell. Cardiol.*. 2016.04; 99; 123-137
10. Miyazaki H, Ito Y, Ohshiro T, Kato J, Romeo U, Nomura T, Makiguchi T, Ogawa M, Watanabe H, Yokoo S. Laser treatments of oral vascular lesions - Approach to the oral vascular lesions with the intralesional laser photocoagulation technique - *Journal of Japanese Society for Laser Surgery and Medicine*. 2016.04; 37(1); 58-65

11. Thanakun S, Izumi Y. Effect of Periodontitis on Adiponectin, C-Reactive Protein, and Immunoglobulin G Against *Porphyromonas gingivalis* in Thai People With Overweight or Obese Status. *J. Periodontol.* 2016.05; 87(5); 566-576
12. Park K, Mima A, Li Q, Rask-Madsen C, He P, Mizutani K, Katagiri S, Maeda Y, Wu IH, Khamaisi M, Preil SR, Maddaloni E, Sørensen D, Rasmussen LM, Huang PL, King GL. Insulin decreases atherosclerosis by inducing endothelin receptor B expression. *JCI Insight.* 2016.05; 1(6); e86574
13. Tooi M, Komaki M, Morioka C, Honda I, Iwasaki K, Yokoyama N, Ayame H, Izumi Y, Morita I. Placenta Mesenchymal Stem Cell Derived Exosomes Confer Plasticity on Fibroblasts. *J. Cell. Biochem.* 2016.07; 117(7); 1658-1670
14. Suzuki J, Imai Y, Aoki M, Fujita D, Takeda N, Aoyama N, Wakayama K, Ikeda Y, Kumagai H, Akazawa H, Izumi Y, Isobe M, Komuro I, Hirata Y. Periodontitis May Deteriorate Sinus of Valsalva Dilatation in Marfan Syndrome Patients. *Int Heart J.* 2016.07; 57(4); 456-460
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16. Taniguchi Y, Aoki A, Sakai K, Mizutani K, Meinzer W, Izumi Y. A Novel Surgical Procedure for Er:YAG Laser-Assisted Periodontal Regenerative Therapy: Case Series. *Int J Periodontics Restorative Dent.* 2016.07; 36(4); 507-515
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#### [Books etc]

1. Izumi Y. *NHK Today's Health June issue.* NHK Publishing, 2016.05
2. Izumi Y. *The latest countermeasures of "muscle" "bone" "teeth" "dementias".* SHUFU TO SEIKATSU SHA CO., 2016.09 (ISBN : 978-4391638776)
3. Izumi Y, Nikaidou M. *Correspondence to vertical bone defects.* Igaku Joho-sha, 2016.10
4. Izumi Y, Oda S, Takeuchi Y, Mizutani K. *Incident and Recovery of periodontal surgery Q&A96.* Quintessence, 2016.11
5. Watanabe H. *Ultra-Illustrated Periodontal Disease.* Hoken, 2016.12 (ISBN : 978-4-86513-281-6)
6. Izumi Y, Akizuki T. *Periodontal treatment 1 - Periodontal tissue examination, initial treatment -.* Morita, 2016.12

#### [Misc]

1. Taniguchi Y, Aoki A, Mizutani K, Izumi Y. Periodontal therapy applying features of Er:YAG laser *JSLSM.* 2016.03; 37(1); 43-51
2. Aoki A. *Introdacution of laser institution JSLSM.* 2016.03; 37(1); 124-126
3. Mizutani K, Aoki A, Coluzzi D, Yukna R, Wang C, Pavlic V, Izumi Y. Lasers in minimally invasive periodontal and peri-implant therapy. *Periodontol.* 2000. 2016.06; 71(1); 185-212
4. Aoki A, Takeuchi Y, Hiratsuka K, Izumi Y. Antibacterial photodynamic therapy in periodontal therapy - Current status of aPDT in clinical and Latest research on LED applications *Journal of Clinical and Experimental Medicine.* 2016.09; 258(11); 1058-1062
5. Takeuchi Y. General risk factors for peri-implant disease *Journal of the Japanese Society of Oral Implantology.* 2016.12; 29(4); 219-225

#### [Conference Activities & Talks]

1. Aoki A. *New periodontal therapy using lasers - Periodontal Phototherapy.* The 36th Laser Society Annual Meeting 2016.01.10 Nagoya
2. Izumi Y. *The relation between general health condition and periodontal disease as oral infectious disease.* The 19th Annual Scientific Meeting of the Japan Society of Metabolism and Clinical Nutrition 2016.01.10 Yokohama
3. Aoki A. *Periodontal treatment with Er:YAG laser seen in the light of basic and clinical evidence .* Er:YAG Laser Users Conference 2016.01.17 Omiya
4. Aoki A. *Periodontal Er:YAG Laser Operation.* Tokyo Medical and Dental University Dental Alumni association CDE Practice course 2016.02.21 Tokyo

5. Shiba T, Watanabe T, Kachi H, Maruyama F, Takeuchi Y, Koyanagi T, Maruyama N, Murase K, Izumi Y, Nakagawa I. Dissimilarities of functional keystone species in co-occurrence network enable discrimination of intractable polymicrobial infectious diseases. SMBE Satellite Workshop on Genome Evolution in Pathogen Transmission and Disease 2016.02.24 Nagano
6. Watanabe H. Basis of periodontal diseases and its flow of periodontal therapy. GC dental college 2016.02.29 Tokyo
7. Akizuki T. Role of the high bioavailable curcumin of the treatment and prevention of the life-style diseases. Symposium 21. The 89th Annual Meeting of the Japanese Pharmacological Society 2016.03.10 Yokohama
8. Ikeda E, Takeuchi Y, Suda W, Ikeda Y, Nakasato A, Hattori M, Izumi Y. Pyrosequencing analysis of subgingival microbiota in chronic periodontitis. 45th Annual Meeting and Exhibition of the American Association for Dental Research 2016.03.18 Los angeles, USA
9. Kido D, Maruyama K, Izumi Y. A case report of comprehensive treatment for a patient with generalized severe chronic periodontitis based on a bacteriological examination. The 30th anniversary KYUSYU IMPLANT RESEARCH GROUP (KIRG) workshop 2016.03.26 Fukuoka
10. Koyanagi T, Kobayashi H, Takeuchi S, Izumi Y. Analysis of peri-implant bone defect configuration using cone beam CT. 2016.03.26
11. Otsu A, Suda T, Takeuchi Y, Izumi Y. Clinical effect of sodium hypochlorite dilution water applied in dental supply duct line. 17th Annual meeting of the Japan Society for Oral Functional Water 2016.03.27 Osaka
12. Sudo T, Okada Y, Kobayashi H, Gokyu M, Tanaka T, Izumi Y. Whole-exome sequencing reveals a novel gene as a cause of Aggressive periodontitis in Japanese consanguineous families. The 13th International Congress of Human Genetics 2016.04.04 Kyoto
13. Sugawara Y, Kashimada A, Moriyama K, Baba S, Imai K, Nishikomori R, Motegi M, Takeuchi Y, Morio T. Aicardi-Goutieres and Singleton-Merten overlapping phenotype due to IFIH1 mutation.. The 13th International Congress of Human Genetics 2016.04.06 Kyoto, Japan
14. Taniguchi Y. Best clinical case clinical case description. Geistlich Biomaterials 2016.04.12 on line
15. Aoki A. Er:YAG Laser in Periodontics. The 23rd Academy of Laser Dentistry Annual Conference 2016.04.14 Orlando,USA
16. Watanabe H. Novel dental therapy developed by laser. 6th annual meeting of Japan Association of Dental traumatology 2016.04.17 Tokyo
17. Ikawa T, Akizuki T, Matsuura T, Hoshi S, Ono W, Maruyama K, Shujaa Addin A, Izumi Y. Histological evaluation of the tunnel  $\beta$ -tricalcium phosphate blocks for ridge preservation after tooth extraction with buccal bone deficiency in beagle dogs. Osteology International Symposium 2016.04.21 Principauté de Monaco
18. Mikami R, Aoki A, Mizutani K, Tamura Y, Aoki K, Izumi Y. Low-level laser irradiation using a high-frequency ultra-short pulsed blue laser enhances osteoblasts proliferation and differentiation. The 59th Spring Meeting of The Japanese Society of Periodontology 2016.05.20 Kagoshima
19. Aoki A. Effects of lights on periodontal pathogens and basic studies of aPDT - Applications of LED. Symposium I : Is antimicrobial photodynamic therapy effective in the periodontal therapy ?. The 59th Spring Meeting of the Japanese Society of Periodontology 2016.05.20 Kagoshima
20. Yashima A, Morozumi T, Ujiie Y, Yoshie H, Hokari T, Izumi Y, Mizutani K, Takamatsu H, Minaba M, Akizuki T, Miyauchi S, Yoshino T, Tanaka M, Tanaka Y, Gomi K. Effectiveness of Azythromycin on one-stage full-mouth SRP. -Biological response and clinical outcome-. The 59th Spring Meeting of The Japanese Society of Periodontology. 2016.05.20 Kagoshima
21. Morozumi T, Yashima A, Gomi K, Ujiie Y, Izumi Y, Mizutani K, Takamatsu H, Minabe M, Akizuki T, Miyauchi S, Yoshino T, Tanaka M, Tanaka Y, Hokari T, Yoshie H. Biological response and Clinical outcome after application of one-stage full-mouth SRP. The 59th Spring Meeting of The Japanese Society of Periodontology. 2016.05.20 Kagoshima

22. Katagiri S, Shigaki-Katagiri A, Takeuchi Y. A case report of oral rehabilitation for severe chronic periodontitis with occlusal trauma. The 59th Spring Meeting of The Japanese Society of Periodontology 2016.05.21 Kagoshima
23. Shiba T, Watanabe T, Koyanagi T, Maruyama N, Takeuchi Y, Maruyama F, Nakagawa I, Izumi Y. Homeostasis maintenance mechanism inferred from polymicrobial oral diseases with similar symptoms. 2016.05.21 Kagoshima
24. Komaki M, Aoki A, Iwasaki K, Izumi Y. Coverage of class III gingival recession localized at anterior mandibular teeth using connective tissue graft. The 59th Spring Meeting of The Japanese Society of Periodontology 2016.05.21
25. Shujaa Addin A, Akizuki T, Hoshi S, Matsuura T, Ikawa T, Maruyama K, Ono W, Fukuba S, Izumi Y. Effect of rhFGF-2 Combined with Gelatin/ $\beta$ -TCP Sponge on Root Coverage: a Pilot Study in Beagle Dogs. The 59th Spring Meeting of The Japanese Society of Periodontology 2016.05.22 Kagoshima
26. Aoki A. Current status of Er:YAG Laser in periodontics and peri-implant therapy - From basic studies to clinical applications: Part I and Part II. 10th Congress of the Asia Pacific Laser Institute 2016.05.29 Taipei, Taiwan
27. Takeuchi S, Koyanagi T, Ogawa M, Ikawa T, Suda T, Takeuchi Y, Izumi Y. The application of corn beam computed topography data for the diagnosis of furcation defects. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.06 Utsunomiya
28. Tooi M, Komaki M, Iwasaki K, Yokoyama N, Nagata M, Izumi Y, Morita I. Placenta mesenchymal stem cell derived exosomes alter differentiation competence in fibroblasts. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya
29. Akazawa K, Iwasaki K, Komaki M, Yokoyama N, Izumi Y, Morita I. Construction of double-layered cell transferred-amnion using osteoblasts and periodontal ligament stem cells by cell transfer technology. The 37th Spring Meeting of The Japanese Society of Inflammation and Regeneration 2016.06.17 Kyoto
30. Watanabe H. Novel periodontal plastic surgery using Er:YAG laser. 94th General Session & Exhibition of the International Association for Dental Research (IADR) 2016.06.22 Seoul, Republic of Korea
31. Shujaa Addin A, Akizuki T, Hoshi S, Matsuura T, Ikawa T, Maruyama K, Ono W, Fukuba S, Izumi Y. Effect of rhFGF-2/Gelatin- $\beta$ -TCP on Root Coverage in Beagle Dogs. 94th General Session & Exhibition of the International association for Dental Research Meeting 2016.06.23 Seoul, Republic of Korea.
32. Shinkai K, Oda S, Yamaguch K, Yamada M, Yoshikawa K, Mitani A, Watanabe H. A proposal of guideline for lecture of laser dentistry. 35th annual meeting of Japanese Dental Education Association 2016.07.02 Osaka
33. Watanabe C, Wada J, Mizutani K, Watanabe H, Wakabayashi N. The effect of removable partial denture placement on periodontal structures of abutment teeth in patients of periodontitis: A digital subtraction analysis. The 125th Scientific Meeting of Japan Prosthodontic Society 2016.07.10 Kanazawa
34. Izumi Y. The clinical epidemiologic survey on periodontal conditions of patients with cardiovascular diseases. The 48th Annual Scientific Meeting of the Japan Atherosclerosis Society 2016.07.14 Tokyo
35. Aoki A. Soft tissue application. Basic Laser Certification Course, 15th Congress of the World Federation for Laser Dentistry 2016.07.16 Nagoya
36. Lin Tai-Chen, Aoki A, Kawamura T, Takagi T, Uekubo A, Mikami R, Mizutani K, Izumi Y. Soft and hard tissue ablation using a Q-switched 2.81  $\mu$  m Er:ZBLAN fiber laser. The 28th Annual Meeting of Japanese Society for Laser Dentistry 2016.07.16 Nagoya
37. Taniguchi Y. A novel surgical procedure of Er:YAG laser-assisted bone regenerative therapy. 15th Congress of the World Federation for Laser Dentistry 2016.07.16 Nagoya
38. Watanabe H. Novel periodontics in laser dentistry. 15th Congress of World Federation for Laser Dentistry 2016.07.17 Nagoya



39. Watanabe H, Belal MH. Comparative study on morphologic changes and cell attachment of periodontitis-affected root surfaces following conditioning with CO<sub>2</sub> and Er:YAG laser irradiations. 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya
40. Aoki A, Mizutani K, Taniguchi Y, Komaki M, Oda S, Watanabe H, Izumi Y. Er:YAG Laser-assisted comprehensive periodontal pocket therapy (Er-LCPT): case series. 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya
41. Eguro T, Takanori Suzuki T, Aoki A, Mizoguchi T, Izumi Y. Soft tissue management with the Er:YAG laser in implant therapy. 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya
42. Miyazaki H, Romeo U, Wada Y, Vecchio AD, Kato J, Tanaka K, Noguchi T, Maruoka Y, Watanabe H, Harada H, Asamura S. Treatment strategies for oral vascular anomalies using intralesional laser photocoagulation. 15th Congress of World Federation for Laser Dentistry 2016.07.18 Nagoya
43. Tsukui A, Watanabe H. Clinical applications of Er:YAG laser in peri-implantitis therapy - Case report. 15th Congress of World Federation for Laser Dentistry 2016.07.18 Nagoya
44. Yano K, Washio K, Tsumanuma Y, Iwata T, Yamato M, Ohta K, Okano T, Izumi Y. Phenotypic analysis of bone and cartilage in Tsukushi-deficient mice. The 34th Annual Meeting of the Japanese Society for Bone and Mineral Research 2016.07.21 Osaka
45. Komaki M, Tooi M, Iwasaki K, Morita I. Mesenchymal stem cell derived exosomes alter differentiation competence in fibroblasts. The 34th Annual Meeting of the Japanese Society for Bone and Mineral Research 2016.07.22 Osaka
46. Taniguchi Y. The application of Er:YAG laser-assisted bone regenerative therapy for periodontics and implant treatment: case report and bibliographical consideration. Clinical research institute for Er:YAG laser treatment, 19th meeting 2016.08.07 Tokyo
47. Watanabe T, Shiba T, Kachi H, Takeuchi Y, Maruyama F, Izumi Y, Nakagawa I. Metatranscriptomic analyses of microbiota in peri-implantitis and periodontitis lesions. The 58th Annual Meeting of Japanese Association for Oral Biology 2016.08.25 Sapporo
48. Iwata T, Yamato M, Washio K, Tsumanuma Y, Yamada A, Onizuka S, Izumi Y, Ando T, Okano T, Ishikawa I. Periodontal Regeneration with Autologous Periodontal Ligament-derived Cell Sheets in humans.. TERMIS-AP2016 2016.09.04 Taipei, Taiwan
49. Benhamou V, Sarmiento HL, Aoki A. Er:YAG laser: Hands-on course, Er: YAG Lasers - Daily Applications in Periodontics: Training Course. Morita Er:YAG laser user meeting 2016.09.09 San Diego, USA
50. Aoki A. Er:YAG Laser in Periodontics and Implant Therapy - From Basic Studies to Clinical Applications. Er: YAG Lasers - Daily Applications in Periodontics: Training Course. Morita Er:YAG laser user meeting 2016.09.09 San Diego, USA
51. Aoki A. Current status of Er:YAG laser therapy in management of peri-implant disease. 5th Pan Pacific Session "Implant Therapy For the Periodontally Compromised Patient. The 102nd Annual Meeting of American Academy of Periodontology 2016.09.09 San Diego, USA
52. Mikami R, Aoki A, Mizutani K, Tamura Y, Aoki K, Izumi Y. Low-level blue laser irradiation enhances osteoblast proliferation and differentiation. The 102nd Annual Meeting of the American Academy of Periodontology 2016.09.10 San Diego, USA
53. Maekawa S, Katagiri S, Takeuchi Y, Komazaki R, Ohtsu A, Udagawa S, Izumi Y. Bone metabolic microarray analysis of ligature-induced periodontitis in streptozotocin- induced diabetic mice. The 102nd Annual Meeting of American Academy of Periodontology 2016.09.10 San Diego, USA
54. Ono W, Ogiso M, Maruyama K, Mineno S, Izumi Y. Histological analysis of implantation to augmented bone using "Casing Method". The 102nd Annual Meeting of the American Academy of Periodontology 2016.09.10 San Diego, USA
55. Maruyama K, Ogiso M, Ono W, Mineno S, Izumi Y. The histological analysis of great-sized ridge augmentation applying the "Casing Method". The 102nd Annual Meeting of the American Academy of Periodontology 2016.09.10 San Diego, USA

56. Shiba T, Watanabe T, Koyanagi T, Maruyama N, Takeuchi Y, Maruyama F, Izumi Y, Nakagawa I. Functional keystone species enable discrimination of peri-implantitis and periodontitis. The 102nd Annual Meeting of the American Academy of Periodontology 2016.09.10 San Diego, USA
57. Shujaa Addin A, Hoshi S, Matsuura T, Ikawa T, Maruyama K, Ono W, Fukuba S, Izumi Y. rhFGF-2/gelatin- $\beta$  TCP in the treatment of gingival recessions in dogs. The 102nd meeting of American Academy of Periodontology 2016.09.12 San Deigo, USA
58. Watanabe H. Novel periodontal therapy using Er:YAG laser- Basis and clinical outcome. The 102nd Annual Meeting of the American Academy of Periodontology 2016.09.13 San Diego, USA
59. Takagi T, Aoki A, Lin T, Taniguchi Y, Tachikawa N, Shinoki T, Izumi Y. The effectiveness of Erbium family laser on dental implant surface -Investigation of appropriate parameter for irradiation and removability of artificial calcified deposits on dental implant-. The 46th Annual Meeting of the Japanese Society of Oral Implantology 2016.09.17 Nagoya
60. Taniguchi Y, Koyanagi T, Lin T, Izumi Y. Simultaneous fixture placement with various bone augmentation techniques using new designed fixtures: a case report. European association for osseointegration 25th annual scientific meeting 2016.09.30 Paris, France
61. Masahiro Noda, Akira Aoki, Koji Mizutani, Taichen Lin, Motohiro Komaki, Shunichi Shibata, Yuichi Izumi. Effect of low level laser irradiation on early stage of wound healing of tooth extraction socket. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10 Fukuoka
62. Tsubokawa M, Aoki A, Kakizaki S, Lin T, Mizutani K, Oda S, Sumi Y, Izumi Y. Optical measurement of periodontal pocket depth using optical coherence tomography (OCT) . The 59th Autumn Meeting of The Japanese Society of Periodontology 2016.10.06 Niigata
63. Maruyama K, Ogiso M, Ono W, Mineno S, Izumi Y. The histological analysis of great-sized ridge augmentation applying the "Casing Method". The 59th Autumn Meeting of The Japanese Society of Periodontology 2016.10.07 Niigata
64. Kakizaki S, Mizutani K, Osugi Y, Katagiri S, Aoki A, Izumi Y. The questionnaire survey about explanation of intra-oral photography using iPad in dental student clinic. The 59th Autumn Meeting of The Japanese Society of Periodontology 2016.10.07 Niigata
65. Nagata M, Iwasaki K, Akazawa K, Komaki K, Yokoyama N, Izumi Y, Morita I. Conditioned medium from periodontal ligament stem cells enhances periodontal regeneration. The 59th Autumn Meeting of The Japanese Society of Periodontology 2016.10.07 Niigata
66. Aoki A. Er:YAG laser-assisted comprehensive periodontal pocket therapy. the 23rd General Meeting of the Japanese Association for Dental Science 2016.10.21 Fukuoka
67. Watanabe H, Shinoki T (Moderator), Yoshimine Y, Fujitani M, Aoki A. Symposium: Inovation of conservative dentistry by laser. The 23rd General Meeting of The Japanese Association for Dental Science 2016.10.22 Fukuoka
68. Aoki A, Mizutani K, Taniguchi Y, Watanabe H, Izumi Y. Application of Er:YAG laser in periodontal pocket therapy and flap surgery. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10.23 Fukuoka
69. Ogawa M, Koyanagi T, Takeuchi T, Katagiri S, Ikawa T, Takeuchi S, Sekiuchi T, Arai Y, Kazama R, Wakabayashi N, Izumi Y. Evaluation of palatal mucosal thickness measurements using CBCT. 145th Meeting of the Japanese Society of Conservative Dentistry 2016.10.28 Matsumoto
70. Aoki A. Periodontal Disease - Pathogenesis, Diagnosis and Management. 2016 Tokyo Medical and Dental University - Taipei Medical University. Joint Symposium on Immunity, Inflammation, and Infection 2016.11.12 Taipei, Taiwan
71. Aoki A. Effects of ultraviolet LEDs on periodontal pathogenic bacteria. Heisei 28 fiscal year Development cost of longevity medical research 26-6 "Research on the development of new diagnostic and treatment devices using infrared lights and lasers" Group meeting 2016.11.17 Obu
72. Aoki A. Application of Er:YAG laser in periodontal therapy. The 18 th Advanced Laser Application Technology Seminar 2016.11.17 Yokohama

73. Ikeda E, Grazieli M, Ikeda Y, Wang y, Fine N, Sheikh Z, Casati M, Ganss B, Glogauer M, Tenenbaum H. Antioxidants/Aryl hydrocarbon-Receptor Antagonist Resveratorol and Curcumin Both Prevent and Reverse Periodontitis-Mediated Bone Loss in Rodents. 4th international conference of resveratrol and health 2016.11.18 Taipei, Taiwan
74. Watanabe H. Laser dentistry - its basis and clinical application . 4th educational seminar of Japanese Association for Laser Dentistry 2016.11.24 Sapporo
75. Hatase M, Watanabe H, Ejiri K, Tsumanuma Y, Izumi Y. Role of Calprotectin in Periodontal Diagnosis. The 81st Annual Meeting of the Stomatological Society 2016.11.26 Tokyo
76. Ode T, Podyma-Inoue KA, Terasawa K, Watabe T, Izumi Y, Yokoyama M. PDMP, a ceramide analogue, acts as an inhibitor of mTORC1 by inducing its translocation from lysosome to endoplasmic reticulum. The 81th Annual Meeting of the Stomatological Society 2016.11.26 Tokyo
77. Aoki A. Periodontal Er:YAG Laser Operation. Dental Alumni Association Tokyo Medical and Dental University CDE Practical training course 2016.12.04 Tokyo
78. Takahashi H, Katagiri S, Eguchi Y. Periodontal Pathogens affect on NAFLD/NASH. The 41st meeting of Eastern Branch of the Japan Society of Hepatology 2016.12.09 Tokyo

#### **[Awards & Honors]**

1. The 37th Spring Meeting of The Japanese Society of Inflammation and Regeneration. Excellence Award (Akazawa K), The Japanese Society of Inflammation and Regeneration, 2016
2. 2016 Research encouragement award for postgraduate student (Sudo T), 2016.03
3. 2016 Morita Scholarship Foundation (Sudo T), Morita Scholarship Foundation, 2016.07
4. Young Researcher's Award, Japanese Society of Laser Dentistry (Sawabe M), The 28th Annual Meeting of Japanese Society for Laser Dentistry, 2016.07
5. 2016 Iwadare Scholarship Foundation (Sudo T), Iwadare Scholarship Foundation, 2016.08
6. Sunstar Young Investigator Award (Nagata M), The Japanese Society of Periodontology, 2016.10

#### **[Others]**

1. Platina Life TOKYO MX TV (Aoki A), 2016.02  
Periodontology and Alzheimer disease
2. Platina Life TOKYO MX TV (Aoki A), 2016.02  
Periodontology and Premature labor



## Global Health Promotion

Professor: Takeo Fujiwara, MD, MPH, PhD (Apr-)

Assistant Professor: Keiko Nakamura, MD, PhD (-Mar)

Junior Associate Professor: Masashi Kizuki, MD, MPH, PhD; Kaoruko Seino, PhD (-Mar)

Assistant Professor: Ayako Morita, PhD

Research Fellow of Japan Society for the Promotion of Science: Yukako Tani, PhD; Satomi Doi, PhD (Apr-Sep)

Project Researcher: Aya Isumi, PhD; Satomi Doi, PhD (Oct-)

### (1) Outline

The purpose of this course is to develop the knowledge and skills of the participants to prevent diseases. Participants will: understand broad risk factors from individual factors (e.g., genetic factor) and environmental factors, especially social determinants, their interactions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or program to prevent diseases in a real life setting.

### (2) Research

The main focus of the department is as follows:

1. Social epidemiology (impact of social inequality, social capital, social network, and social support on health)
2. Life-course epidemiology (impact of child poverty and adverse childhood experiences on health) and international comparison study
3. Prevention on child abuse and neglect
4. Disaster and child and their family's mental health
5. Nutrition during pregnancy or early childhood and health

### (3) Education

The faculty of department teach Public Health and Social Medicine for grade 3 medical students, Public Health Practice for grade 4 medical students, and graduate students seminars.

### (4) Lectures & Courses

The purpose of this course is to develop the knowledge and skills of the participants to prevent diseases. Participants will: understand broad risk factors from individual factors (e.g., genetic factor) and environmental factors, especially social determinants, their interactions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or program to prevent diseases in a real life setting.

The participants will be able to: 1. explain the risk of disease.

2. verbalize own research question and develop a hypothesis to test it.

3. develop research field or access secondary data to test the hypothesis.
4. explain an epidemiologic study design.
5. calculate a sample size.
6. analyse basic model (multivariate analysis, logistic analysis, etc) and conduct advnaced analysis (multilevel analysis, propensity score moathcing, multiple imputation, etc)
7. justify the research question logically, in scientific writing in English.
8. develop an intervention (policy or program) and design a study protocol to assess its effectiveness.

## ( 5 ) Publications

### [Original Articles]

1. Sachiko Baba, Hiroyasu Iso, Takeo Fujiwara. Area-Level and Individual-Level Factors for Teenage Motherhood: A Multilevel Analysis in Japan. *PLoS ONE*. 2016; 11(11); e0166345
2. Akiko Mizuta, Takeo Fujiwara, Toshiyuki Ojima. Association between economic status and body mass index among adolescents: a community-based cross-sectional study in Japan. *BMC Obes*. 2016; 3; 47
3. Yosuke Inoue, Andrew Stickley, Aki Yazawa, Kokoro Shirai, Airi Amemiya, Naoki Kondo, Katsunori Kondo, Toshiyuki Ojima, Masamichi Hanazato, Norimichi Suzuki, Takeo Fujiwara. Neighborhood Characteristics and Cardiovascular Risk among Older People in Japan: Findings from the JAGES Project. *PLoS ONE*. 2016; 11(10); e0164525
4. Naho Morisaki, Takeo Fujiwara, Reiko Horikawa. The Impact of Parental Personality on Birth Outcomes: A Prospective Cohort Study. *PLoS ONE*. 2016; 11(6); e0157080
5. Seung Chik Jwa, Kohei Ogawa, Minatsu Kobayashi, Naho Morisaki, Haruhiko Sago, Takeo Fujiwara. Validation of a food-frequency questionnaire for assessing vitamin intake of Japanese women in early and late pregnancy with and without nausea and vomiting. *J Nutr Sci*. 2016; 5; e27
6. Kei Nagaoka, Takeo Fujiwara. Impact of Subsidies and Socioeconomic Status on Varicella Vaccination in Greater Tokyo, Japan. *Front Pediatr*. 2016; 4; 19
7. Yosuke Inoue, Andrew Stickley, Aki Yazawa, Takeo Fujiwara, Katsunori Kondo, Naoki Kondo. Month of birth is associated with mortality among older people in Japan: Findings from the JAGES cohort. *Chronobiol. Int.*. 2016; 33(4); 441-447
8. Satomi Doi, Kengo Yokomitsu, Yuji Sakano. The relationships between valued action, behavioral activation, avoidance, and reinforcement in a sample of college students *Psychological Reports*. 2016; 118(1); 5-22
9. Ayako Morita, Kazumi Natsuhara, Gwendalyn Vengiau, Cindy Chia-Jung Chen, Shingo Odani, Tsukasa Inaoka, Kiyoshi Tadokoro, Kazuhiro Suda, Takuro Furusawa, Peter Siba, Suparat Phuanukoonnon, Masahiro Umezaki. Reduced morning cortisol concentration in saliva was associated with obesity: Evidence from community-dwelling adults in papua new guinea. *Am. J. Hum. Biol.*. 2016.01;
10. Masahiro Umezaki, Yuichi I Naito, Takumi Tsutaya, Jun Baba, Kiyoshi Tadokoro, Shingo Odani, Ayako Morita, Kazumi Natsuhara, Suparat Phuanukoonnon, Gwendalyn Vengiau, Peter M Siba, Minoru Yoneda. Association between sex inequality in animal protein intake and economic development in the Papua New Guinea highlands: The carbon and nitrogen isotopic composition of scalp hair and fingernail. *Am. J. Phys. Anthropol.*. 2016.01; 159(1); 164-173
11. Satomi Doi. The elaboration of behavioral activation approach focusing on promoting value-based behavior 2016.03;
12. Satomi Doi, Kengo Yokomitsu, Yuji Sakano. Behavioral Activation Approach with Focus on Values : A Meta-Analysis 2016.03; 16(2); 207-218
13. Hiroaki Honma, Makiko Okuyama, Takeo Fujiwara, Shukei Gouzu. Large-scale disasters and PTSD in young children: A follow-up study of preschool children severely affected by the Great East Japan Earthquake *Japanese Journal of Child and Adolescent Psychiatry*. 2016.04; 57(2); 283-297

14. Shihoko Koyama, Jun Aida, Masashige Saito, Naoki Kondo, Yukihiro Sato, Yusuke Matsuyama, Yukako Tani, Yuri Sasaki, Katsunori Kondo, Toshiyuki Ojima, Tatsuo Yamamoto, Toru Tsuboya, Ken Osaka. Community social capital and tooth loss in Japanese older people: a longitudinal cohort study. *BMJ Open*. 2016.04; 6(4); e010768
15. Mashal MO, Nakamura K, Kizuki M. Hidden burden of non-medical spending associated with inpatient care among the poor in Afghanistan. *International Journal of Public Health*. 2016.05; 61; 661-671
16. Airi Amemiya, Takeo Fujiwara. Association between maternal intimate partner violence victimization during pregnancy and maternal abusive behavior towards infants at 4 months of age in Japan. *Child Abuse Negl*. 2016.05; 55; 32-39
17. Sayaka Aoki, Keiji Hashimoto, Natsuha Ikeda, Makoto Takekoh, Takeo Fujiwara, Naho Morisaki, Hidetoshi Mezawa, Yoshiyuki Tachibana, Yukihiro Ohya. Comparison of the Kyoto Scale of Psychological Development 2001 with the parent-rated Kinder Infant Development Scale (KIDS). *Brain Dev*.. 2016.05; 38(5); 481-490
18. Rami Al Rifai, Keiko Nakamura, Kaoruko Seino. Decline in the prevalence of anaemia among children of pre-school age after implementation of wheat flour fortification with multiple micronutrients in Jordan. *Public Health Nutr*. 2016.06; 19; 1486-1497
19. Aya Isumi, Takeo Fujiwara. Association of adverse childhood experiences with shaking and smothering behaviors among Japanese caregivers. *Child Abuse and Neglect*. 2016.07; 57; 12-20
20. Nakamura K, Chiba M, Seino K. Factors influencing reduction of risk of lifestyle related disease among children. 2016.08; 31; 381-386
21. Katsura Igai, Manabu Itakura, Suguru Nishijima, Hirohito Tsurumaru, Wataru Suda, Takumi Tsutaya, Eriko Tomitsuka, Kiyoshi Tadokoro, Jun Baba, Shingo Odani, Kazumi Natsuhara, Ayako Morita, Minoru Yoneda, Andrew R Greenhill, Paul F Horwood, Jun-Ichi Inoue, Moriya Ohkuma, Yuichi Hongoh, Taro Yamamoto, Peter M Siba, Masahira Hattori, Kiwamu Minamisawa, Masahiro Umezaki. Nitrogen fixation and nifH diversity in human gut microbiota. *Sci Rep*. 2016.08; 6; 31942
22. Junko Yagi, Takeo Fujiwara, Takehito Yambe, Makiko Okuyama, Ichiro Kawachi, Akio Sakai. Does social capital reduce child behavior problems? Results from the Great East Japan Earthquake follow-up for Children Study. *Soc Psychiatry Psychiatr Epidemiol*. 2016.08; 51(8); 1117-1123
23. Nobuyuki Nosaka, Takeo Fujiwara, Emily Knaup, Ayumi Okada, Hirokazu Tsukahara. Validity of Mothers' Reports of Children's Weight in Japan. *Acta Med. Okayama*. 2016.08; 70(4); 255-259
24. Yukako Tani, Naoki Kondo, Yuiko Nagamine, Tomohiro Shinozaki, Katsunori Kondo, Ichiro Kawachi, Takeo Fujiwara. Childhood socioeconomic disadvantage is associated with lower mortality in older Japanese men: the JAGES cohort study. *Int J Epidemiol*. 2016.08; 45(4); 1226-1235
25. Manami Ochi, Takeo Fujiwara. Association Between Parental Social Interaction and Behavior Problems in Offspring: a Population-Based Study in Japan. *Int J Behav Med*. 2016.08; 23(4); 447-457
26. Yukako Tani, Takeo Fujiwara, Naoki Kondo, Hisashi Noma, Yuri Sasaki, Katsunori Kondo. Childhood Socioeconomic Status and Onset of Depression among Japanese Older Adults: The JAGES Prospective Cohort Study. *Am J Geriatr Psychiatry*. 2016.09; 24(9); 717-726
27. Naho Morisaki, Ichiro Kawachi, Emily Oken, Takeo Fujiwara. Parental Characteristics can Explain Why Japanese Women Give Birth to the Smallest Infants in the United States. *Paediatr Perinat Epidemiol*. 2016.09; 30(5); 473-478
28. Shafiqullah H, Morita A, Nakamura K, Seino K. The family planning conundrum in Afghanistan Health Promotion International. 2016.10;
29. Al-Sobaihi S, Nakamura K, Kizuki M.. Undernutrition among children under 5 years of age in Yemen: Role of adequate childcare provided by adults under conditions of food insecurity. *Journal of Rural Medicine*. 2016.11; 11(2); 47-57
30. Tumurkhuu T, Fujiwara T, Komazaki Y, Kawaguchi Y, Tanaka T, Inazawa J, Ganburged G, Bazar A, Ogawa T, Moriyama K. Association between maternal education and malocclusion in Mongolian adolescents: a cross-sectional study. *BMJ Open*. 2016.11; 6(11);

31. Munehiro Furuichi, Takeo Fujiwara, Akinari Fukuda, Mureo Kasahara, Isao Miyairi. Fulminant Hepatic Failure as a Risk Factor for Cytomegalovirus Infection in Children Receiving Preemptive Therapy After Living Donor Liver Transplantation. *Transplantation*. 2016.11; 100(11); 2404-2409
32. Aki Yazawa, Yosuke Inoue, Takeo Fujiwara, Andrew Stickley, Kokoro Shirai, Airi Amemiya, Naoki Kondo, Chiho Watanabe, Katsunori Kondo. Association between social participation and hypertension among older people in Japan: the JAGES Study. *Hypertens. Res.*. 2016.11; 39(11); 818-824
33. Hisashi Eguchi, Akihito Shimazu, Takeo Fujiwara, Noboru Iwata, Kyoko Shimada, Masaya Takahashi, Masahito Tokita, Izumi Watai, Norito Kawakami. The effects of workplace psychosocial factors on whether Japanese dual-earner couples with preschool children have additional children: a prospective study. *Ind Health*. 2016.12; 54(6); 498-504
34. Yusuke Matsuyama, Takeo Fujiwara, Jun Aida, Richard G Watt, Naoki Kondo, Tatsuo Yamamoto, Katsunori Kondo, Ken Osaka. Experience of childhood abuse and later number of remaining teeth in older Japanese: a life-course study from Japan Gerontological Evaluation Study project. *Community Dent Oral Epidemiol*. 2016.12; 44(6); 531-539

### [Misc]

1. Takeo Fujiwara, Naho Morisaki, Yukiko Honda, Makiko Sampei, Yukako Tani. Chemicals, Nutrition, and Autism Spectrum Disorder: A Mini-Review. *Front Neurosci*. 2016; 10; 174

### [Conference Activities & Talks]

1. Nakamura K. Post-disaster excess deaths of NCD and Disaster Health Emergency Assistance Team.. WHO Meeting on Healthy and Resilient Cities 2016.01.11 Gandong-gu, Seoul, Republic of Korea
2. Nakamura K. Healthy Cities and Food is Asia. HCSO-AFHC Symposium 2016.02.02 Tokyo
3. Nakamura K. Examples of actions to address urban health challenges: Urban health system roles and functions: Emergency Preparedness Plan. Meeting on Implementation of the Regional Framework for Urban Health in the Western Pacific (2016-2020) 2016.02.29 Manila, Philippines
4. Takeo Fujiwara, Yukako Tani. Does eat-vegetable-first policy prevent children' s caries?. 8th Annual Meeting, International Society for Social Capital research 2016.05.27
5. Satomi Doi, Takeo Fujiwara. The association between leaving children home alone and mental health: Result from A-CHILD study.. The 8th Annual Meeting International Society for Social Capital research 2016.05.30
6. Kaori Honjo, Naoki Kondo, Yukako Tani, Masashige Saitoh, Katsunori Kondo. Living arrangements and risk of depressive symptoms among older adults in Japan: The JAGES longitudinal survey. Society of Epidemiologic Research 49th Annual Meeting 2016.06 Miami, USA
7. Aya Isumi, Takeo Fujiwara. Shaken Baby Syndrome and Social Capital: A Multilevel Analysis of Caregivers of Infants in Japan. The Society for Pediatric and Perinatal Epidemiologic Research 29th Annual Meeting 2016.06.21 Miami, Florida, USA
8. Aya Isumi, Takeo Fujiwara. Association of Adverse Childhood Experiences with Shaking and Smothering Behaviors among Japanese Caregivers . The 2016 Epidemiology Congress of the Americas 2016.06.22 Miami, Florida, USA
9. Takeo Fujiwara, Aya Isumi. Interaction effect of unexpected pregnancy and younger motherhood on infant abuse: A retrospective cohort study in Japan. 2016.06.23
10. Satomi Doi, Kengo Yokomitsu, Koki Takagaki et al.. The effect of values intervention in behavioral activation in college students: Randomized controlled trial. The 8th World Congress of Behavioral and Cognitive Therapies 2016.06.24
11. Shihoko Koyama, Jun Aida, Masashige Saito, Naoki Kondo, Yukihiro Sato, Yusuke Matsuyama, Yukako Tani, Yuri Sasaki, Katsunori Kondo, Toshiyuki Ojima, Tatsuo Yamamoto, Toru Tsuboya, Ken Osaka. Community social capital and oral health in Japanese older people. IADR PBRG Symposium 2016 2016.06.27 Nagoya, Japan

12. Nakamura K. Health Supportive City Development. The 12th Annual Conference of the Japan Chapter of the Alliance for Healthy Cities 2016.07.26
13. Nakamura K. Public Health. Graduate School Seminar at School of Public Health, MUHAS 2016.08.03 Dar es Salaam, Tanzania
14. Nakamura K, Fawkes S. The Foresight Approach towards Healthy and Resilient Cities. The 7th Global Conference of the Alliance for Healthy Cities 2016.08.29 Wonju, Republic of Korea
15. Aya Isumi, Takeo Fujiwara. Association of positive parenting practice with shaking and smothering among caregivers of infants in Japan. 21st International Congress on Child Abuse and Neglect 2016.08.29 Calgary, Canada
16. Nakamura K. Nationwide program for prevention and control of lifestyle related disease, Japan.. 8th NCD Forum Seminar 2016.09.28 Seoul, Republic of Korea
17. Masashi Kizuki, Manami Ochi, Aya Isumi, Tsuguhiko Kato, Takeo Fujiwara. Association between mental health of children and time parents return home from work. 75th Annual Meeting of Japanese Society of Public Health 2016.10.26 Osaka city, Osaka
18. Aya Isumi, Makiko Sampei, Takeo Fujiwara. The effect of the educational video on infant crying on prevention of Shaken Baby Syndrome among Japanese caregivers. 75th Annual Meeting of Japanese Society of Public Health 2016.10.27 Osaka city, Osaka
19. Masashi Kizuki, Takeo Fujiwara. Association between family support and psychological distress, as modified by attachment patterns. 9th European Public Health Conference 2016.11.10 Vienna, Austria
20. Aya Isumi, Takeo Fujiwara. Interaction effects of unintended pregnancy and maternal age on infant abuse in Japan. 9th European Public Health Conference 2016.11.12 Vienna, Austria
21. Takeo Fujiwara, Manami Ochi, Aya Isumi, Tsuguhiko Kato. Modifiable mediators on the association between child poverty and health in Japan. 9th European Public Health Conference 2016.11.12
22. Aya Isumi, Manami Ochi, Tsuguhiko Kato, Takeo Fujiwara. Child maltreatment among economically disadvantaged families: Evidence from A-CHILD Study . 22th Annual Meeting of Japanese Society for Prevention of Child Abuse and Neglect 2016.11.26 Osaka city, Osaka
23. Kaori Honjo, Koichiro Shiba, Yukako Tani, Yuri Sasaki, Katsunori Kondo, Naoki Kondo. The risk of depressive symptoms according to living alone and social support among Japanese older people: A fixed effects analysis of longitudinal data from the Japan Gerontological Evaluation Study. ICBM2016 2016.12.10 Melbourne, Australia

# Environmental Parasitology

Professor Nobuo OHTA  
 Associate Professor Nobuaki AKAO  
 Lecturer Takashi KUMAGAI  
 Assistant Professor Akina HINO, Wataru KAGAYA (2016.4 ~)  
 Project Lecturer Mitsuko OHASHI (AMED J-GRID)  
 PhD Course Students : Masafumi YAMABE, Emmanuel BLAY, Kofi KWOFIE,  
 Ripa JAMAL (~ 2016.9), Daisuke KOBAYASHI, Katsumi MAEZAWA, Nobuhide HATA,  
 Michael AMOA-BOSOMPEM (2016.10 ~)  
 Master Course Students: Junya NAKAMICHI  
 Research student: Kiichi YAMAMOTO

## (1) Outline

Parasitic diseases are still serious health matters in the developing world. In spite of those situations, there is still no enough achievement in the disease control. Moreover, recent situations such as global warming or development of rapid transportations, parasitic infections are rather spreading even in developed countries. Our purpose of research and education are based on the global view, and comprehensive research should be done involving development of new tools for disease control. Parasites are highly evolved animals and host-parasite interplay is complicated. Uncovering those enigma is a big challenge for health and welfare of people all over the world.

Purpose of our Department is developing human resources to make contributions for health and welfare of the people living in areas with parasitic infections.

Our Department manages the Joint research project with Noguchi Memorial Institute for Medical Research, Ghana, supported by AMED, Japan.

## (2) Research

- (1) Pathological Research on zoonotic parasitoses: Toxocariasis, Dilofilariasis
- (2) Epidemiological survey of parasitic diseases: Opisthorchis infection, Schistosomiasis were analyzed by the use of new diagnostic tools in SE Asian areas.
- (3) Molecular epidemiology of tropical diseases: Drug resistance of Aedes mosquitoes, Molecular detection of arthropod viruses in mosquitoes, and their metagenomic analyses..
- (4) Immunopathology of schistosomiasis: Regulation of egg-granuloma formation in schistosomiasis japonica.
- (5) Drug development against parasitic infection: New drug candidates for schistosomiasis were investigated for their target compounds.
- (6) Regulation of gene expression in parasitic helminthes: RNAi and parasitism in schistosome parasites.
- (7) Molecular and epidemiological research on parasitic infections and vector mosquitoes in West African sub-region.

## (3) Education

Because of the recent development and the global changes in social system and life style, parasitic infections are becoming more heterogeneous. When we consider about factors promoting spreading parasitic diseases, multidisciplinary approaches are needed: medical, zoological and sociological.



Our laboratory mainly deals with pathophysiology and epidemiology of parasitic infections. Immunology, molecular biology and clinico-pathology are approaches employed. Main subjects in our laboratory are schistosomiasis, zoonotic helminthiasis, malaria and trypanosomiasis, all of which include laboratory and field investigations. In the schistosomiasis research, we focus on developing new diagnostic method by DNA detection in the sample, and uncovering immunopathogenesis of the typical hepatic inflammation. For zoonotic helminthiasis, developments of diagnostic tools are urgent matters to be studied. Our laboratory is one of the reference stations for the diagnosis in Japan.

Since 2008, TMDU started collaboration project on research on infectious diseases at Noguchi Memorial Institute for Medical Research. At the collaboration center at NMIMR, molecular approaches to discover new drug targets for African trypanosomiasis are underway.

Our Department managed Public Health Medicine Course under the special grant from Ministry of Education, Culture, Sports, Science and Technology, Japan.

#### (4) Lectures & Courses

Lecture and practices of basic and clinical parasitology are given. Further more, Field practice is important for future career. It is important to have field experiences where each student find matters and problems to be clarified. Together with those, final goal is to develop human resources with enough knowledge and experiences.

#### (5) Clinical Services & Other Works

Clinical services for the diagnosis of parasitic infections are our routine activities. Furthermore, epidemiological surveillance and disease control activities in the endemic fields are intended to enhance health and welfare of residents.

#### (6) Publications

##### [Original Articles]

1. Ikeuchi N, Itoi T, Tonozuka R, Mukai S, Koyama Y, Tsuchiya T, Matsumoto T, Mizuno Y, Nakamura I, Hino A, Moriyasu F. Strongyloides stercoralis Infection Causing Obstructive Jaundice and Refractory Pancreatitis: A Lesson Learned from a Case Study. Internal Medicine. 2016; 55(15); 2081-2086
2. Hino A, Maruyama H, Kikuchi T.. A novel method to assess the biodiversity of parasites using 18S rDNA Illumina sequencing; parasitome analysis method. Parasitology international. 2016.01;
3. Ayi I, Kwofie KD, Blay EA, Osei JH, Frempong KK, Koku R, Ghansah A, Lartey M, Suzuki T, Boakye DA, Koram KA, Ohta N.. Clonal types of Toxoplasma gondii among immune compromised and immune competent individuals in Accra, Ghana. Parasitology International. 2016.06; 65(3); 238-244
4. Motomura A, Norose K, Hoshioka Y, Torimitsu S, Chiba F, Makino Y, Inokuchi G, Yajima D, Ohta N, Kumagai T, Iwase H.. Forensic study of Schistosoma japonicum eggs found in an autopsy case. Parasitology International. 2016.06; 65(3); 285-287
5. Ayumi Motomura, Kazumi Norose, Yumi Hoshioka, Suguru Torimitsu, Fumiko Chiba, Yohsuke Makino, Go Inokuchi, Daisuke Yajima, Nobuo Ohta, Takashi Kumagai, Hirotaro Iwase. Forensic study of Schistosoma japonicum eggs found in an autopsy case. Parasitol. Int.. 2016.06; 65(3); 285-287
6. Kofi D Kwofie, Nguyen Huu Tung, Mitsuko Suzuki-Hashi, Michael Amoa-Bosompem, Richard Adegle, Maxwell M Sakyiamah, Frederick Ayertey, Kofi Baffour-Awuah Owusu, Isaac Tuffour, Philip Atchoglo, Kwadwo K Frempong, William K Anyan, Takuhiro Uto, Osamu Morinaga, Taizo Yamashita, Frederic Aboagye, Alfred A Appiah, Regina Appiah-Opong, Alexander K Nyarko, Yasuchika Yamaguchi, Dominic Edoh, Kwadwo A Koram, Shoji Yamaoka, Daniel A Boakye, Nobuo Ohta, Yukihiro Shoyama, Irene Ayi. Antitrypanosomal Activities and Mechanisms of Action of Novel Tetracyclic Iridoids from Morinda lucida Benth. Antimicrob. Agents Chemother.. 2016.06; 60(6); 3283-3290
7. Kawada H, Higa Y, Futami K, Muranami Y, Kawashima E, Osei JH, Sakyi KY, Dadzie S, de Souza DK, Appau M, Ohta N, Suzuki T, Minakawa T.. Discovery of point mutations in the voltage-gated sodium channel from African Aedes aegypti populations: Potential phylogenetic reasons for gene introgression. PLoS Neglected Tropical Diseases. 2016.06; 15(6); e0004780

8. Ayi I, Sowah AO, Blay EA, Suzuki T, Ohta N, Aye-Kumi PF.. Toxoplasma gondii infections among pregnant women, children and HIV infected persons in Accra, Ghana. Tropical Medicine and Health. 2016.06; 44(1); 17-24
9. Suzuki T, Osei JH, Sasaki A, Adimazoya M, Appau M, Boakye DA, Ohta N, Dadzie S.. Risk of transmission of viral haemorrhagic fevers and the insecticide susceptibility status of Aedes aegypti (Linnaeus) in some sites in Accra, Ghana. Ghana Medical Journal. 2016.06; 50(3); 136-141
10. Amoa-Bosompem M, Ohashi M, Mosore MT, Agyapong J, Tung NH, Kwofie KD, Ayetey F, Owusu KBA, Tuffour I, Achogle P, Djameh GI, Azerygyik FA, Botchie SK, Anyan WK, Appiah-Opong R, Uto T, Morinaga O, Appiah FA, Ayu I, Shoyama M, Ohta N.. In vitro anti-leishmania activity of tetracyclic iridoids from Morinda lucida benth. Tropical Medicine and Health. 2016.08; 44(1); 25
11. Jamal R, Shimogawara R, Yamamoto K, Ohta N.. Anti-trypanosome effects of nutritional supplements and vitamin D3: in vitro and in vivo efficacy against Trypanosoma brucei brucei. Tropical Medicine and Health. 2016.08; 44(2); 26
12. Taisei Kikuchi, Akina Hino, Teruhisa Tanaka, Myo Pa Pa Thet Hnin Htwe Aung, Tanzila Afrin, Eiji Nagayasu, Ryusei Tanaka, Miwa Higashiarakawa, Kyu Kyu Win, Tetsuo Hirata, Wah Win Htike, Jiro Fujita, Haruhiko Maruyama. Genome-Wide Analyses of Individual Strongyloides stercoralis (Nematoda: Rhabditoidea) Provide Insights into Population Structure and Reproductive Life Cycles. PLoS Neglected Tropical Diseases. 2016.12; 10(12); e0005253
13. Kwofie KD, Ghansah A, Osei JH, Frempong KK, Obed S, Frimpong EH, Boakye DA, Suzuki T, Ohta N, Ayi I.. Indication of risk of mother-to-child Toxoplasma gondii transmission in the Greater Accra region of Ghana. Maternal and Child Health Journal. 2016.12; 20(12); 2581-2588
14. Kobayashi D, Isawa H, Ejiri H, Sasaki T, Sunahara T, Futami K, Tsuda Y, Katayama Y, Mizutani T, Minakawa N, Ohta N, Sawabe K.. Complete genome sequencing and phylogenetic analysis of a Getah virus strain (Genus Alphavirus, Family Togaviridae) isolated from Culex tritaeniorhynchus mosquitoes in Nagasaki, Japan in 2012. Vector Borne Zoonotic Diseases. 2016.12; 16(12); 769-776

#### [Books etc]

1. Nobuo Ohta. Current Therapy 2016. Igaku Shoin Co., 2016.01

#### [Conference Activities & Talks]

1. Takashi Kumagai, Koichiro Ichimura, Masafumi Yamabe, Rieko Shimogawara, Nobuo Ohta. Female-biased miRNAs productions through the extracellular vesicles induced by the erythrocyte uptake in the adult worms of Schistosoma japonicum. U.S.-Japan Cooperative Medical Sciences Program (USJCMSP) Parasitic Disease Panel 2016.01.14 Bethesda, Maryland, USA
2. Akina Hino, Taisei Kikuchi, Kosuke Tanimoto, Chinami Sonobe, Takashi Kumagai, Yasuhide Saitoh, Rieko Shimogawara, Haruhiko Maruyama, Nobuo Ohta. Phylogenetic analysis of Oncomelania spp. , intermediate snails of Schistosoma japonicum, with whole mitochondria genome. The 85th Annual meeting of the Japanese society of Parasitology 2016.03.19
3. Wataru Kagaya, Chim Chan, James Kongere, Jesse Gitaka, Lucy Okell, Akira Kaneko. Mass drug administration to eliminate malaria on Ngodhe Island in Lake Victoria, Kenya: a pilot study. RSTMH Biennial Meeting - Challenges in Disease Elimination 2016.09.15 Cambridge
4. Takashi Kumagai, Moritoshi Iwagami, Masafumi Yamabe, Sengdeuane Keomalaphet, Phonepadith Khat-tignavong, Lavy Lorphacan, Pheovaly Soundala, Bouasy Hongvanthong, Nobuo Ohta, Paul T. Brey, Shigeyuki Kano. The application of the LAMP method to Opisthorchis viverrini and Schistosoma mekongi infections in Champasak Province, southern Lao PDR.. The 10th National Health Research Forum 2016.10.27 Savannakhet Province, Lao PDR



## Forensic Medicine

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Specially Appointed Assistant Professor  
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Graduate Student  
Atsushi YAMADA  
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Naho HIRAYAMA  
Yusuke FUJII  
Haruka KOJIMA  
Ryo WATANABE  
Rina KASEDA  
Tomomi SANO

### ( 1 ) Research

Research Subjects

- 1) Toxicology
- 2) Alcohol medicine
- 3) Forensic pathology

### ( 2 ) Education

Purpose of education

Forensic medicine provides fundamental human rights, public safety and nation's welfare to make a fair judgment on the items on the law which requires the medical knowledge. Education of forensic medicine is included forensic medicine in a narrow sense and medical law. Purpose of education in forensic medicine is to provide students opportunity to study the essential knowledge of the relationship between medical and society (include law, ethics, suit and administration). Students are also taught a blood type and an alcohol medicine

in a practical training.

### ( 3 ) Clinical Services & Other Works

Practical services

Forensic Medicine provides the expert opinion on a living body and a corpse to clarify causes of wound and death, mainly entrusted by a public prosecutor or the police, thereby, contributing fair trial in a court.

### ( 4 ) Publications

#### [Original Articles]

1. Watanabe M, Unuma K, Makino Y, Komatsu A, Yamada A, Nagai H, Uemura K. An Autopsy Case of Asphyxia Caused by Uncontrolled Hemorrhage Following Transbronchial Lung Biopsy J Clin Respir Dis Care. 2016;
2. Yusuke Fujii, Takeshi Funakoshi, Kana Unuma, Kanako Noritake, Toshihiko Aki, Koichi Uemura. Hydrogen sulfide donor NaHS induces death of alveolar epithelial L2 cells that is associated with cellular shrinkage, transgelin expression and myosin phosphorylation. J Toxicol Sci. 2016; 41(5); 645-654
3. Haruka Kimura-Kojima, Kana Unuma, Takeshi Funakoshi, Chizuru Kato, Ayumi Komatsu, Toshihiko Aki, Koichi Uemura. Increased MFG-E8 expression and its implications in the vascular pathophysiology of cocaine abuse. J Toxicol Pathol. 2016.04; 29(2); 131-138
4. Takeshi Funakoshi, Toshihiko Aki, Masateru Tajiri, Kana Unuma, Koichi Uemura. Necroptosis-like Neuronal Cell Death Caused by Cellular Cholesterol Accumulation. J. Biol. Chem.. 2016.11; 291(48); 25050-25065

# Health Care Management and Planning

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Ritsuki NEGISHI

Katsunori OHYAMA

## (1) Outline

By analyzing the Japanese healthcare policies and system and by reviewing their interaction with society, the structural characteristics and issues can be clarified. To resolve or find better ways to handle these issues, we conduct research into public health and welfare, and its related disciplinary areas. With the cooperation of active policy makers and personnel from the healthcare departments, the research results can be applied to the present healthcare policies and system. Through this education on collecting data, clarifying issues, analyzing the situation, and evaluating options, students taking this course are expected to grow in their ability to make healthcare policies.

## (2) Research

In the academic areas mentioned above, we conduct research under the following topic areas:

- 1) The significance of public healthcare planning, its challenges, and influences on the healthcare system  
We conduct research on issues related to new healthcare policies including planning, analysis, issue resolution, and making positive changes to the healthcare plan. This research area includes the Japanese emergency medical service and the impartial evaluation of the travel distance of aid agents and the time required for them to reach their destination.
- 2) Structural choices concerning national blood services  
In Japan, we experienced HIV infection from tainted blood products. There were various causes for this event, and improvements are required in all processes: collecting blood, screening blood, manufacturing blood products, and following-up on the usage of these products. By analyzing background information related to the adverse events and their causes, we can propose the most appropriate policies related to blood services, thus ensuring safety, and securing a stable supply. To achieve a stable supply of blood products, we also conduct epidemiological studies to review guidelines on collecting blood.
- 3) The government role in preventing medical errors

Issues related to medical errors and adverse events have recently attracted a great deal of attention in Japan. We study the role that the government should play regarding various medical errors and their prevention as well as review and address the financial loss caused by blood-related adverse events and policies on prevention.

4) Structural analyses of healthcare system in the community

By reviewing and analyzing activities related to disease prevention and health promotion conducted by local healthcare centers, we research the role of the local healthcare system and its effectiveness and efficiency.

5) Systemizing and evaluating public health policies

We review the processes of creating public health policies and systems, address the association with the creating processes and stakeholders such as political parties and lobby groups, evaluate their policies, and then suggest improvements to these policies and systems.

6) The role of healthcare communication to fill in gaps between medical providers and patients, and to share the uncertainties related to medicine and healthcare

7) The influence of healthcare communication on patient and medial safety

8) Reviewing communication tools and skills, and their systematic introduction into the healthcare system in order to realize patient participation and proactive involvement in treatment processes

### ( 3 ) Publications

#### [Original Articles]

1. Takamichi Kogure, Masahiko Sumitani, Hiroaki Abe, Jun Hozumi, Reo Inoue, Kazuhito Mietani, Kazuo Kawahara, and Yoshitsugu Yamada. . Ischemic Ulcer Pain Is Both Nociceptive and Neuropathic Pain Based on a Discriminant Function Analysis Using the McGill Pain Questionnaire Journal of Pain& Palliative Care Pharmacotherapy. 2017.04; 0(0); 1-7

# Molecular Epidemiology

Professor: Masaaki MURAMATSU

Associate Professor : Noriko SATO

Assistant Professor : Chihiro Imai

Adjunct Instructor : Katsuko SUDO, Jun-ichi TAGUCHI

Graduate Student: Kaung Si Thu,

Khin Thet Thet Zaw, Yuko Maeda, Fujitani,

Tay Zar Kyaw, Tadaaki Katsuta, Jyun-ya Hagiwara, Shilpa Pavethynath

Norihiko Satake, Maidina Abudushataer, Ake Ko Ko Minn, Zong Yuan, Kenji Suzuki, Hirokazu Sakamoto, Yui Tsubota

Research Student: Tong Daike

## ( 1 ) Outline

Many common chronic diseases are multifactorial in that they are caused by multiple genetic and environmental factors. By applying the technology and information of human genome to epidemiological studies, we aim to clarify the role of genetic polymorphisms, epigenetic changes, as well as their interaction with environmental factors, which may contribute to the development of these diseases.

## ( 2 ) Research

Our research subjects are as follows.

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
4. The role of epigenetic regulation and fetal programming in common diseases.
5. Application of personal genome to preemptive & preventive medicine.

## ( 3 ) Education

Masaaki Muramatsu: Holistic Study of Disease Prevention I

Masaaki Muramatsu: Environmental/Social Health

Masaaki Muramatsu: Negotiation and Debate in English

Noriko Sato, Masaaki Muramatsu: Bioscience I

Noriko Sato: Molecular and Cellular Biology

**(4) Lectures & Courses**

We focus on common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis which are caused by multiple genetic and environmental factors, and aim to decipher these factors as well as their interactions by applying the technology and information of human genome to epidemiology. Our goal is not only to identify disease genes and polymorphisms but also to elucidate gene-environment interactions that contribute to the onset and progression of the diseases. Epigenetic changes in common diseases are also in our scope. A new project has been started to study methods for educating genome-based health literacy by employing information generated from personal genome sequences.

**(5) Publications****[Original Articles]**

1. Kumpei Tanisawa, Yasumichi Arai, Nobuyoshi Hirose, Hiroshi Shimokata, Yoshiji Yamada, Hisashi Kawai, Motonaga Kojima, Shuichi Obuchi, Hirohiko Hirano, Hideyo Yoshida, Hiroyuki Suzuki, Yoshinori Fujiwara, Kazushige Ihara, Maki Sugaya, Tomio Arai, Seiji Mori, Motoji Sawabe, Noriko Sato, Masaaki Muramatsu, Mitsuru Higuchi, Yao-Wen Liu, Qing-Peng Kong, Masashi Tanaka. Exome-wide Association Study Identifies CLEC3B Missense Variant p.S106G as Being Associated With Extreme Longevity in East Asian Populations. *J. Gerontol. A Biol. Sci. Med. Sci.* 2016.05; 72(3); 309-318
2. Kaung Si Thu, Noriko Sato, Shinobu Ikeda, Makiko Naka-Mieno, Tomio Arai, Seiji Mori, Motoji Sawabe, Masaaki Muramatsu, Masashi Tanaka. Association of polymorphisms of the transporter associated with antigen processing (TAP2) gene with pulmonary tuberculosis in an elderly Japanese population. *APMIS*. 2016.08; 124(8); 675-680
3. Heying Zhou, Seiji Mori, Tatsuro Ishizaki, Masashi Tanaka, Kumpei Tanisawa, Makiko Naka Mieno, Motoji Sawabe, Tomio Arai, Masaaki Muramatsu, Yoshiji Yamada, Hideki Ito. Genetic risk score based on the lifetime prevalence of femoral fracture in 924 consecutive autopsies of Japanese males. *J. Bone Miner. Metab.* 2016.11; 34(6); 685-691
4. Khin Thet Thet Zaw, Noriko Sato, Shinobu Ikeda, Kaung Si Thu, Makiko Naka Mieno, Tomio Arai, Seiji Mori, Tetsushi Furukawa, Tetsuo Sasano, Motoji Sawabe, Masashi Tanaka, Masaaki Muramatsu. Association of ZFHX3 gene variation with atrial fibrillation, cerebral infarction, and lung thromboembolism: An autopsy study. *J Cardiol*. 2016.12; 70(2); 180-184
5. Yuko Maeda, Noriko Sato, Makiko Naka-Mieno, Seiji Mori, Tomio Arai, Masashi Tanaka, Masaaki Muramatsu, Motoji Sawabe. Association of non-synonymous variants in WIPF3 and LIPA genes with abdominal aortic aneurysm: an autopsy study. *J Geriatr Cardiol*. 2016.12; 13(12); 960-967

**[Conference Activities & Talks]**

1. Noriko Sato, Hidemi Takimoto, Tay Zar Kyaw, Nay Chi Htun, Chihiro Imai, Asako Igarashi, Yui Tsubota, Reiko Tajirika-Shirai, Satoshi Yago, Tomoko Aoyama, Motoko Okamitsu, Naoyuki Miyasaka. Cohort profile: Birth Cohort – Gene and Environment Interaction Study of TMDU (BC-GENIST). The 5th Annual Meeting of the Japan Society for Developmental Origins of Health and Disease
2. Noriko Sato. To understand the mechanisms by which metabolic disease develop due to antenatal nutritional environment . The 63rd meeting for the Japanese society of nutrition and dietetics 2016.09.08
3. Kaung Si Thu, Noriko Sato, Shinobu Ikeda, Makiko Naka-Mieno, Tomio Arai, Seiji Mori, Motoji Sawabe, Masashi Tanaka, Masaaki Muramatsu. Association of polymorphisms of the transporter associated with antigen processing (TAP2) gene with pulmonary tuberculosis in an elderly Japanese population. The Molecular Biology Society of Japan 2016 2016.12.02 Yokohama
4. Khin Thet Thet Zaw, Noriko Sato, Shinobu Ikeda, Kaung Si Thu, Makiko Naka-Mieno, Tomio Arai, Seiji Mori, Tetsushi Furakawa, Tetsuo Sasano, Motoji Sawabe, Masashi Tanaka, Masaaki Muramatsu. Phenome scan of ZFHX3 gene variation: association with atrial fibrillation, cerebral infarction, and lung thromboembolism. The Molecular Biology Society of Japan 2016 2016.12.02

## Research Development

Faculty Staff  
Professor  
Kozo TAKASE

Graduate Students  
Doctor course  
Akemi HIRABAYASHI  
Tomoko IZUGAMI  
Akira MIURA  
Hidehiro ANDO  
Yasumasa OOSHIRO  
Hideki TERUYA  
Masakazu HARAMO  
Rinshuu SHIMABUKURO  
Kazushige ENDOH

Master course (Master of Medical Administration)  
Ai SONODA  
Yoshimi NAKANISHI  
Daisuke NAMEKI  
Jun HATTORI  
Satoshi YABE  
Atsushi YOSHIDA

### ( 1 ) Research

- 1) Introduction of Clinical Pathway in hospital
- 2) Medical law suit and professional information
- 3) Quality management of medical law suit
- 4) Organizational logic for hospital
- 5) Health care policy and rational
- 6) Management of medical information and privacy
- 7) Hospitality in medicine
- 8) Clinical guideline and medical quality
- 9) Development of medical engineering apparatus

### ( 2 ) Education

- 1) Hospital Information Management
- 2) Medical Informatics, statistics
- 3) TQM in medicine
- 4) Biological bias and data management
- 5) Medical Law and Ethics

- 6) Medical induction course for Judges and Prosecutors (collaborated with the Supreme Court and Department of Justice)
- 7) Medical Engineering special program with Tokyo Institute of Technology
- 8) Health Promotion Policy program (General Medicine, Risk Management in Medicine) with Hitotsubashi University

### **( 3 ) Lectures & Courses**

Study on development of medical system and hospital management

Goals/outline:

The goals supposed in the lecture are mastering the technique of implementation of research development and acquiring the ability of management of projects.

### **( 4 ) Clinical Services & Other Works**

Kozo TAKASE

Committee member of Legal Training for Judicial Apprentice, Japanese Supreme Court

Chief Editorial Board of Japanese Society for Clinical Pathway

### **( 5 ) Publications**



## Health Policy and Informatics

Professor: Kiyohide FUSHIMI

Graduate Student: Asako TUKASAKI, Kyoko SHINODA,  
Ayako MATSUO, Motoko TAIMA(SANO), Toshihiro TAMAKI,  
Yuya MIZUNO, Hiroki AIZAWA, Tetu OHNUMA, Akira HOMMA,  
Eishi UECHI, Nobuo SAKATA, Tomomitsu ICHIKAWA,  
Mariko KODAN, Norihiko INOUE, Kyoko HIRANO, Mihoko OTA,  
Ken KAWASAKI, Natsuko KANAZAWA, Shunsuke EDAKUBO,  
Yoshiteru YANO, Yoko NUKAYA

Graduate Research Student: Masahiro INOUE

### (1) Research

- 1) Functional differentiation and coordination of healthcare facilities
- 2) Development and application of patient case mix system for Japanese healthcare settings
- 3) Application of information technology to standardization of health care and sharing of health care information.

### (2) Education

Health policy informatics is a branch of health policy science which deals with the application of information technology to health policy research. Main objective of health policy informatics in the graduate course is to acquire ability to independently design, manage and accomplish researches in health policy and health informatics fields.

### (3) Publications

#### [Original Articles]

1. So Kato, Hirotaka Chikuda, Junichi Ohya, Takeshi Oichi, Hiroki Matsui, Kiyohide Fushimi, Katsushi Takeshita, Sakae Tanaka, Hideo Yasunaga. Risk of infectious complications associated with blood transfusion in elective spinal surgery-a propensity score matched analysis. *Spine J.* 2016.01; 16(1); 55-60
2. Takashi Tagami, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Prophylactic Antibiotics May Improve Outcome in Patients With Severe Burns Requiring Mechanical Ventilation: Propensity Score Analysis of a Japanese Nationwide Database. *Clin. Infect. Dis.* 2016.01; 62(1); 60-66
3. Tomoki Wada, Hideo Yasunaga, Hiromasa Horiguchi, Takehiro Matsubara, Kiyohide Fushimi, Susumu Nakajima, Naoki Yahagi. Outcomes of Argatroban Treatment in Patients With Atherothrombotic Stroke: Observational Nationwide Study in Japan. *Stroke.* 2016.02; 47(2); 471-476
4. Sayaka Suzuki, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Yuki Saito, Tatsuya Yamasoba. Factors Associated With Neck Hematoma After Thyroidectomy: A Retrospective Analysis Using a Japanese Inpatient Database. *Medicine (Baltimore).* 2016.02; 95(7); e2812

5. Junichi Ohya, Yasushi Oshima, Hirotaka Chikuda, Takeshi Oichi, Hiroki Matsui, Kiyohide Fushimi, Sakae Tanaka, Hideo Yasunaga. Does the microendoscopic technique reduce mortality and major complications in patients undergoing lumbar discectomy? A propensity score-matched analysis using a nationwide administrative database. *Neurosurg Focus*. 2016.02; 40(2); E5
6. Tsuyoshi Hamada, Hideo Yasunaga, Yousuke Nakai, Hiroyuki Isayama, Hiroki Matsui, Kiyohide Fushimi, Kazuhiko Koike. Interstitial lung disease associated with gemcitabine: A Japanese retrospective cohort study. *Respirology*. 2016.02; 21(2); 338-343
7. Masao Iwagami, Hideo Yasunaga, Eisei Noiri, Hiromasa Horiguchi, Kiyohide Fushimi, Takehiro Matsubara, Naoki Yahagi, Masaomi Nangaku, Kent Doi. Potential Survival Benefit of Polymyxin B Hemoperfusion in Septic Shock Patients on Continuous Renal Replacement Therapy: A Propensity-Matched Analysis. *Blood Purif*.. 2016.02; 42(1); 9-17
8. Hanako Ishikawa, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Norito Kawakami. Differences in cancer stage, treatment and in-hospital mortality between patients with and without schizophrenia: retrospective matched-pair cohort study. *Br J Psychiatry*. 2016.03; 208(3); 239-244
9. Takashi Tagami, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Changes in Therapeutic Hypothermia and Coronary Intervention Provision and In-Hospital Mortality of Patients With Out-of-Hospital Cardiac Arrest: A Nationwide Database Study. *Crit. Care Med*.. 2016.03; 44(3); 488-495
10. Yusuke Tsuda, Hideo Yasunaga, Hiromasa Horiguchi, Kiyohide Fushimi, Hirotaka Kawano, Sakae Tanaka. Complications and Postoperative Mortality Rate After Surgery for Pathological Femur Fracture Related to Bone Metastasis: Analysis of a Nationwide Database. *Ann. Surg. Oncol*.. 2016.03; 23(3); 801-810
11. Ryo Momosaki, Hideo Yasunaga, Wataru Kakuda, Hiroki Matsui, Kiyohide Fushimi, Masahiro Abo. Very Early versus Delayed Rehabilitation for Acute Ischemic Stroke Patients with Intravenous Recombinant Tissue Plasminogen Activator: A Nationwide Retrospective Cohort Study. *Cerebrovasc. Dis*.. 2016.03; 42(1-2); 41-48
12. Sayaka Suzuki, Hideo Yasunaga, Hiroki Matsui, Hiromasa Horiguchi, Kiyohide Fushimi, Tatsuya Yamasoba. Pharyngocutaneous fistula and delay in free oral feeding after pharyngolaryngectomy for hypopharyngeal cancer. *Head Neck*. 2016.04; 38(S1); E625-E630
13. Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. In-hospital mortality and successful weaning from venoarterial extracorporeal membrane oxygenation: analysis of 5,263 patients using a national inpatient database in Japan. *Crit Care*. 2016.04; 20(1); 80
14. Y Sasabuchi, H Yasunaga, H Matsui, A K Lefor, K Fushimi. Prolonged propofol infusion for mechanically ventilated children. *Anaesthesia*. 2016.04; 71(4); 424-428
15. Momosaki Ryo, Yasunaga Hideo, Matsui Hiroki, Horiguchi Hiromasa, Fushimi Kiyohide, Abo Masahiro. Predictive factors for oral intake after aspiration pneumonia in older adults. *Geriatr Gerontol Int*. 2016.05; 16(5); 556-560
16. Toshiaki Isogai, Hideo Yasunaga, Hiroki Matsui, Hiroyuki Tanaka, Kiyohide Fushimi. Relationship between hospital volume and major cardiac complications of rotational atherectomy: A nationwide retrospective cohort study in Japan. *J Cardiol*. 2016.05; 67(5); 442-448
17. Ryo Momosaki, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Masahiro Abo. Proton Pump Inhibitors versus Histamine-2 Receptor Antagonists and Risk of Pneumonia in Patients with Acute Stroke. *J Stroke Cerebrovasc Dis*. 2016.05; 25(5); 1035-1040
18. Sachiko Ono, Miho Ishimaru, Yosuke Ono, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Impact of Body Mass Index on the Outcomes of Open Reduction for Mandibular Fractures. *J. Oral Maxillofac. Surg*.. 2016.05; 74(5); 1024:e1-1024:e5
19. Junko Hirashima, Hayato Yamana, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Effect of intravenous magnesium sulfate on mortality in patients with severe acute asthma. *Respirology*. 2016.05; 21(4); 668-673
20. Michio Naganuma, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Clinical features of isolated dissections of abdominal aortic branches. *Heart Vessels*. 2016.06; 31(6); 1006-1009

21. Miho Ishimaru, Sachiko Ono, Sayaka Suzuki, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Risk Factors for Free Flap Failure in 2,846 Patients With Head and Neck Cancer: A National Database Study in Japan. *J. Oral Maxillofac. Surg.*. 2016.06; 74(6); 1265-1270
22. Yutaka Yamaji, Hideo Yasunaga, Yoshihiro Hirata, Atsuo Yamada, Shuntaro Yoshida, Hiromasa Horiguchi, Kiyohide Fushimi, Kazuhiko Koike. Association Between Colorectal Cancer and Atherosclerotic Diseases: A Study Using a National Inpatient Database in Japan. *Dig. Dis. Sci.*. 2016.06; 61(6); 1677-1685
23. Yasuhiro Yamauchi, Hideo Yasunaga, Wakae Hasegawa, Yukiyo Sakamoto, Hideyuki Takeshima, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Effect of outpatient therapy with inhaled corticosteroids on decreasing in-hospital mortality from pneumonia in patients with COPD. *Int J Chron Obstruct Pulmon Dis.* 2016.06; 11; 1403-1411
24. Keishi Oda, Kazuhiro Yatera, Yoshihisa Fujino, Hiroshi Ishimoto, Hiroyuki Nakao, Tetsuya Hanaka, Takaaki Ogoshi, Takashi Kido, Kiyohide Fushimi, Shinya Matsuda, Hiroshi Mukae. Efficacy of concurrent treatments in idiopathic pulmonary fibrosis patients with a rapid progression of respiratory failure: an analysis of a national administrative database in Japan. *BMC Pulm Med.* 2016.06; 16(1); 91
25. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Kiyohide Fushimi, Hideo Yasunaga. Early  $\beta$ -blocker use and in-hospital mortality in patients with Takotsubo cardiomyopathy. *Heart.* 2016.07; 102(13); 1029-1035
26. Yusuke Sasabuchi, Hiroki Matsui, Alan K Lefor, Kiyohide Fushimi, Hideo Yasunaga. Risks and Benefits of Stress Ulcer Prophylaxis for Patients With Severe Sepsis. *Crit. Care Med.*. 2016.07; 44(7); e464-e469
27. Hironori Uematsu, Susumu Kunisawa, Kazuto Yamashita, Kiyohide Fushimi, Yuichi Imanaka. Impact of weekend admission on in-hospital mortality in severe community-acquired pneumonia patients in Japan. *Respirology.* 2016.07; 21(5); 905-910
28. Sayaka Suzuki, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Tatsuya Yamasoba. Factors associated with prolonged duration of post-tympanoplasty local treatment in adult chronic otitis media patients: A retrospective observational study using a Japanese inpatient database. *Auris Nasus Larynx.* 2016.08; 43(4); 377-381
29. Tetsu Ohnuma, Daisuke Shinjo, Kiyohide Fushimi. Hospital mortality of patients aged 80 and older after surgical repair for type A acute aortic dissection in Japan. *Medicine (Baltimore).* 2016.08; 95(31); e4408
30. Sayaka Suzuki, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Yuki Saito, Tatsuya Yamasoba. Cerebral infarction after intraarterial and intravenous chemoradiotherapy for head and neck cancer: A retrospective analysis using a Japanese inpatient database. *Head Neck.* 2016.09; 38(9); 1354-1358
31. Yasuhiro Yamauchi, Hideo Yasunaga, Yukiyo Sakamoto, Wakae Hasegawa, Hideyuki Takeshima, Hirokazu Urushiyama, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Mortality associated with bone fractures in COPD patients. *Int J Chron Obstruct Pulmon Dis.* 2016.09; 11; 2335-2340
32. Seiko Mizuno, Susumu Kunisawa, Noriko Sasaki, Kiyohide Fushimi, Yuichi Imanaka. In-hospital mortality and treatment patterns in acute myocardial infarction patients admitted during national cardiology meeting dates. *Int. J. Cardiol.*. 2016.10; 220; 929-936
33. Nobuo Sakata, Sayuri Shimizu, Fumio Hirano, Kiyohide Fushimi. Epidemiological study of adult-onset Still's disease using a Japanese administrative database. *Rheumatol. Int.*. 2016.10; 36(10); 1399-1405
34. Hayato Yamana, Hiroki Matsui, Takashi Tagami, Junko Hirashima, Kiyohide Fushimi, Hideo Yasunaga. De-escalation versus continuation of empirical antimicrobial therapy in community-acquired pneumonia. *J. Infect.*. 2016.10; 73(4); 314-325
35. Hayato Yamana, Hiromasa Horiguchi, Kiyohide Fushimi, Hideo Yasunaga. Comparison of Procedure-Based and Diagnosis-Based Identifications of Severe Sepsis and Disseminated Intravascular Coagulation in Administrative Data. *J Epidemiol.* 2016.10; 26(10); 530-537
36. Takumi Matsumoto, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Naohiro Izawa, Tetsuro Yasui, Yuho Kadono, Sakae Tanaka. Time trends and risk factors for perioperative complications in total ankle arthroplasty: retrospective analysis using a national database in Japan. *BMC Musculoskelet Disord.* 2016.10; 17(1); 450

37. Takashi Tagami, Hiroki Matsui, Masamune Kuno, Yuuta Moroe, Junya Kaneko, Kyoko Unemoto, Kiyohide Fushimi, Hideo Yasunaga. Early antibiotics administration during targeted temperature management after out-of-hospital cardiac arrest: a nationwide database study. *BMC Anesthesiol.* 2016.10; 16(1); 89
38. Takashi Tagami, Hiroki Matsui, Chie Tanaka, Junya Kaneko, Masamune Kuno, Saori Ishinokami, Kyoko Unemoto, Kiyohide Fushimi, Hideo Yasunaga. Amiodarone Compared with Lidocaine for Out-Of-Hospital Cardiac Arrest with Refractory Ventricular Fibrillation on Hospital Arrival: a Nationwide Database Study. *Cardiovasc Drugs Ther.* 2016.10; 30(5); 485-491
39. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Kiyohide Fushimi, Hideo Yasunaga. Atrial natriuretic peptide therapy and in-hospital mortality in acute myocardial infarction patients undergoing percutaneous coronary intervention. *Int. J. Cardiol.* 2016.11; 222; 163-170
40. Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. The Effect of Intraaortic Balloon Pumping Under Venoarterial Extracorporeal Membrane Oxygenation on Mortality of Cardiogenic Patients: An Analysis Using a Nationwide Inpatient Database. *Crit. Care Med.* 2016.11; 44(11); 1974-1979
41. Yasuo Nakahara, Hideo Yasunaga, Haruhi Inokuchi, Naoshi Ogata, Hiromasa Horiguchi, Shinya Matsuda, Kiyohide Fushimi, Nobuhiko Haga. Mortality-Reducing Effect of Rehabilitation for COPD: Observational Propensity-Matched Cohort Study Using a Nationwide Database. *Respir Care.* 2016.11; 61(11); 1497-1504
42. Tsuyoshi Hamada, Hideo Yasunaga, Yousuke Nakai, Hiroyuki Isayama, Hiroki Matsui, Kiyohide Fushimi, Kazuhiko Koike. No weekend effect on outcomes of severe acute pancreatitis in Japan: data from the diagnosis procedure combination database. *J. Gastroenterol.* 2016.11; 51(11); 1063-1072
43. Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Hospital volume and mortality due to preterm patent ductus arteriosus. *Pediatr Int.* 2016.11; 58(11); 1171-1175
44. Maiko Yagi, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Masashi Fujimoto, Teruyuki Koyama, Junko Fujitani. Effect of early rehabilitation on activities of daily living in patients with aspiration pneumonia. *Geriatr Gerontol Int.* 2016.11; 16(11); 1181-1187
45. Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. Reducing Length of Hospital Stay Does Not Increase Readmission Rates in Early-Stage Gastric, Colon, and Lung Cancer Surgical Cases in Japanese Acute Care Hospitals. *PLoS ONE.* 2016.11; 11(11); e0166269
46. Ryuji Sasaki, Hideo Yasunaga, Hiroki Matsui, Nobuaki Michihata, Kiyohide Fushimi. Hospital Volume and Mortality in Mechanically Ventilated Children: Analysis of a National Inpatient Database in Japan. *Pediatr Crit Care Med.* 2016.11; 17(11); 1041-1044
47. Hironori Uematsu, Kazuto Yamashita, Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. The economic burden of methicillin-resistant *Staphylococcus aureus* in community-onset pneumonia inpatients. *Am J Infect Control.* 2016.12; 44(12); 1628-1633
48. Ryota Niikura, Hideo Yasunaga, Atsuo Yamada, Hiroki Matsui, Kiyohide Fushimi, Yoshihiro Hirata, Kazuhiko Koike. Factors predicting adverse events associated with therapeutic colonoscopy for colorectal neoplasia: a retrospective nationwide study in Japan. *Gastrointest. Endosc.* 2016.12; 84(6); 971-982.e6
49. Takashi Tagami, Hiroki Matsui, Saori Ishinokami, Masao Oyanagi, Akiko Kitahashi, Reo Fukuda, Kyoko Unemoto, Kiyohide Fushimi, Hideo Yasunaga. Amiodarone or nifekalant upon hospital arrival for refractory ventricular fibrillation after out-of-hospital cardiac arrest. *Resuscitation.* 2016.12; 109; 127-132
50. Tomoki Wada, Hideo Yasunaga, Hiromasa Horiguchi, Kiyohide Fushimi, Takehiro Matsubara, Susumu Nakajima, Naoki Yahagi. Ozagrel for Patients With Noncardioembolic Ischemic Stroke: A Propensity Score-Matched Analysis. *J Stroke Cerebrovasc Dis.* 2016.12; 25(12); 2828-2837

**[Conference Activities & Talks]**

1. Kiyoshi Murata, Yasuhiro otomo, Kiyohide Fushimi. . Quality Management of Acute Care Surgery Training Program based on PDCA cycle. 17th European Congress of Trauma and Emergency Surgery 2016.04.24 Vienna, Austria
2. Ohta, M., Fushimi, K. . Real-World Comparing Intravenous Busulfan to Total Body Irradiation in Hematopoietic Stem Cell Transplantation with A Japanese Diagnosis Procedure Combination(DPC) Database. ISPOR 7th Asia-Pacific Conference 2016.09.03 Singapore
3. Mutsuko Moriwaki, Yuko Sase, Mikayo Toba, Kiyohide Fushimi. . Visualization of the current situation of the use of antibacterial drugs by using medical data and an approach to improvement activities. International Forum on Quality and Safety in Healthcare. 2016.09.26 Singapore
4. Mikayo Toba, Mutsuko Moriwaki, Noriko Oshima, Kimio Wakana, Akira Wakabayashi, Satoshi Kobayashi, Kiyohide Fushimi.. Caluculation of inpatient mortality after surgeryfor uterine endometrial cancer using a anationwide administractive database. International Forum on Quality and Safety in Healthcare. 2016.09.26 Singapore

# Life Sciences and Bioethics

Masayuki Yoshida  
Yusuke Ebana  
Hiroko Kohbata  
Mizuko Osaka  
Eiichiro Kanda

## (1) Outline

Department of Life Sciences and Bioethics (Bioethics Research Center) offers classes and seminars regarding bioethics, research ethics, and clinical ethics in Graduate School of Medical and Dental Sciences, Graduate School of Health Care Sciences, and School of Medicine. Our lecture includes fundamental bioethics and research ethics so that students can absorb the current concept of the bioethics and research ethics. We try to include clinical materials such as cases of genetic counseling, where ethics-based approach is critically important.

Apart from class for juniors, we give bioethics seminars for hospital staff and faculties based on the research ethics guideline revised 2008, in which attendance of bioethics lecture is mandatory for any person who conducts medical research.

We dynamically participated in extra-campus activities; such as the ethical committee members of the National Institute of Health etc.

## (2) Publications

### [Original Articles]

1. Yuki Hasegawa, Satomi Hamada, Takuro Nishimura, Takeshi Sasaki, Yusuke Ebana, Mihoko Kawabata, Masahiko Goya, Mitsuaki Isobe, Takatoshi Koyama, Tetsushi Furukawa, Kenzo Hirao, Tetsuo Sasano. Novel Dielectric Coagulometer Identifies Hypercoagulability in Patients with a High CHADS2 Score without Atrial Fibrillation. PLoS ONE. 2016; 11(6); e0156557
2. Yusuke Ebana, Hiroko Terui-Kohbata, Sayako Takahashi, Yoshida Masayuki.. Genetic counseling for a case with breast cancer who underwent a whole-exome sequencing in a private company The 13th International Congress of Human Genetics Program. 2016; 229
3. Eiichiro Kanda, Masumi Ai, Mitsuyo Okazaki, Masayuki Yoshida, Yoshitaka Maeda. Association of High-Density Lipoprotein Subclasses with Chronic Kidney Disease Progression, Atherosclerosis, and Klotho. PLoS ONE. 2016; 11(11); e0166459
4. Kataoka H, Ariyama Y, Deushi M, Osaka M, Nitta K, Yoshida M.. Inhibitory Effect of Serotonin Antagonist on Leukocyte-Endothelial Interactions In Vivo and In Vitro. PROS ONE. 2016.01; 11(1); e0147929
5. Ito S, Osaka M, Edamatsu T, Itoh Y, Yoshida M.. Crucial Role of the Aryl Hydrocarbon Receptor (AhR) in Indoxyl Sulfate-Induced Vascular Inflammation. Journal of Atherosclerosis Thrombosis. 2016.02;
6. Mizuko Osaka, Shunsuke Ito, Masaki Honda, Yukihiro Inomata, Kensuke Egashira, Masayuki Yoshida. Critical role of the C5a-activated neutrophils in high-fat diet-induced vascular inflammation. Scientific Reports. 2016.02; 6; 21391

7. Yoichi Otaki, Yusuke Ebana, Shunji Yoshikawa, Mitsuaki Isobe. Dielectric permittivity change detects the process of blood coagulation: Comparative study of dielectric coagulometry with rotational thromboelastometry. *Thromb. Res.* 2016.06; 145; 3-11
8. Hirokazu Ohigashi, Natsuko Tamura, Yusuke Ebana, Masayoshi Harigai, Yasuhiro Maejima, Takashi Ashikaga, Mitsuaki Isobe. Effects of immunosuppressive and biological agents on refractory Takayasu arteritis patients unresponsive to glucocorticoid treatment. *J Cardiol.* 2016.08;
9. Shunsuke Ito, Mizuko Osaka, Takeo Edamatsu, Yoshiharu Itoh, Masayuki Yoshida. Crucial Role of the Aryl Hydrocarbon Receptor (AhR) in Indoxyl Sulfate-Induced Vascular Inflammation. *J. Atheroscler. Thromb.* 2016.08; 23(8); 960-975
10. Michiyo Deushi, Mizuko Osaka, Kaku Nakano, Kyoichi Osada, Kensuke Egashira, Masayuki Yoshida. Ezetimibe reduced hepatic steatosis induced by dietary oxysterols in nonhuman primates. *FEBS Open Bio.* 2016.10; 6(10); 1008-1015
11. Tani M, Horvath KV, Lamarche B, Couture P, Burnett JR, Schaefer EJ, Asztalos BF. Effects of Lipoprotein Lipase and Hepatic Lipase Deficiency on High-Density Lipoproteins. *Atherosclerosis* . 2016.10; 253; 7-14
12. Lian Liu, Yusuke Ebana, Jun-Ichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Toshihiro Tanaka, Masatoshi Komura, Mitsuaki Isobe, Tetsushi Furukawa. Genetic Variants Associated With Susceptibility to Atrial Fibrillation in a Japanese Population. *Can J Cardiol.* 2016.11;

#### [Misc]

1. Yusuke Ebana. Ethics in Clinical Research Obstet. Gynecol.. 2016.10; 83(10); 1119-1123

#### [Conference Activities & Talks]

1. Osaka Mizuko, Ito Shunsuke, Yoshida Masayuki. High-Fat Diet-triggered Neutrophil Activation Initiates Leukocyte Adhesion to Murine Femoral Artery in vivo. Japanese Circulation Society Scientific Meeting 2016.03
2. Yusuke Ebana, Hiroko Terui-Kohbata, Sayako Takahashi, Yoshida Masayuki. Genetic counseling for a case with breast cancer who underwent a whole-exome sequencing in a private company. The 13th International Congress of Human Genetics 2016.04
3. Yusuke Ebana Hiroko Kohbata, Sayako Takahashi, Masayuki Yoshida. Genetic counselling for a case with breast cancer who underwent a whole-exome sequencing in a private company. The 13th International Congress Society of Human Genetics 2016.04.06
4. Hiroko Kohbata, Yusuke Ebana, Sayako Takahashi, Masayuki Yoshida. Genetic Counseling for the Result of a Company's Personal Exome Sequencing: a Case Report. Japanese Society for Genetic Counseling 2016.04.08 Kyoto
5. Osaka M, Yoshida M. Role of complement component C5a for development of atherosclerosis.. The 48th Annual Scientific Meeting of the Japan Atherosclerosis Society 2016.07.14 Tokyo
6. Mizuko Osaka, Masaki Honda, Yukihiro Inomata, Kensuke Egashira, Masayuki Yoshida. C5a play an important role in high fat diet-induced neutrophil activation. XXVth INTERNATIONAL COMPLEMENT WORKSHOP 2016.09.04
7. Mariko Tani, Yuko Kamata, Michiyo Deushi, Mizuko Osaka, Masayuki Yoshida. 7-ketocholesterol Induces Leukocyte Interaction to Endothelial Cells thorough p38MAPK-dependent pathway. 19th International Vascular Biology Meeting 2016.10 Sheraton Boston Hotel, Boston, USA
8. Mizuko Osaka, Masaki Honda, Yukihiro Inomata, Masayuki Yoshida. Critical role of complement C5a and neutrophils during high-fat diet-induced vascular inflammation.. 19th International vascular biology meeting 2016.10.30 Boston
9. Osaka M, Yoshida M. High fat diet induces vascular inflammation via upregulation of complement component C5a.. the Society of Cerebral-Cardio-Vascular Anti-Aging 2016.12.17 Tokyo



# Forensic Dentistry

Professor Koichi SAKURADA  
 Assistant Professor Hajime UTSUNO  
 Assistant Professor Namiko ISHII  
 Graduate Student Saki MINEGISHI

## (1) Outline

Forensic dentistry plays an important role in society through the use identification of victims after major accidents or disasters using dental findings, as well as the identification of cadavers or persons from biological samples in relation to crime. In particular, the establishment of two laws related to cause of death investigation in June 2012 further promoted research, identification, and education related to individual identification. The primary function of our laboratory is the identification of individuals from hard tissues such as teeth and bones, soft tissues, body fluids, or facial images, using the latest molecular biological and imaging techniques.

## (2) Research

1. Individual identification
  - Identification based on dental findings
  - Identification using hard tissues such as teeth and bones, soft tissues, and body fluids
  - Identification based on facial reconstruction and image analysis
2. Child abuse and neglect
3. Dental accidents and lawsuits
4. Problems associated with the dental care system
5. Forensic toxicology

## (3) Education

We teach dental students a relation between death investigation systems and dentists and make them understand that society expects them as dentists to perform individual identification based on dental findings. Also, students are likely to have opportunities to assist the regional administrative and police activities in the future. To protect the rights of the deceased individuals and improve public health, dental students need to acquire basic knowledge about forensic medical sciences including postmortem changes and cause of death identification. To foster independent researchers, we teach graduate students the latest research directions in forensic dentistry and how to plan their own research project. In addition, students learn practical individual identification methods and their importance through forensic autopsy.

## (4) Lectures & Courses

We believe that students learn more effectively in an environment where they can simultaneously conduct practical work and research.



**( 5 ) Clinical Services & Other Works**

Forensic autopsy for the identification of cadavers and other related activities. Individual identification following accidents or disasters. Participation in disaster prevention and individual identification training programs held by various communities.

**( 6 ) Publications****[Original Articles]**

1. Ken Watanabe, Tomoko Akutsu, Koichi Sakurada. Development of a Real-Time PCR-Based Method for Analyzing Semen-Specific Unmethylated DNA Regions and Methylation Status in Aged Body Fluid Stains. *J. Forensic Sci.*. 2016.01; 61 Suppl 1; S208-S212
2. Suguru Torimitsu, Yohsuke Makino, Hisako Saitoh, Ayaka Sakuma, Namiko Ishii, Daisuke Yajima, Go Inokuchi, Ayumi Motomura, Fumiko Chiba, Rutsuko Yamaguchi, Mari Hashimoto, Yumi Hoshioka, Hirotaro Iwase. Stature estimation from skull measurements using multidetector computed tomographic images: A Japanese forensic sample. *Leg Med (Tokyo)*. 2016.01; 18; 75-80
3. Ken Watanabe, Tomoko Akutsu, Ayari Takamura, Koichi Sakurada. Evaluation of a blood-specific DNA methylated region and trial for allele-specific blood identification from mixed body fluid DNA. *Leg Med (Tokyo)*. 2016.09; 22; 49-53
4. Namiko Ishii, Ayaka Sakuma, Yohsuke Makino, Suguru Torimitsu, Daisuke Yajima, Go Inokuchi, Ayumi Motomura, Fumiko Chiba, Yumi Hoshioka, Hirotaro Iwase, Hisako Saitoh. Incidence of three-rooted mandibular first molars among contemporary Japanese individuals determined using multidetector computed tomography. *Leg Med (Tokyo)*. 2016.09; 22; 9-12
5. Suguru Torimitsu, Yohsuke Makino, Hisako Saitoh, Ayaka Sakuma, Namiko Ishii, Daisuke Yajima, Go Inokuchi, Ayumi Motomura, Fumiko Chiba, Rutsuko Yamaguchi, Mari Hashimoto, Yumi Hoshioka, Hirotaro Iwase. Sexual determination based on multidetector computed tomographic measurements of the second cervical vertebra in a contemporary Japanese population. *Forensic Sci. Int.*. 2016.09; 266; 588.e1-588.e6
6. N Ishii, Y Makino, M Fujita, A Sakuma, S Torimitsu, F Chiba, D Yajima, G Inokuchi, A Motomura, N H Iwase, H Saitoh. Assessing age-related change in Japanese mental foramen opening direction using multidetector computed tomography. *J Forensic Odontostomatol*. 2016.12; 2(34); 11-20

**[Books etc]**

1. Koichi Sakurada. Teeth speak louder than words the great mission that a dentist can contribute to the society . *DENTAL DIAMOND*, 2016.07
2. Koichi Sakurada. Teeth speak louder than words what methods are used for private identification ? . *DENTAL DIAMOND*, 2016.08
3. Koichi Sakurada. Teeth speak louder than words why is the tooth useful for private identificatoin? . *DENTAL DIAMOND*, 2016.09
4. Koichi Sakurada. Teeth speak louder than words private identification by forensic autopsies . *DENTAL DIAMOND*, 2016.10
5. Koichi Sakurada. Teeth speak louder than words oral photograph and dental chart . *DENTAL DIAMOND*, 2016.11
6. Koichi Sakurada. Teeth speak louder than words dental X-rays and CT images . *DENTAL DIAMOND*, 2016.12

**[Misc]**

1. Victor A Voicu, Andrei Valentin Medvedovici, Koichi Sakurada, Hikoto Ohta, Flavian Stefan Rădulescu, Dalia Simona Miron. The forgotten or underestimated relevance of biopharmaceutical-based assessments for the oral absorption studies of oxime reactivators. *Expert Opin Drug Metab Toxicol*. 2016.07; 12(7); 743-752

**[Conference Activities & Talks]**

1. Susumu Ohtani, Ran Iguchi, Hidenori Nene, Noboru Adachi, Kanako Noritake, Joji Funakoshi, Koichi Sakurada, Koichi Uemura, Yoshihiro Yamada. A case that the age estimation from the tooth by the amino acid racemization method was particularly effective for identification . The 100 Congress of the Japanese Society of Legal Medicine 2016.06.17 Shinagawa-ku, Kyurian
2. Torimitsu S, Makino Y, Saitoh H, Sakuma A, Ishii N, Yajima D, Inokuchi G, Motomura A, Chiba F, Yamaguchi R, Hashimoto M, Hoshioka Y, Iwase H.. Stature estimation from skull measurements using multidetector computed tomographic images: A Japanese forensic sample.. The 100st Congress Of The Japanese Society Of Legal Mrdicine 2016.06.17 Kyuriann,Higashiooi, Shinagawa-ku, Tokyo
3. Saitoh H, Yusa K, Moriya T, Takeyama M, Sakuma A, Ishii N, Abe H, Takahashi S, Chiba F, Torimitsu S, Iwase H, Iino M, Tokanai H.. The radiocarbon birth-dating estimation using teeth : a study of sample processing. The 100th Congress Of The Japanese Society Of Legal Medicine 2016.06.17 Kyuriann, Higashiooi, Shinagawa-ku, Tokyo
4. Hajime Utsuno, Namiko Ishii, Saki Minegishi, Koichi Sakurada. Oculusion state of the gender gap which should be noted when performing the face restruction method. The 15th National Meeting of Police Dentist Society 2016.09.03 Gifu city
5. Hajime Utsuno, Namiko Ishii, Saki Minegishi, and Koichi Sakurada.. Significant difference of occlusion and Sexual demorphisms for then performing facial reconstruction.. The 15th National Meeting of Police Dentist Society 2016.09.03 Gifu
6. Saegusa F, Saitoh H, Ishii N, Sakuma A, Hiraga T, Takahashi T, Nakayama S, Hayashi K, Omori M, Uchida K, Shishikura K, Kimata S, Saito H.. For the dental identification , the Japan dental association in cooperation with the police work with the department of Legal Medicine at Chiba University . The 15th National Meeting of Police Dentist Society 2016.09.03 Gifu Grand Hotel, Gifu-shi
7. Hajime Utsuno, Namiko Ishii, Saki Minegishi, Koichi Sakurada. Oculusion state of the gender gap which should be noted when performing the face restruction method. The 15th National Meeting of Police Dentist Society 2016.09.03 Gifu city
8. Hajime Utsuno. Archaeological Facial Reconstruction from Juvenile Skull. The 70th Annual Meeting of the Anthropological Society of Nippon 2016.10.10 Niigata
9. Koichi Sakurada, Ken Watanabe, Tomoko Akutsu. Seminar 4 :Introduction of forensic scientific methods from bloodstains and body fluid stains. 10th Anniversary Meeting of Japanese Society of Forensic Dental Science 2016.11.06 Station Conference Tokyo
10. Torimitsu S, Makino Y, Saitoh H, Sakuma A, Ishii N, Yajima D, Inokuchi G, Motomura A, Chiba F, Yamaguchi R, Hashimoto M, Hoshioka Y, Iwase H.. Sex estimation based on scapula analysis in a Japanese population using multidetector computed tomography.. The 10th Congress Of The Japanese Society Of Forensic Dental Science 2016.11.06 Station Conference Tokyo
11. Sugimoto T., Utsuno H.. Questionnair survey on relaps of post orthodontic treatment in the patients of Omiya Orthodontic Clinin. The 75th Annual Meeting of the Japanese Orthodontic Society 2016.11.08 Tokushima
12. Koichi Sakurada. Project for Promoting Leading-edge Research in Oral Science, Kickoff Symposium, Session 2:Society and Education. The 81st Annual Meeting of the Stomatological Society of Japan 2016.11.26 Tokyo Medical and Dental University

**[Social Contribution]**

1. Individual identification using dental findings (50 cases), 2016, 2016.01.01 - 2016.12.31

# Health Care Economics

Koichi Kawabuchi  
Isao Igarashi

## ( 1 ) Outline

The role of health care extends to improving such aspects of life as dietary habit and relationship with others, and is deeply connected to quality of life. Looking back, however, discussion on healthcare has too often originated from political dynamics and interests of parties involved, and not from the voices of general public. This is due partially to the lack of quality data available among the people. The reality of healthcare and what it brings to the society are not necessarily always clear to the general public. In terms of dental care especially, it is hard to say that enough evidences have been established and widely recognized among people to the extent that matches to its importance in providing quality life. Thus, we apply economics in conducting interdisciplinary review of healthcare along with other related fields, and pursue how the healthcare system should be for the people.

## ( 2 ) Research

Research activities involve conducting analysis on phenomena and observations in health care from the viewpoint of macro as well as micro economics.

Main focuses are:

- 1) Cross-sectional research on healthcare, dental care, nursing care, long-term care, and pharmaceuticals from the viewpoint of economics
- 2) Proposals on policy making in efficient delivery of healthcare, nursing care, and long-term care
- 3) Borderless and mutual development of various specialties such as dental care, healthcare, economics, management and accounting.

## ( 3 ) Education

Understanding the methods of research on phenomena and observations in health care field through economics point of view. As we have many part-time students with jobs as well as foreign students, the lecture will be centered around such topics as the approach to a research theme in economics and other social sciences (especially empirical studies) , how to proceed with the research, and paper writing. Specifically, we will provide outline of healthcare economics by a weekly lecture for Ph. D. candidates as well as once a year lecture for the master course. Some of them adapt more interactive style of problem solving with input from visiting lecturers. Emphasis is placed on methods of quantitative analysis, learning both theoretical and empirical approaches to phenomena and observations in health care field through economics point of view. Lectures for undergraduate education will be focused on the outline of healthcare economics in dental care, with specific themes as 1) Economical analysis of dental healthcare, 2) Expenditure on dental care, 3) Reimbursement, and 4) Quality assessment of dental care.

**( 4 ) Lectures & Courses**

Faced with recent changes in healthcare and long-term care, core hospitals and other healthcare related institutions in communities with responsibility of supporting front-line healthcare long for personnel competent in healthcare management. Call for such personnel is strong among research organizations and public offices as well, looking for those who are proficient in qualitative and quantitative analysis. Therefore, we aim to train students to be capable in making immediate contribution to the healthcare and welfare field, and to educate future "academic doctors" who can voice their messages in policy making.

**( 5 ) Clinical Services & Other Works**

Igarashi, Assistant Professor in our department, practices three times a week in the clinic for Oral Diagnosis and General Dentistry of the Dental Hospital. Findings from our research activities are shared to the public through papers, reports, lectures and symposiums in both academic and less academic settings. Comments on healthcare reform, for instance, have been televised on and printed in various media.

**( 6 ) Publications****[Misc]**

1. Kazumitsu Nawata, Koichi kawabuchi. Comparison of the Length of Stay and Medical Expenditures among Japanese Hospitals for Type 2 Diabetes Treatments: The Box-Cox Transformation Model under Heteroscedasticity Health. 2016.01; 8(1);
2. Koichi Kawabuchi, Yusuke Kabeya. FY2016 Estimating the Impact of the New Income Deduction System for Over-the-Counter Drug Expenses- JAPAN HOSPITALS. 2016.07; 35;

**[Conference Activities & Talks]**

1. Policies on Healthcare and Nursing care in Japan and The Integrated Community Care System.. International (Sino-Japan) Summit on Integrated Care 2016.04.09
2. Koichi Kawabuchi. Looking for solutions to issues in elderly care. CHINA-HOSPEQ 2016 2016.08.19
3. Koichi Kawabuchi, Yusuke Kabeya. Impact of promoting self-medication on medical costs in Japan: a new research proposal. 11th WSMI Asia-Pacific Conference & 3rd APSMI General Assembly Meeting at Nagoya 2016.10.13
4. Koichi Kawabuchi. Promoting self-medication in Japan~focusing on OTC drugs and tax cut policy. the 26th International Symposium at the Center for Japanese Studies, Fudan University 2016.11.05

## Dental Education Development

Professor: Ikuko MORIO  
Assistant: Professor Naoko SEKI  
Graduate Student: Chinatsu MATSUKAWA  
Graduate Student: Akira TAKINAGA  
Graduate Student: NGUYEN THI THANH TAM  
Graduate Student: Mio NAITO

### ( 1 ) Research

- 1) Research on curriculum for health care professional education
- 2) Comparative study of domestic and international dental education
- 3) Research and development of educational methods in health care professional education
- 4) Research and development of English education programs in health care professional education

### ( 2 ) Education

Main educational goal of this section as part of graduate school is to help students in health care sciences learn the basics of medical/dental curriculum: educational objectives, strategies and evaluation. This section is currently involved in the undergraduate dental education as the coordinators of multiple modules: the students' research project, courses for global communication, and the electives including various English courses and courses for international exchange for dental students.

### ( 3 ) Clinical Services & Other Works

[ Coordination for Seminar, Symposium, Workshop or other events]

1. Essential Expertise for Clinical Dentistry 1 (Seminar), Tokyo, Japan (TMDU). February 26, March 25, April 15, May 20, June 17, July 15.
2. Essential Expertise for Clinical Dentistry 2 (Seminar), Tokyo, Japan (TMDU). October 27, November 24, December 15.
3. TMDU Dental Training Program 2016, Tokyo, Japan. October 7-18.

### ( 4 ) Publications

#### [Original Articles]

1. Takehara S, Wright FAC, Kawaguchi Y, Ishida Y, Morio I, and Tagami J. Characteristics of undergraduate dental students in Japan: English competency and willingness to study abroad International Dental Journal. 2016; 66; 311-317
2. Seki N, Moross J, Sunaga M, Hobo K, Miyoshi T, Nitta H, Kinoshita A, Morio I. Evaluation of simulation learning materials use to fill the gap in Japanese dental English education. Journal of Medical and Dental Sciences. 2016.03; 63(1); 1-8
3. Rena Oguro, Masatoshi Nakajima, Naoko Seki, Alireza Sadr, Junji Tagami, Yasunori Sumi. The role of enamel thickness and refractive index on human tooth colour. J Dent. 2016.08; 51; 36-44

4. Asami Aida, Masatoshi Nakajima, Naoko Seki, Yukinori Kano, Richard M Foxton, Junji Tagami. Effect of enamel margin configuration on color change of resin composite restoration. *Dent Mater J.* 2016.08; 35(4); 675-683

### [Conference Activities & Talks]

1. Naito M, Shinada K, Kunitsuka K, Yamamoto R, Onishi T, Nishi M, Seki N, Morio I, Taniyama K. Intervention survey on oral health at newspaper printing factories. 89th Annual Meeting of the Japan Society for Occupational Health 2016.05.27 Fukushima city
2. Morio I. Quality Assurance System in Japanese Dental Education. The 12th International Conference of Asian Academy of Preventive Dentistry 2016.05.29 Tokyo, Japan
3. Kurumi IDE, Masatoshi NAKAJIMA, Keiichi HOSAKA, Masahiro TAKAHASHI, Naoko SEKI, Junji TAGAMI. Effect of cavity depth on Ultimate Tensile Strength of bulk fill flowable resin. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.10 Tochigi, Japan
4. Morio I. Dental Education and Accreditation in Japan. The 1st East Asian Conference on Dental Education and Accreditation 2016.06.25 Seoul, Republic of Korea
5. Morio I. Globalization of universities - current situation and future direction. Annual Meeting of the 35th Japanese Dental Education Association 2016.07.02 Osaka, Japan
6. Nguyen T, Seki N, Morio I. Comparing stress of dental students in clinical/preclinical practices at the University of Ho Chi Minh City, Vietnam. Annual Meeting of the 35th Japanese Dental Education Association 2016.07.02 Osaka, Japan
7. Moross J, Seki N, Sunaga M, Otsuka H, Naito M, Shinada K, Morio I, Kinoshita A. Development of ESL clinical simulation teaching materials for dental hygienist education. Annual Meeting of the 35th Japanese Dental Education Association 2016.07.02 Osaka, Japan
8. Nguyen T, Seki N, Morio I. Association between stress and academic performance in dental students. The 27th annual scientific meeting, South East Asia Association for Dental Education. 2016.09.09 Ho Chi Minh City, Vietnam
9. Tsuruta J, Noritake K, Mizutani K, Seki N, Kondo K, Arakawa S, Araki K. A new IPW course -working in a dental team. The 27th annual scientific meeting, South East Asia Association for Dental Education. 2016.09.09 Ho Chi Minh City, Vietnam
10. Morio I, Araki K. Quality Assurance of Dental Education in Japan. 27th Annual Scientific Meeting South East Asia Association for Dental Education (SEAADE) 2016.09.09 Ho Chi Minh City, Vietnam
11. Morio I. What has been brought about by the implementation of this 5-year project. Re-Inventing Japan Project\_Inter-university exchange program toward medical and dental networking in Southeast Asia International Symposium "Developing Global Health Leaders" 2016.10.11 Tokyo, Japan
12. Anna Miyayasu, Manabu Kanazawa, Yuri Komagamine, Naoko Seki. Decision making for prosthodontics treatment in a case of multiple tooth loss. *Essential Expertise for Clinical Dentistry 2* 2016.10.27 Tokyo, Japan
13. Seki N, Moross J, Otsuka H, Sunaga M, Naito M, Takatsuna Y, Kondo K, Shinada K, Morio I, Kinoshita A. Learning outcome provided by ESL clinical simulation teaching materials for dental hygiene education. 81st Annual Meeting of the Stomatological Society 2016.11.26 Tokyo
14. Takinaga A, Seki N, Morio I. Present Situation after Employing the Foreign Nurses Based on the Economic Partnership Agreement (EPA nurses) -From the Experience at Japanese Red Cross Ashikaga Hospital-. 81st Annual Meeting of the Stomatological Society 2016.11.26 Tokyo
15. Nguyen T, Seki N, Morio I. Stress and academic performance in dental students at Tokyo Medical and Dental University. 81st Annual Meeting of the Stomatological Society 2016.11.26 Tokyo

## Oral Health Promotion

Professor Yoko Kawaguchi  
Associate Professor Masayuki Ueno  
Assistant Professor Takashi Zaito  
Hospital Staff Akiko Ohshiro  
Office administrator Reika Nagaoka  
Research Assistant Professor Sachiko Takehara (the Institute of Global Affairs)  
Registered Resident Hiromi Nishiyama  
Graduate Student Anastasiya Blizniuk(~September)  
Nguyen Thi Hoang Yen  
Yuka Shizuma  
Kaung Myat Thwin  
Toshiya Kanazawa  
Takashi Tanemura  
Jin Aoki  
Mitsue Kamisawa

### ( 1 ) Research

#### Research Subjects

Research topics are innovative, academic and international research in the field of dental public health and preventive dentistry to proceed with oral health promotion that contributes to human health. The current main research themes are:

1. Epidemiology and prevention of dental disease
2. Oral health care system
3. Relationship between oral health and general health
4. Oral health promotion
5. Diagnosis and treatment system construction of oral malodor
6. International oral health

### ( 2 ) Lectures & Courses

#### 1) Graduate School, Oral Health Promotion

The educational purpose is to foster professionals in dental public health and preventive dentistry who can think oral health problems as related issues with living environment, life style, health policy and social condition, and can conduct innovative, academic and international research on oral health for maintaining and improving oral health.

#### 2) Undergraduate Education

The department is in charge of module units of “Introduction to dentistry” , “Environment and society II” and “Comprehensive problem exercise” for the third year dental students, and module units of “Basis for dentistry” , “Prevention and health management I” , “Prevention and health management II” and “Dentistry and nutrition” for the fourth year dental students. The department is also in charge of “Experiential research



exercise” for the fourth year dental students, and “Comprehensive clinical practice phase I & II” for the fourth and fifth year dental students, in cooperation with other departments.

### (3) Clinical Services & Other Works

#### Clinical Services

“Fresh breath clinic” in Dental hospital, Tokyo Medical and Dental University is a special clinic for diagnosis, treatment and prevention of oral malodor. About half of oral malodor patients are referred from other departments in the dental hospital or outside dental clinics. Other patients visit the clinic by finding the information of the clinic from mass media such as the internet, newspapers and television.

For oral malodor examination, gas chromatography and gas sensor instrument are used to measure the concentration of volatile sulfur compounds (VSCs) along with the organoleptic test. Oral malodor is treated based on diagnosis by precise measurement and oral examination, besides psychological aspects of the patient are paid attention. Treatment of oral malodor needs continuous periodontal disease management and oral care in cooperation with oral care department in the dental hospital and patient’s family dentist.

### (4) Publications

#### [Original Articles]

1. S Takehara, FAC Wright, Y Kawaguchi, Y Ishida, I Morio, J Tagami. Characteristics of undergraduate dental students in Japan: English competency and willingness to study abroad *International Dental Journal*. 2016; 66; 311-317
2. Kaung Myat Thwin, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi.. Early Childhood Caries and Related Risk Factors among Myanmar Preschool Children *Int J Clin Prev Dent*. 2016; 12(4); 229-235
3. Masayuki Ueno, Norie Sawada, Manami Inoue, Shoichiro Tsugane, Yoko Kawaguchi.. Association between adult’s height and dentition status: JPHC oral health study *Asian Pac J Health Sci*. 2016; 3(4s); 81-88
4. Sachiko Komori, Takashi Zaitzu, Sachiko Takehara, Masayuki Ueno, Yoko Kawaguchi. The relationship of salivary viscosity with halitosis *Int J Clin Prev Dent*. 2016; 12(1); 13-22
5. H Rani, Ueno M, Zaitzu T, Kawaguchi Y. Oral malodour among adolescents and its association with health behaviour and oral health status *International Journal of Dental Hygiene*. 2016; 14; 135-141
6. Blizniuk A, Ueno M, Zaitzu T, Kawaguchi Y. Association between self-reported and clinical oral health status in Belarusian adults. *Journal of Investigative and Clinical Dentistry*. 2016.01; 0(0); 1-6
7. Blizniuk A, Furukawa S, Ueno M, Kawaguchi Y. Evaluation of English Websites on Dental Caries by Using Consumer Evaluation Tools 2016.01; 0(0); 1-7
8. Tumurkhuu T, Fujiwara T, Komazaki Y, Kawaguchi Y, Tanaka T, Inazawa J, Ganburged G, Bazar A, Ogawa T, Moriyama K. Association between maternal education and malocclusion in Mongolian adolescents: a cross-sectional study. *BMJ Open*. 2016.11; 6(11);

#### [Books etc]

1. Yoko Kawaguchi, Sachiko Takehara, Yuji Ishida, Kazuhiro Yonemoto. *Dental Terminology in 8 Languages*. Oral Health Association of Japan, 2016.05

#### [Conference Activities & Talks]

1. Yoko Kawaguchi. Strategies and approaches for tackling Early Childhood Caries (ECC). The 36th Myanmar Dental Conference 2016.01.26 University of dental Medicine Yangon, Myanmar



2. Sachiko Takehara, Ikuko Morio, Yoko Kawaguchi. Effects of exchange programs on perception among Japanese/overseas dental students. The 12th International Conference of Asian Academy of Preventive-Dentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
3. Mitsue Kamisawa, Mitsue Onodera, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi,. Oral health care for psychiatric inpatients by nurses. The 12th International Conference of Asian Academy of Preventive-Dentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
4. Akiko Oshiro, Yuka Shizuma, Toshiya Kamisawa, Mitsue Kamisawa, Sachiko Takehara, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Relationship between oral malodor and the number of bacteria in tongue coating,. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
5. Masayuki Ueno, Satoko Ohara, Yoko Kawaguchi. The association of active and passive smoking with oral health in adults, The 12th International Conference of Asian Academy of PreventiveDentistry. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
6. Takashi Zaitzu, Toshiya Kanazawa, Kaung Myat Thwin, Thi Hoang Yen Nguyen, Akiko Oshiro, Masayuki Ueno, Yoko Kawaguchi. Oral health behaviors and symptoms of employees classified by worksite industry. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
7. Takashi Zaitzu, Mitsue Kamisawa, Yuka Shizuma, Anastasiya Blizniuk, Sachiko Takehara, Reika Nagaoka, Masayuki Ueno, Yoko Kawaguchi. Oral health status of employees classified by worksite industry. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
8. Yuka Shizuma, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Association of self-assessment with oral health status and behavior among adolescents. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
9. Haslina Rani, Masayuki Ueno, Takashi Zaitzu, Yoko Kawaguchi. A case report on volatile sulfide compounds changes in breath. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
10. Takashi Zaitzu. Space Dentistry –Teledental System in Space and Antarctic Environments-, The 12th International Conference of Asian Academy of PreventiveDentistry.. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
11. Nguyen Thi Hoang Yen, Takashi Zaitzu, Sachiko Takehara, Masayuki Ueno, Yoko Kawaguchi. Early childhood caries and related risk factors in Vietnam, The 12th International Conference of Asian Academy of PreventiveDentistry.. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
12. Kaung Myat Thwin, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Early childhood caries and related risk factors among Myanmar preschool children,. The 12th International Conference of Asian Academy of PreventiveDentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
13. Anastasia Blizniuk, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Oral Health Literacy and its impact on oral health in Belarusian adults. The 12th International Conference of Asian Academy of Preventive-Dentistry. Joint meeting with The 65th General Meeting of Japanese Society for Oral Health 2016.05.27 Tokyo Medical and Dental University
14. Zaitzu T, Kawaguchi Y. Oral health status on of employees classified by work schedule. IADR/APR General Session & Exhibition 2016.06.23 Seoul, Republic of Korea

15. Yen Hoang Thi Nguen, Masayuki Ueno, Takashi Zaito, Yoko Kawaguchi. Early Childhood Caries of Preschool Children in Hue, Vietnam. The 23rd General Meeting of The Japanese Association for Dental Science 2016.10.21 Fukuoka international Congress Center
16. Takashi Zaito, Yoko Kawaguchi. Teledental System in the Environments of Space and Antarctica. The 5th Tri-University Consortium on Oral Science and Education 2016.10.27 China

## Sports Medicine and Dentistry

[ Associate Professor] Toshiaki Ueno  
[ Assistant Professor] Toshiyuki Takahashi, Hiroshi Churei  
[ Clinical fellow] Katsuhide Kurokawa  
[ Graduate Student] Abhishekhi Shrestha, Mai Ikegawa, Takahiro Sirako, Yuriko Yoshida, Nana Shiota, Gen Tanabe, Kiyonobu Yamamura, Chiho Shibata, Phyu Sin Tun  
[ Research Student] Satoshi Kawabata, Aki Kanasaki  
[ Part-time Instructor] Goshi Kondo, Yukio Sasaki, Ryo Sato, Takuto Yamanaka, Sachiko Fujino  
[ Part-time Resident] Hiromi Miura, Koichiro Adachi, Keisuke Abe, Kenji Takeuchi, Takayuki Ishigami, Kairi Hayashi, Takaaki Fukuda, Akihiro Mitsuyama, Sinto Fukasawa,

### ( 1 ) Outline

Sport medicine/dentistry is a branch of clinical medical and dental sciences which deals with the clinical management of oral health of athletes and sports-active people, the safety measures of sports-related traumatic injuries and disorders, and medical and dental supports to improve athletic performance.

### ( 2 ) Research

- 1) Oral health promotion of athletes and sports-active people
  - (1) Field survey of oral health conditions in athletes and sports-active people
  - (2) Changes of oral environment associated with physical and sporting activities
  - (3) Influences of sports drinks and supplements on oral health
- 2) Safety measures of sports-related dental and maxillofacial traumatic injuries
  - (1) Diagnosis and treatment techniques for sports-related dental and maxillofacial injuries
  - (2) Development and innovation of sports mouthguard
  - (3) Development and innovation of sports faceguard
  - (4) Development and innovation of scuba diving mouthpiece
- 3) Correlations between occlusion and general motor functions
  - (1) Biomechanical assessment of motor performance associated with occlusion
  - (2) Electrophysiological analysis of neuromuscular function associated with occlusion
- 4) Correlations between occlusion and body posture
  - (1) Effect of occlusion on static posture
  - (2) Influence of occlusion on dynamic posture
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

### ( 3 ) Education

academic classes for sports medicine/dentistry in undergraduate and graduate courses in undergraduate and graduate courses are listed as follows;

- 1) D1: Shigaku-Gaietu
- 2) D3: Sogo-Kadai-Ensyu
- 3) D3: Rinsyo-Taiken-Jissyu

- 4)D4:Kenkyu-Taiken-Jissyu
- 5)D5:Hatten-Shika-Rinsyo/Sports Dentistry
- 6)D5-D6:Hokatsu Rinsyo-Jissyu Phase I to II
- 7)OH2:Kiso-Kagaku-Jissyu
- 8)OH3:Seijin-Koukuhoken-Eiseigaku
- 9)OH3-OH4:Koukuhoken-Eisei-Jissyu
- 10)OE4:Sports dental engineering
- 11)Master course:Kankyo-Syakai-Ishigaku
- 12)PhD course: Tokuron, Ensyu and Kenkyu-Jissyu of Sports Medicine and Dentistry
- 13)Clinical training course:Sports Dentistry

#### ( 4 ) Lectures & Courses

Main objectives of academic education programs of sports medicine/dentistry in from undergraduate to graduate courses is to provide the students to study the oral health conditions in athletes and sports-active people, the changes of oral environment associated with physical and sporting activities, the possible correlations between occlusion and general motor functions and body posture, the novel techniques of sports mouthguard and faceguard, the relations between mastication and occlusion and brain functions, and so on. Students are also taught to advanced knowledge on sports medicine/dentistry and up-to-date techniques to fabricate custom mouthguard and faceguard.

#### ( 5 ) Clinical Services & Other Works

Sports dentistry clinic in Dental Hospital of Tokyo Medical and Dental University offers comprehensive care and clinical management for athletes and sports-active people suffered dental diseases and traumatic injuries. Custom-fitted protective gears such as mouthguard and faceguard against sports-related dental and maxillofacial trauma are also handled for participants in contact sports such as a boxing, American football, rugby football, hockey, lacrosse, and martial art. Sports dentistry clinic is positioned as a dental branch of Clinical Center for Sports Medicine and Dentistry under TMDU Sports Science Organization. In addition, Our clinic maintains close cooperation with Japan Institute of Sports Science/National Training Center under Japan Sport Council.

#### ( 6 ) Clinical Performances

< Certified specialists>

Toshiaki Ueno (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by Japanese Academy of Sports Dentistry, 3.Mouthguard technical instructor certified by JASD, 4.Dental specialist certified by Japanese Academy of Maxillofacial Prosthetics)

Toshiyuki Takahashi (1.MG technical instructor certified by JASD)

Hiroshi Churei (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3. MG technical instructor certified by JASD)

Katsuhide Kurokawa (1.MG technical instructor certified by JASD)

Sachiko Fujino (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Keisuke Abe (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3.MG technical instructor certified by JASD)

Takayuki Ishigami (1.MG technical instructor certified by JASD)

Kairi Hayashi (1.MG technical instructor certified by JASD)

Akihiro Mitsuyama (1.MG technical instructor certified by JASD, 2.Dental specialist certified by Japan Association of Dental Traumatology)

Shintaro Fukasawa (1.MG technical instructor certified by JASD, 2.Dental materials adviser certified by Japanese Society of Dental Materials and Devices)

Mai Tanabe (1. Sports dental hygienist certified by JASD)

Takahiro Shirako(1.MG technical instructor certified by JASD, 2.Dental specialist certified by JADT)

Aki Kanasaki(1. Sports dental hygienist certified by JASD)

**(7) Publications****[Original Articles]**

1. Hayashi K, Takahashi T, Tanabe M, Horie M, Oyaizu T, Enomoto M, Shibata S, Yagishita K, Ueno T. The facilitatory effects of hyperbaric oxygen treatment on membrane bone wound healing in a rat calvarial defect model *Undersea Hyperb Med.* 2016.03; 43(2); 135-142
2. Mitsuyama A, Takahashi T, Ueno T. Effects of teeth clenching on soleus H reflex during lower limb muscle fatigue *J Prosthodontic Res.* 2016.06; Epub ahead of print
3. Fukasawa S, Churei H, Chowdhury RU, Shirako T, Shahrin S, Shrestha A, Wada T, Uo M, Takahashi H, Ueno T. Application of addition-cured silicone denture relining materials to mouthguard adjustment *Dent Mater J.* 2016.07; 35(4); 635-643
4. Shrestha A, Takahashi T, Kurokawa K, Mitsuyama A, Hayashi K, Ishigami T, Shahrin S, Chowdhury RU, Churei H, Ueno T. Effects of mouthguards on electromyographic activity of masticatory muscles *Int J Sports Dent.* 2016.10; 9(1); 27-37
5. Ishigami T, Takahashi T, Kurokawa K, Ueno T. Effects of occlusal supporting area on dynamic posture against disturbance by electrical stimulation *Int J Sports Dent.* 2016.10; 9(1); 7-17
6. Takahiro Wada, Hiroshi Churei, Toshiaki Ueno, Motohiro Uo. High shock absorbing faceguard using fiber-reinforced plastic (FRP) and elastomer *The Journal of the Japanese Society for Dental Materials and Devices.* 2016.11; 35(6); 325-328
7. Nakamura T, Yoshida Y, Churei H, Aizawa J, Hirohata K, Ohmi T, Ohji S, Takahashi T, Enomoto M, Ueno T, Yagishita K. The effect of teeth clenching on dynamic balance at jump-landing: a pilot study *J Appl Biomech.* 2016.12; Epub ahead of print
8. Fukasawa S, Churei H, Chowdhury RU, Shahrin S, Shrestha A, Wada T, Uo M, Takahashi H, Ueno T. Differences among shock-absorbing capabilities of mouthguard materials *Dent Traumatol.* 2016.12; 32(6); 474-479

**[Conference Activities & Talks]**

1. Ikegawa M, Takahashi T, Ueno T. Effects of water gargling on changes of saliva pH and buffering capacity by taking sports drinks during exercise. 7th International Conference of Sports & Society 2016.06.02 Hawaii, U.S.A.
2. Takahiro Wada, Hiroshi Churei, Shintaro Fukasawa, Takahiro Shirako, Toshiaki Ueno, Motohiro Uo. Shock-absorbing property of face guard by incorporating a glass-fiber reinforced plastic and space. 2016.06.12
3. Shirako K, Churei H, Ueno T. Splinting by use of novel luxated tooth model and Periotest. 19th World Congress on Dental Traumatology 2016.08.11 Brisbane, Australia
4. Takahiro Wada, Hiroshi Churei, Haruka Takayanagi, Mako Yokose, Shintaro Fukasawa, Takahiro Shirako, Toshiaki Ueno, Naohiko Iwasaki, Hidekazu Takahashi, Motohiro Uo. Development of a faceguard using a glass-fiber reinforced thermoplastic (GFRTTP) and shock escape space. Visual-JW 2016 2016.10.17 Suita, Osaka, Japan
5. Takahiro Wada, Hiroshi Churei, Shintaro Fukasawa, Takahiro Shirako, Toshio Hongo, Toshiaki Ueno, Motohiro Uo. Analysis of shock absorption ability of a faceguard by incorporating a glass-fiber reinforced thermoplastic and space. International Dental Materials Congress 2016 2016.11.05 Bali, Indonesia
6. Tanabe G, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Effect of the use of commercial cleaning liquid in thermoforming process of mouthguard materials. International Dental Materials Congress 2016 2016.11.05 Bali, Indonesia

## Educational Media Development

Professor KINOSHITA Atsuhiko  
 Assistant Professor SUNAGA Masayo  
 Graduate Student MIYOSHI Tomoe  
 Graduate Student HOB0 Koki  
 Graduate Student CAO Ridan  
 Graduate Student AKIYAMA Kyoko  
 Graduate Student TAKATSUNA Yukiko

### (1) Research

1) Development of computer-assisted clinical simulation system for medical and dental practice training.

In our university, we executed the Establishment of Computer-Assisted Education System on Clinical Simulation for Medical and Dental Practice Training project, which was adopted as part of the Support Program for Distinctive University Education in 2005, and developed the computer simulation materials on clinical education by utilizing digital clinical data from our Medical and Dental hospitals. We have expanded our study into a new project, 'Progress of Computer-Assisted Simulation for Medical and Dental Practice Training. Computer-Assisted Simulation Promoting Clinical Inference, Decision-making, Problem Solving and Cooperation Abilities of Health Professionals', which was subsequently selected to be part of the Program for Promoting the University Education Reform in 2009 by the Ministry of Education, Culture, Sports, Science and Technology. After utilizing the simulation materials for our students, we will evaluate and analyze their educational efficacy. Furthermore, we will develop a computer-assisted clinical simulation system for the entire university.

2) Development of new education system using information and communication technologies for medical and dental students.

At our university, we executed the Integration of Information and Communication Technologies into Clinical Training project, which was adopted as part of the Support Program for the Contemporary Educational Needs in 2007. The aim of this program is to integrate traditional educational methods with advanced information and communication technologies in order to allow clinical training, practical training and lectures to be effectively interlinked. By expanding digital content and employing an automatic visual recording system, we are planning to establish a digital archive of treatments and surgeries, demonstrations of dental techniques, lectures and student training. We will then launch an on-demand distribution system in order to incorporate this content into clinical education, which the students will be able to use for their self-evaluation and learning.

3) Development and utilization of an educational media for medical and dental students.

- Development and Study of Computerized Dental Simulator for Training of Dental Cavity Preparation and Prosthodontic Tooth Preparation practices:

We plan to develop a new computerized dental simulator and evaluate its effectiveness for training in dental cavity preparation and prosthodontic tooth preparation.

- Development and Study of Dental Model and Kit for Practical Training:

Dental and dental hygiene students must acquire skills for measuring periodontal pockets and must learn to identify the base of the pocket. However, few dental models are commercially available, and students cannot measure deep periodontal pockets by practicing on one another. Thus, we developed a new dental model with which the students can practice the probing of deep periodontal pockets, and plan to evaluate its effectiveness in training and evaluation of examiners.

- Development of Composing and Screening System for Original 3D Movies from Operator's Viewpoint:

If students can experience and recognize three-dimensional space from the operator's (instructor's) viewpoint during their practice sessions and lectures, it would have educational benefits. Thus, we plan to develop a Composing and Screening System for Original 3D Movies from an Operator's Viewpoint. Furthermore, we will improve the quality of distance learning and remotely operated instruction using the superimposing method.

- Development of Dental Handpiece System with CCD camera:

We plan to develop a system equipped with a CCD camera, mirror and reverse image units in order to allow students in the lecture room to observe dental treatment sites in real-time, thereby giving them a sense of being at a clinic.

## (2) Education

We will assist graduate students in understanding new educational systems and media utilizing information-communication technologies, such as the computer-assisted education system, the e-learning system and the live broadcasting lecture system. We will also assist these students in mastering how to create related educational media and apply it to medical, dental, nursing and dental hygiene education, as well as interprofessional cooperation.

First-year students at the School of Dentistry, and first and second-year students at the School of Oral Health Care Sciences will learn to process media information and create media content, as well as how to search the Internet for information that is necessary for their study and research activities. They will also learn how to make use of various databases.

Fourth-year students at the School of Dentistry will acquire the practical knowledge, communication skills and attitude to build good relationships with patients by gaining clinical experience at an early stage. This practice consists of two units; clinical experience in the teaching clinic and the computer-assisted simulation practice. This experience will enhance the students' abilities, enabling them to be effective clinicians.

## (3) Publications

### [Original Articles]

1. Yuka Tsumanuma, Takanori Iwata, Atsuhiko Kinoshita, Kaoru Washio, Toshiyuki Yoshida, Azusa Yamada, Ryo Takagi, Masayuki Yamato, Teruo Okano, Yuichi Izumi. Allogeneic Transplantation of Periodontal Ligament-Derived Multipotent Mesenchymal Stromal Cell Sheets in Canine Critical-Size Supra-Alveolar Periodontal Defect Model. *Biores Open Access*. 2016.01; 5(1); 22-36
2. Michiyo Kurosa, Ken-ichi Tonami, Satoko Ohara, Sachi Umemori, Kanako Noritake, Masayo Sunaga, Atsuhiko Kinoshita, Kouji Araki. Differences between Computer-Based and Paper-Based Assessments of the Clinical Reasoning Competency of Dental Students. *Kokubyo Gakkai Zasshi*. 2016.03; 83(1); 25-33
3. Naoko Seki, Janelle Moross, Masayo Sunaga, Koki Hobo, Tomoe Miyoshi, Hiroshi Nitta, Atsuhiko Kinoshita, Ikuko Morio. Evaluation of simulation learning materials use to fill the gap in Japanese dental English education. *J. Med. Dent. Sci.*. 2016.03; 63(1); 1-8
4. Hiromi Otsuka, Keiko Kondo, Yuki Ohara, Masayo Yasuda, Natsuki Kishimoto, Masayo Sunaga, Keiko Endo, Shinichi Arakawa, Atsuhiko Kinoshita, Kayoko Shinada. An Inter- and Intraprofessional Education Program in Which Dental Hygiene Students Instruct Medical and Dental Students. *J Dent Educ*. 2016.09; 80(9); 1062-1070
5. Masayo Sunaga, Masato Minabe, Koji Inagaki, Atsuhiko Kinoshita. Effectiveness of a Specially Designed Dental Model for Training, Evaluation, and Standardization of Pocket Probing. *J Dent Educ*. 2016.12; 80(12); 1430-1439



# Insured Medical Care Management

Professor Masumi AI  
J Associate Professor Junichiro ISHIOKA  
Graduate Student Hiroshi KAWAMURA

## ( 1 ) Outline

Our department supports an appropriate practice on insured medical care and billing for medical service fees at the TMDU medical hospital.

We also focus on development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

## ( 2 ) Research

1) Development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

2) Studies on management and supports for billing for medical service fees at insurance medical institutions.

3) Studies on affairs of medical insurance system and provision of medical services.

In addition, the staff has been engaged in clinical studies and epidemiological studies on lipid metabolism, diabetes mellitus, atherosclerosis, laboratory medicine, and urology.

## ( 3 ) Education

The staff has been in charge for education of social health insurance system and rules for insured medical treatment at the TMDU medical hospital (May 2016 and February 2017).

A doctor course student is in his second year.

## ( 4 ) Lectures & Courses

\*Providing practical supports for an appropriate insured medical care in the clinical fields.

Providing individual support for an appropriate billing for medical service fees at the medical hospital.

We also focus on development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

## ( 5 ) Clinical Services & Other Works

The staff has been in charge for assisting appropriate medical fee claims, and also providing clinical service on diabetes, dyslipidemia, atherosclerosis, geriatrics, and Urology.



**(6) Clinical Performances**

As a managing section of the medical hospital, we collaborate all kinds of hospital workers practically and efficiently to provide an appropriate insured medical care.

**(7) Publications****[Original Articles]**

1. Eiichiro Kanda, Masumi Ai, Mitsuyo Okazaki, Masayuki Yoshida, Yoshitaka Maeda. Association of High-Density Lipoprotein Subclasses with Chronic Kidney Disease Progression, Atherosclerosis, and Klotho. *PLoS ONE*. 2016; 11(11); e0166459
2. Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Hiroshi Tanaka, Jiro Kumagai, Soichiro Yoshida, Junichiro Ishioka, Fumitaka Koga, Hitoshi Masuda, Satoru Kawakami, Yasuhisa Fujii, Kazunori Kihara. Candidate selection for quadrant-based focal ablation through a combination of diffusion-weighted magnetic resonance imaging and prostate biopsy. *BJU Int.* 2016.01; 117(1); 94-101
3. Takayuki Nakayama, Noboru Numao, Soichiro Yoshida, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. A novel interactive educational system in the operating room—the IE system. *BMC Med Educ*. 2016.02; 16; 44
4. Naoko Kawamura, Minato Yokoyama, Yasuhisa Fujii, Junichiro Ishioka, Noboru Numao, Yoh Matsuoka, Kazutaka Saito, Chizuru Arisawa, Tetsuo Okuno, Akira Noro, Shinji Morimoto, Kazunori Kihara. Recovery of renal function after radical nephrectomy and risk factors for postoperative severe renal impairment: A Japanese multicenter longitudinal study. *Int. J. Urol.* 2016.03; 23(3); 219-223
5. Hiroaki Ikezaki, Masumi Ai, Ernst J Schaefer, Seiko Otokozawa, Bela F Asztalos, Katsuyuki Nakajima, Yanhua Zhou, Ching-Ti Liu, Paul F Jacques, L Adrienne Cupples, Norihiro Furusyo. Ethnic Differences in Glucose Homeostasis Markers between the Kyushu-Okinawa Population Study and the Framingham Offspring Study. *Sci Rep*. 2016.11; 6; 36725
6. Yoshio Fujitani, Shimpei Fujimoto, Kiyohito Takahashi, Hiroaki Satoh, Takahisa Hirose, Toru Hiyoshi, Masumi Ai, Yosuke Okada, Masahiko Goshō, Tomoya Mita, Hirotaka Watada. Effects of linagliptin monotherapy compared with voglibose on postprandial blood glucose responses in Japanese patients with type 2 diabetes: Linagliptin Study of Effects on Postprandial blood glucose (L-STEP). *Diabetes Res. Clin. Pract.* 2016.11; 121; 146-156

**[Misc]**

1. Matsuoka Y, Inoue M, Ito M, Yoshida S, Yokoyama M, Ishioka J, Numao N, Saito K, Fujii Y, Kihara K. Gassless single-port RoboSurgeon radical prostatectomy using an endoscopic manipulator robot 2016.07; 8(1); 31-35

**[Conference Activities & Talks]**

1. Yoshida S et al. . Potential utility of standardized apparent diffusion coefficient value as a biomarker predicting clinical aggressiveness of bladder cancer with various MRI protocols at various institutions. European Association of Urology annual congress 2016.03.12 Munich, Germany
2. Tanaka H et al. Novel stepwise algorithm using CT and MRI for differential diagnosis of fat-poor angiomyolipoma in small renal masses: Development and external validation. European Association of Urology annual congress 2016.03.12 Munich, Germany
3. Ishioka J et al. When should patients undergo prostate biopsy? Decision analysis using differences in the health-related quality-of-life between pre-biopsy healthy men and patients with castration-resistant prostate cancer. European Association of Urology annual congress 2016.03.12 Munich, Germany
4. Fujiwara M et al.. Antibiotic prophylaxis is avoidable in minimally invasive clean surgery for renal or adrenal tumors: A prospective study of 678 cases. Munich, Germany 2016.03.12 Munich, Germany

5. 1.Fujii Y, Kihara K, Tanaka H, Saito K., Yoshida S, Yokoyama M., Ishioka J, Matsuoka Y, Numao N. . Bladder-sparing protocol consisting of low-dose chemoradiotherapy and consolidative partial cystectomy against muscle-invasive bladder cancer: Oncological and functional outcome in elderly patients.. European Association of Urology annual congress 2016.03.13 Germany
6. 5.Yokoyama M, Kawamura N, Fujii Y, Inoue M, Ishioka J, Numao N, Matsuoka Y, Saito K, Arisawa C, Okuno T, Noro A, Morimoto S, Kihara K. . Longitudinal changes in renal function after radical nephrectomy and risk factors for postoperative severe renal impairment: A Japanese multicenter study using a linear mixed model analysis. European Association of Urology annual congress 2016.03.13 Germany
7. Moriyama S et al. A new quantitative method for characterizing small renal masses: MRI intensity ratio curve analysis. European Association of Urology annual congress 2016.03.13 Munich, Germany
8. Waseda Y. et al.. Elevation of urinary metanephrine/normetanephrine and impairment of glucose tolerance predict the development of hypoglycemia after resection of pheochromocytoma. European Association of Urology annual congress 2016.03.13
9. Nakamura Y et al. Renal dysfunction manifestation in patients with adrenal Cushing's syndrome after adrenalectomy. European Association of Urology annual congress 2016.03.13 Munich, Germany
10. 4.Kawamura N, Yokoyama M, Fujii Y, Inoue M, Ito M, Yoshida S, Ishioka J, Numao N, Matsuoka Y, Saito K, Kihara K.. Longitudinal preservation of renal function after clamp-less partial nephrectomy: An analysis of patients with chronic kidney disease.. European Association of Urology annual congress 2016.03.14 Germany
11. 14.Yasuda Y, Saito K, Kawamura N, Yuasa T, Yokoyama M, Matsuoka Y, Ishioka J, Numao N, Okuno T, Yamamoto S, Takahashi S, Yonese J, Fujii Y, Kihara K. Prognostic significance of early CRP response for metastatic renal cell carcinoma treated with tyrosine kinase inhibitor. European Association of Urology annual congress 2016.03.14 Germany
12. Matsuoka Y, Ishioka J, Tanaka H, inoue M, Ito M, Yoshida S, Yokoyama M, Numao N, Saito K, Fujii Y, Kihara K. Impact of PI-RADS version 2 on MRI diagnosis for extracapsular extension of prostate cancer: A multireader study. European Association of Urology annual congress 2016.03.14 Munich, Germany
13. Inoue M et al. . Prediction of therapeutic resistance using ERBB2 expression status and Ki-67 labelling index in muscle-invasive bladder cancer patients treated with chemoradiation-based selective bladder-sparing approach. European Association of Urology annual congress 2016.03.14 Munich, Germany
14. Matsuoka Y, Numao N, Saito K, Tanaka H, Inoue M, Ito M, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Kihara K. Applicability analysis of focal therapy to intermediate- and high-risk prostate cancer. .annual meeting of the American Urological Association 2016.05.06 San Diego, USA
15. Numao N et al. Optimal combination of MRI-targeted biopsy and systematic biopsy for men with suspicion of prostate cancer. annual meeting of the American Urological Association 2016.05.06 San diego, USA
16. Ishioka J et al.. The incidence of late bladder tumor recurrence of upper tract urothelial carcinoma and optimal cystoscopic follow-up: A multicenter study.. annual meeting of the American Urological Association 2016.05.06 San diego, USA
17. Nakamura Y et al.. Masked renal dysfunction in patients with adrenal Cushing's syndrome manifested by adrenalectomy. annual meeting of the American Urological Association 2016.05.06 San diego, USA
18. Tanaka H et al. Development and validation of a novel stepwise algorithm using CT and MRI for diagnosis of fat-poor angiomyolipoma in small renal masses. .annual meeting of the American Urological Association 2016.05.07

19. Ito M et al. Likelihood of underlying Lynch syndrome in Japanese upper tract urothelial carcinoma patients. annual meeting of the American Urological Association 2016.05.07 San diego, USA,
20. Kobayashi M et al. Maximum standardized uptake value of 18F-FDG PET/CT predicts survival of patients with advanced urothelial carcinoma. annual meeting of the American Urological Association 2016.05.07 San diego, USA
21. Fujii Y et al.. Bladder-sparing protocol consisting of low-dose chemoradiotherapy and consolidative partial cystectomy against muscle-invasive bladder cancer: Comparison of oncological and functional outcomes between older and younger patients. annual meeting of the American Urological Association 2016.05.08 USA
22. Ishioka J et al. Prognostic impact of C-reactive protein kinetics on survival of patients with advanced urothelial carcinoma. A multicenter study. . annual meeting of the American Urological Association 2016.05.08 San diego, USA
23. 8.Ishioka J et al. Yokoyama M., Kawamura N., Fujii Y., Inoue M., Ishioka J., Numao N., Matsuoka Y., Saito K., Arisawa C., Okuno T., Noro A., Morimoto S., Kihara K.. Longitudinal renal function recovery after radical nephrectomy and risk factors for postoperative severe renal impairment: a Japanese multicenter study.. annual meeting of the American Urological Association 2016.05.08 San diego, USA
24. Matsuoka Y, Ishioka J, Tanaka H, Inoue M, Ito M, Yoshida S, Yokoyama M, Numao N, Saito K, Fujii Y, Kihara K. Impact of the Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) on the assessment of extracapsular extension in prostate cancer: A multireader study.. annual meeting of the American Urological Association 2016.05.09 San Diego, USA
25. 13.Nakayama T, Kazutaka S, Fujii Y, Waseda Y, Moriyama S, Tanaka H, Kawamura N, Inoue M, Ito M, Yoshida, S, Yokoyama M, Matsuoka Y, Numao N, Kihara K. Association of M2 macrophage invasion with C-reactive protein in renal cell carcinoma.. annual meeting of the American Urological Association 2016.05.09 San diego, USA
26. Masaharu Inoue, Fumitaka Koga, Soichiro Yoshida, Hajime Tanaka, Shuichiro Kobayashi, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Predictive model for therapeutic resistance using ERBB2 expression status and Ki-67 labeling index in muscle-invasive bladder cancer patients treated with chemoradiotherapy-based bladder-sparing protocol. AUA2016 Annual Meeting 2016.05.09 San Diego, USA
27. Matsuoka Y, Saito K, Numao N, Tanaka H, Inoue M, Ito M, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Kihara K. Risk assessment for undertreatment in focal therapy and its applicability to intermediate- and high-risk prostate cancer. 9th International Symposium on Focal Therapy and Imaging in prostate & kidney cancer 2016.06.23 Durham, USA
28. Saito K, Matsuoka Y, Numao N, Hayashi K, Toda K, Ito M, Inoue M, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Yoshimura R, Kihara K. Hemi-gland brachytherapy for localized prostate cancer. 9th International Symposium on Focal Therapy and Imaging in prostate & kidney cancer 2016.06.23 Durham, USA

## **[Others]**

1. IRB Member, Tokyo Institute of Technology 2011-
2. IRB Member, Sony Corporation 2012-

# Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD  
 Junior Associate Professor: Kaoruko Seino, PhD  
 International Researcher: Layla McCay, MBChB  
 Graduate Student: Nguen Huu Chau Duc, MD; Rakprasit Jutarat, MPH;  
 Shagdarsuren Tserendulam, MA; Saber Al-Sobaihi, MPH;  
 Aya Anzai, RN; Omar Mohammad Mashal, MD;  
 Shiro Ochi, MSc, PhD; Tomoko Terada, MD,  
 Dasavanh Manivong, MD, MSc; Delgermaa Doshzeveg, MPH;  
 Iskander Isaac Maro, MD, MPH; Yoshiko Shimozawa, PT, MMs;  
 Hoang Thuy Linh Nguyen, MD, MPH; Ahmad Shekib Arab, MD;  
 Yuri Tashiro, MPharm, MPH; Deogratius Bintabara MD, MSc;  
 TJ Robionson Moncatar, RN, MPH; Kathryn Lizbeth Lucena Siongco, RN, RM, MAN

## ( 1 ) Outline

The department of Global Health Entrepreneurship seeks to elucidate physical, social, economic and cultural factors determining inequity in health. The department works closely with WHO and other international agencies to help develop guidelines of scientific evaluation and recommended practices.

## ( 2 ) Research

Major Research Topics:

- 1) Transfiguration of the ecosystem and its interaction with human health
- 2) Socio-cultural factors determining health
- 3) Social entrepreneurship development through applying the Healthy Settings approach
- 4) Use of information technology to improve public health
- 5) International health workforce and trade in health services
- 6) Universal health coverage in ageing society

## ( 3 ) Education

PhD programs

Our doctoral program provides a flexible curriculum that allows students to customize their research goals, methods, and activities based upon their own interests and preferences. Students on the Public Health Medicine (PHM) track of the Disease Prevention Global Leader Program (DP-GLP) attain the skills required for public health professionals with an international perspective. The program prepares them for leadership roles in public institutions. Advanced students from many countries around the world are now enrolled. All the classes are conducted in English, thus facilitating the acquisition of international communication skills.

A rich variety of educational activities have been arranged in the program. These include: individual discussion sessions with professors and other faculty members; field investigations; and seminars on various topics such as community health care, community medicine, public health policy, biostatistics, academic presentation, development of foreign language skills, and communication skills. Students work closely with faculty members on an individual basis in setting the right direction for their research and confirmation of their progress.

## Master Programs

Master degree students receive systematic intensive training that leads to the acquisition of broad expertise in the field of global public health. This program is open to students who have majored in any field.

## ( 4 ) Lectures & Courses

The objective of our postgraduate education is to provide professional qualifications to high-caliber people who exhibit leadership in the advancement of public health and promotion of health on an international scale. The department helps students attain the knowledge, skills, attitude, and experiences that are necessary for competent health specialists and social entrepreneurs in healthcare.

By completion of the doctoral course, the participants are expected to be able to:

- Assess health and well being the populations in local, national, and international settings,
- Assess evidence to show effectiveness of health interventions, programs and strategies,
- Think strategically to develop local, national, and international policies,
- Manage projects to successful completion
- Demonstrate leadership in local, national, or international public health programs
- Communicate properly when listening, presenting, writing, and negotiating
- Pursue a full-cycle of an academic, public health research project
- Facilitate learning of staff, students, and colleagues, and
- Practice and respect professional ethics in a socio-culturally diverse environment.

## ( 5 ) Publications

### [Original Articles]

1. Mashal MO, Nakamura K, Kizuki M. Hidden burden of non-medical spending associated with inpatient care among the poor in Afghanistan. *International Journal of Public Health*. 2016.05; 61; 661-671
2. Rami Al Rifai, Keiko Nakamura, Kaoruko Seino. Decline in the prevalence of anaemia among children of pre-school age after implementation of wheat flour fortification with multiple micronutrients in Jordan. *Public Health Nutr*. 2016.06; 19; 1486-1497
3. Nakamura K, Chiba M, Seino K. Factors influencing reduction of risk of lifestyle related disease among children. 2016.08; 31; 381-386
4. Shafiqullah H, Morita A, Nakamura K, Seino K . The family planning conundrum in Afghanistan *Health Promotion International*. 2016.10;
5. Al-Sobaihi S, Nakamura K, Kizuki M.. Undernutrition among children under 5 years of age in Yemen: Role of adequate childcare provided by adults under conditions of food insecurity. *Journal of Rural Medicine*. 2016.11; 11(2); 47-57

### [Conference Activities & Talks]

1. Nakamura K. Post-disaster excess deaths of NCD and Disaster Health Emergency Assistance Team.. WHO Meeting on Healthy and Resilient Cities 2016.01.11 Gandong-gu, Seoul, Republic of Korea
2. Nakamura K. Healthy Cities and Food is Asia. HCSO-AFHC Symposium 2016.02.02 Tokyo
3. Nakamura K. Examples of actions to address urban health challenges: Urban health system roles and functions: Emergency Preparedness Plan. Meeting on Implementation of the Regional Framework for Urban Health in the Western Pacific (2016-2020) 2016.02.29 Manila, Philippines
4. Nakamura K. Health Supportive City Development. The 12th Annual Conference of the Japan Chapter of the Alliance for Healthy Cities 2016.07.26

5. Nakamura K. Public Health. Graduate School Seminar at School of Public Health, MUHAS 2016.08.03 Dar es Salaam, Tanzania
6. Nakamura K, Fawkes S. The Foresight Approach towards Healthy and Resilient Cities. The 7th Global Conference of the Alliance for Healthy Cities 2016.08.29 Wonju, Republic of Korea
7. Nakamura K. Nationwide program for prevention and control of lifestyle related disease, Japan.. 8th NCD Forum Seminar 2016.09.28 Seoul, Republic of Korea

## Geriatrics and Vascular Medicine

Professor : Kentaro SHIMOKADO

Associate Professor : Eiji KANEKO, Shohei SHINOZAKI

Junior Associate Professor : Masashi BEPPU

Assistant Professor : Yasuko ABE

Graduate Student : Kenji TOYOSIMA, Norihiko IZUMIMOTO

Yasuko USHIO, I, Hirofumi MASUTOMI

Tomomi HAKAMADA, Marie NAKAMURA

Rie MASUDO, Suguru MABUCHI, Mari SASAKI

### ( 1 ) Research

- 1) Cell biological mechanisms of atherogenesis
- 2) Mechanisms involved in dyslipidemia
- 3) Mechanisms of aging and age-related diseases
- 4) Undergraduate and postgraduate education in geriatrics

### ( 2 ) Education

- 1) Undergraduate education of medical students with a particular emphasis on geriatrics
- 2) Development of research on aging and age-related diseases with a particular emphasis on atherosclerosis

### ( 3 ) Clinical Services & Other Works

As a division of the Department of Internal Medicine, we are taking care of elderly patients who are better treated by us rather than by highly specialized experts both at the outpatient clinics and the ward of our university hospital. We also provide subspecialty service such as oriental herbal medicine, mononuclear cell transplantation for PAD, and dyslipidemia clinic.

### ( 4 ) Publications

#### [Original Articles]

1. Takahashi Keita, Takisawa Shoko, Shimokado Kentaro, Kono Nozomu, Arai Hiroyuki, Ishigami Akihito. Age-related changes of vitamin E: alpha-tocopherol levels in plasma and various tissues of mice and hepatic alpha-tocopherol transfer protein. *Eur J Nutr.* 2016.02;
2. Sasaki Mari, Shinozaki Shohei, Shimokado Kentaro. Sulforaphane promotes murine hair growth by accelerating the degradation of dihydrotestosterone. *Biochem Biophys Res Commun.* 2016.03; 472(1); 250-254

3. Masutomi Hirofumi, Kawashima Saki, Kondo Yoshitaka, Uchida Yoshiaki, Jang Byungki, Choi Eun-Kyoung, Kim Yong-Sun, Shimokado Kentaro, Ishigami Akihito. Induction of peptidylarginine deiminase 2 and 3 by dibutyl cAMP via cAMP-PKA signaling in human astrocytoma U-251MG cells. *J Neurosci Res.* 2016.10;
4. Chiba Tsuyoshi, Noji Keiko, Shinozaki Shohei, Suzuki Sachina, Umegaki Keizo, Shimokado Kentaro. Diet-induced non-alcoholic fatty liver disease affects expression of major cytochrome P450 genes in a mouse model. *J Pharm Pharmacol.* 2016.12; 68(12); 1567-1576



## Rehabilitation Medicine

Associate Professor Tetsuya JINNO

Graduate Student

Tomoko ARAKI,

Kashitarou HYOUDOU

Chisato HOSHINO

Kazuko KATSUKI

Takanori KOKUBUN

Takashi IKEDA

### ( 1 ) Research

Research Subjects

- 1) Rehabilitation for total joint arthroplasty
- 2) Three dimensional motion analysis of upper/lower extremities and gait analysis
- 3) Nutritional management in rehabilitation
- 4) Biomechanical research for prevention of sports injury

### ( 2 ) Lectures & Courses

Purpose of Education:

Rehabilitation medicine consists of physical, occupational and speech therapy. Main theme of rehabilitation medicine in graduate course is to study 3-dimensional motion analysis in activities of daily living and molecular biological analysis of disuse atrophy.

### ( 3 ) Publications

#### [Original Articles]

1. Takashi Ikeda, Junya Aizawa, Hiroshi Nagasawa, Ikuko Gomi, Hiroyuki Kugota, Keigo Nanjo, Tetsuya Jinno, Tadashi Masuda, Sadao Morita. Effects and feasibility of exercise therapy combined with branched chain amino acid supplementation on muscle strengthening in frail and pre-frail elderly people requiring long-term care: A crossover trial *Applied Physiology, Nutrition, and Metabolism*. 2016; 41(4); 438-445
2. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Yuki Yamauchi, Yoshinori Asou, Takeshi Muneta, Atsushi Okawa. Limited significance of screening computed tomography after cementless total hip arthroplasty with highly cross-linked polyethylene at 7 to 10 years of follow-up *Mod Rheumatol*. 2016; 26(5); 757-760
3. Tsuyoshi Yamada, Toshitaka Yoshii, Satoru Egawa, Ryohei Takada, Takashi Hirai, Hiroyuki Inose, Tsuyoshi Kato, Tetsuya Jinno, Atsushi Okawa. Drain tip culture is not prognostic for surgical site infection in spinal surgery under prophylactic use of antibiotics *Spine (Phila Pa 1976)*. 2016; 41(14); 1179-1184
4. Takanori Kokubun, Naohiko Kanemura, Kenji Murata, Hideki Moriyama, Sadao Morita, Tetsuya Jinno, Hidetoshi Ihara, Kiyomi Takayanagi. Effect of changing the joint kinematics of knees with a ruptured anterior cruciate ligament on the molecular biological responses in a spontaneous healing in a rat model *Am J Sports Med*. 2016; 44(11); 2900-2910

5. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Masanobu Hirao, Takeshi Muneta, Atsushi Okawa. Comparison of wear rate and osteolysis between annealed and remelted highly cross-linked polyethylene in total hip arthroplasty. A 7 to 10 year follow-up Orthop Traumatol Surg Res. 2016; 102(6); 707-721

**[Conference Activities & Talks]**

1. Gaku Koyano, Tetsuya Jinno, Daisuke Koga, Takeshi Muneta, Atsushi Okawa. Bilateral Comparison of Hip Joint Morphology between the Hips with and without Herniation Pit. Orthopaedic Research Society 2016.03
2. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Masanobu Hirao, Takeshi Muneta, Atsushi Okawa. Comparison of wear rate and osteolysis between annealed and remelted highly cross-linked polyethylene in total hip arthroplasty. 17th EFORT 2016.06
3. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Masanobu Hirao, Takeshi Muneta, Atsushi Okawa. Limited significance of screening computed tomography after cementless total hip arthroplasty with highly cross-linked polyethylene. 17th EFORT 2016.06

## Gerodontology and Oral Rehabilitation

Professor

MINAKUCHI Shunsuke

Associate Professor

TOHARA Haruka, OWATARI Tsuneto

Junior Associate Professor

SEKITA Toshiaki, KOBAYASHI Ken-ichi

Assistant Professor

AKIBA Norihisa, INOKOSHI Masanao, KANAZAWA Manabu, KOMAGAMINE Yuriko, MOTOMURA Kazuo, NAKANE Ayako, SATO Yusuke, WAKASUGI Yoko, OKUBO Mai

Project Assistant Professor

HAMA Youhei

Dental Resident

YOSHIZAKI Taro, NAKMURA Toshinarim, HIRAYAMA Daisuke, INOUE Minoru, JOU Ayami, TANOUE Mariko, YAMAGA Eijirou, YOSHIZUMI Yuu, NOMOTO Akiko, SATO Marie, OZAWA Emi

Graduate Student

AMAGAI Noriko, ANNDOU Mariko, ARAKIDA Toshio, ASAMI Mari, BABA Yuuya, CHANTARAMANEE Ariya, DOUKE Midori, KAGIFUKU Yuko, KAIDILIYA Yalikun, Sato Eriko, KAMOECHI Gou, KHAING Myat Thu, KUROSAWA Yukiko, KYOSAKA Yuka, MATSUBARA Mariko, MATSUDA Yuhei, MIURA Akemi, MIYAYASU Anna, OOWADA Gaku, SHIMIZU Haruki, SHIMIZUBATA Makoto, SHINOZAKI Hiromichi, SOEDA Hitomi, SUZUKI Hiroyuki, Shimada Ryo, TAGASHIRA Itoe, TUN Min Bo, VO Lam Thuy, YAMAGUCHI Kouhei, YAMAZAKI Yasuhiro, YOSHIMI Kanako, YOSHINAKA Shinn, HIROKO Namai, KUBOTA Chieko, OBA Shoko

Student

HIGASHINAKAGAWA Anri, JOKO Natsuka, KAKU Jakuenn, KANEKO Seiko, KAWASHIMA Mina, MACHIDA Nami, NAMIKI Chizuru, NISHIKI Gen, NISHIMIYA Yui, ODA Ken, OKANO Sakiko, TAKADA Shintaro, TAMURA Atsuko, TANIMOTO Hiroyuki, UEDA Kaori, UENO Taro, Tsugawa Eriko, YAGUCHI Shiho, YOSHII Eiji, AOKI Yumi, AWANO Mikiko, NAITO Yoko,

Staff

YAJIMA Yuriko, YOSHIZAKI Ayaka

Visiting Lecturer

Ando Kazuo, Fujishima Ichiro, SANO Haruo, Hiratsuka Tomohiro, INOKUCHI Nobuhiro FUJITANI Junko, KAGAWA Tomonori, UEMURA Ken'ichi, KIKUCHI Keisuke, SATOU Koutetsu, Kobayashi Shoji, Kojo Akiko, MURATA Shino, Matsuo Koichiro, Hino Naohiko, Nishibori Masakazu Osada Eiji, Ozaki Ken-ichiro, SUSA Chiaki, Saito Eiichi, Satoda Takahiro, Terasaka Satoshi, Hirano Shigezo, Kunimitsu Takashi, TAKESHITA Shin, TAKEUCHI Shuhei, TANAKA Shinji, Takahashi Noboru Takeuchi Satoshi, Usui Yoshie, Watanabe Ikki, YAMADA Ayako, YAMAMOTO Shinta, Yoneyama Takeyoshi Yuki Hirazima, ZHAO Hui Zi, Akimoto Kazuhiro, HAYASHI Keiji, HAYASHI Yukiko, Seki Takeo, Oono Tomohisa YAMADA Azusa, YAMAMOTO Katsura

### (1) Research

- 1) Medical management of Elderly Patients During Dental Treatment
- 2) New Examination Method for Dry Mouth
- 3) Oral Stereognosis Ability in the Elderly
- 4) Threshold of Mucous Membrane under Denture Base in Elderly Oral Mucosa Patients
- 5) State of the art Lasers in Zirconia Prosthetic Processing and Pain-free Treatment

- 6) Denture Mobility
- 7) Deglutition in Elderly Patients Requiring Nursing Care
- 8) Eating and Swallowing Rehabilitation in Post-Oral Tumor Surgery Patients
- 9) Dysphagia of Medullary Infarction Patients
- 10) Dental Approaches to Dysphagia
- 11) Screening Methods of Silent Aspiration
- 12) Swallowing Dynamics and Brain Activity
- 13) Stress analyses of implant overdenture
- 14) Factorial analysis of complete denture prosthesis
- 15) Resilient denture lining material
- 16) CAD/CAM system for fabricating complete dentures
- 17) Evaluations of masticatory performance using color-changeable chewing gum

## ( 2 ) Education

Given the increased health needs of an aging society, we aim to integrate diverse clinical specialties related to geriatric dental practice and to educate individuals of fundamental studies in each field. We emphasize a comprehensive approach to patient interactions by examining daily life functionality rather than focusing only on their diseases.

With regard to dysphagia, which can lead to aspiration pneumonia, we provide comprehensive education on causes, diagnostic methods, and rehabilitation options from a dentistry point of view. Since we regard rehabilitation as the medicine of daily living, we emphasize that dysphagia rehabilitation should be considered a method to ameliorate disability rather than diseases by introducing practical approaches in addition to factual knowledge.

## ( 3 ) Clinical Performances

We manage the prosthodontic, special care and dysphagia rehabilitation departments.

## ( 4 ) Publications

### [Original Articles]

1. Marie Sato. Effectsof Thyroid Cartilage Skin Traction on Swallowing Function in Elderly People 2016; 31(2); 100-107
2. Enri Nakayama, Haruka Tohara, Kotomi Sakai, Mayumi Hayata, Sayako Ohnishi, Sekino Jumpei, Hidetaka Tsuzuki, Koichiro Ueda. Predictive Factors associated with oral intake ability in gastrostomy patients under long-term care Journal of Nutrition Health & Aging,. 2016;
3. Inokoshi M, Yoshihara K, Nagaoka N, Nakanishi M, De Munck J, Minakuchi S, Vanmeensel K, Zhang F, Yoshida Y, Vleugels J, Naert I, Van Meerbeek B. Structural and Chemical Analysis of the Zirconia-Veneering Ceramic Interface. J Dent Res. 2016.01; 95(1); 102-109
4. Sato D, Kanazawa M, Kim YK, Yokoyama S, Omura Y, Ozeki M, Minakuchi S, Kasugai S, Baba K. Immediate loading of two freestanding implants placed by computer-guided flapless surgery supporting a mandibular overdenture with magnetic attachments. J Prosthodont Res. 2016.01; 60(1); 54-62
5. Nami Machida, Haruka Tohara, Koji Hara, Ayano Kumakura, Yoko Wakasugi, Ayako Nakane, Shunsuke Minakuchi. Effects of aging and sarcopenia on tongue pressure and jaw-opening force. Geriatr Gerontol Int. 2016.01;
6. Yamamoto S, Kanazawa M, Hirayama D, Nakamura T, Arakida T, Minakuchi S. In vitro evaluation of basal shapes and offset values of artificial teeth for CAD/CAM complete dentures. Computers in Biology and Medicine. 2016.01; 68(1); 84-89

7. Zhang F, Batuk M, Hadermann J, Manfredi G, Marien A, Vanmeensel K, Inokoshi M, Van Meerbeek B, Naert I, Vleugels J.. Effect of cation dopant radius on the hydrothermal stability of tetragonal zirconia: Grain boundary segregation and oxygen vacancy annihilation *Acta Mater.* 2016.03; 106; 48-58
8. Huizi Zhao, Norihisa Akiba, Hiroyuki Tanimoto, Taro Yoshizaki, Kaidiliya Yalikun, Shunsuke Minakuchi. Effects of temperature-responsive hydrogel on viscosity of denture adhesives. *Dent Mater J.* 2016.04; 35(2); 210-215
9. Inokoshi M, Pongprueksa P, De Munck J, Zhang F, Vanmeensel K, Minakuchi S, Vleugels J, Naert I, Van Meerbeek B. Influence of Light Irradiation Through Zirconia on the Degree of Conversion of Composite Cements. *J Adhes Dent.* 2016.04; 18(2); 161-171
10. Uchida Yoko, Kubota Chieko. Study on the relation between LUTS and xerostomia in community residents *International Nursing Care Research.* 2016.04; 15(1); 95-103
11. Effect of Added Oil and Fat on the Easiness of Swallow of Modified Diet for Dysphagia Persons 2016.06; 31(1); 58-65
12. Omura Y, Kanazawa M, Sato D, Kasugai S, Minakuchi S. Comparison of patient-reported outcomes between immediately and conventionally loaded mandibular two-implant overdentures: A preliminary study. *J Prosthodont Res.* 2016.07; 60(3); 185-192
13. Komagamine Y, Kanazawa M, Sasaki Y, Sato Y, Minakuchi S. Prognoses of new complete dentures from the patient's denture assessment of existing dentures. *Clinical Oral Investigations.* 2016.07;
14. Oda K, Kanazawa M, Takeshita S, Minakuchi S.. Influence of implant number on the movement of mandibular implant overdentures. *J Prosthet Dent..* 2016.09;
15. Sakai K, Nakayama E, Tohara H, Maeda T, Sugimoto M, Takehisa T, > Takehisa Y, Ueda K. Tongue Strength is Associated with Grip Strength and Nutritional Status in Older Adult Inpatients of a Rehabilitation Hospital. 2016.09;
16. Miura Y, Nakagami G, Yabunaka K, Tohara H, Hara K, Noguchi H, Mori T, Sanada H.. Detecting pharyngeal post-swallow residue by ultrasound examination: a case series *Med Ultrason.* 2016.09; 18(3); 288-293
17. Takahiro Arakawa, Yusuke Kuroki, Hiroki Nitta, Prem Chouhan, Koji Toma, Shin-ichi Sawada, Shuhei Takeuchi, Toshiaki Sekita, Kazunari Akiyoshi, Shunsuke Minakuchi, Kohji Mitsubayashi. Mouthguard biosensor with telemetry system for monitoring of saliva glucose: A novel cavity sensor *Biosensors and Bioelectronics* . 2016.10; 84; 106-111
18. Suguru Kimoto, Yasuhiko Kawai, Atsuko Gunji, Hisatomo Kondo, Taro Nomura, Tomohiko Murakami, Akito Tsuboi, Guang Hong, Shunsuke Minakuchi, Yusuke Sato, Gaku Ohwada, Tetsuya Suzuki, Katsuhiko Kimoto, Noriyuki Hoshi, Makiko Saita, Yoshikazu Yoneyama, Yohei Sato, Masakazu Morokuma, Joji Okazaki, Takeshi Maeda, Kenichiro Nakai, Tetsuo Ichikawa, Kan Nagao, Keiko Fujimoto, Hiroshi Murata, Tadafumi Kurogi, Kazuhiro Yoshida, Masahiro Nishimura, Yasuhiro Nishi, Mamoru Murakami, Toshio Hosoi, Taizo Hamada. Study protocol for a multi-center, randomized controlled trial to develop Japanese denture adhesive guidelines for patients with complete dentures: the Denture Adhesive Guideline trial: study protocol for a randomized controlled trial *Trials.* 2016.10; 17;
19. Komagamine Y, Kanazawa M, Iwaki M, Jo A, Suzuki H, Amagai N, Minakuchi S. Combined effect of new complete dentures and simple dietary advice on nutritional status in edentulous patients: study protocol for a randomized controlled trial. *Trials.* 2016.11; 17(1); 539-546
20. Zhang F, Inokoshi M, Batuk M, Hadermann J, Naert I, Van Meerbeek B, Vleugels J. Strength, toughness and aging stability of highly-translucent Y-TZP ceramics for dental restorations. *Dent Mater.* 2016.12; 32(12); e327-e337
21. Mariko Tanoue, Manabu Kanazawa, Shin Takeshita, Shunsuke Minakuchi. Effects of clip materials on stress distribution to maxillary implant overdentures with bar attachments *Journal of Prosthetic Dentistry.*
22. Khaing Myat Thu, Khin Swe Aye, Aung Htang. In vitro study of Coronal Leakage of Four Temporary Filling Materials Immersed in Alcoholic Methylene Blue Dye *Myanmar Dental Journal* . 20(1); 49-57

23. Yu Yoshizumi, Shinya Mikushi, Ayako Nakane, Haruka Tohara, Shunsuke Minakuchi. Dynamics of Swallowing Tablets during the Recovery Period following Surgery for Tongue Cancer Otolaryngology.

#### [Books etc]

1. Shinya Mikushi, Haruka Tohara. Anatomy for Plastic Surgery of the Face, Head and Neck. 2016

#### [Misc]

1. Manabu Kanazawa, Maiko Iwaki, Shinta Yamamoto, Toshio Arakida and Shunsuke Minakuchi. The complete denture with using CAD/CAM system 2016.06; 35(3); 185-188
2. Inokoshi M, Minakuchi S. Bond strategy for zirconia ceramics The Journal of the Japanese Society for Dental Materials and Devices. 2016.07; 35(4-5); 265-268

#### [Conference Activities & Talks]

1. Jo A, Kanazawa M, Sato Y, Akiba N, Iwaki M, Komagamine Y, Minakuchi S. Influence of the different impression methods for complete denture fabrication on masticatory ability. 2016.01.24
2. Manabu Kanazawa. Live border molding for complete dentures. Essential Expertise for Clinical Dentistry 2 2016.02.09
3. Manabu Kanazawa. Mandibular 2-implant overdenture. Essential expertise for clinical density 2016.02.26
4. Yuka Kyosaka, Shusaku Tayama, Tsuneto Owatari. A case report of prilocaine-induced methemoglobinemia in a medically compromised elderly. 2016.03.06
5. Arakida T, Kanazawa M, Yamamoto S, Iwaki M, Minakuchi S, Suzuki T. The effect if external light of digital impression. The effect of external light of digital impression 2016.05.29
6. Inokoshi M, Zhang F, De Munck J, Vanmeensel K, Minakuchi S, Vleugels J, Naert I and Van Meerbeek B. Influence of surface treatment on the bending strength of zirconia. 94th General Session & Exhibition of the IADR 2016.06 Seoul, Korea
7. M. Kanazawa, M. Iwaki, D. Sato, Y. Omura, A. Miyayasu, S. Kasugai, S. Minakuchi.. Immediate Loading of two-implants mandibular overdentures: 4-years prospective study.. 94th General Session & Exhibition of the IADR 2016.06 Seoul, Republic of Korea
8. Y. Komagamine, M. Kanazawa, H. Suzuki, N. Amagai, S. Minakuchi.. Effect of New Removable Dentures on Foods and Nutrients Intakes. 94th General Session & Exhibition of the IADR 2016.06 Seoul, Republic of Korea
9. Yuka Kyosaka, Tsuneto Owatari, Kazuki Takahashi, Natsuka Joko, Ayano Hayashi, Kazuhiro Shimoyama, Shunsuke Minakuchi. A case report of drug-induced arrhythmia : Excessive use of tiotropium in a medically compromised elderly in dental treatment.. 2016.06.18
10. Eriko Kajisa, Haruka Tohara, Ayako Nakane, Atsuko Tamura, Kohei Yamaguchi, Kanako Yoshimi, Mina Kawashima, Mikiko Awano, Shunsuke Minakuchi. The Relationship between Jaw Opening Force and Skeletal Muscle Mass including Suprahyoid Muscles. 2016.06.18
11. Hiromichi Shinozaki, Haruka Tohara, Mariko Matsubara, Yasuhiro Yamazaki, Koji Hara, Ayako Nakane, Yoko Wakasugi, Shunsuke Minakuchi. Effect of Decreased Jaw Opening Force on Hyoid bone Movement and its Resting Position in Healthy Elderly Subjects. 2016.06.18 Asty Tokushima
12. Minoru Inoue, Tsuneto Owatari, Hiroyuki Suzuki, Seiko Kaneko, Makoto Shimizubata, Noriko Amagai, Syunsuke Minakuchi, Kazuhiro Shimoyama. A case report of the urgent hospitalization of an elderly patient due to the actualized lung infection after the tooth extraction. 2016.06.19
13. Kanako Yoshimi, Haruka Tohara, Eriko Kajisa, Kohei Yamaguchi, Mikiko Awano, Mina Kawashima, Yoko Wakasugi, Ayako Nakane, Shunsuke Minakuchi. The Relationship between Oral Function and Leisure Activity in Community-dwelling Elderly People. 2016.06.19

14. M. YAMAMOTO, K. MOTOMURA, H. NAKAMURA, T. YOSHIOKA, F. YOSHIKAWA, S. TANAKA. Optimum conditions for resistance-heat-bending of NiTi arch wire. 94rd General Session & Exhibition of the IADR, 3rd Meeting of the Asia Pacific Region, 35th Annual Meeting of the IADR Korean Division 2016.06.23 Seoul
15. F.YOSHIKAWA, K.MOTOMURA, H.NAKAMURA, T.YOSHIOKA, M.YAMAMOTO, S.TANAKA. Improving adhesion of zirconia by surface modification. 94rd General Session & Exhibition of the IADR, 3rd Meeting of the Asia Pacific Region, 35th Annual Meeting of the IADR Korean Division 2016.06.24 Seoul
16. Anna Miyayasu, Ayami Jo, Manabu Kanazawa, Yusuke Sato, Maiko Iwaki, Norihisa Akiba, Shunsuke Minakuchi. Cost Analysis of the different impression methods for complete dentures. 94th General Session & Exhibition of the IADR 2016.06.25 Seoul, Korea
17. Y Kaidiliya, M Kanazawa, S Takeshita, K Oda ,M Tanoue, A Miyayasu, V L Thuy, K M Thu, M Asami, H Shimizu, S Minakuchi. Stress Analysis of Mandibular Implant Overdentures with Different Implant Positions. 94th General Session & Exhibition of the IADR 2016.06.25 Seoul, Korea
18. Hama Y, Minakuchi S, Sasaki K, Maeda T, Hamura A, Ichinohe T, Keiji M. The Dental Education Consortium to promote healthy longevity -Second report- Agendas after the second year. 2016.07.02
19. Multicenter Randomized Clinical Study of Denture Adhesive to Establish the Guideline: Study by the Subgroup Analysis for a Denture Adhesive on the Effect of the Masticatory Performance. 2016.07.09
20. Arakida T,Kanazawa M,Yamamoto S,Iwaki M, Minakuchi S,Suzuki T,Oki M,Kamijo S,Ando K,Morisawa K. The effect of external light of digital impression time and accuracy. 2016.07.09
21. Miyayasu A, Jo A, Kanazawa M, Sato Y, Iwaki M, Akiba N, Minakuchi S. Cost-effectiveness analysis of the impression methods for mandibular complete dentures in randomized controlled trial. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07.09 Kanazawa
22. Hiroyuki Suzuki,Manabu Kanazawa,Yuriko Komagamine,Maiko Iwaki,Ayami Jo,Noriko Amagai,Shunsuke Minakuchi. Combined effect of new complete dentures and simple dietary counseling on nutritional status in edentulous patients : study protocol for a randomized controlled trial. The 125th Scientific Meeting of Japan Prosthodontic Society 2016.07.09 Kanazawa
23. Asami Mari,Miyayasu Anna,Kanazawa Manabu,Takeshita Shin,Tanoue Mariko,Sato Daisuke,Oda Ken,Shimizu Haruki,Morisawa Masayuki,Kasugai Shohei,Minakuchi Shunsuke. Cost-effectiveness analysis of mandibular single-implant overdentures and conventional complete dentures Study protocol for a randomized controlled clinical trial . The 125th Scientific Meeting of Japan Prosthodontic Society 2016.07.09 Kanazawa
24. Kobayashi K, Sekita T, Kobayashi K, Hoshino T, Takeuchi S. A 25-year Follow-up of the Patient with Advanced Periodontal Disease Treated by Cross-arch Fixed Bridge. 2016.07.09
25. Kobayashi K, Sekita T, Kobayashi K, Hoshino T, Takeuchi S. A 25-year Follow-up of the Patient with Advanced Periodontal Disease Treated by Cross-arch Fixed Bridge. The 125rd Annual Meeting of Japan Prothodontic Society 2016.07.09 Kanazawa
26. Zhang F, Vanmeensel K, Inokoshi M, Van Meerbeek B, Naert I, Vleugels J.. Towards aging resistant zirconia: Grain boundary engineering. International Congress on Ceramics (ICC6) 2016.08 Dresden
27. Yoko Wakasugi, Toshiyuki Yamamoto, Miho Murata, Haruka Tohara, Syunsuke Minakuchi. Effect of an impaired oral stage of swallowing in patients with Parkinson's disease. 2016.09.23
28. Y. Komagamine, M. Kanazawa. N. Akiba, Y. Sato, M. Okubo, Y. Hama, S. Minakuchi. The comparison of the nutritional status between pre- and post- provision with new complete denture among edentulous people. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10.21 Fukuoka Convention Center, Hakata, Fukuoka
29. Anna Miyayasu, Manabu Kanazawa, Yuriko Komagamine, Naoko Seki. Decision making for prosthodontics treatment in a case of multiple tooth loss. Essential Expertise for Clinical Dentistry 2 2016.10.27 Tokyo, Japan
30. Inokoshi M. Basics of dental zirconia. Tokyo Meister Course Lecture 2016 2016.10.30 Tokyo



31. Kaidiliya Yalikun, Manabu Kanazawa, Shin Takeshita, Ken Oda ,Mariko Tanoue, Anna Miyayasu, Vo Lam Thuy, Khaing Myat Thu, Mari Asami, Haruki Shimizu, Ryo Shimada, Shunsuke Minakuchi. Strain Analysis of Mandibular Implant Overdentures in Different Dislodging Position with Different Implant Number.. International Dental Materials Congress 2016 (IDMC2016) 2016.11 Bali, Indonesia
32. Shimada Ryo, Kanazawa Manabu, Miyayasu Annna, Tanoue Mariko, Sato Daisuke, Kusumoto Yuriko, Abe Yuka, Yokowama Sawako, Baba Kazemi, Minakuchi Syunnsuke. Prospective clinical trial of IARPD with short implants -research protocol- . 2016.11.06 gihu
33. Go KAMOCHI, Norihisa AKIBA, Toshinari NAKAMURA, Shunsuke MINAKUCHI. Effect of water absorption on stress relaxation behavior of home reliner. 2016.11.26

#### **[Others]**

1. Kobayashi K, Principle of tooth preparation, 2016.04  
Hands-oncourse
2. Kobayashi K, Principle of tooth preparation, 2016.10  
Hands-on course
3. Kobayashi K, Principle of tooth preparation for molar teeth, 2016.11  
Hands-on course



## Laboratory Medicine

Professor Shuji TOHDA

Research Associate Mai ITOH

Graduate Students Mika OHTAKA, Erika SHIRATORI, Shohei NOGAMI, Yuki KOHDA

### ( 1 ) Outline

Laboratory medicine is a field of research to develop analytical methods of pathophysiology of various diseases, new diagnostic tests, and diagnosis-supporting system using laboratory tests.

### ( 2 ) Research

Our research subjects are as follows:

- 1) Cellular and molecular mechanism of abnormal growth of acute leukemia cells and drug-sensitivity tests for molecularly targeted therapy
- 2) Molecular diagnostic tests for cancer and detection of minimal residual cancer cells
- 3) Mechanism of abnormal growth of lymphoma cells
- 4) Molecular diagnostic tests for infectious diseases

### ( 3 ) Education

To graduates students, we provide opportunity to study and develop novel diagnostic tests using cellular and molecular biological technique in our laboratories.

To undergraduate students, we give a lecture and practical training on laboratory medicine.

### ( 4 ) Lectures & Courses

Main objective of Laboratory Medicine in the graduate course is to provide students opportunity to study analysis of pathophysiology, development of new diagnostic tests, and establishment of diagnosis-supporting system using laboratory tests. We focus on the analysis of pathophysiology of hematological malignancies and the development of molecular diagnostic tests for cancer and infectious diseases.

### ( 5 ) Clinical Services & Other Works

We are performing laboratory tests for hematology, clinical chemistry, immunology, and microbiology in cooperation with doctors and technologists of clinical laboratory in University hospital. We give a lecture on laboratory tests at meetings of laboratory medicine-related societies.

### ( 6 ) Clinical Performances

We are developing new diagnostic methods collaborating with various clinical departments. We are also supporting them in their diagnostic procedure.

**(7) Publications****[Original Articles]**

1. Mari Kamiya, Peter Y Shane, Makoto Soejima, Shuji Tohda, Nobuyuki Miyasaka, Hitoshi Kohsaka. IgG4-Related Sialoadenitis with a Skin Lesion and Multiple Mononeuropathies Suggesting Coexistent Cryoglobulinemic Vasculitis. *Intern. Med.*. 2016; 55(10); 1355-1361
2. Megumi Akiyama, Kota Yoshifuji, Tetsuya Fukuda, Shuji Tohda, Tohru Miki, Osamu Miura, Masahide Yamamoto. Fulminant visceral disseminated varicella-zoster virus infection without skin involvement in a patient with autoimmune hemolytic anemia on prednisolone therapy. *Rinsho Ketsueki*. 2016.04; 57(4); 467-471
3. Noriko Kawaguchi-Ihara, Mai Itoh, Ikuo Murohashi, Shuji Tohda. Establishment of a quenching probe method for detection of NPM1 mutations in acute myeloid leukemia cells. *Oncol Lett.* 2016.04; 11(4); 2429-2432
4. Hiroko Nagata, Mina Nakagawa, Yuki Nishimura-Sakurai, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Fumio Goto, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Naoko Tojo, Shuji Tohda, Yasuhiro Asahina, Mamoru Watanabe, . Serial measurement of Wisteria floribunda agglutinin positive Mac-2-binding protein is useful for predicting liver fibrosis and the development of hepatocellular carcinoma in chronic hepatitis C patients treated with IFN-based and IFN-free therapy.[ Epub ahead of print] *Hepatol Int.* 2016.07;
5. Shinji Ogihara, Ryoichi Saito, Etsuko Sawabe, Michio Hagihara, Shuji Tohda. First Japanese case of infectious endocarditis due to *Enterococcus faecalis* small-colony variants. *J. Infect. Chemother.*. 2016.10; 22(10); 716-719
6. Gene Igawa, Mika Casey, Etsuko Sawabe, Yoko Nukui, Shu Okugawa, Kyoji Moriya, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Comparison of agar dilution and broth microdilution methods for *Clostridium difficile* antimicrobial susceptibility testing. *J Glob Antimicrob Resist.* 2016.12; 7; 43-45

**[Conference Activities & Talks]**

1. Amano E, Suzuki M, Ozaki K, Ishibashi S, Akaza M, Kanouchi T, Tohda S, Yokota T. A case of sensory dominant CIDP with conduction delay predominantly in the most distal segment (Japanese). 10th Tokyo Metropolitan Neuromuscular Electrodiagnosis Forum 2016.01.30 Tokyo
2. Shohei Nogami, Mai Itoh, Shuji Tohda. Clinical usefulness of allele-specific/quenching probe method for detection of the MYD88 L265P mutation. The 14th Asian Society for Clinical Pathology and Laboratory Medicine Congress 2016.03.26 Taipei
3. Ohta N, Kanouchi T, Akaza M, Aoyagi E, Narumi J, Yanagi N, Sumi Y, Yokota T, Hagihara M, Tohda S. A study of quality control of nerve conduction study. 57th annual meeting of the Japanese Society of Neurology 2016.05.20 Kobe
4. Kazuaki Yamamoto, Seiya Watanabe, Michio Hagihara, Shuji Tohda. Development of a novel measurement method for L-hydroxyproline using a new enzyme. The 32th World Congress of Biomedical Laboratory Science 2016.09.02
5. Naoya Ichimura, Ayako Itoi, Yuki Ohkubo, Yuki Koda, Michio Hagihara, Shuji Tohda. Development of an internal quality control application for immature granulocytes differential. The 32th World Congress of Biomedical Laboratory Science 2016.09.02 Kobe
6. Naoya Ichimura, Ayako Itoi, Yuki Ohkubo, Yuki Koda, Michio Hagihara, Shuji Tohda. Evaluation of an internal QC application for correctly recognizing immature granulocytes on blood smear. The 32th World Congress of Biomedical Laboratory Science 2016.09.02 Kobe
7. Kanouchi T, Sekiguchi T, Tohda S, Yokota T. Does the impairment of upper motor neurons have an influence upon the speed of degeneration of lower motor neurons in ALS. 46th annual meeting of the Japanese Society of Clinical Neurophysiology 2016.10.28 Kohriyama

8. Aoyagi E, Kanouchi T, Akaza M, Iida S, Narumi J, Ohta N, Sumi Y, Yokota T, Hagihara M, Tohda S. A study of quality control of nerve conduction study. 46th annual meeting of the Japanese Society of Clinical Neurophysiology 2016.10.29 Kohriyama
9. Erika Shiratori, Mai Itoh, Mika Ohtaka, Shohei Nogami, Shuji Tohda. Mechanisms of suppressive effects of MYD88 Inhibitors on the Growth of Lymphoma and Leukemia Cells. The 58th American Society of Hematology 2016.12.04 San Diego

# Intensive Care Medicine

Professor:

Hidenobu Shigemitsu (2016.9.1 -)

Associate Professor

Hideo Takahashi(2016.4.1 -)

Yushi Adachi(2015.4.1 - 2016.6.30)

Assistant Professor:

Takahiro Masuda (Intensive Care Unit) (2014.4.1 -)

Kenji Wakabayashi (2015.4.1 -)

Akihiro Haramo (Intensive Care Unit) (2015.4.1 - 2017.3.31)

Nobuhiro Shiota (Intensive Care Unit) (2015.4.1 -)

Arisa Fukagawa (Intensive Care Unit) (2016.4.1 - 2017.3.31)

Kanae Ochiai (Intensive Care Unit) (2016.7.1 - 2017.1.31)

Takafumi Ohmori (Anesthesiology) (2016.4.1 - 2017.3.31)

Fellow:

Fumi Maruyama (Intensive Care Unit) (2014.4.1 -)

Postgraduate students:

Mariko Senda (2014.4.1 -)

Yusuke Mitsui (2016.4.1 -)

Shotaro Matsumoto (2016.4.1 -)

## ( 1 ) Outline

Critical care medicine provides intensive care and treatment for critically ill patients. To treat critically ill patients, intensivists have to catch the changes of the patients' condition by monitoring and evaluation, and practice appropriate therapy. It is important that intensivists practice minute-to-minute titration therapy in cooperation with other multidisciplinary professionals.

Practice of critical care medicine includes intensive care for various types of shock, acute respiratory distress syndrome/acute lung injury, sepsis, multiple organ dysfunction syndrome, abnormal acid-base balance, electrolyte disturbance, acute kidney injury, central nervous system dysfunction, and hospital-acquired infection, mechanical ventilation, pharmacological support, cardiopulmonary support system, blood purification, and nutrition support.

## ( 2 ) Research

Our themes of research are derived from clinical questions in critically ill patients.

Clinical research:

1) Conducted Multiple institutes randomized control trial: Japanese Trial for Acute Kidney Injury in Post-cardiovascular Surgery by Atrial Natriuretic Peptide (JAPAN study).

2) Participated multiple center clinical investigation: Mechanical ventilation practice investigation (MVP investigation).

3) Participated multiple center randomized control trial: Acid-base Balance & Oxygen management in patients required mechanical Ventilation - Evaluation study (ABOVE study).

Eleven Japanese hospitals were included in this trial.

Basic research:

1) Effect of inhaled insulin on acute lung injury (Nakazawa, Funded by Grant-in-Aid for challenging Exploratory Research)

2) Interaction between different anaesthetics (Adachi, funded by Grant-in-Aid for Scientific Research C)

3) Mechanism of inflammation in acute lung injury (Wakabayashi, funded by Grant-in-Aid for Young Scientists B)

4) Role of microvesicles in bronchopulmonary dysplasia (Wakabayashi, funded by Grant-in-Aid for Young Scientists B)

5) Role of urinary microvesicles in acute liver failure (Wakabayashi, funded by National Center of Child Health and Development)

### (3) Education

Undergraduate education

Lectures: Fourth-year medical students

1) Mechanical ventilation (Wakabayashi)

Clinical clerkship: Fifth-year and Sixth-year medical students

Critical care medicine is a branch of faculty of medicine which deals with monitoring and care of critically ill patients. Main objective of critical care medicine is to provide students opportunity to study diagnosis and treatment of critically ill patients in the intensive care unit (ICU). Students are taught on clinical practice in the ICU. Students take charge of 1-2 patients with attending physician and intensivist. Students check clinical data every morning and evening and make system-oriented presentation at ICU rounds.

Conference: Students are assigned to read recent articles of critical care medicine and make presentations by power point at the conference.

Residents: Residents are training in the ICU for 2-3 months. They study respiratory, circulatory, and metabolic management of critically ill patients. They learn how to use ultrasound and bronchoscope.

### (4) Clinical Services & Other Works

Intensivists are staying in the ICU, and take charge treatment of critically ill patients in the ICU.

Every morning, intensivists, nurses, pharmacist, nutritionist, rehabilitation staffs, infection control staffs, medical engineers, and attending physicians get together, go round, and talk about the best treatment of the patients.

### (5) Publications

#### [Original Articles]

1. Yukako Obata, Yushi U Adachi, Katsumi Suzuki, Taiga Itagaki, Hiromi Kato, Maiko Satomoto, Yoshiki Nakajima. The Influence of Differences in Solvents and Concentration on the Efficacy of Propofol at Induction of Anesthesia. *Anesthesiol Res Pract.* 2016.01; 2016; 9178523
2. Chieko Mitaka, Takahiro Masuda, Koji Kido, Tokujiro Uchida, Shinya Abe, Taku Miyasho, Makoto Tomita, Eiichi Inada. Polymyxin B hemoperfusion prevents acute kidney injury in sepsis model. *J. Surg. Res.* 2016.03; 201(1); 59-68
3. Z Sun, M Satomoto, Y U Adachi, H Kinoshita, K Makita. Inhibiting NADPH oxidase protects against long-term memory impairment induced by neonatal sevoflurane exposure in mice. *Br J Anaesth.* 2016.05; 117(1); 80-86
4. Takahiro Masuda, Koichi Nakazawa, Chieko Mitaka. A case of atypical hemolytic uremic syndrome triggered by a surgery, and treated with eculizumab. *J Jpn Soc Intensive Care Med.* 2016.11; 23(6); 673-674

**[Misc]**

1. Koichi Nakazawa, Ken Shinoda. An overview of incidence and outcome of perioperative pulmonary aspiration The Japanese Journal of Anesthesiology . 2016.01; 65(1); 4-12

**[Conference Activities & Talks]**

1. Wakabayashi K, Adachi YU, Tateishi T, Inase N, Nakazawa K. Ventilator management for the patient with acute exacerbation of interstitial pneumonia. Japanese Society of Intensive Care Society 2016.02
2. Effects of non-invasive positive airway pressures on right internal jugular vein size. . 2016.05.30
3. Kenji Wakabayashi. Biotrauma and multiple organ dysfunction syndrome. The 38th annual congress of Japanese Society of Respiratory Care Medicine 2016.07 Nagoya, Japan

## Liaison Psychiatry and Palliative Medicine

Associate Professor Eisuke MATSUSHIMA  
Assistant Professor Miho MIYAJIMA  
Visiting Lecture Tetsuya Matsuda, Katsuya Ota,  
Kanao Ichikura, Takashi Hosaka,  
Clinical Psychologist Aya Yamashita, Nao Nakayama,  
Graduate Student Noriko Ishiduka, Miho Itou,  
Toshi Kuriyama, Hiroshi Koubou,  
Toshimi Takano, Rie Tani,  
Takamasa Noda, Noriko Yoshida,  
Hiroko Arioka, Nami Kondou,  
Hiroki Sakurai, Mariko Takaki,  
Sumie Nemoto, Reiko Matsuda,  
Kisaragi Suzuki, Yoko Suzuki,  
Jun Nakagawa, Mayo Fujiwara,  
Kanao Amano, Sayaka Ozaka,  
Saori Koshimoto, Shiho Matsuoka,  
Kazuhiro Kosugi, Takafumi Watanabe,  
Mayuko Iijima, Yu Okura, Jun Kakou,  
Kensuke Komatsu,  
Research Student Okihiko Aihara, Ryuho Ibaraki.  
Secretary Yoriko Mizukane

### ( 1 ) Outline

The purpose of the section is to help understanding characteristics of psychosocial distress in patients with physical and mental disorders from a comprehensive viewpoint. Objects are mainly physical patients accompanied with pain, anxiety, depressive mood and so on. Students study these patients' symptoms, how to diagnose, practice of treatment and methods of preventive measures.

### ( 2 ) Research

- 1) Assessment of mental state in cancer and other physical patients using written questionnaire
- 2) Research on quality of life (QOL) in cancer patients and their families
- 3) Investigation cognitive function of patients with organic disorders (SLE, diabetics, and so on) undergoing a battery of psychometry tests and neuroimaging examinations
- 4) Explanation for the relationship between physical symptoms and mental states in patients with psychosomatic diseases including chronic pain and irritable bowel syndrome (IBS)
- 5) Examination for physiological phenomenon of psychiatric patients using eye mark recorder, electroencephalogram (EEG) and functional MRI (fMRI)

### (3) Clinical Services & Other Works

Psychosomatic clinic provides consultation-liaison psychiatry services at the request of the treating medical or surgical staffs. Patients accompanied with insomnia, anxiety, depressive mood and delirium are treated with psychotherapy and prescription medicines.

### (4) Publications

#### [Original Articles]

1. Fujiwara K, Miyajima M, Yamakawa T, Abe E, Suzuki Y, Sawada Y, Kano M, Maehara T, Ota K, Sasai-Sakuma T, Sasano T, Matsuura M, Matsushima E. Epileptic seizure prediction based on multivariate statistical process control of heart rate variability features *IEEE Trans Biomed Eng*. 2016; 63(6); 1321-1332
2. Kanako Ichikura, Aya Yamashita, Taro Sugimoto, Seiji Kishimoto, Eisuke Matsushima. Persistence of psychological distress and correlated factors among patients with head and neck cancer. *Palliat Support Care*. 2016.02; 14(1); 42-51
3. Shiho Matsuoka, Naoko Kato, Takahiro Kayane, Michiyo Yamada, Masako Koizumi, Toshimi Ikegame, Miyuki Tsuchihashi-Makaya. Development and Validation of a Heart Failure-Specific Health Literacy Scale. *J Cardiovasc Nurs*. 2016.03; 31(2); 131-139
4. Jun Hamano, Takashi Yamaguchi, Isseki Maeda, Akihiko Suga, Takayuki Hisanaga, Tatsuhiko Ishihara, Tomoyuki Iwashita, Keisuke Kaneishi, Shohei Kawagoe, Toshiyuki Kuriyama, Takashi Maeda, Ichiro Mori, Nobuhisa Nakajima, Tomohiro Nishi, Hiroki Sakurai, Satofumi Shimoyama, Takuya Shinjo, Hiroto Shirayama, Takeshi Yamada, Tatsuya Morita. Multicenter cohort study on the survival time of cancer patients dying at home or in a hospital: Does place matter? *Cancer*. 2016.05; 122(9); 1453-1460
5. Koichi Fujiwara, Miho Miyajima, Toshitaka Yamakawa, Erika Abe, Yoko Suzuki, Yuriko Sawada, Manabu Kano, Taketoshi Maehara, Katsuya Ohta, Taeko Sasai-Sakuma, Tetsuo Sasano, Masato Matsuura, Eisuke Matsushima. Epileptic Seizure Prediction Based on Multivariate Statistical Process Control of Heart Rate Variability Features. *IEEE Trans Biomed Eng*. 2016.06; 63(6); 1321-1332
6. Naoki Matsuo, Tatsuya Morita, Yoshinobu Matsuda, Kenichiro Okamoto, Yoshihisa Matsumoto, Keisuke Kaneishi, Takuya Odagiri, Hiroki Sakurai, Hideki Katayama, Ichiro Mori, Hirohide Yamada, Hiroaki Watanabe, Taro Yokoyama, Takashi Yamaguchi, Tomohiro Nishi, Akemi Shirado, Shuji Hiramoto, Toshio Watanabe, Hiroyuki Kohara, Satofumi Shimoyama, Etsuko Aruga, Mika Baba, Koki Sumita, Satoru Iwase. Predictors of Responses to Corticosteroids for Cancer-Related Fatigue in Advanced Cancer Patients: A Multicenter, Prospective, Observational Study. *J Pain Symptom Manage*. 2016.07; 52(1); 64-72
7. Kanako Ichikura, Yasuyuki Okumura, Takashi Takeuchi. Associations of Adverse Clinical Course and Ingested Substances among Patients with Deliberate Drug Poisoning: A Cohort Study from an Intensive Care Unit in Japan. *PLoS ONE*. 2016.08; 11(8); e0161996
8. Miho Ito, Eisuke Matsushima. Presentation of Coping Strategies Associated with Physical and Mental Health During Health Check-ups. *Community Ment Health J*. 2016.08; 53(3); 297-305
9. Ando K, Soshi T, Nakazawa K, Noda T, Okada T. Risk Factors for Problematic Behaviors among Forensic Outpatients under the Medical Treatment and Supervision Act in Japan. *Front Psychiatry*. 2016.08; 7; 144
10. Shiho Matsuoka, Miyuki Tsuchihashi-Makaya, Akiko Okada, Yoshiyuki Aoki, Mariko Fukawa, Yoko Ishida, Etsuko Nakatsugawa, Debra K. Moser. . Japanese Version of the Control Attitude Scale-Revised is Valid and Reliable in Patients With Heart Failure *J Card Fail*. 2016.08; 22(8); s78
11. Shiho Matsuoka, Miyuki Tsuchihashi-Makaya, Takahiro Kayane, Michiyo Yamada, Rumi Wakabayashi, Naoko P Kato, Miyuki Yazawa. Health literacy is independently associated with self-care behavior in patients with heart failure. *Patient Educ Couns*. 2016.09; 99(6); 1026-1032



12. Shiho Matsuoka, Akiko Hayashi, Miyuki Tsuchihashi-Makaya. Daily Physical Symptom Burden in Patients with Heart Failure: A Systematic Review. *J Card Fail.* 2016.09; 22(9); s210
13. Midori Ninomiya-Baba, Junko Matsuo, Daimei Sasayama, Hiroaki Hori, Toshiya Teraishi, Miho Ota, Kotaro Hattori, Takamasa Noda, Ikki Ishida, Shigenobu Shibata, Hiroshi Kunugi. Association of body mass index-related single nucleotide polymorphisms with psychiatric disease and memory performance in a Japanese population. *Acta Neuropsychiatr.* 2016.12; 1-10
14. Go Taniguchi, Miho Miyajima, Masako Watanabe, Yoshiko Murata, Daichi Sone, Yutaka Watanabe, Mitsutoshi Okazaki, Motonori Kobayashi-Kimura, Masaaki Kato, Teiichi Onuma. . Nonconvulsive status epilepticus in the elderly associated with newer antidepressants used at therapeutic doses: A report of three cases. *Epilepsy Behav.* (accepted).

### [Conference Activities & Talks]

1. Jun Kako, Masamitsu Kobayashi, Yusuke Kanno, Asao Ogawa. Establishing a binary cut-off point for the physical scores of edmonton symptom assessment system-revised Japanese version. The MASCC/ISOO 2016 Annual Meeting 2016.06.23
2. Jun Kako, Masamitsu Kobayashi, Yusuke Kanno, Keita Tagami, Chiemi Saito. Administration of intranasal vinegar was effective for persistent hiccups with an advanced cancer patient in palliative care setting a case report. The MASCC/ISOO 2016 Annual Meeting 2016.06.23
3. Masamitsu Kobayashi, Jun Kako, Yusuke Kanno, Asao Ogawa. Evaluation of physical symptoms using the edmonton symptom assessment system-revised Japanese version and binary data. The MASCC/ISOO 2016 Annual Meeting 2016.06.23
4. Sasaki A, Tomita N, Kawashima I, Nishi Y, Nomura M, Setoyama S, Noda T, Kumano H. Effectiveness and mechanism of Attention Training Technique on depressed patients by observing two cases.. 8th World Congress of Behavioural and Cognitive Therapies 2016.06.24 Australia (Melbourne Convention and Exhibition Centre)
5. Kanako Ichikura, Shin-ichi Suzuki. Experience-oriented learning vs. lecture-based learning about cognitive behavioral therapy for lifestyle modification: a pilot study. 8th World Congress of Behavioural and Cognitive Therapies 2016.06.25 Melbourne, Australia
6. A randomized controlled trial evaluating the effect of workbook intervention on QOL in patients receiving chemotherapy. . 2016.07.28
7. Miho Miyajima. Real-Time Epileptic Seizure Prediction System Employing a Wearable HRV Telemeter and a Smartphone. 38TH Annual International Conference of The IEEE Engineering in Medicine and Biology Society 2016.08.19 Orlando
8. Changes of heart rate and heart rate variability in the patients who found prolonged seizure during electroconvulsive therapy. 2016.10
9. Changes of corrected QT interval during electroconvulsive therapy relate to the risk of ventricular arrhythmias. 2016.10
10. Kanako Amano, Osamu Takahashi. Psychological issues and interventions for young partners in palliative care ward-How can we support young partners in short term?-. 18th World Congress International Psycho-oncology Society 2016.10.18 Dublin/Ireland

# Pharmacokinetics and Pharmacodynamics

Professor Masato Yasuhara  
Associate Professor Masashi Nagata  
Research student Yuri Kimura  
Secretary Takako Iguchi

## ( 1 ) Research

- 1) Kinetics of drug action in disease states
- 2) Therapeutic drug monitoring and clinical pharmacokinetics

## ( 2 ) Education

Department of Pharmacokinetics and Pharmacodynamics is in charge of the education of pharmacokinetics and pharmacodynamics for the establishment of safe and effective drug therapy. In the graduate course, the lecture on the recent progress of the pharmacokinetic analysis and drug transport will be given. Students will have the practice of pharmacokinetic analysis and animal experiments.

## ( 3 ) Publications

### [Original Articles]

1. Yuki Aoki, Reiji Miyawaki, Kohsuke Imai, Masatoshi Takagi, Michiko Kajiware, Yasuyoshi Ishiwata, Masato Yasuhara, Tomohiro Morio, Shuki Mizutani, Daisuke Tomizawa. Haploidentical Bone Marrow Transplantation With Clofarabine and Busulfan Conditioning for a Child With Multiple Recurrent Acute Lymphoblastic Leukemia. *J. Pediatr. Hematol. Oncol.* 2016.01; 38(1); 39-41
2. M. Nagata, M. Nakajima, Y. Ishiwata, Y. Takahashi, H. Takahashi, K. Negishi and M. Yasuhara. Mechanism underlying induction of hyperglycemia in rats by single administration of olanzapine. *Biol. Pharm. Bull.* 2016.05; 39(5); 754-761
3. Yasuyoshi Ishiwata, Masashi Nagata, Takafumi Arai, Misato Makiishi, Maho Yoshikawa, Hiromitsu Takahashi, Hitoshi Kohsaka, Masato Yasuhara. Effects of Miconazole Oral Gel on Blood Concentrations of Tacrolimus and Cyclosporine: A Retrospective Observational Study. *Ther Drug Monit.* 2016.12; 38(6); 717-721

### [Conference Activities & Talks]

1. M. Nagata, M. Nakajima, Y. Ishiwata, Y. Takahashi, H. Takahashi, M. Yasuhara. Pharmacokinetic-pharmacodynamic modeling of olanzapine-induced acute hyperglycemia in rats. ISSX2016 2016.06.12 Busan, Korea
2. Ishiwata Y, Nagata M, Arai T, Makiishi M, Yoshikawa M, Takahashi H, Kohsaka H, Yasuhara M. Drug-drug Interaction of Miconazole Oral Gel with Tacrolimus and Cyclosporine After Oral Administration. 2016 AAPS Annual Meeting and Exposition 2016.11.15 Denver, USA

## Medical Education Research and Development

Professor Yujiro TANAKA  
Junior Associate Professor Makoto TAKAHASHI  
Junior Associate Professor Yasuhiro ITSUI  
Junior Associate Professor Toshifumi KUDO  
Junior Associate Professor Eriko OKADA  
Senior Resident Fukiko KITAHATA

### (1) Outline

Department of General Medicine was established in 2000, when Prof. Yujiro Tanaka assumed the role of chairman of the department. Since then, our aim has been to coordinate and support a wide range of new innovations for the department of medicine and its affiliated hospitals. Accordingly, we launched the following projects to carry out our mission; 1) Designing a new postgraduate clinical training program for TMDU affiliated hospitals, 2) Forming a patient support system including social casework, 3) Establishing the Center for Cell Therapy, and 4) Reforming undergraduate medical education.

In response to the expansion of our activities, we have had some reforms in our organizations. 1) We founded the Center for Postgraduate Medical Education in 2002. (Director: Prof. Tanaka. Associate Director: Dr. Masanaga Yamawaki/former, Dr. Yoshihito Momohara/former, and Dr. Makoto Takahashi/previous) 2) In 2002, we also established the Center for Health and Welfare. And two years later in 2004, it was developed into an independent center as the Department of Medicine when Dr. Masayoshi Shichiri was appointed as the Director. 3) The Center for Cell Therapy, which was first established as a part of the Blood Transfusion Department in March, 2001, became an independent organization in 2003. Then Dr. Tomohiro Morio became the director. 4) Prof. Tanaka became a member of the Board of Education and worked at the committee for curriculum renovations in the Department of Medicine. Then he became the chair of the Education Committee in 2004.

In addition to the curriculum reforms, the Department of General Medicine has been in charge of early clinical training, PBL implementation, supervising patient-doctor communication education, OSCE (objective structured clinical examination) preparation, and BSL (bedside learning). We have also promoted educational alliances with Harvard University since 2002 and with Imperial College, London since 2003.

As mentioned above, a couple of years after their launch, the Center for Health and Welfare and the Center for Cell Therapy became independent from the Department of General Medicine. Meanwhile, new working groups were formed within the department in 2004; the Working Group for Ward Management and the Safety Management Committee. The Department of General Medicine also devised an evaluation system for the residency training program (EPOC), which was later adopted as a national online evaluation system for postgraduate clinical training. We are working in close cooperation with Center for Interprofessional Education which we took in part of its establishment to materialize the interprofessional education introduced due to a revision of new curriculum in 2011.

### (2) Research

Research on continuing education in clinical EBM (Tanaka)

Although the theory of EBM (Evidence-Based Medicine) has become common knowledge, there are many practical problems yet to be solved. Research on teaching and assessment techniques for under- and post-

graduate clinical training are ongoing.

Medical risk education using the HAZOP method-through analyzing basic surgical procedure (Takahashi)  
Structured risk analysis methods, HAZOP, are applied for medical risk management. We have also developed computer software for risk analysis with HAZOP. As a method of medical education for medical risk as well, HAZOP is a comprehensive method that is effective in reducing medical errors.

Review of clinical training in postgraduate clinical education (Takahashi)  
The performance evaluation system using EPOC, which is used in 60% of educational hospitals in Japan, was primarily developed at Tokyo Medical and Dental University. We applied this system to a clerkship program to compare its educational effect with that of a residency program.

General research on medical education (Tanaka, Takahashi, Itsui, Kudou, Okada)  
We are developing a comprehensive research project regarding postgraduate medical education, primary care in rural regions, development of clinical competence, and a new PBL system.

### (3) Education

#### Undergraduate Education

As a division, which is responsible for the education of students and residents, our primary goal is to foster doctors who have both a 'patient-centered perspective as a specialist' and 'up-to-date knowledge as a generalist'. To achieve our goal, we are designing and offering a continuing medical educational (CME) program for clerkship students, emphasizing on educational systems spreading among multiple departments. Since we think it is crucial to foster medical prospective with a patient-centered perspective, we introduced an early exposure course (MIC: Medical Introductory Course) for the 1st and 2nd year medical students, as well as some medicine oriented English courses, including a special course titled "Language and Philosophy of Western Medicine" regarding some of the needs of this globalized era of medicine. In addition, we are managing a training course for simulated patients who can contribute to medical education cooperating with the International Center for Medical Education at the University of Tokyo. To improve the quality of clinical training, we are currently developing an evaluation system for tutors and trainers.

#### Postgraduate Education (Clinical Training)

Our department has offered the postgraduate clinical training since 2004 according to the new national residency system in Japan. We have also played an important role in developing the online evaluation system for postgraduate clinical training (EPOC), which is used in 60% of education hospitals in Japan. Results of the questionnaire in March, 2013 showed one of the highest satisfaction rate among all national universities.

#### Postgraduate Education (Master's degree courses)

We have been offering master's degree courses in Medical Administration since this MMA program started in 2004, and were in charge of two courses this year, "Human resources management" and "Leadership in the medical care."

### (4) Clinical Services & Other Works

#### Second Opinion (Itsui)

Our hospital is open to the public who ask for second opinions about their recommended treatments so that we can continue to contribute to the provision of safe and high-quality advanced medical technology. Over 300 consultation cases have been performed for patients coming from other hospitals nationwide. The purpose of this section is to assist the patients to exercise their right of self-determination and to be informed of new treatments and diagnostic tests. To provide a qualified second opinion, we have organized the network of specialists in TMDU.

#### Patient Safety (Kudou)

Dr.Ooka is the General Risk Manager of our university hospital, and our department regularly organizes seminars and training courses. In collaboration with other departments (e.g., Skills Laboratory Center, Infectious Control Committee, etc.), we are working for greater safety and quality of healthcare.

## ( 5 ) Publications

### [Original Articles]

1. Zainuer A, Inoue Y, Kudo T, Toyofuku T, Igari K, Kawano T.. Usefulness of the tranfer function index for diagnosing peripheral arterial disease in patients with arterial calcification. *J Med Dent Sci.* 2016; 63(1); 29-35
2. Igari K, Kudo T, Toyofuku T, Inoue Y.. A novel approach to infrainguinal arteries with chronic total occlusions using the high frequency vibrational device. *Int Angiol.* 2016; 35(2); 212-216
3. Igari K, Kudo T, Toyofuku T, Inoue Y.. The outcomes of endovascular aneurysm repair with the chimney technique for juxtarenal aneurysms. *Ann Throac Cardiovasc Surg.* 2016; 22(3); 174-180
4. Yamamoto Y, Igari K, Toyofuku T, Kudo T, Inoue Y.. Late stent graft infection after the emergency endovascular repair of a secondary iliac artery-enteric fistula treated with graft removal and in situ aortic reconstruction using femoral veins. *Ann Thorac Cardiovasc Surg.* 2016; [ Epub ahead of print]
5. Yamamoto Y, Kudo T, Igari K, Toyofuku T, Inoue Y.. Radial artery aneurysm in the anatomical snuff box: A case report and literature review. *Int J Surg Case Rep.* 2016; 27; 44-47
6. Igari K, Kudo T, Toyofuku T, Inoue Y.. Relationship of inflammatory biomarkers with severity of peripheral arterial disease. *Int J Vasc Med.* 2016; 6015701
7. Igari K, Kudo T, Toyofuku T, Inoue Y.. A case of successful coil embolization for a late-onset type Ia endoleak after endovascular aneurysm repair with the chimney technique. *Case Rep Vasc Med.* 2016; 5307416
8. Igari K, Kudo T, Toyofuku T, Inoue Y.. Endothelial dysfunction of patients with peripheral arterial disease measured by peripheral arterial tonometry. *Int J Vasc Med.* 2016; 3805380
9. Igari K, Kudo T, Toyofuku T, Inoue Y.. The relationship between endothelial dysfunction and endothelial cell markers in peripheral arterial disease. *PLoS ONE.* 2016; 11(11); e0166840
10. Ryohei Hayashi, Kiichiro Tsuchiya, Keita Fukushima, Nobukatsu Horita, Shuji Hibiya, Keisuke Kitagaki, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Eriko Okada, Akihiro Araki, Kazuo Ohtsuka, Shinji Fukuda, Hiroshi Ohno, Ryuichi Okamoto, Tetsuya Nakamura, Shinji Tanaka, Kazuaki Chayama, Mamoru Watanabe. Reduced Human  $\alpha$ -defensin 6 in Noninflamed Jejunal Tissue of Patients with Crohn's Disease. *Inflamm. Bowel Dis.* 2016.05; 22(5); 1119-1128

### [Misc]

1. Makoto Takahashi. Residency and board certification of orthopaedic surgery in USA Orthopaedic Surgery and Traumatology. 2016.09; 59(10); 1319-1332

### [Conference Activities & Talks]

1. Igari K, Kudo T, Toyofuku T, Inoue Y.. Relationship of inflammatory biomarkers, PTX3 with severity of peripheral arterial disease.. 84th European Atherosclerosis Society Congress 2016.05.31 Innsbruck (Austria)
2. Igari K, Kudo T, Toyofuku T, Inoue Y.. Total endovascular treatment for acute deep venous thrombosis by catheter-directed thrombolysis.. Asian Society for Vascular Surgery 2016 2016.10.21 Singapore
3. Yamamoto Y, Ichinose T, Nakamura M, Nishizawa M, Igari K, Toyofuku T, Kudo T, Inoue Y.. Multiple recurrent pseudoaneurysms after EVAR in a patient with Behçet' s disease.. The 13th Tokyo Shanghai International Symposium for Vascular Surgery 2016.11.13 Tokyo (Japan)

# Acute Critical Care and Disaster Medicine

Professor Yasuhiro Otomo

## (1) Outline

### 1. Purpose of Education

We, the department of acute critical care and disaster medicine, investigate following wide range of fields, such as the search for mechanisms of biological response to severe stresses, the development of strategy for multiple organ dysfunction from the view of intensive care medicine, basic and clinical research about trauma, trauma preventive medicine and disaster medicine. Our targets of research are practical and cutting edge to work not only as a medical scientist but as a researcher for government projects.

### 2. Research Subjects

Basic research of the mechanism of multiple organ dysfunction following hemorrhagic/septic shock

Development of strategy for multiple organ dysfunction

Basic and clinical research of multiple trauma

Trauma epidemiology and trauma preventive medicine

Disaster medicine

Clinical research of cerebrovascular disease on acute phase

### 3. Clinical Services

Our emergency center was authorized to hold the 21st level I center in Tokyo on April 1, 2007. We give treatments over 8000 patients annual who are under critical condition like multiple organ dysfunction, severe sepsis and septic shock, life-threatening trauma as well. We also contribute to medical services, rushing to the emergency scene by a Doctor-Car/Helicopter at times.

## (2) Publications

### [Original Articles]

1. Junichi Inoue, Atsushi Shiraishi, Ayako Yoshiyuki, Koichi Haruta, Hiroki Matsui, Yasuhiro Otomo. Resuscitative endovascular balloon occlusion of the aorta might be dangerous in patients with severe torso trauma: a propensity score analysis. *J Trauma Acute Care Surg.* 2016.01;
2. Mukawa, M. Nariai, T. Inaji, M. Tamada, N. Maehara, T. Matsushima, Y. Ohno, K. Negi, M. Kobayashi, D.. First autopsy analysis of a neovascularized arterial network induced by indirect bypass surgery for moyamoya disease *J Neurosurg.* 2016.05; 124(5); 1211-1214
3. Akira Endo, Atsushi Shiraishi, Shigeki Kushimoto, Yasushiro Otomo. Verification of conventional criteria of the lethal triad and development of novel criteria as an indicator of decision making
4. Akira Endo, Atsushi Shiraishi, Yasuhiro Otomo, Shigeki Kushimoto. Development of novel criteria of the ‘lethal triad’ as an indicator of decision making in current trauma care: a retrospective multicenter observational study in Japan Critical Care Medicine.

**[Conference Activities & Talks]**

1. Jun-ichi Inoue, Atushi Shiraishi, Ayako Yoshiyuki, Koichi Haruta, Yasuhiro Otomo. RESUSCITATIVE ENDOVASCULAR BALLOON OCCLUSION OF THE AORTA (REBOA) MIGHT BE DANGEROUS IN PATIENTS WITH SEVERE TORSO TRAUMA — A PROPENSITY SCORE ANALYSIS SAYS —. 74th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery 2016.09.09 Las Vegas, NV, United States

# Clinical Oncology

Professor MIYAKE Satoshi  
 Project Associate Professor  
 OOOKA Shinya  
 Project Assistant Professor

SAKASHITA Hiroyuki  
 Project Assistant Professor  
 ITOU Hiromitsu  
 Graduate Student  
 SATOU Noriyuki

## ( 1 ) Outline

Department of Clinical Oncology was established in May 2012 to promote the field of palliative medicine and cancer chemotherapy according to “Training Program for Next Generation Specialists to Promote Cancer Therapy” . As for the education in medical school, we are involved in the course of Hematology-Oncology block and have a class of palliative medicine in the third year grade. In addition, we have a class of clinical ethics mainly focusing on the end-of-life care. As for the post-graduate education, we organized the “Training Program for Next Generation Specialists to Promote Cancer Therapy” .

## ( 2 ) Research

- 1)Application of palliative care when the patient is diagnosed as cancer.
- 2)Improvement of QOL in the end-of -life care of cancer patients.
- 3)Communication skills in the team health care.
- 4)Multi-institutional research in pancreatic cancer treatment.
- 5)The role of biomarkers for newly developed anti-cancer drugs in lung cancer.

## ( 3 ) Education

- 1)Hematology/Oncology
- 2)GI tract cancer
- 3)Lung cancer
- 4)Ethics
- 5)Communication

## ( 4 ) Clinical Services & Other Works

Department of Clinical Oncology manages Cancer Center of the medical school hospital.  
 There are five divisions below.

- 1)Division of palliative medicine



- 2)Division of cancer chemotherapy
- 3)Division of cancer registry
- 4)Division of coordination of cancer treatment
- 5)Division of cancer consultation and support

## **( 5 ) Publications**

### **[Original Articles]**

1. Nakajima Y, Kawada K, Tokairin Y, Tomita M, Miyake S, Kawano T.. Prognostic Factors for Post-Recurrence Survival in Patients with Thoracic Esophageal Squamous Cell Carcinoma after Curative Resection. Dig Surg. 2016; 33(2); 136-145
2. Retrospective Analyses of Esophageal Bypass Surgery for Patients with Esophagorespiratory Fistulas Caused by Esophageal Carcinomas. World J Surg. 2016.05; 40(5); 1158-1164

## Dentistry for Persons with Disabilities

Associate Professor  
Osamu SHINOZUKA

Junior Associate Professor (Part-time)  
Minoru INADA  
Goro SEKIGUCHI  
Naoki HAYASHI  
Yohei TAKEUCHI  
Syohei TAMURA  
Moriyuki NAKAMURA

Assistant Professor  
Yasuka KUSUMOTO

Graduate Student  
Aiko HOSHIAI

Hospital Staff  
Taiji HOSHIAI  
Ayana NATORI  
Anna KUMAKURA  
Hirotoshi Yamawaki

Graduate International Research Student  
Shohei TAKAHASHI  
Clinical Junior Associate Professor (Part-time)  
Seiji SAKURAI  
Tomo SUZUKI  
Yosuke KINOSHITA

### ( 1 ) Research

- 1) Formation of oral biofilm
- 2) Elimination of oral biofilm of persons with disabilities
- 3) Oral health status of the medically compromised patients
- 4) Oral management of genetic syndrome

### ( 2 ) Lectures & Courses

Our department was started as a graduate course of the special dentistry section on April, 1999. The sections are the dentistry for persons with disabilities and medically compromised individuals .

The main objective of this course is to provide the opportunity for students to understand the outline of the reconstruction of functional and esthetic disorders of oral and/or maxillofacial areas by means of the high-

advanced dental cares for patients with special needs.

### **( 3 ) Clinical Performances**

The clinical purpose of our department is to treat oral problems of special patients who are unable to receive normal dental care by reason of a disability which may be physical, mental, medical, or emotional, or combination of any of these under using behavior management and systemic support.

For example,

- 1) The patients requiring behavior management are physically disabled, intellectual disability, autistic spectrum disorder, etc.
- 2) The patients requiring systemic support are internal impediment, dental phobia, etc.

### **( 4 ) Publications**

#### **[Original Articles]**

1. Takutoshi Inoue, Tomoyuki Miyamoto, Haruhisa Fukayama, Yasuka Kusumoto, Osamu Shinozuka. Intravenous Sedation for Dental Treatment in a Patient with Wiskott-Aldrich Syndrome Journal of Japanese Dental Society of Anesthesiology. 2016.01; 44(1); 17-19

## General Dentistry

Associate Professor Shigeru ODA  
 Junior Associate Professor Masayuki HIDEISHIMA  
 Junior Associate Professor Satoko OHARA  
 Junior Associate Professor Ken-ichi TONAMI  
 Assistant Professor Azusa YAMADA  
 Assistant Professor Sachi UMEMORI  
 Assistant Professor Kanako NORITAKE  
 Hospital Staff Shuuhei NAKAMURAI  
 Hospital Staff Yuko MITSUMA  
 Hospital Staff Mina GOTO  
 Hospital Staff Maiko IWAKI  
 Hospital Staff Yasuyuki KIMURA  
 Hospital Staff Shota HAYASHI  
 Hospital Staff Naoki ISHIHARA  
 Hospital Staff Shogo MAEKAWA

### ( 1 ) Outline

Recent dentistry is sectionalized into various specialized fields of research and education. On the other hand, as a general practitioner, a dentist must possess not only integrated knowledge and skills of all the fields but also should be competent to apply such generalized knowledge and skills to individual patients. The department of General Dentistry performs researches and education for practicing such general and holistic dentistry. General dentistry related to clinical and affective education for dental students and residents. Therefore, the research theme includes dental education as well as oral diagnosis and general dentistry, cooperating with the department of Educational System in Dentistry, Behavioral Dentistry and Educational Media Development. Researches for sleep apnea syndrome have been also conducted in association with Dental Clinic for Sleep Disorders. The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry which missions in the Dental Hospital are initial diagnosis for new outpatients and general dental practice. Clinics of General Dentistry 1 and 2, where dental students and residents are trained, also relate to the department of General Dentistry.

### ( 2 ) Research

Recent research themes are listed below.

1. Study for structure of health problems and treatment planning for dental patients.
2. Study for verification and improvement of oral diagnosis.
3. Study for dental education for dental students and residents.

### ( 3 ) Education

The educational objective of General Dentistry is that the students/residents acquire transversal academic framework of dental knowledge and skills and competency to provide patients with personalized treatment.

### ( 4 ) Lectures & Courses

1. Introduction to the Behavioral Science. (For the 2nd-year dental students)
2. Holistic Oral Diagnosis. (For the 5th-year dental students)
3. Comprehensive Clinical Training Phase I Phase II. (For the 5th and 6th-year dental students)
4. Clinical training (For the dental residents)

### ( 5 ) Clinical Services & Other Works

The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry. In the clinic, dental examination and health assessment for new outpatients are conducted to decide initial treatment plan and a clinic in charge for the patients. The patients who need comprehensive dental care and who cannot cooperate students' practice also attend this clinic to receive general dental practice.

### ( 6 ) Clinical Performances

In the Dental Hospital, the clinic of Oral Diagnosis and General Dentistry is the first clinic for new outpatients. That is, the clinic is responsible for constructing good relationship between patients and the hospital. Therefore, the doctors pay attention actively to psychosocial aspects of patients during examination. In diagnosing and deciding clinic for patients, initial-treatment plans are introduced to patients. In this process, doctors think treatment plans together with patients thoroughly to obtain sound informed consent. Many patients who visits the dental hospital demands high medical level of the university hospital while not a few patients needs primary care. Oral Diagnosis and General Dentistry provides such patients with general dental practice to meet various kinds of patients' needs, makes effort to improve patients' satisfaction.

### ( 7 ) Publications

#### [Original Articles]

1. Yuka Tsumanuma, Takanori Iwata, Atsuhiko Kinoshita, Kaoru Washio, Toshiyuki Yoshida, Azusa Yamada, Ryo Takagi, Masayuki Yamato, Teruo Okano, Yuichi Izumi. Allogeneic Transplantation of Periodontal Ligament-Derived Multipotent Mesenchymal Stromal Cell Sheets in Canine Critical-Size Supra-Alveolar Periodontal Defect Model BioResearch Open Access. 2016.01; 5(1); 22-36
2. Hoshi S, Akizuki T, Matsuura T, Ikawa T, Kinoshita A, Oda S, Tabata Y, Matsui M, Izumi Y . Ridge augmentation using recombinant human fibroblast growth factor-2 with biodegradable gelatin sponges incorporating  $\beta$ -tricalcium phosphate: a preclinical study in dogs Journal of Periodontal Research. 2016.01; 51(1); 77-85
3. Ikawa T, Akizuki T, Matsuura T, Hoshi S, Ammar S, A, Kinoshita A, Oda S, Izumi Y. Ridge Preservation After Tooth Extraction With Buccal Bone Plate Deficiency Using Tunnel Structured B-Tricalcium Phosphate Blocks: A 2-Month Histological Pilot Study in Beagle Dogs Journal of Periodontology. 2016.02; 87(2); 175-183
4. Kurosa Michiyo, Tonami Ken-ichi, Ohara Satoko, Umemori Sachi, Noritake Kanako, Sunaga Masayo, Kinoshita Atuhiko and Araki Kouji. Differences between Computer-Based and Paper-Based Assessments of the Clinical Reasoning Competency of Dental Students The Journal of The Stomatological Society, Japan. 2016.03; 83(1); 25-33
5. Komagamine Y, Kanazawa M, Iwaki M, Jo A, Suzuki H, Amagai N, Minakuchi S. Combined effect of new complete dentures and simple dietary advice on nutritional status in edentulous patients: study protocol for a randomized controlled trial. Trials. 2016.11; 17(1); 539-546

**[Books etc]**

1. Shunsuke Minakuchi, Manabu Kanazawa, Norihisa Akiba, Yusuke Sato, Maiko Iwaki, Mai Okubo, Yuriko Komagamine. The live lecture of the complete denture -The first step of the full mouth reconstruction-. 2016.05
2. Izumi Y, Nikaidou M. Correspondence to vertical bone defects. Igaku Joho-sha, 2016.10

**[Misc]**

1. Masayuki Hideshima, Syuhei Nakamura, Hisashi Matsubara, Tatsu Suzuki. Oral Appliances for Sleep Apnea Syndrome The Journal of the Japanese Society for Dental Materials and Devices, The Journal of Dental Engineering. 2016.01; 35(1); 10-13
2. Manabu Kanazawa, Maiko Iwaki, Shinta Yamamoto, Toshio Arakida and Shunsuke Minakuchi. The complete denture with using CAD/CAM system 2016.06; 35(3); 185-188
3. ODA Shigeru and HOTTA Yasunori. Preface: With a View to Reconsidering Peri-Implant Disease: Prevention and Treatment Journal of Japanese Society of Oral Implantology. 2016.12; 29(4); 207

**[Conference Activities & Talks]**

1. Jo A,Kanazawa M,Sato Y,Akiba N,Iwaki M, Komagamine Y, Minakuchi S. Influence of the different impression methods for complete denture fabrication on masticatory ability. 2016.01.24
2. Arakida T,Kanazawa M,Yamamoto S,Iwaki M, Minakuchi S,Suzuki T. The effect if external light of digital impression. The effect of external light of digital impression 2016.05.29
3. M. Kanazawa, M. Iwaki, D. Sato, Y. Omura, A. Miyayasu, S. Kasugai, S. Minakuchi.. Immediate Loading of two-implants mandibular overdentures: 4-years prospective study.. 94th General Session & Exhibition of the IADR 2016.06 Seoul, Republic of Korea
4. Tonami K,Sano K,Iwasaki N,Takahashi H,Araki K. TEM image of dentin after Xe excimer lamp irradiation. The 144th Meeting of the Japanese Society of Cnsevative Dentistry 2016.06.09
5. Anna Miyayasu, Ayami Jo, Manabu Kanazawa, Yusuke Sato, Maiko Iwaki, Norihisa Akiba, Shunsuke Minakuchi. Cost Analysis of the different impression methods for complete dentures. 94th General Session & Exhibition of the IADR 2016.06.25 Seoul, Korea
6. Ken-ichi TONAMI, Azusa YAMADA, Sachi UMEMORI, Kanako NORITAKE, Yasuyuki KIMURA1, Maiko IWAKI, Masayo SUNAGA, Masayuki HIDEISHIMA, Shigeru ODA, Hiroshi NITTA, Atsuhiro KINOSHITA, Kouji ARAKI, Shiro MATAKI. Influential factor in medical ethics practice on class evaluation by students after three years. 2016.07.01
7. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Chisato Ida, Yuko Mitsuma, Shota Hayashi, Akihito Uesato, Toshihide Fujie, Meiyo Tamaoka, Yasunari Miyazaki, Masahiko Shimada, Noriyuki Wakabayashi . Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy and compliance in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial.. Japanese Society of Sleep Research the 41th Annual Meeting 2016.07.07 Tokyo
8. Multicenter Randomized Clinical Study of Denture Adhesive to Establish the Guideline: Study by the Subgroup Analysis for a Denture Adhesive on the Effect of the Masticatory Performance. 2016.07.09
9. Arakida T,Kanazawa M,Yamamoto S,Iwaki M, Minakuchi S,Suzuki T,Oki M,Kamijo S,Ando K,Morisawa K. The effect of external light of digital impression time and accuracy. 2016.07.09
10. Miyayasu A, Jo A, Kanazawa M, Sato Y, Iwaki M, Akiba N, Minakuchi S. Cost-effectiveness analysis of the impression methods for mandibular complete dentures in randomized controlled trial. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07.09 Kanazawa
11. Hiroyuki Suzuki,Manabu Kanazawa,Yuriko Komagamine,Maiko Iwaki,Ayami Jo,Noriko Amagai,Shunsuke Minakuchi. Combined effect of new complete dentures and simple dietary counseling on nutritional status in edentulous patients : study protocol for a randomized controlled trial. The 125th Scientific Meeting of Japan Prosthodontic Society 2016.07.09 Kanazawa

12. Wada J, Hideshima M, Inukai S, Matsuura H, Wakabayashi N. Influence of shape of dental arch and palate on the accuracy of speech production disturbed by major connector of maxillary removable partial denture. The 125th Annual Meeting of the Japan Prosthodontic Society 2016.07.09 Kanazawa
13. Akira Aoki, Koji Mizutani, Yoichi Taniguchi, Motohiro Komaki, Shigeru Oda, Hisashi Watanabe, Yuichi Izumi. Er:YAG Laser-assisted Comprehensive Periodontal Pocket Therapy (Er-LCPT): Case Series. The 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya, Japan
14. Jun Tsuruta, Kanako Noritake, Kouji Mizutani, Naoko Seki, Keiko Kondou, Shin-ichi Arakawa, Kouji ARAKI. A Trial for a new IPW course for Dental students and Oral health sciences students working in a dental team. Association of Dental Education in Europe, Annual Conference 2016.08.25 Barcelona
15. Jun Tsuruta, Kanako Noritake, Kouji Mizutani, Naoko Seki, Keiko Kondou, Shin-ichi Arakawa, Kouji ARAKI. A new IPW course working in a dental team. 27th Annual meeting, Southeast Asia Association for Dental Education 2016.09.08 Ho Chi Minh City
16. Son Hoang le, Ly Thi-Bich Nguyen, Lan Thi-Quynh Ngo, Sachi Umemori, Ken-ichi Tonami, Shiro Mataka. Impact of preparatory information on patient undergoing third molar surgery. 27th SEAADE Annual Scientific Meeting 2016.09.08 Ho Chi Minh City, Viet Nam
17. Maekawa S, Katagiri S, Takeuchi Y, Komazaki R, Ohtsu A, Udagawa S, Izumi Y. Bone metabolic microarray analysis of ligature-induced periodontitis in streptozotocin-induced diabetic mice. 102nd Annual Meeting of American Academy of Periodontology 2016.09.10 San Diego, USA
18. Kenichi Tonami, Yasuyuki Kimura, Miyuki Umemori, Masayuki Hideshima, Shiro Mataka, Kouji Araki. Basic research for morphological diagnosis using fractal dimension. 2016.09.22
19. Jun Tsuruta, Kanako Noritake, Koji Mizutani, Naoko Seki, Keiko Kondo, Shinichi Arakawa, Kouji Araki. Implementing a new IPW course in the dental student clinic. The 5th Tri-University Consortium on Oral Science and Education 2016.10.27 Beijing, China

#### [Awards & Honors]

1. Naoki Ishihara. JADSM KIKUCHI Award 2016, 2016.11

# Psychosomatic Dentistry

Professor	Akira Toyofuku
Assistant Professor	Miho Takenoshita
Hospital Staff	Takeru Kyuragi, Anna Suzuki-Miura, Yojiro Umezaki
Graduate Student	Yukiko Shinohara, Anna Suzuki-Miura, Rou Mikuzuki Kaoru Kawasaki, Shiori Sugawara, TU Thi Huyen Trang
Lecturer (part-time)	Haruhiko Motomura, Ayano Katagiri, Tatsuya Yoshikawa

## ( 1 ) Outline

Psychosomatic dentistry is the only one department in Japan, which research and develop new diagnosis and treatment methods for MUOS such as BMS, AO, PBS etc.

## ( 2 ) Research

- 1) Study on pathophysiological mechanisms of oral psychosomatic disorders
- 2) Psychosomatic study on oro-facial medically and psychiatrically unexplained symptoms
- 3) Brain imaging of oral psychosomatic disorders
- 4) Psychopharmacological study on oral psychosomatic disorders

## ( 3 ) Education

It is not uncommon to see the patients diagnosed with “Oral Psychosomatic Disorders”, so there is a growing need for proper treatment of the disorders from both sides of doctors and patients. It is, therefore, extremely important for dental students to instruct in psychosomatic dentistry. However, few Dental Universities in Japan are following this. At the same time, there’s a great deal of misunderstanding about psychosomatic dentistry, in spite of we have many years of consistent education. For example, “Your work is only hearing to complaints from patients”, “Patients with not otherwise specified mental illness is eventually referred to your clinic”, or “The mission of your clinic is to calm down your patients with unidentified dental and oral complaints”.

So, regarding undergraduate medical education, we focus on not only lessons from lectures and books but also practical experience through clinical training. We have comprehensive medical teaching for fifth and sixth-year students. Students can listen to patient’s complaints directly and deepen their understanding. Actually they can see patients with dental psychosomatic disorders, and they know that these disorders are treatable. Moreover, they can learn negative effects of wrong ideas as a psychogenic disorder, and they can understand serious distress in patients and family members.

This practice is arduous effort, but in the future, it is hoped that efforts will be made to facilitate uniformed services for patients with dental psychosomatic disorders, enhance coping skills for refractory cases, and reduce trouble with patients by the graduates of our department who mastered psychosomatic dentistry.

It is important to have identity as a dentist on practice of psychosomatic dentistry. Therefore we have advanced



strengthening of human resource development. In particular, we focus on cultivation of dentists who can be readily applied their knowledge of psychosomatic medicine to clinical practice. And we are working towards establishment of ‘psychosomatic dentistry’ introduced psychotherapy.

Also regarding education for graduate student, we focus on clinical practice for development of dentists who have great skill in psychosomatic dentistry.

#### (4) Clinical Services & Other Works

We take charge of “Psychosomatic Dentistry clinic” in dental hospital of Tokyo Medical and Dental University. This special clinic is for patients with oral psychosomatic disorders, such as glossodynia (burning mouth syndrome), atypical facial pain, atypical odontalgia, oral dysesthesia, occlusal discomfort(dysesthesia).

Main psychosomatic treatment is psychopharmacological one with SSRIs(Selective Serotonin Reuptake Inhibitors), SNRI(Serotonin-Noradrenaline Reuptake Inhibitor), SDAs(Serotonin-Dopamin antagonists) etc. And supportive psychotherapies are applied.

Intractable cases are increasing year by year, we take care of every patient and have good clinical courses about 70% of them.

We believe there are exactly “oral psychosomatic disorders”, and dentists should be in charge of treatment. Psychosis, as a matter of course, should be taken care by psychiatrists, so we discriminate them from oral psychosomatic disorders, and properly refer to psychiatry.

On the other hand, on “functional somatic symptoms secondary to psychiatry disorders”, which are refer to us from psychiatrists, we do our best in cooperation with psychiatrists.

We have about 600 new outpatients per year, and almost of them were referred from other specialists not only in dentistry but also internal medicine, otorhinolaryngology, dermatology, psychosomatic medicine, and psychiatry. They come from the Metropolitan area, of course, Osaka, Kyushu, Hokkaido and so on. We take fine-grained care and follow up, total number of patients is up to 10,000 per year.

We have a mission to meet the demand of these patients and their families, so better treatment outcome and increasing efficiency are required, and cooperation with other medical specialists is needed.

#### (5) Clinical Performances

Psychosomatic dentistry clinic is very unique, specialized for patients with MUOS. We have treated a large number of patients with various oral psychosomatic problems. With our unrivalled clinical experiences for MUOS, we offer our best clinical setting for the treatments of every MUOS.

#### (6) Publications

##### [Original Articles]

1. Yojiro Umezaki, Bashar W Badran, William H DeVries, Jkeonye Moss, Theresa Gonzales, Mark S George. The Efficacy of Daily Prefrontal Repetitive Transcranial Magnetic Stimulation (rTMS) for Burning Mouth Syndrome (BMS): A Randomized Controlled Single-blind Study. *Brain Stimul.* 2016.03; 9(2); 234-242
2. Yojiro Umezaki, Miho Takenoshita, Akira Toyofuku. Low-dose aripiprazole for refractory burning mouth syndrome. *Neuropsychiatr Dis Treat.* 2016.05; 12; 1229-1231
3. Miho Takenoshita, Haruhiko Motomura, Akira Toyofuku. Low-Dose Aripiprazole Augmentation in Amitriptyline-Resistant Burning Mouth Syndrome: Results from Two Cases. *Pain Med.* 2016.08;

##### [Misc]

1. Yojiro Umezaki, Anna Miura, Motoko Watanabe, Miho Takenoshita, Akihito Uezato, Akira Toriihara, Toru Nishikawa, Akira Toyofuku. Oral cenesthopathy. *Biopsychosoc Med.* 2016; 10; 20
2. Akira Toyofuku. Psychosomatic problems in dentistry. *Biopsychosoc Med.* 2016.04; 10; 14

**[Conference Activities & Talks]**

1. Akira Toriihara, Shin Nakamura, Akira Toyofuku, Ukihide Tateishi. Usefulness of Molecular Imaging for Patients with Dental Diseases.. SNMMI annual meeting 2016.06.13 San Diego, California, USA
2. Yojiro Umezaki, Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Shiori Sugawara, Kaoru Kawasaki, Takeru Kyuragi, Motoko Watanabe, Miho Takenoshita, Akira Toyofuku . Clinicostatistical Study on the Patients with Oral Cenesthopathy. 17th Congress of the Asian College of Psychosomatic Medicine (ACPM) 2016.08.21 Fukuoka, Japan
3. Miho TAKENOSHITA, Anna MIURA, Yukiko SHINOHARA, Lou MIKUZUKI, Kaoru KAWASAKI, Shiori SUGAWARA, Trang THI HUYEN YU, Takeru KYURAGI, Yojiro UMEZAKI, Motoko WATANABE, Ayano KATAGIRI, Tatsuya YOSHIKAWA, Akira TOYOFUKU. Two Cases of Atypical Odontalgia Successfully Treated by Adding Low-Dose of Aripiprazole to Mirtazapine. 17th Congress of the Asian College of Psychosomatic Medicine (ACPM) 2016.08.21 Fukuoka, Japan
4. Motoko Watanabe, Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Yojiro Umezaki, Takeru Kyuragi, Tatsuya Yoshikawa, Miho Takenoshita, Akira Toyofuku . Psychopharmacological Outcomes and Its Predictors for Burning Mouth Syndrome: 2 Years Follow Up Study. 17th Congress of the Asian College of Psychosomatic Medicine (ACPM) 2016.08.21 Fukuoka, Japan
5. Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Shiori Sugawara, Kaoru Kawasaki, Tu Thi Huyen Trang, Yojiro Umezaki, Miho Takenoshita, Akira Toyofuku . Psychiatric Comorbidities in Patients with Persistent Dento-Alveolar Pain Disorder (Atypical Odontalgia). 17th Congress of the Asian College of Psychosomatic Medicine (ACPM) 2016.08.21 Fukuoka, Japan

## Behavioral Dentistry

Professor	Shiro Matak
Associate Professor	Hiroshi Nitta
Research Associate	Azusa Yamada
Research Associate	Sachi Umemori
Graduate Student	Ayako Kubota
Graduate Student	Le Son Hoang (Vietnam)
Graduate Student	Shizuka Tanaka

### (1) Research

- 1) Construction of educational system of behavioral dentistry for dental students
- 2) Application of behavioral science to development of dental educational curriculum
- 3) Patients' evaluation of the dental hospital and the dental educational system
- 4) Application of behavioral science to dental clinic

### (2) Lectures & Courses

Topic of Behavioral Dentistry included characteristics of human behavior, especially of relationship between patients and dental staff based on the informed consent. Main objective of behavioral dentistry in the graduate course is to provide students opportunity to study application of behavioral science to deal with dental patients showing various perception and behavior in clinic.

### (3) Clinical Services & Other Works

Behavioral Dentistry provides medical interview for preliminary diagnosis and general dental practice at the clinic of oral diagnosis and general dentist cooperating with General Dentistry.

### (4) Publications

#### [Original Articles]

1. Yuka Tsumanuma, Takanori Iwata, Atsuhiko Kinoshita, Kaoru Washio, Toshiyuki Yoshida, Azusa Yamada, Ryo Takagi, Masayuki Yamato, Teruo Okano, Yuichi Izumi. Allogeneic Transplantation of Periodontal Ligament-Derived Multipotent Mesenchymal Stromal Cell Sheets in Canine Critical-Size Supra-Alveolar Periodontal Defect Model BioResearch Open Access. 2016.01; 5(1); 22-36
2. Michiyo Kurosa, Ken-ichi Tonami, Satoko Ohara, Sachi Umemori, Kanako Noritake, Masayo Sunaga, Atsuhiko Kinoshita, Kouji Araki. Differences between Computer-Based and Paper-Based Assessments of the Clinical Reasoning Competency of Dental Students. Kokubyo Gakkai Zasshi. 2016.03; 83(1); 25-33
3. Seki N, Moross J, Sunaga M, Hobo K, Miyoshi T, Nitta H, Kinoshita A, Morio I. Evaluation of simulation learning materials use to fill the gap in Japanese dental English education. Journal of Medical and Dental Sciences. 2016.03; 63(1); 1-8

4. Yuki Ohara, Hirohiko Hirano, Hideyo Yoshida, Shuichi Obuchi, Kazushige Ihara, Yoshinori Fujiwara, Shiro Mataki. . Prevalence and factors associated with xerostomia and hyposalivation among community-dwelling older people in Japan. *Gerodontology*. 2016.03; 33(1); 20-27
5. Yuki Ohara, Naomi Yoshida, Hisashi Kawai, Shuichi Obuchi, Hideyo Yoshida, Shiro Mataki, Hirohiko Hirano, Yutaka Watanabe. Development of an oral health-related self-efficacy scale for use with older adults. *Geriatr Gerontol Int*. 2016.08;

#### **[Books etc]**

1. Hiroshi Nitta, Sayaka Katagiri. Happening recovery in periodontal surgery. Quintessence Publishing Co.,Ltd, 2016.11 (ISBN : 978-4-7812-0522-9)

#### **[Conference Activities & Talks]**

1. Ayako Kubota, Yoko Kono, Hiroko Imura, Hiroji Shimomura, Kiyoko Kanamori, Yasuko Kawakami, Shiro Mataki, Kumiko Sugimoto. Oral health status and behavior of Japanese university students. International Symposium on Dental Hygiene 2016 2016.06 Basel, Switzerland
2. Naomi Yoshida, Kumiko Sugimoto, Sato Yamanaka, Hiroyuki Sakamaki, Yoko Yamazaki, Asako Kimura, Hiroko Imura, Yoko Kono, Ayako Kubota. Oral and holistic health evaluation and dental health status in dental hygienists at menopausal stage. International Symposium on Dental Hygiene 2016 2016.06.23 Basel
3. Ken-ichi TONAMI, Azusa YAMADA, Sachi UMEMORI, Kanako NORITAKE, Yasuyuki KIMURA1, Maiko IWAKI, Masayo SUNAGA, Masayuki HIDESHIMA, Shigeru ODA, Hiroshi NITTA, Atsuhiko KINOSHITA, Kouji ARAKI, Shiro MATAKI. Influential factor in medical ethics practice on class evaluation by students after three years. 2016.07.01
4. Son Hoang le, Ly Thi-Bich Nguyen, Lan Thi-Quynh Ngo, Sachi Umemori, Ken-ichi Tonami, Shiro Mataki. Impact of preparatory information on patient undergoing third molar surgery. 27th SEAAGE Annual Scientific Meeting 2016.09.08 Ho Chi Minh City, Viet Nam
5. Kenichi Tonami, Yasuyuki Kimura, Miyuki Umemori, Masayuki Hideshima, Shiro Mataki, Kouji Araki. Basic reseach for morphological diagnosis using fractal dimension. 2016.09.22

## Professional Development in Health Sciences

Professor Kazuki Takada  
Associate Professor Jun Tsuruta  
Associate Professor Mina Nakagawa  
Junior Associate Professor Kumiko Yamaguchi

### (1) Outline

Worldwide, accelerated aging and the shift in disease burdens have created a demand for innovations in health sciences, healthcare, and the healthcare delivery system. Innovation requires not only a vast amount of knowledge and superior skills, but also critical and creative thinking skills. Innovation concerning new drugs and medical devices further requires understanding of the entire flow and process of research and development. In our department, we provide educational opportunities for learners to acquire high-level and practical knowledge of the followings: history of medical and dental education in Japan, professional education/development/certification in Japan and North American/European countries, key pedagogical theories and learning methods, process-based approach and logic models in curriculum development, and competencies and their assessment/evaluation.

### (2) Research

- Needs assessment in health care and in professional development in health science fields · Curriculum development for professionals of the future needs in health sciences
- Interprofessional education curriculum development

### (3) Clinical Services & Other Works

Medical Hospital  
Kazuki TAKADA : Rheumatology  
Mina NAKAGAWA : Gastroenterology and Hepatology

Dental Hospital  
Jun TSURUTA : Oral Diagnosis and General Dentistry

### (4) Publications

#### [Original Articles]

1. Satoshi Otani, Sei Kakinuma, Akihide Kamiya, Fumio Goto, Shun Kaneko, Masato Miyoshi, Tomoyuki Tsunoda, Yu Asano, Fukiko Kawai-Kitahata, Sayuri Nitta, Toru Nakata, Ryuichi Okamoto, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Yasuhiro Asahina, Tomoyuki Yamaguchi, Naohiko Koshikawa, Motoharu Seiki, Hiromitsu Nakauchi, Mamoru Watanabe. Matrix metalloproteinase-14 mediates formation of bile ducts and hepatic maturation of fetal hepatic progenitor cells. *Biochem. Biophys. Res. Commun.* 2016.01; 469(4); 1062-1068
2. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shinji Tanaka, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Satoshi Otani, Miki Taniguchi, Fumio Goto, Hiroko Nagata, Shun Kaneko, Megumi

Tasaka-Fujita, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Mina Nakagawa, Minoru Tanabe, Shinichi Takano, Mitsuharu Fukasawa, Minoru Sakamoto, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma with clinicopathological features. *J. Gastroenterol.* 2016.03; 51(5); 473-486

3. Miki Taniguchi, Megumi Tasaka-Fujita, Mina Nakagawa, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Fumio Goto, Hiroko Nagata, Shun Kaneko, Sayuri Nitta, Miyako Murakawa, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Kenichi Mori, Shintaro Yagi, Sei Kakinuma, Yasuhiro Asahina, Mamoru Watanabe. Evaluation of Interferon Resistance in Newly Established Genotype 1b Hepatitis C Virus Cell Culture System. *J Clin Transl Hepatol.* 2016.03; 4(1); 5-11
4. Seishin Azuma, Yasuhiro Asahina, Yuki Nishimura-Sakurai, Sei Kakinuma, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Ootani, Fukiko Kawai-Kitahata, Miki Taniguchi, Miyako Murakawa, Takako Watanabe, Megumi Tasaka-Fujita, Yasuhiro Itsui, Mina Nakagawa, Mamoru Watanabe. Efficacy of additional radiofrequency ablation after transcatheter arterial chemoembolization for intermediate hepatocellular carcinoma. *Hepatol Res.* 2016.04; 46(4); 312-319
5. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihhide Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Hironori Nishitsuji, Saneyuki Ujino, Kunitada Shimotohno, Masashi Iwamoto, Koichi Watashi, Takaji Wakita, Mamoru Watanabe. Human induced pluripotent stem cell-derived hepatic cell lines as a new model for host interaction with hepatitis B virus. *Sci Rep.* 2016.07; 6; 29358
6. Hiroko Nagata, Mina Nakagawa, Yuki Nishimura-Sakurai, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Fumio Goto, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Naoko Tojo, Shuji Tohda, Yasuhiro Asahina, Mamoru Watanabe, . Serial measurement of Wisteria floribunda agglutinin positive Mac-2-binding protein is useful for predicting liver fibrosis and the development of hepatocellular carcinoma in chronic hepatitis C patients treated with IFN-based and IFN-free therapy.[ Epub ahead of print] *Hepatol Int.* 2016.07;
7. Fumio Goto, Sei Kakinuma, Masato Miyoshi, Tomoyuki Tsunoda, Shun Kaneko, Ayako Sato, Yu Asano, Satoshi Otani, Seishin Azuma, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Yasuhiro Asahina, Mamoru Watanabe. Bone morphogenetic protein-4 modulates proliferation and terminal differentiation of fetal hepatic stem/progenitor cells. *Hepatol. Res.* 2016.09;
8. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Mina Nakagawa, Sayuri Nitta, Satoshi Otani, Hiroko Nagata, Shun Kaneko, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhito Tanaka, Sayuki Iijima, Kaoru Tsuchiya, Namiki Izumi, Shuji Tohda, Mamoru Watanabe. Hepatic IFNL4 expression is associated with non-response to interferon-based therapy through the regulation of basal interferon-stimulated gene expression in chronic hepatitis C patients. [ Epub ahead of print] *J. Med. Virol.* 2016.12;

#### [Conference Activities & Talks]

1. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H, Goto F, Otani S, Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A Model for Interaction between HBV and Host Cells Derived from Human Induced Pluripotent Stem Cells. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
2. Nakagawa M. 【HCV】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
3. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Otani S, Goto F, Nagata H, Kaneko S, Asano Y, Miyoshi M, Tsunoda T, Azuma S, Itsui Y, Nakagawa M, Tanabe M, Maekawa S, Enomoto N, Watanabe M. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)

4. Nagata H, Sakurai Y, Nakagawa M, Kakinuma S, Azuma S, Murakawa M, Nitta S, Itsui Y, Asahina Y, Watanabe M. Serial changes in M2BPGi levels as predictors of fibrosis and HCC in chronic hepatitis C. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
5. Nakagawa M. 【HCV 11】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.23 International Convention Center Pamir, Tokyo (JAPAN)
6. Nakagawa M. 【HCV 12】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.23 International Convention Center Pamir, Tokyo (JAPAN)
7. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H , Goto F, Otani S, Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A new model for studying interaction between hepatitis B virus and host cells derived from human induced pluripotent stem cells. EASL The International Liver Congress 2016 2016.04.14 Barcelona (Spain)
8. Jun Tsuruta, Kanako Noritake, Kouji Mizutani, Naoko Seki, Keiko Kondou, Shin-ichi Arakawa, Kouji ARAKI. A Trial for a new IPW course for Dental students and Oral health sciences students working in a dental team . Association of Dental Education in Europe, Annual Conference 2016.08.25 Balcelona
9. Jun Tsuruta, Kanako Noritake, Kouji Mizutani, Naoko Seki, Keiko Kondou, Shin-ichi Arakawa, Kouji ARAKI. A new IPW course working in a dental team. 27th Annual meeting, Southeast Asia Association for Dental Education 2016.09.08 Ho chi ming city
10. Jun Tsuruta. Implementing a new IPW course in the dental student clinic. The 5th Tri-University Consortium on Oral Science and Education 2016.10.27 Peking, China
11. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihhide Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Ayako Sato, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Mamoru Watanabe. Genetically modified human induced pluripotent stem cell-derived hepatic progenitor-like cell lines as a model for interaction between hepatitis B virus and host cells. AASLD The Liver meeting 2016 2016.11.11 Boston (USA)

#### **[Awards & Honors]**

1. Poster Presentation Award, 2016.09

#### **[Others]**

1. Recognized Reviewer Status, 2016.02  
As a reviewer; reviewing for Journal of Prosthodontic Research

# Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio

Assistant Professor: KAWAGISHI Masahiko

Assistant Professor: SAITO Kenta

Assistant Professor: SATO Keisuke

Graduate Student, MD-PhD Course, Research Fellow of the Japan Society for the Promotion of Science:  
SATO Fumiya(until March)

Lab Manager, Administrative Assistant: TAGUCHI Mie

## ( 1 ) Research

Our lab has focused in two major directions:

(1) How are cytoplasmic proteins transported in cells, and what other intracellular elements are necessary for their quality control during transport? How are the dynamics of cytoskeletal proteins in neurons regulated and coordinated?

Neuronal cells such as neurons and glial cells are atypical and asymmetric in their morphology; both of them having long processes. They have to endure the burden of energy-consuming long-distance intracellular transport, and develop specialized cytoskeletal structures. Both intracellular transport and cytoskeletal dynamics are inseparably interrelated, and essential for the cellular homeostasis and function. One of the main interests of our laboratory is to understand how their dynamics are regulated and how these dynamics define neuronal morphologies and functions.

(2) How do inhalation anesthetics exert their effects on synaptic transmissions?

Our interests are in deciphering the long-lasting mystery of inhalation anesthetic effects on synaptic transmissions, major mechanism in mammals that insures secure and painless surgical operations. We use electrophysiological preparations as well as newly developed spectroscopic techniques to identify their principles.

## ( 2 ) Education

Department of neuroanatomy and cellular neurobiology takes charge of basic neuroscience education for medical undergraduate student (Lectures and Wet labs), especially from the morphological point of view.

For graduate school students, our group offers introductory courses on both optical and electron microscopy (Lectures and Wet labs), with close relation to molecular and cellular neurobiology.

## ( 3 ) Publications

### [Original Articles]

1. Fumiya Sato, Hitoshi Asakawa, Takeshi Fukuma, Sumio Terada. Semi-in-situ atomic force microscopy imaging of intracellular neurofilaments under physiological conditions through the 'sandwich' method.



Microscopy (Oxf). 2016.08; 65(4); 316-324

**[Misc]**

1. Kenta Saito, Masafumi Nakano, Takeharu Nagai. Luminescence Imaging: (a) Multicolor Visualization of  $\text{Ca}^{2+}$  Dynamics in Different Cellular Compartments and (b) Video-Rate Tumor Detection in a Freely Moving Mouse. *Meth. Mol. Biol.*. 2016.01; 1461; 289-297

**[Conference Activities & Talks]**

1. Terada S.. Cytoskeletal dynamics in neurons and beyond. Lecture 2016.01 China Soochow University CAM-SU GRC
2. Terada S.. Close-up pictures of cytoskeletal dynamics in neurons. The 7th Asia Pacific International Congress of Anatomists 2016.03 Singapore
3. Masahiko Kawagishi, Yuki Obara, Takayuki Suzuki, Masumi Hayashi, Kazuhiko Misawa, Sumio Terada. Direct Label-Free Measurement of the Distribution of Small Molecular Weight Compound Inside Thick Biological Tissue using Coherent Raman Microspectroscopy. Biophysical Society 60th Annual Meeting 2016.03.01 Los Angeles, California, USA

# Systems Neurophysiology

Professor Izumi Sugihara  
 Associate Professor Yuriko Sugiuchi  
 Lecturer Yoshiko Izawa  
 Assistant Professor Mayu Takahashi  
 JSPS Postdoctoral Research Fellow Hermina Nedelcescu  
 Students (doctoral) 6  
 Part-time lecturer Hirofumi Fujita

## (1) Outline

Department of Systems Neurophysiology, formerly Department of Physiology #1 of the medical school, is one of the basic medicine departments and take charge of research and education in the field of neurophysiology and related neurosciences.

## (2) Research

Our main interest lies in clarifying the structures that underlies function of the central nervous system and then understanding their function. We are focused on the part of the central nervous system that is involved in control of eye movements. The eye movement control system is located in the cerebrum, brainstem and cerebellum, has been studied in great detail and is important clinically. The cerebellum itself is another site of focus. Dysfunction of the cerebellum causes ataxia, a movement disorder associated with impaired control of movement. We use electrophysiological, morphological and cell-biological approaches.

### 1) Cerebellar function

Distinct regions in the cerebellum make specific connections with different areas of the brain and are involved in the control of various movements including eye movements. For example, the neuronal circuitry that connects the lateral cerebrum, pontine nuclei, cerebellar cortex (hemisphere), cerebellar nucleus (dentate nucl.), thalamus and cerebrum is important for initiation, execution and control of movements. To understand cerebellar function, it is important to understand the organization of the cerebellum into distinct anatomical regions, to characterize the specific neuronal circuitry of these regions, and to identify how the cerebellum is organized into regions and functions by way of the input and output systems. Our systematic approach to this question includes (developmental) anatomy, molecular biology, and electrophysiology. We have expertise in neuronal labeling with marker molecules and tracers, single-axonal reconstruction, three-dimensional mapping of neuronal projection patterns.

## (3) Education

We participate in Introductory Neurophysiology, Neuroscience and Physiology Lab courses for medical students (2nd year) as well as in courses for graduate students. We mainly teach the neurophysiology sections in these courses. Our goal is for students to understand normal function of nerve cells and the nervous system and,

on this ground, to understand pathological states of the nervous system in disease. For this purpose, we give clinically-oriented lectures and laboratory courses linked with morphology and pharmacology.

#### **( 4 ) Lectures & Courses**

Our lectures cover transport and electric potential of the cell membrane, excitation and synaptic transmission (Introductory Neurophysiology), sensory systems, motor systems, autonomic nervous systems, and higher brain function (Neuroscience), i.e. neurophysiology in general from the molecular, cellular through the organismic levels. To promote students' self-learning attitude, we sometimes employ an "active-learning" style. In the laboratory course, we promote student-teacher discussion in small groups. We have had three "elective research course" students.

#### **( 5 ) Publications**

##### **[Books etc]**

1. Yuanjun Luo, Izumi Sugihara. The Olivocerebellar Tract. Springer, 2016 (ISBN : 978-3-319-24549-2)

##### **[Conference Activities & Talks]**

1. Mayu Takahashi. Functional roles of commissural inhibitory and excitatory connections between the superior colliculi for control of saccades in relation to the VOR system and Listing' s law. Dissecting and Understanding Mechanisms for Functional Shift of Brain Network 2016.03.03
2. Sugiuchi Y, Takahashi M, and Shinoda Y.. Supranuclear pathways for vertical saccade compared with those for horizontal saccade and vestibuloocular reflex. . The 29th Barany Society Meeting 2016 2016.06.05 Seoul, Korea.
3. Yoshiko Izawa, Hisao Suzuki. Activity of frontal eye field fixation neurons and its relation to the suppression of saccades and smooth pursuit. The 29th Barany Society Meeting 2016 2016.06.06 Seoul, Korea
4. Mayu TAKAHASHI. TECTAL COMMISSURAL CONNECTIONS AND THEIR FUNCTIONAL ROLE OF VERTICAL SACCADDES IN RELATION TO LISTING'S LAW AND VOR. 29th Barany Society Meeting 2016 2016.06.06
5. Mayu Takahashi. Neural circuit of the superior colliculus output system for control of coordinated eye and head movements. The 39th Annual Meeting of the Japan Neuroscience Society 2016.07.22

# Pharmacology and Neurobiology

Professor: Tsutomu TANABE  
 Assistant professor: Hironao SAEGUSA  
 Assistant professor: Makoto FUJIKAWA  
 Assistant professor: Daisuke TANAKA

## (1) Outline

Many intriguing mysteries left in the issue of brain function like (1) learning and memory, (2) cognition and behavior, (3) generation of consciousness, (4) personality and mentality. On the other hand, in the modern-day world with a complicated human relations and prolonged life span, necessity of deeper understanding and development of the means to cure the numerous neurological disorders and pain is enormously increased.

## (2) Research

1. Regulation of Microglial function in Neuroinflammation/Neurodegenerative diseases
2. Regulation of Macrophage function in Inflammatory bowel disease and Rheumatoid arthritis
3. Energy metabolic imaging at single cell level of cancer stem cell/cancer cell using Bioluminescence and FRET and Imaging
4. Energy metabolic imaging at single cell level of neuron, microglia and astrocyte in the degenerative area of the mouse model of various neurodegenerative diseases
5. Neural mechanisms of pleasure and motivation in feeding
6. Molecular basis of Calcium channelopathy
7. Alteration of Neuron-Glia interaction in Neurological disorders

## (3) Education

Undergraduate course: Pharmacology course provides the principle of pharmacological basis of therapeutics. Several representative therapeutic drugs in each disease will be picked up and systematic lectures -from basic pharmacology to mechanism of action, drug metabolism, clinical application and side effects- will be provided. Students are projected to acquire self-learning skills during the course and expected to be ready for handling clinical cases by pharmacological means.

We consider education through the pharmacology lab work is important. Students are given opportunity to dissect out several tissues (heart, skeletal muscle, ileum and vas deferens) from living animals by themselves and test the effect of a number of drugs including specific agonist, antagonist and non-selective drugs. Lab work course is divided into two parts. In the first part, students were given several known drugs for testing the known effect on these tissues. In the second part, students are given two unknown drugs and requested to identify the name and concentration of each drug using the tissues they prepare by themselves.

Graduate course: During the first couple of months, students are requested to acquire basic techniques of biochemistry, molecular biology, pharmacology and electrophysiology that are routinely used in our laboratory. Then students will be given a small project to do using the techniques they have learned during the initial

training. Students are also required to read relevant scientific papers and conduct seminar style lectures to other lab members monthly. After completion of the initial phase, students start their own project under the supervision of the faculties in the lab.

## Molecular Neuroscience

Professor Kohichi Tanaka  
 Associate Professor Tomomi Aida  
 Assistant Professor Saeko Ishida  
 Assistant Professor Yuichi Hiraoka (2015/5/1 )

Graduate Student (doctor course)  
 Zhao Zhuoyang  
 Kaori Sugiyama  
 Takehisa Handa

Graduate Student (master course)  
 Mina Kusunose  
 Moeko Tanaka  
 Haruka Takigawa  
 Hiroshi Ogawa

Technical Staff  
 Harumi Ishikubo

Secretary  
 Satomi Ohno

### ( 1 ) Outline

The final goal of our research is to understand molecular, cellular, and neuronal ensemble mechanisms underlying higher order brain functions including learning and memory. For that purpose, we combine molecular genetics, physiological and behavioral methods. The laboratory also studies the mechanism that underlies neuronal cell death and regeneration.

### ( 2 ) Research

#### 1. Functions of glutamate transporters in the brain

Glutamate is a major excitatory neurotransmitter and plays an important role in neuronal plasticity and neurotoxicity in the central nervous system. Glutamate transport proteins provide the mechanism by which synaptically released glutamate is inactivated and kept below toxic levels in the extracellular space. By now, five subtypes of high-affinity glutamate transporters have been identified in the mammalian brain. Our lab studies the physiological and pathological roles of glutamate transporter subtypes using subtype-specific knockout mice. Clinical phenotypes of spinocerebellar ataxia type-5 (SCA5) and spectrin-associated autosomal recessive cerebellar ataxia type-1 (SPARCA1) are mirrored in mice lacking  $\beta$ -III spectrin ( $\beta$ -III<sup>-/-</sup>). One function of  $\beta$ -III spectrin is the stabilization of the Purkinje cell-specific glutamate transporter EAAT4 at the plasma membrane. In  $\beta$ -III<sup>-/-</sup> mice EAAT4 levels are reduced from an early age. In contrast levels of the glutamate transporter GLAST, expressed in Bergmann glia, only fall progressively from 3 months onwards. Here we elucidated the roles of these two glutamate transporters in cerebellar pathogenesis mediated through loss of  $\beta$ -III spectrin function by studying EAAT4 and GLAST knockout mice as well as crosses of both with  $\beta$ -III<sup>-/-</sup> mice. Our

data demonstrate that EAAT4 loss, but not abnormal AMPA receptor composition, in young  $\beta$ -III-/- mice underlies early Purkinje cell hyper-excitability and that subsequent loss of GLAST, superimposed on the earlier deficiency of EAAT4, is responsible for Purkinje cell loss and progression of motor deficits. Yet the loss of GLAST appears to be independent of EAAT4 loss, highlighting that other aspects of Purkinje cell dysfunction underpin the pathogenic loss of GLAST. Finally, our results demonstrate that Purkinje cells in the posterior cerebellum of  $\beta$ -III-/- mice are most susceptible to the combined loss of EAAT4 and GLAST, with degeneration of proximal dendrites, the site of climbing fibre innervation, most pronounced. This highlights the necessity for efficient glutamate clearance from these regions and identifies dysregulation of glutamatergic neurotransmission particularly within the posterior cerebellum as a key mechanism in SCA5 and SPARCA1 pathogenesis.

We investigated the cytoprotective effect of geranylgeranylacetone (GGA) on RGCs degeneration using a normal tension glaucoma (NTG) mouse model, which lacks GLAST. Three-week-old GLAST+/- mice were given oral administration of GGA at 100, 300, or 600 mg/kg/day or vehicle alone, and littermate control mice were given vehicle alone for 14 days, respectively. The number of RGCs of GLAST+/- mice significantly decreased, as compared to that of control mice. RGC loss was significantly suppressed by administration of GGA at 600 mg/kg/day, compared with vehicle alone. Following GGA administration, HSP70 was significantly upregulated together with reduction in the activities of caspase-9 and -3. Our studies highlight HSP70 induction in the retina is available to suppress RGC degeneration, and thus GGA may be applicable for NTG as a promising therapy.

## 2. Development of genome editing technologies

Although CRISPR/Cas enables one-step gene cassette knock-in, assembling targeting vectors containing long homology arms is a laborious process for high-throughput knock-in. We recently developed the CRISPR/Cas-based precise integration into the target chromosome (PITCh) system for a gene cassette knock-in without long homology arms mediated by microhomology-mediated end-joining.

Here, we identified exonuclease 1 (Exo1) as an enhancer for PITCh in human cells. By combining the Exo1 and PITCh-directed donor vectors, we achieved convenient one-step knock-in of gene cassettes and floxed allele both in human cells and mouse zygotes. Our results provide a technical platform for high-throughput knock-in.

## (3) Education

### Goals/Outline:

Students should generate genetically modified animals to comprehensively understand the cognitive mechanisms at the level of molecule to behavior. Then, students should analyze cognitive deficits of mutant animals and those molecular mechanisms.

### Available programs:

Participation in the ongoing research project; as needed

Training for cell biology: five times a year 13:00 – 16:00

### Experiment:

1. Gene cloning and generation of targeting vector.
2. Generation of genetically modified mice
3. Behavioral analysis of the mice
4. Morphological analysis of central nervous systems.

## (4) Lectures & Courses

The aim of this practice is to learn molecular biological, anatomical, electrophysiological and psychological approaches to elucidate the mechanism of cognition. Moreover, based on previous case reports of cognitive deficits, students should plan and discuss what kinds of the researches are possible and meaningful to elucidate the pathology of these diseases, leading to unveil the mechanism of cognition.

**( 5 ) Publications****[Original Articles]**

1. Shinji Miyazaki, Yuichi Hiraoka, Shizu Hidema, Katsuhiko Nishimori. Prenatal minocycline treatment alters synaptic protein expression, and rescues reduced mother call rate in oxytocin receptor-knockout mice *Biochemical and Biophysical Research Communications*. 2016.02; Volume 472( Issue 2); 319-323
2. Elise Marsan, Saeko Ishida, Adrien Schramm, Sarah Weckhuysen, Giuseppe Muraca, Sarah Lecas, Ning Liang, Caroline Treins, Mario Pende, Delphine Roussel, Michel Le Van Quyen, Tomoji Mashimo, Takehito Kaneko, Takashi Yamamoto, Tetsushi Sakuma, Séverine Mahon, Richard Miles, Eric Leguern, Stéphane Charpier, Stéphanie Baulac. Depdc5 knockout rat: A novel model of mTORopathy. *Neurobiol. Dis.* 2016.05; 89; 180-189
3. Shizu Hidema, Tomokazu Fukuda, Yuichi Hiraoka, Hiroaki Mizukami, Ryotaro Hayashi, Ayano Otsuka, Shingo Suzuki, Shinji Miyazaki, and Katsuhiko Nishimori. Generation of Oxtr cDNA(HA) -Ires-Cre Mice for Gene Expression in an Oxytocin Receptor Specific Manner. *Journal of Cellular Biochemistry*. 2016.05; Volume 117, (Number 5 ); 1099-1111
4. Emma M Perkins, Daumante Suminaite, Yvonne L Clarkson, Sin Kwan Lee, Alastair R Lyndon, Jeffrey D Rothstein, David J A Wyllie, Kohichi Tanaka, Mandy Jackson. Posterior cerebellar Purkinje cells in an SCA5/SPARCA1 mouse model are especially vulnerable to the synergistic effect of loss of  $\beta$ -III spectrin and GLAST. *Hum. Mol. Genet.* 2016.10; 25(20); 4448-4461
5. Zhenyu Dong, Yasuhiro Shinmei, Yoko Dong, Saori Inafuku, Junichi Fukuhara, Ryo Ando, Nobuyoshi Kitaichi, Atsuhiko Kanda, Kohichi Tanaka, Kousuke Noda, Takayuki Harada, Shinki Chin, Susumu Ishida. Effect of geranylgeranylacetone on the protection of retinal ganglion cells in a mouse model of normal tension glaucoma. *Heliyon*. 2016.10; 2(10); e00191
6. Tomomi Aida, Shota Nakade, Tetsushi Sakuma, Yayoi Izu, Ayu Oishi, Keiji Mochida, Harumi Ishikubo, Takako Usami, Hidenori Aizawa, Takashi Yamamoto, Kohichi Tanaka. Gene cassette knock-in in mammalian cells and zygotes by enhanced MMEJ. *BMC Genomics*. 2016.11; 17(1); 979



# Neuropathology

Professor: Hitoshi Okazawa

Practical professor: Kazuhiko Tagawa

Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone, Toshiki Uchihara

Project assistant lecturer: Hiroshi Tsuda

Assistant professor: Kyota Fujita

Project Assistant professor: Xigui Chen, Hidenori Homma, Kazumi Motoki, Emiko Yamanishi

Graduate Student : Mao Ying, Juliana Bosso Taniguchi, Eriko Hoshino, Hikari Tanaka, Tomohiro Kumaki

## ( 1 ) Outline

The goals of our research are to elucidate molecular mechanisms of neurodegenerative disorders as well as of mental retardation, and to develop novel therapeutics for those intractable diseases. In neurodegeneration, we are now focusing on polyglutamine diseases including hereditary spinocerebellar degenerations and Huntington's disease. Knowledge from transcriptome and proteome analyses of the pathologies will lead to new types of molecular therapeutics. In reference to mental retardation, we are developing animal models and analyzing molecular pathologies of our original molecule PQBP1 whose mutations cause mental retardation with microcephaly. This line of research is also for developing new therapeutics of the common but intractable diseases.

## ( 2 ) Research

### Research Contents

Following studies have been intensively carried out in our laboratory.

- 1) Investigation of molecular pathologies of neurodegenerative diseases.
- 2) Studies on impairment of DNA-repair in polyglutamine diseases.
- 3) Development of new seed drugs for neurodegeneration.
- 4) Development of new seed drug for mental retardation.
- 5) Investigation of molecular functions of Oct-3/4

Below is the brief report of this year's progress.

#### 1. Gene therapy for Spinocerebellar Ataxia model mice using AAV-RpA1 vector

Spinocerebellar ataxia type-1 (SCA1) is an intractable neurological disease caused by CAG repeat expansion of the Ataxin-1 (Atxn1) gene. This mutant Atxn-1 induces dysfunctions and neurodegeneration mainly of cerebellar Purkinje cells and spinal motor neurons. We previously reported that DNA damage repair is one of the domain of SCA1 molecular pathology. Comprehensive proteome analysis of soluble nuclear proteins indicated that HMGB1/2 were decreased in neurons expressing mutant Atxn1 in comparison to those expressing normal Atxn1 (Qi et al., 2007). We also showed that mitochondrial HMGB1 was decreased in mutant Atxn1-KI mice (Ito et al., 2015). Mutant Atxn1 increased DNA damage, which were rescued by supplementation of HMGB1 (Qi et al., 2007; Ito et al., 2015).

RpA1 is a critical molecule involved in multiple type of DNA damage repair system. We previously revealed that RpA1 was another target molecule of DNA damage repair in SCA1 that was expected from gene screens in *Drosophila* models. In this study, we tested gene therapy of mutant Atxn1-KI mice with adeno-associated

virus (AAV) vector expressing RpA1.

AAV-RpA1 vector was injected into the surface of the cerebellum (subarachnoid space). We found significant effects on motor functions, normalization of DNA damage markers, and improved Purkinje cell morphology. Surprisingly, such effects lasted for 50 weeks following AAV-RpA1 infection. We also confirmed that AAV-RpA1 indirectly recovered multiple cellular functions such as RNA splicing, transcription and cell cycle as well as abnormal morphology of dendrite and dendritic spine of Purkinje cells in *Atn1-KI* mice.

## 2. Strategy of molecular target for pathological signaling before aggregation of beta-Amyloid.

Pathological feature of neurodegenerative disease such as Alzheimer's disease is abnormal protein aggregation inside or outside of cells. In Alzheimer's disease, senile plaque composed of beta-Amyloid and neurofibrillary tangle composed of tau. Based on amyloid hypothesis, clinical trials have been challenged with the aim of clearance of extracellular amyloid aggregation. However, antibody therapy against beta-Amyloid did not succeed the recovery of cognitive decline although it could reduce the amyloid plaque. Therefore, our recent research interest is focusing on the earlier interpretation of antibody treatment before aggregation of beta-Amyloid, or new molecular target therapy based on early-phase (phase 0) change of pathological signaling.

Previously we performed comprehensive phosphoproteome analysis in order to identify the phase 0 molecular events, and we identified 17 core-protein phosphorylation changed from early-phase to late-phase, and among them, 3 phosphoprotein were changed at phase 0. MARCKS, one of these proteins, is known as a substrate of PKC, was phosphorylated not only PKC-phosphorylation site but also other phosphorylation site modified by another kinases. Thus, in the present study, we compared the change of molecular pattern in model mice and human postmortem brain in order to detect the key phosphorylation site. We found that Ser46 were phosphorylated at early-phase, and antibody against pSer46-MARCKS depicted degenerative neuritis surrounded the amyloid plaques. We also found the pSer46-MARCKS lost its ability to bind cytoskeletal protein, actin, and failed to maintain the spine. Phosphorylation of MARCKS at ser46 was due to HMGB1 (one of the DAMPS; damage-associated molecular pattern), not beta-Amyloid. Also, HMGB1 in spinal fluid of patients with early progression was shown higher than others, which suggest that pSer46-MARCKS is closely related to the pathology of Alzheimer's disease in human patients. Finally, we tried the rescue experiments using neutralizing antibody against HMGB1, and we succeeded the decrease of pSer46-MARCKS, rescued the reduction of spine, and improved the cognitive decline in model mice. HMGB1 can be released from not only leakage from dead cells but also hyperactive living neurons. Therefore, antibody therapy targeting HMGB1 have a potential to pathology of phase 0 before aggregation of beta-amyloid, and it might be beneficial for prevention of AD pathogenesis.

## 3. New therapeutic strategy for Huntington's disease: targeting the third atypical cell death.

The common important feature of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, Huntington's disease, Spinocerebellar Ataxia, Amyotrophic lateral sclerosis, is slow-progressive neurodegeneration over the decades. Such slow-progressive dysfunction of neuronal cells and their cell death have different aspects from other neurological disorders such as cerebral infarction or cerebral hemorrhage, which symptoms have been completed within a few minutes or a few hours. The characteristics of cell death in neurodegenerative disease have been greatly debated. The typical types of cell death are apoptosis and necrosis, but there are other types of cell death such as autophagy, necroptosis, and TRIAD (transcriptional repression-induced atypical cell death). We previously identified TRIAD, which can be triggered by specific inhibition of RNA polymerase II and can be executed slow-progressively. The morphological characteristics of TRIAD are different from that of apoptosis or autophagy, but key morphology is abnormal expansion of endoplasmic reticulum (ER). Also, we previously reported that YAP, a candidate molecule obtained through comprehensive expression analysis, might be involved in signal cascade of TRIAD execution. In the present studies, we first performed screening of TRIAD-related molecules associated with several types of cell death, then mixed with bioinformatics by matching the data with protein-protein interaction database in order to comprehensive search for identification of signal network of TRIAD. Then, we found hnRNP, a RNA-binding molecule, and Htt (causative gene for Huntington's disease) are related to TRIAD (Mao et al., 2016a)

On the other hand, we found that mutant-Htt-expressing neurons showed not apoptotic or necrotic cell death but cell death with asymmetric cytoplasmic expansion. This expansion was endoplasmic reticulum expansion, and by two-photon microscopic analysis, we revealed that similar expansion of ER could be seen in living model mice brain carrying mutant Htt (Mao et al., 2016b).

We also tried to understand the molecular mechanism under the execution of TRIAD, and we found that loss of YAP-TEAD dependent survival signal is mainly contributed. Especially activation of Hippo-pathway prevented the intranuclear translocation of YAP, and phosphorylation of YAP by Plk1 increased binding of YAP/p73, also

mutant Htt bounded to and incorporated YAP into its inclusion, which all leads to the loss of survival signaling (figure C in “Highlight”). Finally, we treated S1P to mutant Htt Knockin mice in order to promote YAP translocation to nucleus and prevent Hippo-pathway activation, and we succeeded to improve their behavioral impairment and the abnormal control of ER size. What is more, we found ER expansion in human HD patients by electron microscopy. We also confirmed the biochemical and histological alteration of hippo-pathway in human HD patients as well as HD model mice (Yamanishi et al., 2017). Collectively, our present studies suggest that treatment targeting signaling pathway of TRIAD is beneficial for HD pathology.

#### 4. Identification of candidate seed drugs for Huntington’s disease by integrated screens of chemical libraries.

We previously reported the pathological function of Ku70 in Huntington’s disease. It is a key molecule for non-homologous end-joining (NHEJ), a type of DNA double-strand break repair that functions in non-dividing cells such as differentiated neurons. By protein-protein interaction screenings, we identified Ku70 as molecule that directly interacts with Htt (Enokido et al, 2010). Furthermore, transgenic overexpression of Ku70 resulted in one of the longest lifespan extensions in HD model mice.

Given such previous results have suggested the importance of Ku70 relative to various mediator molecules, we screened chemicals that could inhibit the interaction between Ku70 and mutant Htt. We employed both wet and dry screening (MF20 and Discovery Studio, respectively) for the initial step, performed a secondary screening with single molecule fluorescence spectroscopy, and examined the phenotypic effects in *Drosophila* and mouse models as the third and fourth screens. Then we found that two chemicals exerted an *in vivo* effect in a mouse HD model such as lifespan extension, body weight recovery, motor function recovery, and DNA damage repair. Unexpectedly, the selected chemicals enhanced rather than inhibited Htt aggregation, as indicated by dynamic light scattering analysis. This may provide additional insight about whether polyQ aggregates are toxic, protective or both.

### (3) Education

As educational tasks, we have lecture and experiment classes of neuropathology for medical/dental graduate school program and medical school program. We also have general pathology and neuropathology classes for graduate school for health sciences, and clinical anatomical and therapeutic pathology classes for research students.

### (4) Lectures & Courses

We provide students with opportunities to learn practical research techniques on neuropathology, especially neurodegenerative diseases.

### (5) Publications

#### [Original Articles]

1. Mao, Y., Tamura, T., Yuki, Y., Abe, D., Tamada, Y., Imoto, S., Tanaka, H., Homma, H., Tagawa, K., Miyano, S., and Okazawa, H. The hnRNP-Htt axis regulates necrotic cell death induced by transcriptional repression through impaired RNA splicing. *Cell Death & Disease*. 2016.04; 7; e2207
2. Mizuguchi, M., Obita, T., Kajiyama, A., Kozakai, Y., Nakai, T., Nabeshima, Y. and Okazawa, H.. Allosteric modulation of the binding affinity between PQBP1 and the spliceosomal protein U5-15kD. *FEBS Lett.*. 2016.06; 590(14); 2221-2231
3. Taniguchi, JB., Kondo, K., Fujita, K., Chen, X., Homma, H., Sudo, T., Mao, Y., Watase, K., Tanaka, T., Tagawa, K., Tamura, T., Muramatsu, SI., Okazawa, H.. RpA1 ameliorates symptoms of mutant Ataxin-1 knock-in mice and enhances DNA damage repair. *Hum Mol Genet.*. 2016.08;
4. Fujita, K., Motoki, K., Tagawa, K., Chen, X., Hama, H., Nakajima, K., Homma, H., Tamura, T., Watanabe, H., Katsuno, M., Matsumi, C., Kajikawa, M., Saito, T., Saido, T., Sobue, G., Miyawaki, A., Okazawa, H.. HMGB1, a pathogenic molecule that induces neurite degeneration via TLR4-MARCKS, is a potential therapeutic target for Alzheimer’s disease. *Scientific Reports.*. 2016.08; 6; 31895

5. Mao, Y., Chen, X., Xu, M., Fujita, K., Sasabe, K., Homma, H., Murata, M., Tagawa, K., Tamura, T., Kaye, J., Finkbeiner, S., Blandino, G., Sudol, M., Okazawa, H. . Targeting TEAD/YAP-transcription-dependent necrosis, TRIAD, ameliorates Huntington' s disease pathology. *Hum Mol Genet.*.. 2016.09;
6. Imamura, T., Fujita, K., Tagawa, K., Ikura, T., Chen, X., Homma, H., Tamura, T., Mao, Y., Taniguchi, JB., Motoki, K., Nakabayashi, M., Ito, N., Yamada, K., Tomii, K., Okano, H., Kaye, J., Finkbeiner, S., Okazawa, H.. Identification of hepta-histidine as a candidate drug for Huntington' s disease by in silico-in vitro-in vivo-integrated screens of chemical libraries. *Scientific Reports.*.. 2016.09; 6; 33861
7. Mao, Y., Chen, X., Xu, M., Fujita, K., Sasabe, K., Homma, H., Murata, M., Tagawa, K., Tamura, T., Kaye, J., Finkbeiner, S., Blandino, G., Sudol, M., Okazawa, H. . Targeting TEAD/YAP-transcription-dependent necrosis, TRIAD, ameliorates Huntington' s disease pathology. *Hum Mol Genet.*.. 2016.09;

### [Conference Activities & Talks]

1. Tamura T, Shiraishi R, Sone M, Okazawa H. Systematic Analysis of Fly Models Elucidates Sleep disturbance in Huntington's Disease. The 57th Annual Meeting of the Japanese Society of Neurology 2016.05.18 Kobe International Exhibition Hall (Kobe)
2. Ito H, Fujita K, Chen X, Okazawa H. Analysis of molecular mechanism and development of therapeutic methods in spinocerebellar ataxia type 1 (SCA1). The 57th Annual Meeting of the Japanese Society of Neurology 2016.05.18 Kobe International Exhibition Hall (Kobe)
3. Takuya Tamura, Risa Shiraishi, Masaki Sone, Hitoshi Okazawa. Systematic Analysis of Fly Models Elucidates Sleep disturbance in Huntington's Disease. The 57th Annual Meeting of the Japanese Society of Neurology 2016.05.18 Kobe International Exhibition Hall (Kobe)
4. Hikaru Ito, Kyota Fujita, Xigui Chen, Hitoshi Okazawa. Analysis of molecular mechanism and development of therapeutic methods in spinocerebellar ataxia type 1 (SCA1). The 57th Annual Meeting of the Japanese Society of Neurology 2016.05.18 Kobe International Exhibition Hall (Kobe)
5. Chen X, Kondo K, Motoki K, Homma H, Okazawa H. Fasting activates macroautophagy in neurons of AD mice but is insufficient to degrade amyloid-beta. The 57th Annual Meeting of the Japanese Society of Neurology 2016.05.19 Kobe International Exhibition Hall (Kobe)
6. Mao Y, Tamura T, Yuki Y, Abe D, Tamada Y, Imoto S, Tanaka H, Homma H, Tagawa K, Miyano S, Okazawa H. The hnRNP-Htt axis regulates necrotic cell death induced by transcriptional repression through impaired RNA splicing. The 39th Annual Meeting of the Japan Neuroscience Society 2016.07.20 Pacifico Yokohama (Yokohama)
7. Okazawa H. Gene therapy to conquer spinocerebellar ataxia. The 22nd Annual Meeting of Japan Society of Gene and Cell Therapy 2016.07.30 Toranomon Hills Forum (Tokyo)
8. Mizuguchi M, Nabeshima Y, Obita T, Okazawa H. Interaction of spliceosomal proteins PQBP1, U5-15kD, and WBP11. The XXVIIth International Conference on Magnetic Resonance in Biological Systems 2016.08.22 International Conference Center Kyoto (Kyoto)
9. Furotani K, Yajima T, Toyokawa M, Nakayama M, Tamura T, Okazawa H, Sone M. Effect of inhibition of synaptic delivery of APP by loss-of-function of yata for the Drosophila Alzheimer's disease model. The 12th Japanese Drosophila Research Conference 2016.09.09 Rikkyo University (Tokyo)
10. Okazawa H. Therapeutics development of Alzheimer' s disease targeting on Phase 0. 15th Surugadai International Symposium 2016.11.29 Tokyo Medical and Dental University (Tokyo)
11. Furotani K, Yajima T, Toyokawa M, Nakayama M, Tamura T, Okazawa H, Sone M. Effect of inhibition of synaptic delivery of APP by loss-of-function of yata for the Drosophila Alzheimer's disease model. The 39th Annual Meeting of the Molecular Biology Society of Japan 2016.12.01 Rikkyo University (Tokyo)

## Ophthalmology and Visual Science

Professor;Kyoko Ohno-Matsui

Specially-appointed professor;Makoto Aihara

Junior Associate Professor;Hiroshi Takase, Koju Kamoi, Takeshi Yoshida

Assistant Professor;Shintaro Horie, Kei Morohoshi, Tae Yokoi

Graduate student;Tomoka Ishida, Yuko Iwasaki, Liu hongcling, keijia Cao, Yuxin Fang

### (1) Outline

Our department was established in 1944. Prof. Jin Ohtsuka initiated research on myopia in 1946, and Emeritus Prof. Takashi Tokoro established high myopia clinic in 1974 as the world only clinic specific to pathologic myopia. To date, clinical practice as well as basic research on myopia have continuously been performed in our department. Uveitis clinic was established by Emeritus Prof. Manabu Mochizuki in 1988. Since Prof. Kyoko Ohno-Matsui was appointed to a professorship in our department, clinical practice and basic research on wide variety of fields such as glaucoma, cataract, diabetic retinopathy, vitreoretinal disorder, and macular diseases in addition to myopia and uveitis have been actively performed.

### (2) Research

#### 1. High myopia

- 1) Analysis of retinochoroidal complications in high myopia (choroidal neovascularization, myopic tractional retinopathy)
- 2) Evaluation of the molecular mechanism of choroidal angiogenesis using the cultured cells as well as experimental animals (collaboratory project with Department of Cellular Physiological Chemistry)
- 3) Gene analysis of highly myopic patients (collaborator project with Kyoto University)
- 4) Establishment of a novel therapy to prevent an axial elongation or the formation of posterior staphyloma

#### 2. Ocular immunology and inflammation

- 1) Evaluation of the molecular mechanism of immunoregulation in intraocular inflammation
- 2) Pathogenic mechanism of intraocular inflammatory diseases
- 3) Development of novel treatments of intraocular inflammation
- 4) Molecular diagnosis of virus-infected uveitis and intraocular lymphomas.

#### 3. Neuro-ophthalmology

- 1) Evaluation of the change of the circulation as well as the glucose metabolism in the visual cortex using positron emission tomography (PET) in various ocular disorders
- 2) Mechanism of visual pathway in normal conditions as well as in the patients with amblyopia.

#### 4. Vitreoretinal disorder

- 1) Development of a novel treatment for vitreoretinal disorders like retinal detachment, diabetic retinopathy, and macular holes.

#### 5. Strabismus and amblyopia clinic

- 1) Effect of the visual background on binocular vision as well as the influence of strabismus on dynamic visual acuity.

### ( 3 ) Education

Undergraduate education of ophthalmology is composed of 1) classes on histology and physiology of the eye, and on diagnosis and treatment of ocular disorders, 2) combination block in which clinical examination is trained, and the diagnostic process is actively learned through group discussion using case series, 3) pre-clerkship and clerkship in which the medical students practically learn the major ocular disorders by seeing the patients and discussing in the conference.

After the initial residency of the first two years, the residency in ophthalmology is programmed for four years according to the educational program on diploma of ophthalmology by Japanese ophthalmological society.

The graduate students are expected to be academic doctors who develop and perform highly-qualified ophthalmologists, as well as become scientists who can perform basic research focusing on their clinical interest.

### ( 4 ) Lectures & Courses

Main objective of ophthalmology and visual science in the graduate course is to obtain the highly-advanced knowledge in the diagnosis and the treatment of various ocular disorders and to perform the basic research based on clinical experience.

### ( 5 ) Clinical Services & Other Works

Clinical practice is organized by the general ophthalmology clinic as well as the several subspecialty clinics. When the patients visited our department, they are screened in the general clinic, and then the final decision of the diagnosis and treatment is made in cooperation with each subspecialty clinic. Subspecialty clinics include high myopia clinic, uveitis clinic, glaucoma clinic, vitreoretinal disorder clinic, diabetic retinopathy clinic, neuro-ophthalmology clinic, and medical retina clinic. Approximately, 1,300 surgeries are performed per year (e.g., cataract surgery, vitreoretinal surgery, glaucoma surgery, strabismus surgery).

### ( 6 ) Publications

#### [Original Articles]

1. Koju Kamoi, Yoichi Nagata, Manabu Mochizuki, Daisuke Kobayashi, Nobuhiro Ohno, Kaoru Uchimar, Arinobu Tojo, Kyoko Ohno-Matsui.. Formation of Segmental Rounded Nodules During Infiltration of Adult T-Cell Leukemia Cells Into the Ocular Mucous Membrane. *Cornea*. 2016.01; 35(1); 137-139
2. Kamoi K, Nagata Y, Mochizuki M, Kobayashi D, Ohno N, Uchimar K, Tojo A, Ohno-Matsui K. Formation of segmental rounded nodules during the infiltration of adult T-cell leukemia cells into ocular mucous membrane. *Cornea*. 2016.01; 35(1); 137-139
3. Higashide T, Ohkubo S, Hangai M, Ito Y, Shimada N, Ohno-Matsui K, Terasaki H, Sugiyama K, Chew P, Li KK, Yoshimura N. Influence of clinical factors and magnification correction on normal thickness profiles of macular retinal layers using optical coherence tomography. *PLoS ONE*. 2016.01; 11(1); e0147782
4. Ohno-Matsui K, Jonas JB, Spaide RF. Macular bruch membrane holes in choroidal neovascularization-related myopic macular atrophy by swept-source optical coherence tomography. *Am. J. Ophthalmol.* 2016.02; 162; 133-139.e1
5. Koh V, Tan C, Tan PT, Tan M, Balla V, Nah G, Ching-Yu C, Ohno-Matsui K, Tan MM, Yang A, Zhao P, Wong TY, Seang-Mei S. Myopic maculopathy and optic disc changes in highly-myopic young Asian eyes and impact on visual acuity. *Am. J. Ophthalmol.* 2016.04; 164; 69-79
6. Jonas JB, Xu L, Wang YX, Bi HS, Wu JF, Jiang WJ, Nangia V, Sinha A, Zhu D, Tao Y, Guo Y, You QS, Wu LJ, Tao LX, Guo XH, Ohno-Matsui K, Panda-Jonas S. Education-related parameters in high myopia: Adults versus school children. *PLoS ONE*. 2016.05; 11(5); e0154554
7. Kimura Y, Akagi T, Miyake M, Yamashiro K, Yoshikawa M, Yamada H, Hasegawa T, Suda K, Nakanishi H, Ohashi-Ikeda H, Gotoh N, Hangai M, Moriyama M, Ohno-Matsui K, Yoshimura N. Association between the CDKN2B-AS1 gene and primary open angle glaucoma with high myopia in japanese patients. *Ophthalmic Genet.* 2016.06; 37(2); 242-244



8. Ohno-Matsui K, Jonas JB, Spaide RF. Macular bruch's membrane holes in highly myopic patchy chorioretinal atrophy. *Am. J. Ophthalmol.*. 2016.06; 166; 22-28
9. Holz FG, Tufail A, Leveziel N, Lai TY, Lanzetta P, Wong TY, Yu HG, Chen YX, Heinrichs N, Pilz S, Ohno-Matsui K. Ranibizumab in myopic choroidal neovascularization: A subgroup analysis by ethnicity, age, and ocular characteristics in RADIANCE. *Ophthalmologica.* 2016.06; 236(1); 19-28
10. Shinohara K, Moriyama M, Shimada N, Yoshida T, Ohno-Matsui K. Characteristics of peripapillary staphylomas associated with high myopia determined by swept-source optical coherence tomography. *Am. J. Ophthalmol.* 2016.06; 169; 138-144
11. Iwasaki Y, Sugita S, Mandai M, Yonemura S, Onishi A, Ito S, Mochizuki M, Ohno-Matsui K, Takahashi M. Differentiation/purification protocol for retinal pigment epithelium from mouse induced pluripotent stem cells as a research tool. *PLoS ONE.* 2016.07; 11(7); e0158282
12. Yokoi T, Jonas JB, Shimada N, Nagaoka N, Moriyama M, Yoshida T, Ohno-Matsui K. Peripapillary diffuse chorioretinal atrophy in children as a sign of eventual pathologic myopia in adults. *Ophthalmology.* 2016.08; 123(8); 1783-1787
13. Shinohara K, Moriyama M, Shimada N, Yoshida T, Ohno-Matsui K. Peripheral pigmented streaks in eyes with pathologic myopia. *Retina (Philadelphia, Pa.).* 2016.08; 36(8); 1573-1578
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15. Karube H, Kamoi K, Ohno-Matsui K. Anti-TNF therapy in the management of ocular attacks in an elderly patient with long-standing Behçet's disease. *Int Med Case Rep J.* 2016.09; 9; 301-304
16. Jonas JB, Bi HS, Wu JF, Xu L, Wang YX, Wei WB, Nangia V, Sinha A, Guo Y, You QS, Ohno-Matsui K, Panda-Jonas S. Corneal curvature radius in myopia of schoolchildren versus adult myopia. *Cornea.* 2016.10; 35(10); 1333-1337
17. Hiroki Akiyama, Hiroshi Takase, Fumito Kubo, Tohru Miki, Masahide Yamamoto, Makoto Tomita, Manabu Mochizuki, Osamu Miura, Ayako Arai. High-dose methotrexate following intravitreal methotrexate administration in preventing central nervous system involvement of primary intraocular lymphoma. *Cancer Science.* 2016.10; 107(10); 1458-1464
18. Ohno-Matsui K. Pathologic Myopia. *Asia Pac J Ophthalmol (Phila).* 2016.11; 5(6); 415-423
19. Yoshihiko Usui, Narsing A Rao, Hiroshi Takase, Kinya Tsubota, Kazuhiko Umazume, Daniel Diaz-Aguilar, Takeshi Kezuka, Manabu Mochizuki, Hiroshi Goto, Sunao Sugita. Comprehensive polymerase chain reaction assay for detection of pathogenic DNA in lymphoproliferative disorders of the ocular adnexa. *Sci Rep.* 2016.11; 6; 36621

## [Books etc]

1. Koju Kamoi, Manabu Mochizuki. *Intraocular Inflammation.* Springer, 2016.01 (ISBN : 978-3-540-75387-2)

## [Misc]

1. Ohno-Matsui K, Lai TY, Lai CC, Cheung CM. Updates of pathologic myopia. *Prog Retin Eye Res.* 2016.05; 52; 156-187
2. Manabu Mochizuki, Koju Kamoi. F1000Prime Recommendation of [ Gül A et al., *Ann Rheum Dis* 2012, 71(4):563-6] . F1000 Prime.

**[Conference Activities & Talks]**

1. Kyoko Ohno-Matsui, Tomoka Ishida. OCT angiography for choroidal neovascularization due to pathologic myopia. 39th Annual Macula Society Meeting 2016.02.23 Miami, USA
2. Kyoko Ohno-Matsui, Tomoka Ishida. Examinations of intrasclerally located Zinn-Haller ring by OCT angiography. 39th Annual Macula Society Meeting 2016.02.24 Miami, USA
3. Ohno-Matsui K. Analyses of the Presence and Types of Posterior Staphyloma Using Wide-Field Imaging. Fourth Annual International Retinal Imaging Symposium 2016.03.19 Los Angeles
4. Ohno-Matsui K. Pathologic myopia and its complications. 2016 APAO(Asia-Pacific Academy of Ophthalmology) 2016.03.24 Taiwan,China
5. Ohno-Matsui K. Bruch membrane and myopic maculopathy. 2016 APAO(Asia-Pacific Academy of Ophthalmology) 2016.03.24 Taiwan,China
6. Ohno-Matsui K. Bruch's membrane and pathologic myopia. 2016 APAO(Asia-Pacific Academy of Ophthalmology) 2016.03.25 Taiwan,China
7. Ohno-Matsui K. Swept-source OCT in pathologic myopia. 2016 APAO(Asia-Pacific Academy of Ophthalmology) 2016.03.25 Taiwan,China
8. Ohno-Matsui K. High myopia and myopia control forum. International Retinal Forum / Annual Meeting of Chinese Ocular Fundus Diseases Society 2016.04.14 China
9. Horie S, Ide M, Morohoshi K, Ohno-Matsui K. Evaluation of En-face OCT images in diabetic macular edema with anti-VEGF treatment. ARVO 2016 2016.05.02
10. Yoshida T, Ishida T, Kejia C, Shinohara K, Hongding L, Ohno-Matsui K. The correlation between sirt1 and muller cells in the development of CNV. ARVO 2016 2016.05.04 Seattle, USA
11. Shinohara K, Yoshida T, Ishida T, Honding L, Morita I, Ohno-Matsui K. Establishment of novel therapy using fibroblasts transplantation on sclera for experimental myopia in rats. ARVO 2016 2016.05.04
12. Nagaoka N, Morohoshi K, Jonas JB, Ohno-Matsui K. Optic disc size and visual field defects in high myopia. ARVO 2016 2016.05.05 Seattle, USA.
13. Ishii M, Ishida T, Morohoshi K, Ikegaya Y, Shinohara K, Ohono-Matsui K. Detection of Zinn-Haller arterial ring in highly myopic eyes by optical coherence tomography angiography. ARVO 2016 2016.05.05
14. Ohno-Matsui K. Imaging of pathologic myopia. Samsung Medical Center Retina Symposium 2016.06.25 Seoul, Korea
15. Ohno-Matsui K, Alkabes M, Mateo C, Moriyama M. Features of posterior staphylomas analyzed by wide-field fundus imaging and 3DMRI in patients with pathologic myopia. XXXth Meeting of the Club Jules Gonin 2016.07.07 Bordeaux, France
16. Ohno-Matsui K. Imaging of optic nerve in highly myopic eyes. XXII International society for Eye Research Biennial Meeting(ISER) 2016.09.27 Tokyo
17. Ohno-Matsui K. Diagnosis of pathologic myopia and over view. 3rd International conference on Pathologic Myopia 2016.09.30 Tokyo
18. Ohno-Matsui K. Imaging of Pathologic Myopia. 3rd International conference on Pathologic Myopia 2016.10.01 Tokyo
19. Grzybowski A, Repka MX, Koffler BH, Ohno-Matsui K, Trier K, Morgan I, Tan D. New Approaches to the Prevention and Treatment of Myopia. AAO(American Academy of Ophthalmology)2016 2016.10.17 Chicago,USA
20. Ohno-Matsui K, Cheung G, Lai T, Hirakata A. Diagnosis and Management of Complications due to Pathologic Myopia. AAO(American Academy of Ophthalmology)2016 2016.10.17 Chicago,USA
21. Stanga P, Moussa MS, Ohno-Matsui K, Sadda SR. Spectral Domain and Swept Source OCT in the Diagnosis and Management of Vitreoretinal and Uveitic Disorders. AAO(American Academy of Ophthalmology)2016 2016.10.18 Chicago,USA



22. Ohno-Matsui K. Fundus imaging of Pathologic Myopia. The 70th Annual Congress of Japan Clinical Ophthalmology 2016.11.03 Kyoto
23. Yokoi T, Ohno-Matsui K. Unilateral Multiple Drusenoid Lesions Detected by OCT in Eyes with High Myopia. The 70th Annual Congress of Japan Clinical Ophthalmology 2016.11.04 Kyoto
24. Ohno-Matsui K. Peripapillary diffuse atrophy is an indicator in children for eventual pathologic myopia in adults. 2016 Autumn Meeting of Ophthalmological Society of Taiwan 2016.11.13 Kaohsiung, Taiwan (Chung Gung Memorial Hospital)
25. Ohno-Matsui K. Cutting edge of ocular imaging for pathologic myopia. The 55th Annual Meeting of Japanese Retina and Vitreous Society 2016.12.03 Tokyo

**[Others]**

1. Pathologic Myopia-cutting edge of this blinding disease, 2016.03  
Tung Wah Eastern Hospital

# Otorhinolaryngology

Professor: Takeshi Tsutsumi

Associate Professor: Yoshiyuki Kawashima

Junior Associate Professor: Yasuhiro Suzuki

Assistant Professor: Taku Itou, Tarou Fujikawa, Yuichiro Inaba

Hospital Staff: Takamori Takeda, Ayako Maruyama, Yumiko Tateishi,

Tomohide Hamajima, Tomoki O-oka

Graduate Student: Keiko Ohno, Ayane Makabe, Takamori Takeda, Motomu Honjo

## ( 1 ) Research

- 1) Deafness gene analysis
- 2) Neurophysiological study of hearing
- 3) Histoanatomical study of ear, nose, throat, head, and neck
- 4) Eye movement analysis in patients with dizziness
- 5) Clinical study of treatment and prognosis in patients with allergic rhinitis, acute and chronic sinusitis, and benign tumors
- 6) Treatment of tinnitus
- 7) Treatment using endoscope
- 8) Development of a new mapping procedure for cochlear implant
- 9) Bio-Marker of external ear canal carcinoma

## ( 2 ) Lectures & Courses

Pre-graduate clinical education

Clinical systematic lecture covers anatomy, a general idea of diseases, their pathological conditions and treatments in the field of otorhinolaryngology. Clinical clerkship I (general diagnostic training) provides instruction in the diagnosis and testing techniques of the otorhinolaryngological field; clinical clerkship II (clinical training) provides detailed explanations of disease mechanisms, training in the performance of examinations, and clinical responsibilities involving both inpatient and outpatient care. Clinical clerkship III provides advanced training beyond the scope of clinical clerkship II. In particular, students develop an advanced understanding of otorhinolaryngological diseases by conducting outpatient procedures (including taking histories, visual inspection, and palpation), and gaining practical experience in assessment and diagnosis of patients' conditions. Furthermore, in the clinical clerkship III, students also attend a "micro-conference" on teaching. Finally, students are assigned to patients throughout their treatment, consistently dealing with the same individuals before, during, and after surgery; this allows the students to become familiar with the course of clinical care.

## ( 3 ) Clinical Performances

Otorhinolaryngology clinic provides full examinations and treatment for diseases in ear, nose, throat, head, and neck, including dizziness, sudden deafness, facial palsy, infectious disease and benign as well as malignant disease in the otorhinolaryngeal area. We have performed the first implementation of bone anchored hearing aid implant in Japan and since then we have experienced many patients for this surgery. We also have performed

surgery for patients with malignant disease as well as skull base lesions in collaboration with the Department of the Head and Neck Surgery. Our outpatient clinic includes general ear, nose and throat clinic as well as allergy, sinusitis, dizziness, otitis media, tumor, deafness, and tinnitus clinic.

#### (4) Publications

##### [Original Articles]

1. Yamamoto Y, Hirai C, Takeda T, Tasaki A, Inaba Y, Kiyokawa Y, Fujikawa T, Suzuki Y, Tsutsumi T.. The analysis of up and down-beating nystagmus on electronystagmography. *Equilibrium Research*. 2016; 75; 106-114
2. Yoshihiro Noguchi, Masatoki Takahashi, Taku Ito, Taro Fujikawa, Yoshiyuki Kawashima, Ken Kitamura. Delayed restoration of maximum speech discrimination scores in patients with idiopathic sudden sensorineural hearing loss. *Auris Nasus Larynx*. 2016.10; 43(5); 495-500
3. Ayako Maruyama, Atsunobu Tsunoda, Masatoki Takahashi, Seiji Kishimoto, Masami Suzuki. Nasopharyngeal pleomorphic adenoma presenting as otitis media with effusion: case report and literature review. *Am J Otolaryngol*. 35(1); 73-76
4. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. *Am J Otolaryngol*. 35(3); 402-404

##### [Conference Activities & Talks]

1. Takeda.T, Tasaki.A, InabaY, Kiyokawa.Y, Fujikawa.T, Suzuki.Y, Tsutsumi.T. Evaluating Listing' s plane from video-occulography on spinocerebellar degeneration. 29th Barany Society meeting 2016 2016.06
2. Tsutsumi T, Takeda T, Ikeda T, Fukuoka Y.. Evaluation of gravity perception using Listing' s plane analysis.. 29th Barany Society Meeting 2016.06.05

# Neurology and Neurological Science

Professor	YOKOTA Takanori
Junior Associate Professor	ISHIBASHI Satoru
Junior Associate Professor	NISHIDA Yoichiro
Assistant Professor	OHKUBO Takuya
Assistant Professor	SATO Nozomu
Assistant Professor	OZAKI Kokoro
Assistant Professor	HATTORI Takaaki
Assistant Professor	NUMASAWA Yoshiyuki
Project Professor	SANJO Nobuo
Project Junior Associate Professor	NAGATA Tetsuya
Project Assistant Professor	KUWAHARA Hiroya
Project Assistant Professor	YOSHIOKA Kotaro
Project Assistant Professor	YUI Daishi
Project Assistant Professor	SAKAUE Fumika
Project Researcher	ASADA Ken
Graduate Student	ITO Yoko
Graduate Student	HIGASHI Miwa
Graduate Student	Yagi Yohsuke
Graduate Student	ZENIYA Satoshi
Graduate Student	IWASAWA Eri
Graduate Student	OHYAGI Masaki
Graduate Student	HASEGAWA Jyuri
Graduate Student	SHINTAKU Hiroshi
Graduate Student	FURUKAWA Fumiko
Graduate Student	MIYASHITA Akiko
Graduate Student	FUJITA Kyohe
Graduate Student	MAJIMA Takamasa
Graduate Student	ONO Daisuke
Graduate Student	HIRATA Kose
Graduate Student	ISHIZU Nobutaka
Graduate Student	LI Fu Ying
Graduate Student	SONG Jin Dong
Graduate Student	GUO Huijia
Graduate Student	HU Yajun
Graduate Student	ZHANG Yong Quan
Graduate Student	SU SU Lei Mon
Graduate Student	REYILA Mamuti
Graduate Student	MAMUTI HASIYATI
Graduate Student	DAIZO Kaiichi
Graduate Student	YASUDA Eiji
Graduate Student	MITSUHASHI Yuta
Graduate Student	TAMURA Keigo
Graduate Student	KUNIEDA Taiki
Research Student	SANO Tatsuhiko
Research Student	TAMAKI Toshihiro

## (1) Research

- 1) Development of base technology on nucleic acid medicine and its application to neurological disorders
- 2) Discovery of biomarker in body fluid for neurological diseases
- 3) Pathogenesis of Alzheimer disease
- 4) Pathogenesis and therapies of amyotrophic lateral sclerosis (ALS)
- 5) Pathogenesis and therapies of cerebrovascular diseases

- 6) Genetical and pathomechanical studies of spinocerebellar ataxias
- 7) Regulation of blood-brain barrier
- 8) Electrophysiological studies
- 9) Leading-edge neuroradiological studies
- 10) Neuropathological studies of biopsied and autopsied samples

## (2) Lectures & Courses

Neurology is a medical specialty concerned with the diagnosis and treatment of disorders of the nervous system including the brain, spinal cord, peripheral nerves, autonomic nerves and skeletal muscles. Since the nervous system extends to the whole body and regulate all the organs, neurologists have to examine and understand many symptoms of the whole brain and body.

The Department of Neurology and Neurological Science at Tokyo Medical and Dental University offers a unique “clinical neurological training for specialist” in a three-year residency program. This program is designed to provide the highest quality clinical training in the clinical practice of neurology, either in an academic or a practice career. To accomplish this, the program integrates extensive practical exposure to all aspects of current clinical neurology with a firm grounding in underlying scientific principles and methods of clinical investigations such as electrophysiology, neuromuscular pathology, stroke, dementia, neuroimaging, and neurogenetics. The faculty and staff are committed to facilitate resident education and training.

After completion of their training for three years, senior residents are equipped with a lot of clinical experience as attending doctors or teaching assistants in the university hospital and affiliated hospitals. They are eligible for the board certification by the Japanese Society of Neurology.

## (3) Clinical Services & Other Works

We daily see about 100 out-patients and 36 in-patients, and offer in- and out-patient consultation services through the weekday and on weekends. We diagnose and treat patients with stroke, multiple sclerosis, Parkinson's disease, spinocerebellar ataxia, ALS, myopathies, neuropathies, meningitis/encephalitis, and hundreds of other neurological issues. We also have the “out-patients clinic specialized to patients with amnesia.” Our patients will be reliably evaluated and diagnosed with some skillful techniques, such as the electrophysiological, neuroradiological, and neuropsychological tests and pathological diagnosis of biopsied nerves and muscles.

## (4) Publications

### [Original Articles]

1. Tsutomu Nakamura, Fumiko Arima-Yoshida, Fumika Sakaue, Yukiko Nasu-Nishimura, Yasuko Takeda, Ken Matsuura, Natacha Akshoomoff, Sarah N Mattson, Paul D Grossfeld, Toshiya Manabe, Tetsu Akiyama. PX-RICS-deficient mice mimic autism spectrum disorder in Jacobsen syndrome through impaired GABAA receptor trafficking. *Nat Commun.* 2016; 7; 10861
2. Enomoto M, Hirai T, Kaburagi H, Yokota T. Efficient Gene Suppression in Dorsal Root Ganglia and Spinal Cord Using Adeno-associated Virus Vectors Encoding Short-Hairpin RNA. *Methods Mol Biol.* 2016; 1364; 277-290
3. Yamada K, Kobayashi H, Bo R, Takahashi T, Purevsuren J, Hasegawa Y, Taketani T, Fukuda S, Ohkubo T, Yokota T, Watanabe M, Tsunemi T, Mizusawa H, Takuma H, Shioya A, Ishii A, Tamaoka A, Shigematsu Y, Sugie H, Yamaguchi S. Clinical, biochemical and molecular investigation of adult-onset glutaric acidemia type II: Characteristics in comparison with pediatric cases. *Brain Dev.* 2016; 38(3); 293-301
4. Nobuo Sanjo, Satoko Kina, Yukiko Shishido-Hara, Yurie Nose, Satoru Ishibashi, Tetsuya Fukuda, Taketoshi Maehata, Yoshinobu Eishi, Hidehiro Mizusawa, Takanori Yokota. A Case of Progressive Multifocal Leukoencephalopathy with Balanced CD4/CD8 T-Cell Infiltration and Good Response to Mefloquine Treatment. *Internal Medicine.* 2016.01; 55(12); 1631-1635
5. Eric Vallabh Minikel, Sonia M. Vallabh, Monkol Lek, Karol O. Estrada, Kaitline E. Samocya, J. Fah Sathirapongsasuti, Cory Y. McLean, Joice Y. Tung, Linda P.C. Yu, Pierluigi Gambetti, Janis Blevins, Shuling

- Zhang, Yvonne Cohen, Wei Chen, Masahito Yamada, Tsuyoshi Hamaguchi, Nobuo Sanjo, Hidehiro Mizusawa, Yoshikazu Nakamura, Tetsuyuki Kitamoto, Steven J. Collins, Alison Boyd, Robert G Will, Richard Knight, Claudia Ponto, Inga Zerr, Theo Kraus, Sabina Eigenbrod, Armin Giese, Jesus de Pedro Cuesta, Stéphane Haïk, Jean-Louis Laplanche, Jean Philippe Brandel, Michael Boenke, Markku Laakso, Karen Mohlke, Francis S. Collins, Anna Kähler, Kimberly Chambert, Steven McCarroll, Patrick Sullivan, Christina M. Hultman, Shaun M. Purcell, Pamela Sklar, Cornelia M. van Duijn, F. Rivadeneira Ramirez, Arfan Ikram, Sven J. van der Lee, Jeannette M. Vergeer-Drop, André G. Uitterlinden, Mark J. Daley, Daniel G. MacArthur, . Quantifying prion disease penetrance using large population control cohorts. *Science Translational Medicine* 2016. 2016.01; 8(322); 322R9-322RA9
6. Yokota T, Kanouchi T, Ohkubo T. ALS: Quantitative analysis of disease progression from a new point of view 2015 Annual report of the research committee of CNS degenerative diseases, The ministry of health, labour and welfare of Japan. 2016.03; 58-61
  7. Mutsuki Kuraoka, En Kimura, Tetsuya Nagata, Takashi Okada, Yoshitsugu Aoki, Hisateru Tachimori, Naohiro Yonemoto, Michihiro Imamura, Shin'ichi Takeda. Serum Osteopontin as a Novel Biomarker for Muscle Regeneration in Duchenne Muscular Dystrophy. *Am. J. Pathol.* 2016.05; 186(5); 1302-1312
  8. Koichi Kimura, Hiroyuki Morita, Masao Daimon, Masaru Horio, Takayuki Kawata, Tomoko Nakao, Megumi Hirokawa, Ruriko Kitao, Daisuke Watanabe, Tetsuo Komori, Tetsuya Nagata, Shin'ichi Takeda, Hirofumi Komaki, Kazuhiko Segawa, Takashi Nakajima, Katsu Takenaka, Issei Komuro. Utility of Cystatin C for Estimating Glomerular Filtration Rate in Patients With Muscular Dystrophy. *Int Heart J.* 2016.05; 57(3); 386-388
  9. Koya Ono, Ken Murata, Toshinari Arai, Tomoyuki Kino, Keisuke Onaka, Satoru Takahashi, Hirotaka Sato, Hiroya Kuwahara. Posterior reversible encephalopathy syndrome after iron administration in a patient with chronic severe anemia. *Journal of the Neurological Sciences.* 2016.08; 367; 333-334
  10. Mitsuru Yoneyama, Hiroshi Mitoma, Nobuo Sanjo, Maya Higuma, Hiroo Terashi, Takanori Yokota. Ambulatory Gait Behavior in Patients with Dementia: A Comparison with Parkinson's Disease. *Transactions on Neural System and Rehabilitation Engineering* 2015 . 2016.08; 24(8); 817-826
  11. Ryo Yamasaki, Takuya Matsushita, Toshiyuki Fukazawa, Kazumasa Yokoyama, Kazuo Fujihara, Mieko Ogino, Takanori Yokota, Katsuichi Miyamoto, Masaaki Niino, Kyoichi Nomura, Ryo Tomioka, Masami Tanaka, Izumi Kawachi, Takashi Ohashi, Ken-Ichi Kaida, Makoto Matsui, Yuji Nakatsuji, Hirofumi Ochi, Hikoaki Fukaura, Takashi Kanda, Akiko Nagaishi, Kanae Togo, Hidehiro Mizusawa, Hiroyuki Murai, Jun-Ichi Kira. Efficacy of intravenous methylprednisolone pulse therapy in patients with multiple sclerosis and neuromyelitis optica. *Mult. Scler.* 2016.09; 22(10); 1337-1348
  12. Hitoshi Suzuki, Yoshitsugu Aoki, Toshiki Kameyama, Takashi Saito, Satoru Masuda, Jun Tanihata, Tetsuya Nagata, Akila Mayeda, Shin'ichi Takeda, Toshifumi Tsukahara. Endogenous Multiple Exon Skipping and Back-Splicing at the DMD Mutation Hotspot. *Int J Mol Sci.* 2016.10; 17(10);
  13. Nobutaka Ishizu, Daishi Yui, Akira Hebisawa, Hidenori Aizawa, Wanpeng Cui, Yuko Fujita, Kenji Hashimoto, Itsuki Ajioka, Hidehiro Mizusawa, Takanori Yokota, Kei Watase. Impaired striatal dopamine release in homozygous Vps35 D620N knock-in mice. *Hum. Mol. Genet.* 2016.10; 25(20); 4507-4517
  14. Nobuko Yamaguchi, Sonoko Misawa, Yasunori Sato, Kengo Nagashima, Kanako Katayama, Yukari Sekiguchi, Yuta Iwai, Hiroshi Amino, Tomoki Suichi, Takanori Yokota, Yoichiro Nishida, Nobuo Kohara, Koichi Hirata, Kazutoshi Nishiyama, Ichiro Yabe, Ken-Ichi Kaida, Norihiro Suzuki, Hiroyuki Nodera, Shoji Tsuji, Haruki Koike, Jun-Ichi Kira, Hideki Hanaoka, Susumu Kusunoki, Satoshi Kuwabara, . A Prospective, Multicenter, Randomized Phase II Study to Evaluate the Efficacy and Safety of Eculizumab in Patients with Guillain-Barré Syndrome (GBS): Protocol of Japanese Eculizumab Trial for GBS (JET-GBS). *JMIR Res Protoc.* 2016.11; 5(4); e210

#### [Misc]

1. Yutaro Asami, Kotaro Yoshioka, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. Drug delivery system of therapeutic oligonucleotides. *Drug Discov Ther.* 2016; 10(5); 256-262
2. Eri Iwasawa, Masahiko Ichijo, Satoru Ishibashi, Takanori Yokota. Acute development of collateral circulation and therapeutic prospects in ischemic stroke. *Neural Regen Res.* 2016.03; 11(3); 368-371

3. Masaki Ohyagi, Takanori Yokota. Oligonucleotide therapeutics for treatment of neurological degenerative diseases 2016.08; 67(4); 349-353
4. Takanori Yokota, Kazutaka Nishina, Hiroya Kuwahara. Gene Therapy with therapeutic oligonucleotides Neurological Therapeutics. 2016.11; 33(3); 303-306

# **[Conference Activities & Talks]**

1. Amano E, Suzuki M, Ozaki K, Ishibashi S, Akaza M, Kanouchi T, Tohda S, Yokota T. A case of sensory dominant CIDP with conduction delay predominantly in the most distal segment (Japanese). 10th Tokyo Metropolitan Neuromuscular Electrodiagnosis Forum 2016.01.30 Tokyo
2. Asada K, Canestrari E, Fu X, Li Z, Makowski E, Wu YC, Mito JK, Kirsch DG, Baraban J, Paroo Z.. Rescuing dicer Defects via Inhibition of an Anti-dicing Nuclease. The 2nd Annual Meeting of the Japan miRNA Society 2016.02.06 Nagoya
3. Song J, Shimoura T, Kuwahara H, Yoshida-Tanaka K, Nishina K, Nagata T, Yokota T. New platform technology to regulate the blood-brain barrier function in vivo. 第8回 CBIR+ONSA 共催若手インスパイアシンポジウム 2016.02.20 Tokyo
4. Takanori Yokota. DNA/RNA heteroduplex oligonucleotide as a novel concept of therapeutic oligonucleotide. 8th AsiaTIDES Oligonucleotide and Peptide Therapeutics 2016.02.25 Kyoto
5. Takanori Yokota. DNA/RNA heteroduplex oligonucleotide for highly efficient gene silencing. Oligonucleotide Therapeutics & Delivery 2016.04.04 Boston
6. Hiroya Kuwahara, Takahiro Shimoura, Jindong Song, Kie Yoshida-Tanaka, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. Hetero-duplex oligonucleotide to regulate the blood-brain barrier function in vivo. Oligonucleotide Therapeutics & Delivery 2016.04.04 Boston
7. Fumiko Furukawa ,Nobuo Sanjo,Atsushi Kobayashi,Tsuyoshi Hamaguchi,Masahito Yamada,Tetsuyuki Kitamoto,Hidehiro Mizusawa. Differential association of amyloid- $\beta$  with PrPSc pathology in each genetic prion disease.. Prion2016 2016.05.10 Tokyo,JPN
8. Ryusuke Ae,Yoshikazu Nakamura, Ichiro Takumi,Nobuo Sanjo,Tetsuyuki Kitamoto,Hidehiro Mizusawa. Epidemiologic features of human prion diseases in Japan: a prospective 15-year surveillance study.. Prion2016 2016.05.10 Tokyo,JPN
9. Kenji Sakai,Tsuyoshi Hamaguchi,Nobuo Sanjo,Hiroyuki Murai,Moeko Noguchi-Shinohara,Ichiro Nozaki,Yoshikazu Nakamura,Tetsuyuki Kitamoto,Hidehiro Mizusawa,Masahito Yamada. Diffusion-weighted images in patients with dura mater graft-associated Creutzfeldt-Jakob disease.. Prion2016 2016.05.10 Tokyo,JPN
10. Yuko Ishimura,Tadashi Tsukamoto,Kazuo Kuwata,Masahito Yamada,Katsumi Doh-ura,Yoshio Tsuboi,Katsuya Sato,Yoshikazu Nakamura,Nobuo Sanjo,Chieko Tamura,Hidehiro Mizusawa . The Japan Consortium of Prion diseases (JACOP) for patients' registration and clinical studies of Prion diseases in Japan. . Prion2016 2016.05.10 Tokyo,JPN
11. Ichiro Takumi,Nobuhito Saito,Nobuo Sanjo,Shunsaku Takayanagi,Chieko Tamura,Tadashi Tsukamoto,Yoshiyuki Kuroiwa,Ryusuke Ae,Yoshikazu Nakamura,Tetsuyuki Kitamoto,Tsuyoshi Hamaguchi,Masahito Yamada,Hidehiro Mizusawa. CJD incidents in Japan.. Prion2016 2016.05.10 Tokyo,JPN
12. Tadashi Tsukamoto,Ryusuke Ae,Yoshikazu Nakamura,Nobuo Sanjo,Tetsuyuki Kitamoto,Katsuya Satoh,Tsuyoshi Hamaguchi,Masahito Yamada,Hidehiro Mizusawa. Human Prion Diseases Surveillance and registration system in Japan.. Prion2016 2016.05.10 Tokyo,JPN
13. Tsuyoshi Hamaguchi,Kenji Sakai,Tetsuyuki Kitamoto,Masaki Takao,Shigeo Murayama,Yasushi Iwasaki,Mari Yoshida,Hiroshi Shimizu,Akiyoshi Kakita,Hitoshi Takahashi,Hiroshi Suzuki,Hironobu Naiki,Nobuo Sanjo,Hidehiro Mizusawa,Masahito Yamada. Cerebral  $\beta$ -Amyloidosis in patients with dura mater graft-associated Creutzfeldt-Jakob disease.. Prion2016 2016.05.10 Tokyo,JPN
14. Kanouchi T, Sekiguchi T, Yokota T. A pilot study on disease progression of ALS by quantitative analysis from a new viewpoint. 57th annual meeting of the Japanese Society of Neurology 2016.05.18 Kobe



15. Jindong Song, Tetsuya Nagata, Wenying Piao, Kazutaka Nishina, Takuya Okubo, Keisuke Abe, Masato Hasegawa, Takanori Yokota. Inhibition of alpha-synuclein fibril assembly by antisense oligonucleotide in mice. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.18 Kobe
16. Fuying Li, Satoru Ishibashi, Kotaro Yoshioka, Takehiko Wada, Masahiko Ichijo, Eri Iwasawa, Jindong Song, Yongquan Zhang, Takanori Yokota. Heteroduplex oligonucleotide reduced gene expression in focal ischemic brain in mice. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.18 Kobe
17. Nobuo Sanjo, Hidehiro Mizusawa, Takanori Yokota. Various neurological manifestations of lymphoma. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.18 Kobe
18. Yoichiro Nishida, Winkler Ethan, Sagare Abhay, De Vivo Darryl, Zlokovic Berislav. GLUT1 reductions at the BBB exacerbate Alzheimer disease vasculo-neuronal dysfunction. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.19 Kobe
19. Ogata H, Yamasaki R, Oka N, Kuwahara M, Suzuki H, Kusunoki S, Yagi Y, Yokota T, Matsushita T, Kira J-I. Useful laboratory markers for predicting anti-NF155 antibody status among CIDP patients. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.19 Kobe
20. Hiroya Kuwahara, Takahiro Shimoura, Jindong Song, Kie Yoshida-Tanaka, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. A novel platform technology to regulate the blood-brain barrier in vivo. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.19 Kobe
21. Kazutaka Nishina, Kotaro Yoshioka, Tomoko Nishina, Hiroya Kuwahara, Tetsuya Nagata, Takanori Yokota. Novel oligonucleotide based on DNA/RNA heteroduplex structures. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.19 Kobe
22. Nozomu Sato, Kinya Ishikawa, Hidehiro Mizusawa, Takanori Yokota. Variations in the mutation for spinocerebellar ataxia type 31 require cautious genetic testing. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.19 Kobe
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25. Keisuke Abe, Mio Tajiri, Daishi Yui, Hiroki Sasaguri, Takuya Ohkubo, Takanori Yokota. A C-terminal fragment of TDP-43 in exosomes mediates propagation of ALS pathology. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.20 Kobe
26. Kazumasa Soga, Kinya Ishikawa, Tokuro Huruya, Hidehiro Mizusawa, Takanori Yokota. A clinical and neuropathological study on homozygous mutations with spinocerebellar ataxia type 6. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.20 Kobe
27. Toshiro Kanazawa, Yurie Nose, Yutaro Asami, Jin Nonami, Masahide Iijima, Hiroaki Tanaka, Takanori Yokota. Clinical features of patients with motor fluctuations before intravenous thrombolysis. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.20 Kobe
28. Masahiko Ichijo, Satoru Ishibashi, Kazunori Miki, Eri Iwasawa, Kyohei Fujita, Hiroaki Yokote, Takeshi Amino, Tomoyuki Kamata, Takanori Yokota. Significance of development and reversion of collaterals in outcome after intravenous thrombolysis. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.20 Kobe
29. Shintaku H, Kanouchi T, Yokota T. Pathophysiology of myoclonus in corticobasal syndrome. 57th annual meeting of the Japanese Society of Neurology 2016.05.21 Kobe
30. Hiroshi Doi, Shigeru Koyano, Misako Kunii, Shunta Hashiguchi, Hitaru Kishida, Kenichi Tanaka, Masaaki Shiina, Kazuhiro Ogata, Fumiko Hirashima, Yukichi Inoue, Nozomu Sato, Kokoro Ozaki, Kiyobumi Ohta, Takanori Yokota, Hidehiro Mizusawa, Jun Mitsui, Shoji Tsuji, Naomichi Matsumoto, Kinya Ishikawa, Fumiaki Tanaka. The clinical and pathological features of autosomal-dominant SCA with CACNA1G mutation. 57th Annual Meeting of the Japanese Society of Neurology 2016.05.21 Kobe



31. Hiroya Kuwahara, Hiroto Fujigasaki, Tohru Tanizawa, Ken Matsumura, Mutsufusa Watanabe, Takanori Yokota, Toshiki Uchihara. An autopsy case of ALS with argyrophilic grain disease showing PSP-like cytopathology predominantly in cerebral cortex. The 57th Annual Meeting of the Japanese Society of Neuropathology 2016.06.02 Hiroaki
32. Ogata H, Yamasaki R, Oka N, Kuwahara M, Suzuki H, Kusunoki S, Yagi Y, Matsushita T, Yokota T, Kira J-I. Valuable objective markers for predicting anti-neurofascin 155 antibody status among CIDP patients. The International Inflammatory Neuropathy Consortium 2016 2016.06.22 Glasgow
33. Taiki Kunieda, Kotaro Yoshioka, Yumiko Sujino, Kie Tanaka, Wenying Piao, Hiroya Kuwahara, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. Development of antisense oligonucleotide with a new type of a double stranded structure. The RNA society of Japan 18th annual meeting (The 21st annual meeting of the RNA society) 2016.06.29 Kyoto
34. Kotaro Yoshioka, Yumiko Sujino, Taiki Kunieda, Kie Tanaka, Wenying Piao, Hiroya Kuwahara, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. A new mechanism of microRNA inhibition by a new type of duplex oligonucleotide. The RNA society of Japan 18th annual meeting (The 21st annual meeting of the RNA society) 2016.06.29 Kyoto
35. Fumika Sakaue, Eiji Yasuda, Tatsuhiko Sano, Taro Ishiguro, Tetsuya Nagata, Takanori Yokota. Chemically modified RNAs inhibit TDP-43 aggregation. The RNA society of Japan 18th annual meeting (The 21st annual meeting of the RNA society) 2016.06.29 Kyoto
36. Kazutaka Nishina, Kie Yoshida-Tanaka, Wenying Piao, Takanori Yokota. DNA/RNA heteroduplex oligonucleotide (HDO) for highly efficient gene silencing. The RNA society of Japan 18th annual meeting (The 21st annual meeting of the RNA society) 2016.06.30 Kyoto
37. Yoko Ito, Nobuo Sanjo, Yukiko Matsumoto, Takanori Yokota. Optimal starting time of cholinesterase inhibitors for amnesic MCI. Alzheimer's Association International Conference 2016 2016.07.14 Toronto, Canada
38. Fumiko Furukawa, Nobuo Sanjo, Atsushi Kobayashi, Tsuyoshi Hamaguchi, Masahito Yamada, Tetsuyuki Kitamoto, Hidehiro Mizusawa, Takanori Yokota. Colocalization of A  $\beta$  42 with PrPSc-plaques in the brain of the Gerstmann-Sträussler-Scheinker disease with the P105L mutation. Alzheimer's Association International Conference 2016 2016.07.24 Toronto
39. Yoichiro Nishida, Daishi Yui, Tomoko Nishina, Kaoru Mogushi, Satoru Ishibashi, Itsuki Ajioka, Kinya Ishikawa, Hidehiro Mizusawa, Shigeo Murayama, Takanori Yokota. Enhanced Pla2g3 expression by oxidative stress decreases the IDE and exacerbates AD. Alzheimer's Association International Conference 2016 2016.07.26 Toronto
40. Takanori Yokota. Propagation of TDP-43 in ALS. Propagation in Neurodegenerative Disease Conference 2016 2016.08.11 Dublin
41. Masahito Yamada, Tsuyoshi Hamaguchi, Yu Taniguchi, Kenji Sakai, Tetsuyuki Kitamoto, Masaki Takao, Shigeo Murayama, Yasushi Iwasaki, Mari Yoshida, Hiroshi Shimizu, Akiyoshi Kakita, Hitoshi Takahashi, Hiroyoshi Suzuki, Hironobu Naiki, Nobuo Sanjo, Hidehiro Mizusawa. Possible iatrogenic transmission of cerebral amyloid angiopathy and subpial A  $\beta$  deposition via cadaveric dura mater grafting. 5th International CAA conference 2016 2016.09.08 Boston, USA
42. Hiroya Kuwahara. Development of nucleic acid therapeutics to target the blood-brain barrier. The 22nd Symposium of Forum for Pharmaceutical Technology Innovation 2016.09.09 Tokyo
43. Hiroya Kuwahara, Takahiro Shimoura, Jindong Song, Kie Yoshida-Tanaka, Tadahaya Mizuno, Tatsuki Mochizuki, Masaki Ohyagi, Kazutaka Nishina, Tetsuya Nagata, Hiroyuki Kusuha, Takanori Yokota. New platform technology to regulate the blood-brain barrier function in vivo. 19th International Symposium on Signal Transduction at the Blood-Brain Barriers 2016.09.15 Copenhagen
44. Taiki Kunieda, Kotaro Yoshioka, Yumiko Sujino, Kie Tanaka, Wenying Piao, Hiroya Kuwahara, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. Pharmacokinetic study of double stranded antisense oligonucleotide: Hetero Chimera Duplex Oligonucleotide (HCDO). 12th Annual Meeting of the Oligonucleotide Therapeutics Society 2016.09.26 Montreal

45. Kotaro Yoshioka, Yumiko Sujino, Taiki Kunieda, Kie Tanaka, Wenying Piao, Hiroya Kuwahara, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. Intracellular mechanisms of microRNA inhibition by a new double-stranded structure for therapeutic oligonucleotide. 12th Annual Meeting of the Oligonucleotide Therapeutics Society 2016.09.27 Montreal
46. Takanori Yokota. DNA/RNA heteroduplex oligonucleotide. 12th Annual Meeting of the Oligonucleotide Therapeutics Society 2016.09.27 Montreal
47. Yohsuke Yagi, Takuya Ohkubo, Hideya Kawaji, Akira Machida, Haruka Miyata, Saori Goda, Sugata Roy, Yoshihide Hayashizaki, Harukazu Suzuki, Takanori Yokota. Small RNA profiling of cerebrospinal fluid exosomes using next-generation sequencing. American Society for Exosomes and Microvesicles 2016 2016.10.21 California
48. Iida S, Kanouchi T, Suzuki M, Sanjo N, Nishida Y, Yokota T. Distribution patterns of nerve conduction abnormality in CIDP. 46th annual meeting of the Japanese Society of Clinical Neurophysiology 2016.10.28 Kohriyama
49. Hiroya Kuwahara, Takahiro Shimoura, Jindong Song, Kie Yoshida-Tanaka, Tadahaya Mizuno, Tatsuki Mochizuki, Kazutaka Nishina, Tetsuya Nagata, Hiroyuki Kusuvara, Takanori Yokota. Novel oligonucleotide to regulate the blood-brain barrier. 3rd International Conference on Biomaterials Science 2016.11.28 Tokyo
50. Takanori Yokota. DNA/RNA heteroduplex oligonucleotide for highly efficient gene silencing. 3rd International Conference on Biomaterials Science. 2016.11.30 Tokyo
51. Noriko Nakamura, Yasutaka Anraku, Hiroya Kuwahara, Takanori Yokota, Kazunori Kataoka. Development of innovative therapeutic nanomachines for intractable neurological diseases. 3rd COINS International Symposium 2016.12.15 Kawasaki
52. Hiroya Kuwahara, Yasutaka Anraku, Kazunori Kataoka, Takanori Yokota. Investigation of delivery mechanism of BBB-crossing nanomachine. 3rd COINS International Symposium 2016.12.15 Kawasaki

## Psychiatry and Behavioral Sciences

### **Professor**

Toru NISHIKAWA, Takayuki OKADA

### **Associate Professor**

Akeo KURUMAJI

### **Junior Associate Professor**

Naoki YAMAMOTO(~2016.6), Takashi TAKEUCHI

### **Assistant Professor**

Daisuke JITOKU, Akihito UEZATO, Hiroo MITSUSADA(~2016.3),  
Yuichiro ABE, Kohei HINO(~2016.3), Hitoshi MUTO(2016.4~),  
Mizue HOB0(Department of Sleep Modulatory Medicine)(~2016.3),  
Takehiro TAMURA(2016.7~), Shunsuke TAKAGI(2016.4~9),  
Takako NAKANOTANI(2016.10~)

### **Medical Staff**

Hitoshi MUTO(~2016.3), Takehiro TAMURA(~2016.6),  
Shunsuke TAKAGI(~2016.3), Ryotaro SAITO(~2016.3),  
Hiroki SHIWAKU, Kohei MISE(2016.4~), Satoshi TAKAHASHI(2016.4~),  
Tomonori TOMISHIGE(2016.4~), Masashi NAGASE(2016.7~),  
Mariko SUNAHARA(2016.12~)

### **Medical Fellow**

Sayuri ISHIWATA(~2016.3)

### **Technical Assistant**

Asami UMINO, Sayuri ISHIWATA(2016.4~12), Masakazu UMINO,  
Momoko KOBAYASHI(~2016.3)

### **Clinical Psychologist**

Kazunori MURAKAMI, Yukari WAKAYAMA, Yasuhiro OKA,  
Miyuki SAITO, Hisashi YAMADA

### **Psychiatric Social Worker**

Yoshifumi KANEKO, Noriko NUMAGUCHI,  
Ayano SOMEYA(~2016.3), Sayaka KOJIMA

### **Graduate Students**

Masakazu UMINO, Kazuo TAKIGUCHI, Momoko KOBAYASHI,  
Megumi GOTO, Ko FURUTA, Shigehiro OGATA, Hidetoshi KINOSHITA,  
Ryotaro SAITO, Koji TAKEDA, Mai KATO, Kanae HAYAKAWA

### **( 1 ) Outline**

Our laboratory is committed to comprehensive research on endogenous psychosis, neurosis, and epilepsy through biological, psychological and social approaches. In collaboration with external research facilities, we are also involved in social psychiatry, child and adolescent psychiatry, and brain imaging studies.

### **( 2 ) Research**

1) Studies in neurochemistry

(i) Molecular genetic studies to clarify the causes and conditions of neuropsychiatric diseases:

Using animal models with psychotic symptom-causing agents, we are involved in a study to isolate new candidate gene clusters associated with the pathogenesis and pathophysiology of neuropsychiatric disorders from the viewpoint of developmental pharmacology. We are examining the effects of candidate gene clusters in patients with neuropsychiatric disorders.

(ii) Studies in biochemical pharmacology to develop new therapeutic methods for neuropsychiatric disorders.

2) Neurophysiological and psychophysiological studies

(i) Studies of neurotransmitter receptor binding in neuropsychiatric disorders with PET:

We are working together with the National Institute of Radiological Sciences to investigate the binding activities of dopamine receptors in various brain areas of the patients with schizophrenia and mood disorders.

(ii) A study of sleep stages and behavior in neuropsychiatric diseases:

A study is being carried out to examine sleep stages and behavior using an originally developed automatic analysis device (polysomnography) in patients with various psychiatric disorders.

A study on brain functioning in psychiatric disorders by using the near-infrared spectroscopy (NIRS): To obtain an insight into biological markers of psychiatric disorders, changes in regional brain functions during psychological tasks are examined by measuring the relative concentrations of oxyhemoglobin using NIRS in combination with MRI in the brain areas of the patients with schizophrenia and mood disorders.

3) Psychopathological studies

We are conducting psychological studies of neuropsychiatric diseases from the aspects of phenomenology, anthropology, and linguistics, while employing a psychotherapeutic approach. Other research activities include a review of basic psychiatric concepts and a basic study for the classification and diagnosis of psychiatric disorders, which are important recent issues. In addition to endogenous psychosis including schizophrenia and manic depressive disorder, we are also involved in psychoanalytic studies of neurosis and borderline personality disorder, which are attracting increasing attention, and psychotherapies for them, as well as pathological research on pathography and art therapy in terms of creativity.

### (3) Education

Following the two-year period of mandatory clinical training, basic professional training in psychiatry will be provided for 6-9 months mainly in the university. In the second term of training, they will acquire knowledge and clinical experience necessary for neuropsychiatrists, and undergo practical training at affiliated medical facilities to become qualified psychiatrists. Undergraduate education, which places emphasis on clinical clerkship training after a systematic series of lecture course and seminar-based classes, is designed to develop students' problem-solving skills, and increase their motivation to learn neuropsychiatry, with support from external facilities.

### (4) Lectures & Courses

In the first term (two years) of postgraduate training, residents will learn basic laboratory procedures and diagnostic techniques, psychotherapy and drug treatment and laws and regulations related to clinical practice, and acquire other general knowledge, all being essential for biologic, psychological, social, and ethical approaches to neuropsychiatric diseases.

### (5) Clinical Services & Other Works

Clinical practice

Approximately eighty new outpatients visit our department every month, about 30% of which are classified as having "mood disorders" (F3) by ICD-10, followed by "neurotic, stress-related, and somatoform disorders" (F4) and "schizophrenia, schizophrenic and paranoid disorders" (F2). We are also actively involved in consultation and liaison psychiatry for inpatients in other departments. Patients with senile dementia, child and adolescent psychiatric disorders, substance dependence, and neurosis requiring intensive psychotherapy are often referred to related and advanced facilities for specialized treatment. Since this facility, the psychiatric department of a general hospital, is used for university education and training, most inpatients are classified as F2, followed by F4 and F3 (ICD-10). We also provide care and treatment for patients with sleep rhythm disorders and neurological disorders, including epilepsy and senile dementia. In addition to drug treatment, we have introduced and provided mECT (modified electroconvulsive therapy) for inpatients, and individual and group psychotherapy for the patients in our psychiatric ward and clinic and day care center in close collaboration with rehabilitation facilities in the community. The day care team consists of a doctor, two nurses, and a psycho-social worker or a clinical psychologist. Day care (partial hospitalization) is the transitional element between inpatient

and outpatient care and its indications have a wide range of psychiatric disorders as follows: schizophrenia, depression, bipolar disorder, adjustment disorder and personality disorders. Each member has the own aim and the team gives care with different types of framework. Our day care team regards the potentiality of group very important and the group process could contribute to therapeutic effect. With this kind of experience, patients could develop their ability to communicate with other people and readapt to social situations.

(i) A study of biological indicators in schizophrenia with eye cameras:

We are not only involved in studies of monozygotic twins, early-onset patients, and children at a high risk in Japan, but also in an international joint research project of the WHO as a center in charge of operations.

## (6) Clinical Performances

Since the 2011 fiscal year, we have been conducting the clinical trial of D-cycloserine for negative symptoms such as avolition, flattening of affect, and poverty of thought and cognitive dysfunction of schizophrenia. We also have been treating patients with schizophrenia with clozapine, which has been approved for refractory schizophrenia. We have started getting systematically involved in the treatment of patients complaining of pain or dysesthesia in oral regions in liaison with the Dental Hospital, which is the unique characteristics of our university. In the 2014 fiscal year, we started the psychoeducational program for patients with bipolar disorder, which focuses on the prevention of relapse. In addition, there is an increasing number of liaison activities for the prevention of delirium especially in the surgical wards, the intervention to patients with suicide attempts in the emergency room, and the mental support for peripartum patients in cooperation with the staffs.

## (7) Publications

### [Original Articles]

1. Mizue Hobo, Akihito Uezato, Mitsunori Nishiyama, Mayumi Suzuki, Jiro Kurata, Koshi Makita, Naoki Yamamoto, Toru Nishikawa. A case of malignant catatonia with idiopathic pulmonary arterial hypertension treated by electroconvulsive therapy. *BMC Psychiatry*. 2016; 16(1); 130
2. Yojiro Umezaki, Anna Miura, Motoko Watanabe, Miho Takenoshita, Akihito Uezato, Akira Toriihara, Toru Nishikawa, Akira Toyofuku. Oral cenesthopathy. *Biopsychosoc Med*. 2016; 10; 20
3. Dean B, Gibbons AS, Boer S, Uezato A, Meador-Woodruff J, Scarr E, McCullumsmith RE. Changes in cortical N-methyl-d-aspartate receptors and post-synaptic density protein 95 in schizophrenia, mood disorders and suicide *Aust N Z J Psychiatry* . 2016; 50(3); 275-283
4. Akeo Kurumaji, Michio Itasaka, Akihito Uezato, Kazuo Takiguchi, Daisuke Jitoku, Mizue Hobo, Kiyotaka Nemoto. A Reduced Gray Matter Volume in Patients with Bipolar II Disorder in a Japanese Sample: a Comparison with Schizophrenia Bipolar Disorder: Open Access. 2016; 2(2);
5. Nishida M, Nakashima Y, Nishikawa T. Slow sleep spindle and procedural memory consolidation in patients with major depressive disorder. *Nat Sci Sleep*. 2016.01; 8; 63-72
6. Okumura Y, Hatta K, Wada K, Takeuchi T, Kishi Y; DELIRIA-J Group. Expert opinions on the first-line pharmacological treatment for delirium in Japan: a conjoint analysis *Int Psychogeriatr*. 2016.06; 28(6); 1041-1050
7. Yoshiike T, Nishida M, Yagishita K, Nariai T, Ishii K, Nishikawa T. Altered Sleep Spindles in Delayed Encephalopathy after Acute Carbon Monoxide Poisoning. *J Clin Sleep Med*. 2016.06; 12(6); 913-915
8. Balu DT, Li Y, Takagi S, Presti KT, Ramikie TS, Rook JM, Jones CK, Lindsley CW, Conn PJ, Bolshakov VY, Coyle JT. An mGlu5-Positive Allosteric Modulator Rescues the Neuroplasticity Deficits in a Genetic Model of NMDA Receptor Hypofunction in Schizophrenia. *Neuropsychopharmacology*. 2016.08; 41(8); 2052-2061
9. Ando K, Soshi T, Nakazawa K, Noda T, Okada T. Risk Factors for Problematic Behaviors among Forensic Outpatients under the Medical Treatment and Supervision Act in Japan. *Front Psychiatry*. 2016.08; 7; 144
10. Ichikura K, Okumura Y, Takeuchi T. Associations of adverse clinical course and ingested substances among patients with deliberate drug-poisoning: a cohort study from an intensive care unit in Japan *PLOS ONE*. 2016.08; 11(8);

**[Books etc]**

1. Nishikawa T. Eds: Yoshimura T, Nishikawa T and Homma H. D-Serine signaling and schizophrenia, Chapter 6, Part II “Physiological Functions and Pathophysiology of D-Serine” , In “D-Amino Acids-Physiology, Metabolism, and Application- “. . Springer, Tokyo, 2016
2. Nishikawa T. Eds: Yoshimura T, Nishikawa T and Homma H. Overview, Chapter 2, Part II “Physiological Functions and Pathophysiology of D-Serine” , In “D-Amino Acids-Physiology, Metabolism, and Application- “. . Springer, Tokyo, 2016

**[Conference Activities & Talks]**

1. Masashi Ohta, Masahito Nakataki , Mai Tamaru, Hiroko Kubo, Chiaki Nakayama, Yasuhiro Funakoshi, Akihito Uezato, Shusuke Numata, Jun-ichi Iga, Satsuki Sumitani, Masafumi Harada, Toru Nishikawa, Tetsuro Ohmori. Functional connectivity of the medial prefrontal cortex in schizophrenia patients treated with D-cycloserine: A resting state functional MRI study. 46th Annual Meeting of the Japanese Society of Neuropsychopharmacology. 2016.07.02 Seoul
2. Sayuri Ishiwata, kotaro Hattori, Daimei sasayama, Toshiya teraishi, Tomoko Miyakawa, Yuuki Yokota, Ryo Matsumura, Toru Nishikawa, Hiroshi Kunugi. Evaluation of plasma and cerebrospinal fluid G72 protein levels and their correlations with psychiatric symptoms in schizophrenia and major depression. 30th CINP World congress of Neuropsychopharmacology 2016.07.04 Seoul
3. Yuichiro Abe. IPSRT- a sleep psychotherapeutic intervention based on social zeitgeber theory of bipolar disorder.. Japanese Society of Sleep Research The 41st Annual Meeting InternationalForum 2016.07.09 Tokyo
4. Watanabe K, Ono S, Wachi T, Yokota K, Otsuka Y, Hirama K, Ando K, Okada T. Preliminary development and validity assessment of a culture-free version of the NRIPS and NCNP’ s Forensic Ability Screening Test(N2-FAST). The 31st International Congress of Psychology (ICP2016) 2016.07.24 Yokohama, Kanagawa (PACIFICO Yokohama)
5. Okada T. Indiscriminate Mass Murders in Japan. The 17th Pacific Rim College of Psychiatrists (PRCP) Scientific Meeting 2016.11.03 Kaohsiung, Taiwan (Kaohsiung Exhibition Center)
6. A. UEZATO, N. YAMAMOTO, D. JITOKU, S. HIRAOKA, E.HARAMO, E. HIRAAKI, Y. IWAYAMA, T. TOYOTA, M. UMINO, A. UMINO, Y.IWATA, K. SUZUKI, M. KIKUCHI, T. HASHIMOTO, N. KANAHARA, A. KURUMAJI, T.YOSHIKAWA, T. NISHIKAWA. Genetic Association between DLG1 gene and schizophrenia. Neuroscience 2016 2016.11.15 San Diego
7. Okada T. Social Safety Nets - Crime Prevention, Correction and Victim Protection of Random Killing Spree cases. 2016 Judicial Protection and Crime Prevention Forum: Strengthen Cooperation and Future Challenges 2016.12.16 Taipei, Taiwan (Hsinchuang United Office Building, Exective Yuan)

**[Awards & Honors]**

1. JSNP Excellent Presentation Award for CINP2016 (Sayuri Ishiwata), The Japanese Society of Neuropsychopharmacology, 2016.07

# Neurosurgery

Professor: Taketoshi Maehara

Associate Professor: Tadashi Nariai

Assistant Professors: Yoji Tanaka and Motoki Inaji

Hospital stuffs:

Takashi Sugawara, Kaoru Tamura, Kazutaka Sumita and Takumi Kudo,

Graduate Students: Masahumi Sasaki, Yoshiteru Obata,

Yousuke Ishii, Sakyō Hirai, Yasuhiro Ueda, Jun Karakama, Takahiro Ogishima, Shihori Hayashi, Kazuhide Shimizu, Don

## (1) Outline

There are various attracting subjects in the field of clinical or basic research. It is essential to acquire the sufficient knowledge and insight into the pathological conditions as well as normal functions of the central nervous system and spinal cord, which will directly benefit for the improvement of clinical results. Main educational purpose of neurosurgery in the graduate course is to provide students opportunity to acquire the proper technique as well as the broad knowledge, and to nurture the mind of exploration.

In the clinical practice, it is important to attach priority to the patients, considering their background. Also in surgery, it is important to preserve the normal brain functions by employing the cutting edge technique. In the research field, it is essential to introduce and develop the latest knowledge and technology by establishing the reciprocal relationship with the other laboratory institutions.

## (2) Research

Brain tumors

1. Analysis of the mechanism of tumor proliferation and infiltration, and its application to treatment
2. Analysis of both proliferative and inhibitory cancer genes in cerebral and spinal tumors
3. Studies of photodynamic therapy, irradiation therapy, agents of chemotherapy, immunotherapy, and inhibition of angiogenesis
4. Development of the multi-modal navigation system integrated with anatomical, hemodynamic, and functional information for brain tumor surgery and evaluate its efficacy.

Vascular diseases in the central nervous system and spinal cord

1. Analysis of pathogenesis of vasospasm after subarachnoid hemorrhage and its application to treatment
2. Studies of circulatory disturbance in ischemic and hemorrhagic diseases, and reversibility of the brain tissue
3. Investigations of pathology of Moyamoya disease and the effects of indirect surgical anastomosis on this entity
4. Solutions of problems in the development of endovascular surgery

Neurotrauma

1. Analysis of cell damage and its reversibility, dynamic simulation in cerebrospinal injury
2. Animal experiments concerning treatment of cerebrospinal injury

Functional neurosurgery

1. Pathological analysis and treatment of temporal lobe epilepsy
2. Analysis of intracellular signal transductions



## Others

1. Studies of human cerebral circulation, metabolism, and functions using PET, MRI/S, and MEG
2. Studies of receptors in the central nervous system using PET
3. Experiments of brain diseases using animal model MRI and PET

**( 3 ) Clinical Services & Other Works**

Neurosurgery is a clinical department dealing with various diseases of central nervous system and spinal cord including tumors, vascular diseases, trauma, congenital malformation, functional disorders, and infection.

**( 4 ) Publications****[Original Articles]**

1. Furuse M, Nonoguchi N, Kuroiwa T, Miyamoto S, Arakawa Y, Shinoda J, Miwa K, Iuchi T, Tsuboi K, Houkin K, Terasaka S, Tabei Y, Nakamura H, Nagane M, Sugiyama K, Terasaki M, Abe T, Narita Y, Saito N, Mukasa A, Ogasawara K, Beppu T, Kumabe T, Nariai T, Tsuyuguchi N, Nakatani E, Kurisu S, Nakagawa Y, Miyatake SI.. A prospective, multicentre, single-arm clinical trial of bevacizumab for patients with surgically untreatable, symptomatic brain radiation necrosis. *Neurooncol Pract.* 2016; 3; 272-280
2. Sugawara T, Maehara T, Nariai T, Aoyagi M, Ohno K. Independent predictors of shunt-dependent normal pressure hydrocephalus after aneurysmal subarachnoid hemorrhage. *Journal of neurosurgical sciences.* 2016; 60; 154-158
3. Atsunobu Tsunoda, Yoji Tanaka, Takanobu Sato, Susumu Kirimura, Ken Kitamura. Vertigo by Breast Cancer Metastasis 33 Years after Treatment. *Intern. Med.* 2016; 55(3); 311-313
4. Miho Watanabe, Haiying Li, Aimee G Kim, Aaron Weilerstein, Anteneta Radu, Marcus Davey, Stavros Loukogeorgakis, Melissa D Sánchez, Kazutaka Sumita, Naoki Morimoto, Masaya Yamamoto, Yasuhiko Tabata, Alan W Flake. Complete tissue coverage achieved by scaffold-based tissue engineering in the fetal sheep model of Myelomeningocele. *Biomaterials.* 2016.01; 76; 133-143
5. Nobuo Sanjo, Satoko Kina, Yukiko Shishido-Hara, Yurie Nose, Satoru Ishibashi, Tetsuya Fukuda, Taketoshi Maehara, Yoshinobu Eishi, Hidehiro Mizusawa, Takanori Yokota. A Case of Progressive Multifocal Leukoencephalopathy with Balanced CD4/CD8 T-Cell Infiltration and Good Response to Mefloquine Treatment. *Internal Medicine.* 2016.01; 55(12); 1631-1635
6. Kazutaka Sumita, Yu-Hua Lo, Koh Takeuchi, Miki Senda, Satoshi Kofuji, Yoshiki Ikeda, Jumpei Terakawa, Mika Sasaki, Hirofumi Yoshino, Nazanin Majd, Yuxiang Zheng, Emily Rose Kahoud, Takehiro Yokota, Brooke M Emerling, John M Asara, Tetsuo Ishida, Jason W Locasale, Takiko Daikoku, Dimitrios Anastasiou, Toshiya Senda, Atsuo T Sasaki. The Lipid Kinase PI5P4K  $\beta$  Is an Intracellular GTP Sensor for Metabolism and Tumorigenesis. *Mol. Cell.* 2016.01; 61(2); 187-198
7. Katsushige Sato, Shihori Hayashi, Motoki Inaji, Yoko Momose-Sato. Oscillations in the embryonic chick olfactory bulb: initial expression and development revealed by optical imaging with a voltage-sensitive dye. *Eur. J. Neurosci.* 2016.02;
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16. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. *Am J Otolaryngol.* 35(3); 402-404

#### [Books etc]

1. Tadashi Nariai. Moyamoya Disease. 2016.01

#### [Conference Activities & Talks]

1. Shoko Hara, Yoji Tanaka, Motoki Inaji, Kenji Ishii, Taketoshi Maehara, Masaaki Hori, Shigeki Aoki and Tadashi Nariai. non-invasive evaluation of CBF, perfusion delay and microstructure of moyamoya disease using new analysis techniques of ASL and diffusion MRI. The 45th Annual Meeting of The Japanese Society of Neuroradiology 2016.02.20 Yamagata, Japan
2. Nariai, T. . Early amelioration of hemodynamics of moyamoya disease by indirect bypass surgery.. Seminar at PLA hospital 2016.02.29 Beijing
3. Nariai, T. . Educational Course: Neuroimaging with PET/MRI. Brain. Perfusion & Permeability Imaging.. ISMRM 2016 2016.05.07 .Singapore.

4. Y. Ishii, T. Nariai, Y. Tanaka, M. Yamashina, H. Satoh, S. Wakabayashi, Y. Suyama, H. Aihara, H. Kajikawa, T. Maehara.. Chronological Evaluation of Cerebral Hemodynamics by Dynamic Susceptibility Contrast Magnetic Resonance Imaging after Indirect Bypass Surgery for Moyamoya Disease. ISMRM 2016 2016.05.11 Singapore
5. Tamura, K., Aoyagi, M., Dong, X., Kobayashi, D., Ando, N., Ogishima, T., Yamamoto, M., Maehara, T.. Involvement of COX2, PGE2 and VEGF in vestibular schwannoma growth and cyst formation after gamma knife stereotactic radiosurgery. The 34rd Annual Meeting of the Japan Society of Brain Tumor Pathology 2016.05.27 Tokyo
6. Takashi Sugawara, Masaru Aoyagi, Masashi Tamaki, Yano Tomoyuki, Atsunobu Tsunoda, Kikuo Ohno, Taketoshi Maehara, Seiji Kishimoto. Extended Orbital Exenteration for Sinonasal Malignancy w/ Orbital Apex Extension. 7th International Congress of the World Federation of Skull Base Societies 2016.06.16 Osaka
7. Takashi Sugawara, MD , PhD, Masaru Aoyagi, MD , PhD, Takahiro Ogishima, MD, Masashi Tamaki, MD , PhD, Tomoyuki Yano, MD , Atsunobu Tsunoda, MD , PhD, Kikuo Ohno, MD , PhD, Taketoshi Maehara, MD , PhD, and Seiji Kishimoto, MD , PhD. Extended orbital exenteration for sinonasal malignancy with orbital apex extension: surgical technique and clinical analysis. 28th Annual Meeting of Japanese Society for Skull Base Surgery 2016.06.16 Osaka
8. Tadashi Nariai. . Progress and remaining questions on surgical treatment of juvenile patients with moyamoya disease. . 8th European-Japanese Cerebrovascular Congress 2016.06.24 Zurich. Switzerland
9. Tadashi Nariai.. Novel imaging technique for CBF and cerebrovascular autoregulation in patients with moyamoya disease.. 8th European-Japanese Cerebrovascular Congress. 2016.06.25
10. Akitaka Muta, Mikio Hiura, Tadashi Nariai, Taketoshi Maehara, Muneyuki Sakata, Keiichi Oda, Jun Toyohara, Kiichi Ishiwata, Kenji Ishii. Regional cerebral blood flow during post exercise hypotension following a single bout aerobic exercise examined by PET and TCD.. OHBM2016 2016.06.29 Geneve
11. Shoko Hara, Yoji Tanaka, Ayana Sawayanagi, Daisu Abe, Yasuhiro Ueda, Shihori Hayashi, Motoki Inaji, Kenji Ishii, Taketoshi Maehara, Tadashi Nariai. The meaning of visual assessment of ASL-MRI may differ between moyamoya disease and atherosclerotic cerebrovascular disease. The 75th Annual Meeting of the Japan Neurosurgical Society 2016.09.29 Fukuoka, Japan
12. Satoshi Kaneko, Takashi Sugawara, Kazutaka Sumita, Motoki Inaji, Yoji Tanaka, Tadashi Nariai, Daisuke Kobayashi, Taketoshi Maehara. The outcome and prognosis of malignant meningiomas in our faculty. The 75th Annual Meeting of the Japan Neurosurgical Society 2016.09.29 Fukuoka, Japan
13. Kei Ito, Kaoru Tamura, Daisuke Kobayashi, Kazutaka Sumita, Masashi Tamaki, Taketoshi Maehara. Long term survivors with glioblastoma; clinical and pathological analysis. The 75th Annual Meeting of the Japan Neurosurgical Society 2016.09.29 Fukuoka, Japan
14. Hara S, Nariai T, Murata S, Tsuruta K, Tanaka Y, Hori M, Maehara T, Aoki S. Neurite orientation dispersion and density imaging revealed the brain microstructural ischemic damage of moyamoya disease. Neuroscience 2016 2016.11.15 San Diego, California, U.S.
15. Shoko Hara, Masaaki Hori, Syo Murata, Ryo Ueda, Misaki Nakazawa, Yoji Tanaka, Taketoshi Maehara, Shigeki Aoki, and Tadashi Nariai.. Neurite Orientation Dispersion and Density Imaging revealed the brain microstructural ischemic damage in patients with moyamoya disease.. SfN2016 2016.11.15 San Diego
16. Kei Ito, Kaoru Tamura, Daisuke Kobayashi, Masashi Tamaki, Kazutaka Sumita, Taketoshi Maehara. Long term survivors with glioblastoma. The 34th Annual Meeting of the Japan Society for Neuro-oncology 2016.12.04 Koufu, Japan

## Endovascular Surgery

Professor Shigeru Nemoto  
Associate Professor Yoshikazu Yoshino  
Assistant Professor Kazunori Miki  
Clinical Fellow Jun Karakama  
Secretary Yoko Yanagida, Hitomi Kuwahara

### ( 1 ) Outline

There are various attracting subjects in the field of clinical or basic research. It is essential to acquire the sufficient knowledge and insight into the pathological conditions as well as normal functions of the vascular system, which will directly benefit for the improvement of clinical results. Main educational purpose of Endovascular Surgery in the graduate course is to provide physicians/students opportunity to acquire the proper technique as well as the broad knowledge, and to nurture the mind of exploration.

### ( 2 ) Research

Our experimental research program is objected to elucidate unsolved questions derived from daily clinical experience. To treat vascular diseases of central nervous system, facial and head-neck legions, we need to understand detailed vascular anatomy, accurate function of these organs and exact pathophysiology of each disease. Our essential research target is the hemodynamics in the vascular diseases of these lesions. Especially we are interested in the integration of the fluid engineering technology into the endovascular field in an effort to open a new frontier of surgical treatment.

### ( 3 ) Education

Course objects of Endovascular Surgery in the graduate course is to acquire the proper technique as well as the basic knowledge of neuroendovascular surgery.

### ( 4 ) Lectures & Courses

Main educational purpose of Endovascular Surgery in the graduate course is to provide students the proper technique as well as the basic knowledge of neuroendovascular surgery.

### ( 5 ) Clinical Services & Other Works

Our major clinical and extracurricular activities are as follows. 1. Endovascular surgery for diseases of central nervous system, facial and head-neck legions. 2. Analysis of cerebrovascular diseases using computational fluid dynamics (CFD). 3. Development of integrated training system for the endovascular surgery.

**( 6 ) Clinical Performances**

Endovascular Surgery is a clinical department dealing with various vascular diseases of central nervous system, spinal cord, facial and head-neck lesions including tumors, congenital malformation, and functional disorders.

**( 7 ) Publications****[Conference Activities & Talks]**

1. Shigeru Nemoto. Characteristics of stent retriever on removing clot —bench test using artificial clot and endovascular simulation system.. AAFITN 12th Asian Australasian Federation of Interventional and Therapeutic Neuroradiology 2016.03.24
2. Evaluating the effect of intra arterial fasudil injection for vasospasm of subarachnoid hemorrhage using the novel angiographic analysis.. 2016.04.11
3. The role and controversy of adjunctive technique for cerebral aneurysm coil embolization. . 2016.04.16
4. Shigeru Nemoto. IC occlusion immediately after coil embolization of Pcom aneurysm.. Cerebrovascular Complications Conference (3C) 2016.06.14 Jacksonhole, Wyoming
5. Shigeru Nemoto. 3D vascular model is valuable in neurointervention.. ESNR (European Society of Neuroradiology) 39th annual meeting 2016.09.15 Beograd,Serbia
6. Efficacy of standard endovascular treatment for paraclinoid aneurysms. 2016.10.01
7. Shigeru Nemoto. Multiple Enterprise stents for vertebral aneurysms.. Siemen Advisory Meeting. 2016.11.05 Tokyo RihgaRoyalHotels
8. Endovascular Revascularization for Chronic Total Occlusion of the Internal Carotid Artery.. 2016.11.24
9. Efficacy of standard endovascular treatment for paraclinoid aneurysms. 2016.11.26

## NCNP Brain Physiology and Pathology

### 1. Staffs and Students

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Yu-ichi GOTO
Collaborative Professor	Hiroshi KUNUGI
Collaborative Professor	Manabu HONDA
Collaborative Professor	Noritaka ICHINOHE
Collaborative Associate Professor	Yoshitsugu AOKI

### (1) Research

#### 1) **Investigation of the molecular machinery underlying brain development.**

(Mikio Hoshino; Department of Biochemistry and Cellular Biology, National Institute of Neuroscience, NCNP)

We are investigating molecular machinery underlying nervous system development, especially focusing on neuron-subtype specification, nervous system regionalization and neuronal migration. We are also interested in human diseases/disorders caused by disorganized development of the nervous system.

The AUTS2 (Autism susceptibility candidate 2) gene has been related to various psychiatric disorders, such as ASD (autism spectrum disorders), schizophrenia, ADHD, and epilepsy. We generated mouse model in which AUTS2 gene was disrupted and analyzed its behavior. We also investigated molecular machinery to specify excitatory and inhibitory neurons in the cerebellum and climbing fiber neurons in the hindbrain.

#### 2) **Molecular genetic and genomic study for intellectual disability in Japan.**

(Yu-ichi Goto, Department of Mental Retardation and Birth Defect Research, National Institute of Neuroscience, NCNP)

One of the major causes of intellectual disability (ID) is based on mutations in the related genes, which are timely and locally expressed in concert with one another in central nervous system. ID is a phenotype derived from the inappropriate expression of these genes. Recent advances in molecular genetics and genome medicine have pushed us on with systematic analysis of ID patients, especially on X-linked ones. In 2013, we investigated the genetic causes and pathophysiology of mitochondrial disease, Rett syndrome, and disease with cortical and white matter dysplasia. We found a unique effect of reactive oxygen species to alteration of heteroplasmy (Ling P, et al. Mol Biol

Cell 2016), differential blocking against nerve and cardiac commitment of iPS cells by mitochondrial respiratory dysfunction (Yokota M, et al. Cell Death Dis 2017) and we studied knock-out mice of Igfbp3 that is downstream of mecp2 associated with Rett syndrome (Dai H, et al. Am J Pathol 2017).

### 3) **Clinical research on mood disorders and schizophrenia**

(Hiroshi Kunugi, Department of Mental Disorder Research, National Institute of Neuroscience, NCNP)

The pathogenesis and physiology of mood disorders and schizophrenia remain elusive, and their biomarkers have not yet been established. Our department, which is in collaboration with the National Center of Neurology and Psychiatry Hospital, is trying to develop objective diagnostic markers for these diseases, employing omics approach, brain imaging, and physiological studies. We also aim to develop new treatment on the basis of key molecules and nutrition. In this year, we published genome-wide database regulating protein levels in the cerebrospinal fluid (Hum Mol Genet, 2016), metabolome finding on postmortem schizophrenia samples (Schizophr Res, 2016), the effect of ketogenic diet on cognitive functions in elderly subjects (Psychopharmacology, 2016), reduced bacterial counts of *Bifidobacterium* and *Lactobacillus* in major depression (J Affect Disord, 2016).

### 4) **Noninvasive study on pathophysiology of human higher brain function.**

(Manabu Honda, Department of Functional Brain Research, National Institute of Neuroscience, NCNP)

We try to reveal various human higher brain functions including sensory, motor, thought, emotion and *KANSEI* functions and pathophysiology underlying higher brain function disorders by integrating multiple noninvasive brain imaging techniques. We also pursue researches for developing a new non-pharmacological therapy by means of the hypersonic effect, that is, sounds containing rich high-frequency component of air vibration above the human audible range activate the deep-lying brain structures including midbrain and diencephalon.

In 2016, as basic researches, we showed that the natural life span of mice prolonged by the enrichment of acoustic environment. As clinical researches, we developed the audio system with ultra-wide range and wide directivity available for clinical use and examined effects of hypersonic sounds on clinical symptoms of BPSD using the originally developed audio system with ultra-wide range and wide directivity.

### 5) **Primate Social brains: their development, anatomy, physiology and patho-physiology.**

(Noritaka Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, NCNP)

We are aiming to elucidate the neural circuit mechanisms of primate social brain using Common Marmoset, new primate model animal. Emphases are on their development, anatomy, physiology and patho-physiology.

This year, we studied mechanisms of material perception, especially glossy materials at medial temporal sulcus (Miyawaka and Banno et al., Front Neural Circuits, 2017).

#### **6) Molecular pathogenesis and therapies for neuromuscular diseases**

(Yoshitsugu Aoki, Department of Molecular Therapy, National, National Institute of Neuroscience, NCNP)

Our research group focuses on genetic neuromuscular diseases including fatal Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS). Our lab integrates molecular, pharmacologic, proteomic and genomic methodologies to clarify the molecular mechanisms of disease pathogenesis and develop novel genetic therapies for the diseases. Especially, we are dedicated to the development of antisense-oligonucleotides based drugs for the diseases in collaboration with Profs. Matthew Wood, Oxford, Kevin Talbot, Oxford, Toshifumi Yokota, Alberta, Fazel Shabanpoor, Melbourne and Samir El-Andaloussi, Karolinska Institutet.

During the academic year 15/16, we have discovered a fundamentally disturbed molecular pathway in C9orf72-related ALS and frontotemporal dementia that identifies a novel extracellular vesicle trafficking, determines the molecular mechanisms and for the first time links ALS pathogenesis with extracellular vesicle biogenesis (Aoki et al., BRAIN, 2017). The goal of the laboratory is a better understanding and improved treatment of fatal and currently untreated neuromuscular diseases.

## **(2) Education**

The nervous system is a very fine and complex organ to elicit the higher brain function and its malfunction causes a variety of neurological and psychiatric disorders in humans. In this course, students learn the structure, development and function of the normal nervous and muscle systems as well as pathology of developmental disorders, psychiatric disorders, neurological diseases and muscle diseases. Students also study the latest progress of advanced remedy for neuromuscular diseases.

## **(3) Publications**



## [Original Articles]

- 1) Hanai S, Sukigara S, Dai H, Owa T, Horike S, Otsuki T, Saito T, Nakagawa E, Ikegaya N, Kaido T, Sato N, Takahashi A, Sugai K, Saito Y, Sasaki M, Hoshino M, Goto Y, Koizumi S, Itoh M. Pathologic active mTOR mutation in brain malformation with intractable epilepsy leads to cell-autonomous migration delay. *American Journal of Pathology*, in press
- 2) Ling P, Rong N, Hatakeyama H, Goto Y, Shibata T, Yoshida M. Reactive oxygen species stimulate mitochondrial allele segregation toward homoplasmy in human cells. *Mol Biol Cell* 27(5): 1684-1693, 2016
- 3) Yokota M, Hatakeyama H, Ono Y, Kanazawa M, Goto Y. Mitochondrial respiratory dysfunction disturbs neuronal and cardiac lineage commitment of human iPSCs. *Cell Death Dis* 8: e2551, 2017
- 4) Dai H, Goto Y, Itoh M. Insulin-like growth factor binding protein-3 deficiency leads to behavior impairment with monoaminergic and synaptic dysfunction. *Am J Pathol* 187(2): 390-400, 2017
- 5) Kuroki N, Kashiwagi H, Ota M, Ishikawa M, Kunugi H, Sato N, Hirabayashi N, Ota T. Brain structure differences among male schizophrenic patients with history of serious violent acts: an MRI voxel-based morphometric study. *BMC Psychiatry*. 2017;17(1):105.
- 6) Hidese S, Hattori K, Sasayama D, Miyakawa T, Matsumura R, Yokota Y, Ishida I, Matsuo J, Noda T, Yoshida S, Teraishi T, Hori H, Ota M, Kunugi H. Cerebrospinal fluid neural cell adhesion molecule levels and their correlation with clinical variables in patients with schizophrenia, bipolar disorder, and major depressive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2017;76:12-18.
- 7) Ikeda M, Takahashi A, Kamatani Y, Okahisa Y, Kunugi H, Mori N, Sasaki T, Ohmori T, Okamoto Y, Kawasaki H, Shimodera S, Kato T, Yoneda H, Yoshimura R, Iyo M, Matsuda K, Akiyama M, Ashikawa K, Kashiwase K, Tokunaga K, Kondo K, Saito T, Shimasaki A, Kawase K, Kitajima T, Matsuo K, Itokawa M, Someya T, Inada T, Hashimoto R, Inoue T, Akiyama K, Tanii H, Arai H, Kanba S, Ozaki N, Kusumi I, Yoshikawa T, Kubo M, Iwata N. A genome-wide association study identifies two novel susceptibility loci and trans population polygenicity associated with bipolar disorder. *Mol Psychiatry*. 2017 Jan 24.
- 8) Matsuo J, Ota M, Hidese S, Hori H, Teraishi T, Ishida I, Hiraishi M, Kunugi H. Sexually dimorphic deficits of prepulse inhibition in patients with major depressive disorder and their relationship to symptoms: A large single ethnicity study. *J Affect Disord*. 2017;211:75-82.



- 9) Sasayama D, Hattori K, Ogawa S, Yokota Y, Matsumura R, Teraishi T, Hori H, Ota M, Yoshida S, [Kunugi H](#). Genome-wide quantitative trait loci mapping of the human cerebrospinal fluid proteome. *Hum Mol Genet*, in press
- 10) Ota M, Sato N, Hidese S, Teraishi T, Maikusa N, Matsuda H, Hattori K, [Kunugi H](#). Structural differences in hippocampal subfields among schizophrenia patients, major depressive disorder patients, and healthy subjects. *Psychiatry Res*. 2017;259:54-59.
- 11) Kasahara T, Ishiwata M, Kakiuchi C, Fuke S, Iwata N, Ozaki N, [Kunugi H](#), Minabe Y, Nakamura K, Iwata Y, Fujii K, Kanba S, Ujike H, Kusumi I, Kataoka M, Matoba N, Takata A, Iwamoto K, Yoshikawa T, Kato T. Enrichment of deleterious variants of mitochondrial DNA polymerase gene (POLG1) in bipolar disorder. *Psychiatry Clin Neurosci*, in press
- 12) Setoyama D, Kato TA, Hashimoto R, [Kunugi H](#), Hattori K, Hayakawa K, Sato-Kasai M, Shimokawa N, Kaneko S, Yoshida S, Goto YI, Yasuda Y, Yamamori H, Ohgidani M, Sagata N, Miura D, Kang D, Kanba S. Plasma Metabolites Predict Severity of Depression and Suicidal Ideation in Psychiatric Patients-A Multicenter Pilot Analysis. *PLoS One*. 2016;11(12):e0165267.
- 13) Ninomiya-Baba M, Matsuo J, Sasayama D, Hori H, Teraishi T, Ota M, Hattori K, Noda T, Ishida I, Shibata S, [Kunugi H](#). Association of body mass index-related single nucleotide polymorphisms with psychiatric disease and memory performance in a Japanese population. *Acta Neuropsychiatr*, in press
- 14) Fujii T, Hattori K, Miyakawa T, Ohashi Y, Sato H, [Kunugi H](#). Metabolic profile alterations in the postmortem brains of patients with schizophrenia using capillary electrophoresis-mass spectrometry. *Schizophr Res*, in press
- 15) Ota M, Matsuo J, Ishida I, Hattori K, Teraishi T, Tonouchi H, Ashida K, Takahashi T, [Kunugi H](#). Effect of a ketogenic meal on cognitive function in elderly adults: potential for cognitive enhancement. *Psychopharmacology (Berl)*. 2016;233(21-22):3797-3802.
- 16) Yoshimura A, Kawamata M, Yoshioka Y, Katsuda T, Kikuchi H, Nagai Y, Adachi N, Numakawa T, [Kunugi H](#), Ochiya T, Tamai Y. Generation of a novel transgenic rat model for tracing extracellular vesicles in body fluids. *Sci Rep*. 2016;6:31172.
- 17) Matsuo J, Ota M, Hori H, Hidese S, Teraishi T, Ishida I, Hiraishi M, [Kunugi H](#). A large single ethnicity study of prepulse inhibition in schizophrenia: Separate analysis by sex focusing on effect of symptoms. *J Psychiatr Res*. 2016;82:155-62.
- 18) Ota M, Hori H, Sato N, Yoshida F, Hattori K, Teraishi T, [Kunugi H](#). Effects of ankyrin 3 gene risk variants on brain structures in patients with bipolar disorder and healthy subjects. *Psychiatry Clin Neurosci*. 2016 Nov;70(11):498-506.

- 19) Odaka H, Numakawa T, Yoshimura A, Nakajima S, Adachi N, Ooshima Y, Inoue T, Kunugi H. Chronic glucocorticoid exposure suppressed the differentiation and survival of embryonic neural stem/progenitor cells: Possible involvement of ERK and PI3K/Akt signaling in the neuronal differentiation. *Neurosci Res*. 2016;113:28-36.
- 20) Hidese S, Ota M, Wakabayashi C, Noda T, Ozawa H, Okubo T, Kunugi H. Effects of chronic l-theanine administration in patients with major depressive disorder: an open-label study. *Acta Neuropsychiatr*. 2016 Jul 11:1-8.
- 21) Aizawa E, Tsuji H, Asahara T, Takahashi T, Teraishi T, Yoshida S, Ota M, Koga N, Hattori K, Kunugi H. Possible association of Bifidobacterium and Lactobacillus in the gut microbiota of patients with major depressive disorder. *J Affect Disord*. 2016;202:254-7.
- 22) Yoshimura A, Numakawa T, Odaka H, Adachi N, Tamai Y, Kunugi H. Negative regulation of microRNA-132 in expression of synaptic proteins in neuronal differentiation of embryonic neural stem cells. *Neurochem Int*. 2016;97:26-33.
- 23) Hori H, Koga N, Hidese S, Nagashima A, Kim Y, Higuchi T, Kunugi H. 24-h activity rhythm and sleep in depressed outpatients. *J Psychiatr Res*. 2016;77:27-34.
- 24) Hori Y, Ogura J, Ihara N, Higashi T, Tashiro T, Honda M, Hanakawa T: Development of a removable head fixation device for longitudinal behavioral and imaging studies in rats. *J Neurosci Methods*, 264: 11-15, 2016.
- 25) Yamashita Y, Fujimura T, Katahira K, Honda M, Okada M, and Okanoya K: Context sensitivity in the detection of changes in facial emotion. *Scientific Reports*, 6: 27798-27798, 2016.
- 26) Miyakawa N, Banno T, Abe H, Tani T, Suzuki W, and Ichinohe N. Representation of Glossy Material Surface in Ventral Superior Temporal Sulcal Area of Common Marmosets. *Front. Neural Circuits*, 11, 17.2017.
- 27) Echigoya Y, Nakamura A, Nagata T, Urasawa N, Kuraoka M, Saito T, Aoki Y, Kole R, Partridge T, Takeda S, Yokota T. Effects of systemic multiexon skipping with peptide-conjugated morpholinos in the heart of a dog model of Duchenne muscular dystrophy. **Proc Natl Acad Sci U S A**. 2017, in press.
- 28) Aoki Y, (corresponding author) Manzano R, Lee Y, Aoki M, Takeda S, Fukuda M, Talbot K, Wood MJA. C9ORF72 and RAB7L1 regulate vesicle trafficking in Amyotrophic Lateral Sclerosis and Frontotemporal Dementia. **BRAIN**. 23 Feb 2017.
- 29) Suzuki H, Aoki Y, Kameyama T, Saito T, Masuda S, Tanihata J, Nagata T, Mayeda A, Takeda S, Tsukahara T. Endogenous Multiple Exon Skipping and Back-Splicing

- at the DMD Mutation Hotspot. **Int J Mol Sci.** 2016 Oct 13;17(10).
- 30) Nakamura A, Fueki N, Shiba N, Motoki H, Miyazaki D, Nishizawa H, Echigoya Y, Yokota T, Aoki Y, Takeda S. Deletion of exons 3-9 encompassing a mutational hot spot in the DMD gene presents an asymptomatic phenotype, indicating a target region for multiexon skipping therapy. **J Hum Genet.** 2016 Jul;61(7):663-7.
- 31) Kuraoka M, Kimura E, Nagata T, Okada T, Aoki Y, Tachimori H, Yonemoto N, Imamura M, Takeda S. Serum Osteopontin as a Novel Biomarker for Muscle Regeneration in Duchenne Muscular Dystrophy. **Am J Pathol.** 2016 May;186(5):1302-12.

# Immune Regulation

Professor Hajime Karasuyama, M.D., Ph.D.

Junior Associate Professor Yoshinori Yamanishi, M.D., Ph.D.

Assistant Professor Shingo Sato, Ph.D.

Assistant Professor Soichiro Yoshikawa, Ph.D.

## ( 1 ) Research

- 1) Role of basophils in immune disorders such as allergy
- 2) Role of basophils in protective immunity against infections
- 3) in vivo imaging of basophil-mediated immune responses

## ( 2 ) Education

Main objective of the immunology course for undergraduate students is to provide them the basic ideas how the immune system works and is regulated in various physiological and pathological settings including infections, cancer, autoimmune and allergic disorders, and organ transplantation. In the immunology course for graduate students, they study molecular mechanisms underlying the development of immune diseases including allergy and parasitic infection, by employing advanced technology in molecular biology, biochemistry, cellular biology and developmental engineering.

## ( 3 ) Publications

### [Original Articles]

1. Adachi, T., Kakuta, S., Aihara, Y., Kamiya, T., Watanabe, Y., Osakabe, N., Hazato, N., Miyawaki, A., Yoshikawa, S., Usami, T., Karasuyama, H., Kimoto-Nira, H., Hirayama, K., M Tsuji, N.. Visualization of Probiotic-Mediated Ca(2+) Signaling in Intestinal Epithelial Cells In Vivo. *Front Immunol.* 2016; 7; 601
2. Yoshikawa, S., Usami, T., Kikuta, J., Ishii, M., Sasano, T., Sugiyama, K., Furukawa, T., Nakasho, E., Takayanagi, H., Tedder, T. F., Karasuyama, H., Miyawaki, A., Adachi, T.. Intravital imaging of Ca(2+) signals in lymphocytes of Ca(2+) biosensor transgenic mice: indication of autoimmune diseases before the pathological onset. *Sci Rep.* 2016.01; 6; 18738
3. Matsukawa, T., Izawa, K., Isobe, M., Takahashi, M., Maehara, A., Yamanishi, Y., Kaitani, A., Okumura, K., Teshima, T., Kitamura, T., Kitaura, J.. Ceramide-CD300f binding suppresses experimental colitis by inhibiting ATP-mediated mast cell activation. *Gut.* 2016.05; Epub ahead of print;
4. Baba, T., Tanabe, Y., Yoshikawa, S., Yamanishi, Y., Morishita, S., Komatsu, N., Karasuyama, H., Hirao, A., Mukaida N.. MIP-1  $\alpha$ /CCL3-expressing basophil-lineage cells drive the leukemic hematopoiesis of chronic myeloid leukemia in mice. *Blood.* 2016.05; 127(21); 2607-2617
5. Schiechl, G., Hermann, F.J., Rodriguez Gomez, M., Kutzi, S., Schmidbauer, K., Talke, Y., Neumayer, S., Goebel, N., Renner, K., Brühl, H., Karasuyama, H., Obata-Ninomiya, K., K Utpatel, K., Evert, M., Hirt, S.W., Geissler, E.K., Fichtner-Feigl, S., Mack, M.. Basophils Trigger Fibroblast Activation in Cardiac Allograft Fibrosis Development. *Am. J. Transplant..* 2016.09; 16(9); 2574-2588

6. Horiguchi, K., Yoshikawa, S., Saito, A., Haddad, S., Ohta, T., Miyake, K., Yamanishi, Y., Karasuyama, H.. Real-time imaging of mast cell degranulation in vitro and in vivo. *Biochem. Biophys. Res. Commun.* 2016.10; 479(3); 517-522
7. Kojima, T., Tsuchiya, K., Ikemizu, S., Yoshikawa, S., Yamanishi, Y., Watanabe, M., Karasuyama, H.. Novel CD200 homologues iSEC1 and iSEC2 are gastrointestinal secretory cell-specific ligands of inhibitory receptor CD200R. *Sci Rep.* 2016.11; 6; 36457
8. Venturelli, N., Lexmond, W. S., Ohsaki, A., Nurko, S., Karasuyama, H., Fiebiger, E., Oyoshi, M. K.. Allergic skin sensitization promotes eosinophilic esophagitis through the IL-33-basophil axis in mice. *J. Allergy Clin. Immunol.* 2016.11; 138(5); 1367-1380.e5
9. Iki, M., Tanaka, K., Deki, H., Fujimaki, M., Sato, S., Yoshikawa, S., Yamanishi, Y., Karasuyama, K.. Basophil tryptase mMCP-11 plays a crucial role in IgE-mediated, delayed-onset allergic inflammation in mice. *Blood.* 2016.12; 128(25); 2909-2918

#### [Misc]

1. Yamanishi, Y., Karasuyama, H.. Basophils and mast cells in immunity and inflammation. *Semin Immunopathol.* 2016.09; 38(5); 535-537
2. Yamanishi, Y., Karasuyama, H.. Basophil-derived IL-4 plays versatile roles in immunity. *Semin Immunopathol.* 2016.09; 38(5); 615-622

#### [Conference Activities & Talks]

1. Nagao, T., Takahashi, S., Kawawa, M., Miyake, K., Yoshikawa, S., Sato, S., Yamanishi, Y., Karasuyama, H.. Molecular properties of carrier protein in allergen are critical for the development of IgE- and basophil-mediated allergic inflammation in the skin.. *Environment controlling normal and diseased hematopoietic and immune systems* 2016.03.02 Yokohama, Japan
2. Karasuyama, H.. Emerging roles of basophils and IgE in allergy and immunity.. *FASEB Science Research Conference* 2016.07.26 Florida
3. Yoshikawa, S., Oh-hora, M., Adachi, T., Yamanishi, Y., karasuyama, H. . STIM1/2 plays essential role in basophil activation and development of IgE-mediated chronic allergic inflammation. . *International Congress of Immunology* 2016 2016.08.21 Melbourne, Australia
4. Nagao, T., Takahashi, S., Kawawa, M., Miyake, K., Yoshikawa, S., Yamanishi, Y., Karasuyama, H.. Sugar modification of carrier protein in allergen determines the magnitude of IgE- and basophil-mediated allergic inflammation.. *International Congress of Immunology* 2016 2016.08.23 Melbourne, Australia
5. Tsutsui, H., Yamanishi, Y., Yoshikawa, S., Sato, S., Karasuyama, H.. mMCP-8, a basophil specific protease, triggers an inflammatory response by stimulating fibroblasts to produce chemokines. *The 16th International Congress of Immunology.. International Congress of Immunology* 2016 2016.08.23 Melbourne, Australia
6. Karasuyama, H.. Emerging roles of basophils in acquired protective immunity to tick infestation.. *XXV International Congress of Entomology* 2016.09.29 Orland
7. Yoshikawa, S., Oh-hora, M., Yamanishi, Y., Karasuyama, H.. STIM2 plays essential role in cytokine-induced IL-4 production in basophil.. *The 45th Annual Meeting of The Japanese Society for Immunology* 2016.12.05 Okinawa, Japan
8. Iki, M., Tanaka, K., Deki, H., Nagao, T., Horibe, M., Sato, S., Yoshikawa, S., Yamanishi Y., Karasuyama, H.. Basophil-selective mMCP-11 plays crucial roles in the development of IgE-mediated chronic allergic inflammation in the skin.. *The 45th Annual Meeting of the Japanese Society for Immunology* 2016.12.06 Okinawa
9. Miyake, K., Shiozawa, N., Nagao, T., Kawawa, M., Yoshikawa, S., Yamanishi, Y., Karasuyama, H.. Basophils gain the capacity of antigen presentation by acquiring MHC class II molecules from dendritic cells through trogocytosis.. *The 45th Annual Meeting of the Japanese Society for Immunology* 2016.12.06 Okinawa

10. Karasuyama, H.. Emerging roles of basophils in allergy and immunity.. 41th JSID Annual Meeting 2016.12.09 Sendai

**[Awards & Honors]**

1. Best Presentation Award Winners 2016(The 45th Annual Meeting of the Japanese Society for Immunology) (Misako Iki), The Japanese Society for Immunology, 2016.12

## Molecular Virology

Professor : Shoji YAMAOKA

Project Professor : Eiji IDO

Assistant Professor: Hiroaki TAKEUCHI, Takeshi YOSHIDA,  
Momoe ITSUMI

Medical Technologist : Yoshio INAGAKI

Secretary : Kumiko THORPE-MATSUI

-Students-

Ph.D. course: Miho OHSAKO

Hideki SAITO

Hirona ICHIKAWA

Naoto SUZUKI

NDZINU JERRY KWAME

AZIATI ISHMAEL DZIGBDRDI KWASI

MXWELL MAMFE SAKYIAMAH

Master course: Maiko TAKAGI

Tsuyoshi HORIKAWA

Kensuke WADA

Chie MASAKI

Saki HASHIMOTO

Takuya HYODO

### ( 1 ) Outline

Microbiology covers several aspects of bacteriology, immunology and virology. Through the studies on various microbes it is expected to understand host-parasite relationship and mechanisms of pathogenicity. Unlike the past, microbiology has rapidly been drawn to the center of the biological stage.

Our laboratory mainly deals with viral oncogenesis and immunodeficiency in humans. Several projects are carried out with particular emphasis on investigation into the mechanisms of viral replication and pathogenesis induced by human retroviruses (HIV-1 and HTLV-I) and human herpes viruses. The purpose of many of the studies being undertaken is to identify critical events and molecules responsible for the efficient replication of these viruses, and in case of human retroviruses, those for transformation or destruction of normal lymphocytes. Virological, immunological and molecular approaches are being applied for this purpose.

### ( 2 ) Research

The following studies have been extensively carried out in our laboratory with various biological and molecular biological techniques:

- Pathogenesis of HIV and HTLV (mutation, virulence,

apoptosis, polymorphism).

- Studies on signal transduction pathways targeted by viral proteins.
- Molecular cloning by genetic approaches of components essential for virus replication in mammalian cells.

### (3) Education

We are engaged in the lectures and practices on the basic aspects of infections for the 2nd year medical students and in the pre-clinical clerkship for the 4th year medical students. Students are also accepted in the Project Semester Program. Graduate course students carry out research on virology and oncology in the laboratory and join seminars and progress meetings.

### (4) Lectures & Courses

Students can learn the structure, replication, function and genetics of micro-organisms as well as the host-pathogen interactions based on the front-line molecular and microbiological sciences.

### (5) Publications

#### [Original Articles]

1. Ito H, Tanaka S, Akiyama Y, Shimada S, Adikrisna R, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Arii S, Yamaoka S, Tanabe M. Dominant Expression of DCLK1 in Human Pancreatic Cancer Stem Cells Accelerates Tumor Invasion and Metastasis. *PLoS ONE*. 2016.01; 11(1); e0146564
2. Masaaki Sugimoto · Kenichi Kohashi · Momoe Itsumi · Masaki Shiota · Tatsuro Abe · Yuichi Yamada · Kentaro Kuroiwa · Seiji Naito. Epithelial to Mesenchymal Transition in Clear Cell Renal Cell Carcinoma with Rhabdoid Features *J Natl Cancer Inst*. 2016.02; 108(7);
3. Momoe Itsumi · Masaki Shiota · Ario Takeuchi · Eiji Kashiwagi · Junichi Inokuchi · Katsunori Tatsugami · Shunichi Kajioaka · Takeshi Uchiyumi · Seiji Naito · Masatoshi Eto · Akira Yokomizo. Equol inhibits prostate cancer growth via degradation of the androgen receptor by Skp2 2016.04;
4. Kwofie KD, Tung NH, Suzuki-Ohashi M, Amoa-Bosompem M, Adegle R, Sakyamah MM, Ayertey F, Owusu KB, Tuffour I, Atchoglo P, Frempong KK, Anyan WK, Uto T, Morinaga O, Yamashita T, Aboagye F, Appiah AA, Appiah-Opong R, Nyarko AK, Yamaguchi Y, Edoh D, Koram KA, Yamaoka S, Boakye DA, Ohta N, Shoyama Y, Ayi I. . Antitrypanosomal Activities and Mechanisms of Action of Novel Tetracyclic Iridoids from *Morinda lucida* Benth. *Antimicrob Agents Chemother*.. 2016.05; 60(6); 3283-3290
5. Masaki Shiota · Naohiro Fujimoto · Kenjiro Imada · Akira Yokomizo · Momoe Itsumi · Ario Takeuchi · Hidetoshi Kuruma · Junichi Inokuchi · Katsunori Tatsugami · Takeshi Uchiyumi · Yoshinao Oda ·Seiji Naito. Potential Role for YB-1 in Castration-Resistant Prostate Cancer and Resistance to Enzalutamide Through the Androgen Receptor V7 *Pathobiology*.. 2016.05; 83(6); 277-286
6. Kofi D Kwofie, Nguyen Huu Tung, Mitsuko Suzuki-Ohashi, Michael Amoa-Bosompem, Richard Adegle, Maxwell M Sakyamah, Frederick Ayertey, Kofi Baffour-Awuah Owusu, Isaac Tuffour, Philip Atchoglo, Kwadwo K Frempong, William K Anyan, Takuhiro Uto, Osamu Morinaga, Taizo Yamashita, Frederic Aboagye, Alfred A Appiah, Regina Appiah-Opong, Alexander K Nyarko, Yasuchika Yamaguchi, Dominic Edoh, Kwadwo A Koram, Shoji Yamaoka, Daniel A Boakye, Nobuo Ohta, Yukihiro Shoyama, Irene Ayi. Antitrypanosomal Activities and Mechanisms of Action of Novel Tetracyclic Iridoids from *Morinda lucida* Benth. *Antimicrob. Agents Chemother*.. 2016.06; 60(6); 3283-3290
7. Shiota M, Fujimoto N, Itsumi M, Takeuchi A, Inokuchi J, Tatsugami K, Yokomizo A, Kajioaka S, Uchiyumi T, Eto M.. Gene polymorphisms in antioxidant enzymes correlate with the efficacy of androgen-deprivation therapy for prostate cancer with implications of oxidative stress *Ann Oncol*.. 2016.12;



8. Ito H, Tanaka S, Akiyama Y, Shimada S, Adikrisna R, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Arie S, Yamaoka S, Tanabe M. . Dominant Expression of DCLK1 in Human Pancreatic Cancer Stem Cells Accelerates Tumor Invasion and Metastasis. PLoS One. . 11(1); e0146564

**[Conference Activities & Talks]**

1. Hiroaki Takeuchi. The timing and triggering of HIV-1 uncoating: the essential role of MELK for optimal capsid core disassembly.. U.S-Japan Cooperative Medical Sciences Program (USJCMSP) AIDS Panel Meeting 2016.01.13 Washington DC, USA
2. Momoe Itsumi, Masaki Shiota, Akira Yokomizo, Eiji Kashiwagi, Ario Takeuchi, Kenjiro Imada, Katsunori Tatsugami, Junichi Inokuchi, Takeshi Uchiumi, Shunichi Kajioka, Seiji Naito, Masatoshi Etoh. Serotonin receptor antagonist inhibits prostate cancer progression. The 75th Annual Meeting of the Japanese Cancer Association 2016.10.06 Pacifico Yokohama
3. Takeshi Yoshida, Akiko Hamano, Hiroaki Takeuchi, Shoji Yamaoka. Identification of a new host factor inhibiting HIV-1 replication. 2016.11.24 Kagoshima
4. Hiroaki Takeuchi. Host factors regulated HIV-1 capsid disassembly. The 30th Annual Meeting of the Japanese Society for AIDS Research 2016.11.26 Kagoshima, JAPAN

# Immunotherapeutics

Professor: Mari KANNAGI

Associate Professor: Takao MASUDA

Assistant Professor: Atsuhiko HASEGAWA (Lecturer)

Assistant Professor: Yoshiko NAGANO

Visiting Researcher:: Sayaka ITO

Graduate Student: Yoko SATO, Satomi ANDO, Tatsuro TAKAHATA, Yuji MURAKAMI, Leila SAWADA, Riho KOGA

## (1) Outline

Our research area is in between clinical and basic science, involving immunology, microbiology, and oncology. Persistent viral infection causes various diseases by inducing immunodeficiency, malignancy, autoimmunity, and inflammation. Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS), and Human T-cell leukemia virus type-I (HTLV-I) causes adult T-cell leukemia (ATL) and various chronic inflammatory autoimmune-like diseases. To understand mechanisms of these diseases, investigation on host immunity is indispensable. Immune responses are usually protective but sometimes harmful for the host, and are important determinants for disease manifestation. The goal of our research is elucidation of the role of host immunity in the diseases in order to develop effective immunotherapy. We also investigate intracellular mechanisms of viral replication to target direct molecules for therapy.

### Research Subjects

1. Analysis of immunological risks for ATL development in HTLV-I-carriers.
2. Development of anti-tumor vaccine against ATL.
3. Immunological and molecular mechanism of HTLV-1-induced leukemogenesis.
4. Molecular mechanism of HIV replication especially related to HIV-1 integrase.
5. Experiments based on gene therapy to suppress HIV-1 replication.

## (2) Research

① Development and clinical study of anti-ATL vaccine therapy with Tax peptide-pulsed autologous dendritic cells.

Adult T-cell leukemia/lymphoma (ATL) is a human T-cell leukemia virus type-I (HTLV-I)-infected T-cell malignancy with poor prognosis. We developed a novel therapeutic vaccine designed to augment an HTLV-I Tax-specific cytotoxic T lymphocyte (CTL) response that has been implicated in anti-ATL effects, and conducted a pilot study to investigate its safety and efficacy in collaboration of Tokyo Medical and Dental University, National Kyushu Cancer Center, and Kyushu University. The vaccine consists of autologous dendritic cells pulsed with Tax peptides corresponding to the CTL epitopes. Two of three patients administered with the vaccine achieved partial and complete remission without severe side effects. The clinical outcomes of this pilot study indicate that the Tax peptide-pulsed DC vaccine is a safe and promising immunotherapy for ATL (Suehiro, Y., Hasegawa, A., et al. *Brit J Haematol.* 169: 356-367, 2015. doi: 10.1111/bjh.13302) .

② Involvement of innate immune response in HTLV-1 pathogenesis.

The constitutive activation of NF  $\kappa$  B plays an important role in leukemogenesis of adult T-cell leukemia/lymphoma (ATL) caused by human T-cell leukemia virus type-1 (HTLV-1). Although HTLV-1 Tax is known to activate

NF  $\kappa$  B, ATL cells exhibit NF  $\kappa$  B activities even in the absence of Tax expression, the mechanism of which has been a long-puzzling question. We demonstrate that both double-stranded RNA-dependent protein kinase (PKR) and anti-sense HTLV-1 transcripts are involved in the constitutive NF  $\kappa$  B activation in Tax-negative ATL cells. Our findings elucidate a novel Tax-independent mechanism of NF  $\kappa$  B activation underlying HTLV-1 leukemogenesis in which host antiviral responses are involved (Kinpara, S., et al. *Leukemia*, 29:1425-1444, 2015. doi: 10.1038/leu.2015.1).

### ( 3 ) Education

① For under graduate students of the medical school, we participate in education of basic immunology I, and II, the project semester, and the preclinical clerkship.

② Graduate students are trained for basic skills in the field of immunology and virology to handle biohazard materials. We provide the opportunity to research for mechanisms of the retro-virus-mediated diseases and development of immunological therapeutics. All the staffs and students participate in maintenance of the laboratory and periodical seminars to discuss about their own studies and keep up with the latest knowledge and information in the area.

### ( 4 ) Lectures & Courses

We always think of the clinical significance of the results of basic research. We try to find an effective therapy by approaching from basic research to understand the disease mechanisms and solve the problem. The disease mechanisms that we study include leukemogenesis, inflammation, immunosuppression, and autoimmunity in persistent virus infection. Through these studies, we contribute to clinical therapies as well as medical sciences.

### ( 5 ) Clinical Services & Other Works

We developed an anti-ATL immunotherapy (Tax peptide-pulsed dendritic cell vaccine), which is under clinical studies in collaboration with National Kyushu Cancer Center and Kyushu University. We evaluate anti-tumor and anti-virus T-cell responses in HTLV-1-infected patients with or without various therapies including the immunotherapy and hematopoietic stem cell transplantation, in response to requests from clinical doctors.

### ( 6 ) Publications

#### [Original Articles]

1. Takahata, T., Takeda, E., Tokunaga, K., Yokoyama, M., Huang, Y-L., Hasegawa, A., Shioda, T., Sato H, Kannagi, M., Masuda T. Critical Contribution of Tyr15 in the HIV-1 Integrase (IN) in Facilitating IN Assembly and Nonenzymatic Function through the IN Precursor Form with Reverse Transcriptase. *J. Virol.* 2016; 90; 4563-4578
2. Masako Nomaguchi, Naoya Doi, Yosuke Sakai, Hirotaka Ode, Yasumasa Iwatani, Takamasa Ueno, Yui Matsumoto, Yasuyuki Miyazaki, Takao Masuda, Akio Adachi. Natural Single-Nucleotide Variations in the HIV-1 Genomic SA1prox Region Can Alter Viral Replication Ability by Regulating Vif Expression Levels. *J. Virol.* 2016.05; 90(9); 4563-4578

# Cellular and Environmental Biology

Associate Professor Masayuki HARA

## (1) Research

Research Subjects

- 1) Reaction mechanisms of cellular protection systems against environmental oxidation stresses.
- 2) Modifying mechanisms in higher order structure of chromatin in cellular differentiation.
- 3) Shifting mechanisms in proteome profiles of cell organelle between pre and post conditions in environment, cell differentiation, disease, or drug exposure.

## (2) Education

Living organisms were influenced their life by environment and adapted themselves to it, however, they formed environment and affected it. In other words, the species that cannot fit the changing environment were fallen and replaced by the new species which could adapt itself to. The organisms are as a part of the global environment, so it is thought that the individual structure and working of them are necessary environmental measures for their survival. It may be said that it is excessive suddenness of the change that human activity is environmentally-impacted now.

Main objective of cellular and environmental biology in the graduate course is to provide students opportunity to study the reaction and adaptation of the organisms for the environmental change at cellular level, to consider hazardous property, toxicity, or physiological activity of environmental (or man-made) factor, and to mention the biotechnical action to the environmental problems.

## (3) Publications

### [Original Articles]

1. Masayuki Hara, Kiyoshi Nomura. A Model Calculation and its Interpretation of the Radiation Effects Based on the Ionization of Intracellular Water Molecules. Japanese Journal of Radiation Safety Management. 2016.11; 15(2); 164-172

## Biodefense Research

Professor Toshiaki Ohteki  
Junior Associate Professor (to Dec. 14) Nobuyuki Onai  
Adjunct Lecturer (from Dec.15) Nobuyuki Onai  
Adjunct Lecturer (JST PREST) Taku Sato  
Assistant Professor Yusuke Nakanishi  
Junior Assistant Professor Junpei Asano  
Junior Assistant Professor Mihoko Kajita  
Research Fellow (SONY) Tomohiko Nakamura  
Research Fellow Shunsuke Kawamura  
Graduate Student Minako Inazawa  
Graduate Student Kana Minamide  
Graduate Student Shuhei Imamura  
Research Technician Shoko Kuroda  
Research Technician Kisho Shiseki  
Research Technician Rumiko Nakamura  
Secretarial Assistant Hisako Kamioka

### (1) Outline

Our research projects focus on understanding the dynamic maintenance and transfiguration of homeostasis in the living body. Our goal is to define the homeostasis mechanism under conditions of health and disease. To accomplish this goal, we are trying to clarify the molecular basis of induction and failure of homeostasis by focusing on immune cells in particular mononuclear phagocytes (dendritic cells and macrophages), tissue stem cells, and their functional interplay in the immunological and non-immunological organs, such as skin and intestine. On the basis of our findings, we will further pursue our research in the hope of developing new rational therapies for prevention and treatment of disease.

### (2) Research

#### 1. Research on mononuclear phagocytes

##### 1) Discovery of a novel source of mononuclear phagocytes

In 1968, Drs. Ralph van Fruth and Zanvil A. Cohn proposed a concept of mononuclear phagocytes that include monocytes and macrophages. In 1973, Dr. Ralph Steinman discovered dendritic cells (DCs), thereby redefining the mononuclear phagocytes as a population consisting of monocytes, macrophages and also DCs. It has been recently continuing epoch-making discoveries in the field of mononuclear phagocytes and their functions are now beyond classical Immunology and rather extend to broad life phenomenon, e.g. tissue development/regeneration, wound-healing, and establishment of various inflammatory diseases.

DCs consist of conventional DCs (cDCs) and plasmacytoid DCs (pDCs), both of which play critical regulatory roles in the immune system. cDCs exhibit prominent antigen-presenting ability, whereas pDCs are characterized by their capacity to produce large amounts of type I interferons (IFNs). We have discovered the DC progenitors in the mouse bone marrow, and named common DC progenitors (CDPs) (Immunity 2013; Nat Immunol 2007). Interestingly, CDPs are divided into 2 subpopulations. One is M-CSF receptor (R)+ CDPs mainly producing cDCs, and the other M-CSFR-CDPs producing a large number of pDCs. In addition to CDPs, common monocyte/macrophage progenitors, cMoP, identified in the mouse bone marrow and spleen by other group in

2013.

Based on these achievements in mouse, we have been trying to identify human progenitors of mononuclear phagocytes, and most recently succeeded to identify human cMoP (in revision). Human cMoP gives rise to only monocytes but not other hematopoietic cells including DCs. Given that monocytes and monocyte-derived macrophages cause a variety of inflammatory disorders, including metabolic syndromes and tumor development, our studies shed light on possible therapeutic applications for infectious diseases, cancers and autoimmune diseases.

## 2) Roles of mononuclear phagocytes in inflammatory bowel disease

Breakdown of the intestinal epithelial layer's barrier function results in the inflow of commensal flora and improper immune responses against the commensal flora, leading to inflammatory bowel disease (IBD) development. Using a mouse dextran sodium sulfate (DSS)-induced colitis model, we showed that commensal Gram-positive bacteria trigger the mobilization of inflammatory monocytes and macrophages into the colon (Mucosal Immunol 2015).  $\text{TNF-}\alpha$ , a representative cytokine that aggravates colitis and a promising therapeutic target, was predominantly produced by monocytes/macrophages. Among macrophage subpopulations,  $\text{Ly6c}^+$  macrophages were a major colitogenic subset producing  $\text{TNF-}\alpha$ . In addition,  $\text{IFN-}\gamma$ -Stat1 pathway was required for histone acetylation at the promoter regions of the *Tnf* loci in macrophages, indicating that  $\text{IFN-}\gamma$ -dependent epigenetic regulation instructs the development of colitogenic macrophages. Our study may provide new therapeutic targets, e.g. inhibition of acetyl transferase in macrophage, for treating IBD and colon cancer (in revision).

## 2. Research on tissue stem cells

### 1) Understanding of tissue homeostasis and its breakdown on the basis of immune cell-tissue stem cell interplay

We found that type I IFNs induce proliferation and exhaustion in hematopoietic stem cells (HSCs), and that interferon regulatory factor-2 (IRF2), a transcriptional suppressor of type I IFN signaling, preserves the self-renewal and multi-lineage differentiation capacity of HSCs (Nat Med 2009). Based on this finding, we show that type I IFN preconditioning, without irradiation or DNA alkylating agents, significantly enhanced the HSC engraftment efficiency in wild type (WT) recipient mice (Blood 2013). Based on these achievements, we have further found that physiological levels of type I IFN signaling also affect other tissue stem cells, e.g. intestinal stem cells (ISCs) and hair follicle stem cells (HFSCs). Elucidation of detailed mechanisms is currently in progress.

### 3. Collaborative research with other institutes

In collaboration with RIKEN, Institute of Physical and Chemical Research, we performed microbiota analysis by 16S rRNA sequencing, and found that there is no significant change in the feces of mice with excess IFN signals specifically in intestinal epithelial cells. As the mice showed defective regeneration capacity of ISCs, we concluded that it is unlikely due to the altered commensal composition (manuscript in preparation).

## (3) Education

Immunology lectures in Faculty of Medicine, Masters Degree, and Doctoral Programs, Graduate School Seminar in other universities as a adjunct lecturer, and educational and research guidance for individual graduate students.

## (4) Publications

### [Original Articles]

1. Nobuyuki Onai, Toshiaki Ohteki. Isolation of Dendritic Cell Progenitor and Bone Marrow Progenitor Cells from Mouse. *Methods Mol. Biol.* 2016.01; 1423; 53-59
2. Jiajia Liu, Yong-Mei Guo, Nobuyuki Onai, Hideaki Ohyagi, Makoto Hirokawa, Naoto Takahashi, Hiroyuki Tagawa, Kumi Ubukawa, Isuzu Kobayashi, Hiroyuki Tezuka, Yoshihiro Minamiya, Toshiaki Ohteki, Kenichi Sawada. Cytosine-Phosphorothionate-Guanine Oligodeoxynucleotides Exacerbates Hemophagocytosis by Inducing Tumor Necrosis Factor-Alpha Production in Mice after Bone Marrow Transplantation. *Biol. Blood Marrow Transplant.* 2016.04; 22(4); 627-636

3. Takayuki Yokoi, Kentarou Yokoi, Kazumasa Akiyama, Takashi Higuchi, Yohta Shimada, Hiroshi Kobayashi, Taku Sato, Toshiaki Ohteki, Makoto Otsu, Hiromitsu Nakauchi, Hiroyuki Ida, Toya Ohashi. Non-myeloablative preconditioning with ACK2 (anti-c-kit antibody) is efficient in bone marrow transplantation for murine models of mucopolysaccharidosis type II. *Mol. Genet. Metab.* 2016.11; 119(3); 232-238

**[Awards & Honors]**

1. Young Investigator's Award (Shunsuke Kawamura), The 24th International Symposium on Molecular Cell Biology of Macrophages , 2016.06

## Pathological Cell Biology

Professor : Shigeomi SHIMIZU

Associate Professor : Norio SHIMIZU

Junior Associate Professor : Satoko ARAKAWA

Project Associate Professor : Masatsune TSUJIOKA, Satoshi TORII

Assistant Professor : Shinya HONDA

Project Assistant Professor : Hirofumi YAMAGUCHI,

Michiko MUROHASHI, Nobuhiro FUJIKAKE, Hajime SAKURAI

Tokunin Assistant Professor : Minkyon SHIN, Mariko SUNADA

Postdoctoral fellow (PD1) : Go Yoshida

Secretary : Hitomi Fukabori, Setsu TAMAI, Kayo HATTANDA

Research Assistant : Ikuyo YOSHINO, Kyoko TSUJIMURA, Ikuko NAKANOMYO, Naomi KOJIMA,

Hikari SHIMADA, Yuta YUNOMAE, Yumi IWASAKI, Hiromi KOJIMA

Graduate Student : Yuna SUGIMOTO, Toyokazu SEKI, Saori NOGUCHI, Yuta GOTO,

Miyuki NAKAI, Hatuki ENDO, Hajime MOCHIDUKI, Ryo OKUNO

### (1) Outline

- 1) Analysis of apoptosis mechanism
- 2) Analysis of non-apoptotic cell death (autophagic cell death)
- 3) Physiological and pathological roles of cell death in mammals
- 4) Analysis of alternative macroautophagy mechanism
- 5) Physiological and pathological roles of autophagy in mammals
- 6) Development of novel EBV infection animal models using the hNOG mice
- 7) Development of an exhaustive pathogenic microbe screening system

### (2) Research

Main objective in the graduate course is to provide students opportunity to study the molecular mechanisms of cell death and autophagy, the cell death-related diseases, the physiological and pathological roles of autophagy, and the development mechanism of Epstein-Barr virus (EBV) infection, the employment of immunodeficiency animals for the creation of virus research models and development of an exhaustive pathogenic microbial screening system.

### (3) Education

Main objective in the graduate course is to provide students opportunity to study the molecular mechanisms of cell death and autophagy, the cell death-related diseases, the physiological and pathological roles of autophagy, and the development mechanism of Epstein-Barr virus (EBV) infection, the employment of immunodeficiency animals for the creation of virus research models and development of an exhaustive pathogenic microbial screening system.



#### (4) Publications

##### [Original Articles]

1. Arai A, Sakashita C, Hirose C, Imadome K, Yamamoto M, Jinta M, Fujiwara S, Tomita M, Shimizu N, Morio T, and Miura O.. Hematopoietic stem cell transplantation for adults with EBV-positive T- or NK-cell lymphoproliferative disorders: efficacy and predictive markers Bone Marrow Transplantation. 2016;
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3. Shimizu S. Alterntive Autophagy is Essential for Neuronal Cell Maintenance. Brain Protein Aiging and Dementia Contorol International Workshop 2016.09.09 Nagoya
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## Pediatrics and Developmental Biology

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Department of Pediatrics, Neonatal and Maternal Medicine

Professor: Shozaburo DOI

Associate Professor: Kohsuke IMAI, Masatoshi TAKAGI

### (1) Outline

Our department delivers the most advanced care available today to infants and children. The specialties of our department cover most pediatric diseases, including hematology-oncology, immunology, cardiology, neurology, endocrinology, nephrology, neonatology, allergy and rheumatology. On the other hand, our scientific and academic activities encompass a wide spectrum of basic and clinical areas and all levels of biologic organization, from the molecule to international populations. The goal of our research is to improve the health of children. We focus on innovation and the development of new strategies for clarifying pathogenesis, diagnostic tests, and therapeutic interventions.

### (2) Research

Our research covers many specialties of pediatric diseases, and the researches are based on from bench to bedside. Our current main projects are

1. Identification of responsible genes for primary immunodeficiency (PID) development.
2. Development of therapeutic approach for PID
3. Research in autoimmune lymphoproliferative syndrome (ALPS) and RAS-associated ALPS like syndrome
4. Quality assessment of iPS cells for clinical application
5. Regulation of granulocyte activation and apoptosis
6. Development of innovative techniques for immune therapy after hematopoietic stem cell transplantation.
7. Elucidating the pathogenesis of glomerulosclerosis formation and the mechanisms in podocyte.
8. Research of infectivity in patients with refractory nephrotic syndrome
9. Revealing the mechanisms of immunological relevant to pediatric idiopathic nephrotic syndrome.
10. Mechanisms of idiopathic pulmonary arterial hypertension
11. Guideline for cardiomyopathy in children
12. Social background in pediatric heart transplantation

13. Clinical background of Eisenmenger syndrome in Japan
14. Lung injury induced by cytokines/monocytes/granulocytes
15. Pathogenesis of periventricular leukomalacia and bronchopulmonary dysplasia
16. Elucidating the molecular mechanisms of gonadal development
17. Molecular pathology of congenital adrenal diseases and disorder of sex development
18. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
19. ATM dependent cellular differentiation
20. Neural diseases based on defective DNA damage response
21. Investigation of molecule marker determine the prognosis of infant leukemia
22. Development of therapeutic strategy targeting homologous recombination repair
23. Genetic background of leukemia development

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Science, Hiroshima University, Istituto Nazionale Tumori (Dr. D. Delia), University of Queensland (Prof. Peter Koopman), Erasmus University (Prof. Jacques van Dongen), Yonsei University (Profs. H. Kim, and SK Lee), Sony Life Science Laboratories, National Institute for Longevity Sciences, National Research Institute for Child Health and Development, RIKEN Center for Integrative Medical Science, Kazusa DNA Research Institute, Tokyo Metropolitan Institute for Medical Science, Juntendo University, and many other laboratories.

#### ● Hematology/Oncology/Immunology Group (Basic Research)

Our research focuses on the dissection of molecular basis of immune regulation, cancer development, DNA damage response. Our aim in research focusing on elucidation of molecular pathogenesis and development of therapeutic approach for pediatric catastrophic disease, especially in immunological disorder. Our research area is also located in the field of tumor development, DNA damage response and primary immunodeficiencies. Some of these research is tightly linked each other. The directions; from bench to clinic and clinic to bench is favorably utilized for research style. Nationwide survey for common variable immunodeficiency (CVID) is executing under the leader

ship of Dr. Morio. Through the analysis of patient samples using next generation sequencing technology, we have identified several rare disease causing gene mutations from a CVID patients, and pursuing characterization. Research focusing on X linked lymphoproliferative disease has been conducted by Dr. Kanegane. iPS cell directed innovative drug discovery has been performed by Dr. Takagi collaborated with Dr. Ohtsu in Tokyo University. In terms with ataxia telangiectasia, research group was organized by Dr. Takagi to improve patient outcome. Cellular differentiation has been investigated using patient derived iPS cells. To maintain quality of life in PID, web based interaction between patient side and hospital side has been established under leadership by Dr. Imai.

In the clinical setting, viral infection is one of a critical factor that affect the outcome of hematopoietic stem cell transplantation. To overcome this disadvantage, we have been starting the generation of multi virus specific cytotoxic T cell. This year our group revealed how chromosomal integrated HHV6 is activated in severe combined immunodeficiency patient. This findings is notable discovery in field of infection and immunodeficiency. In regenerative medicine field, Dr. Morio organized research group to evaluate the quality of clinical use iPS cell. Comprehensive microbe monitoring system has been developing collaborate with Dr. Shimizu at TMDU Medical research institute, and non-invasive genomic alteration detection system has been developing collaborate

with Dr. Inazawa at TMDU Medical research institute and Dr. Ohara at Kazusa genome institute.

In the oncology field, we have focusing on that how DNA damage response prevent oncogenic transformation. In addition, development of therapeutics targeting DNA damage and repair pathway is conducting. Comprehensive genome research for leukemia has been conducted. These research will be lead to identification of novel therapeutic approach for pediatric leukemia. Clinical trial based on these discovery is currently under consideration.

#### ● Cardiology Group

We performed both the basic and clinical studies.

As for the basic studies, we have consecutively focused on the theme “inflammation and pulmonary hypertension (PH)” and have engaged in the basic research to clarify the mechanisms of PH and development of treatment. However, we moved to focus on pulmonary hypertension (PH) induced right ventricular (RV) remodeling which is one of the important factors related to its prognosis. We became to be interested in Pannexin (PANX) which can play a role as heart mechanosensor. PANX is a protein which exists in cell membrane and belongs to be the gap junction channel family. Dr. Furukawa is Professor of department of Bio-informational Pharmacology

and clarified that PANX expressed on the left ventricle was associated with TAC-induced left ventricular (LV) hypertrophy by using PANX K/O mice. Our research aim is to clarify that PANX plays an important role for PH-induced RV hypertrophy as heart mechanosensor as well as TAC-induced LV hypertrophy. It may be possible to improve the prognosis in PH patients by regulation of PANX which is expressed on the RV.

As for the clinical studies, we were engaged in three multi-center-associated clinical studies. Two of them “Guideline for cardiomyopathy in children” and “Social background in pediatric heart transplantation” were supported by Health and Labor Sciences Research Grant, and one of them “Clinical backgrounds of Eisenmenger syndrome in Japan” was supported by The Japanese Society of Pediatric Cardiology and Cardiac Surgery.

## ● Neurology Group

Our research is focused on elucidating the pathogenesis of neurological disorders, such as neurodegenerative and neuroinflammatory diseases, based on molecular approach.

Ataxia-telangiectasia (AT) is one of the major neurodegenerative diseases caused by defective DNA damage responses. We established iPS cell lines from AT patients and investigating the neuropathological mechanism and trying to identify a novel therapeutic approach. Further, we are exploring to discover unidentified genetic diseases with DNA repair-deficiency disorders using next-generation sequencing technology.

Marinesco-Sjögren syndrome, a disease associated with ER(Endoplasmic Reticulum) stress, is caused by abnormal unfolded protein response, and we aim to identify the pathological mechanisms at the cellular level. We expect our research would provide therapeutic approach to the disease.

In collaborating with other research institutes, we have identified the adverse effect of BZDs on a mouse model of inflammation-induced status epilepticus. We showed that MDZ therapy significantly increased the risk for neurological sequelae in immature mice, including hyperactivity (collaborative project with Haruo Okado, Tokyo Metropolitan Institute of Medical Science).

Elucidating immunological roles of the purinergic receptor signal for microglial inflammatory reaction is another target of our research. We have established P2RY12 KO microglial cell line that enabled us to investigate purinergic receptor signals on inflammatory cytokine production from microglia (collaborative project with Hiroshi Sakuma, Tokyo Metropolitan Institute of Medical Science).

Clinical and epidemiological study is another priority field. We have been conducting a clinical research to evaluate the efficacy and safety of very-low-dose betamethasone therapy in ataxia-telangiectasia. In multi-institutional study, conducted by Shinichi Hirose, Fukuoka University, we have provided the genetic tests for the patients with epilepsy and febrile-seizures. We have also contributed to a nationwide survey of rare intractable epilepsy syndrome registry project, operated by Yushi Inoue, NHO Shizuoka Institute of Epilepsy and Neurological Disorders.

## ● Endocrinology Group

Currently, our research is focused on elucidating the molecular mechanisms of congenital diseases of endocrine organs, especially adrenal glands and gonads. We are looking at developing the radical treatment systems for the congenital endocrine diseases by using regenerative medicine as a final target.

Our ongoing projects are bellows

#1: Molecular mechanisms of gonadal development

We are trying to elucidate molecular mechanisms of gonadal development, especially, focusing on elucidating epigenetic network of gonadal development and gonadal cell differentiation. Our projects also include identifying the precise function of transcription factors, such as Sf1, Foxl2 and Sox9.

In collaborating with M. Kanai (Department of Experimental Animal Model for Human Disease), Shuji Takada (Department of Systems BioMedicine, National Center for Child Health and Development), P. Koopman (IMB. The university of Queensland, Brisbane, Australia), we use in vitro and in vivo approach.

#2: Molecular pathology in congenital adrenal hyperplasia.

Congenital adrenal hyperplasia is one of disorders of sex development (DSDs), and now we are treating more than 40 patients.

Including the relationships between genotype and phenotype, the molecular mechanisms of the disease have not been clarified yet. Including functional analyses of novel mutations of the steroidogenic enzymes, we are trying to elucidate the pathological mechanisms of the disease.

#3: Elucidating the mechanisms of congenital disorder of endocrine organs

Identifying the molecular mechanisms of congenital disorder of endocrine organs is also our important target. Understanding the molecular pathology of the diseases will lead to develop innovative treatment of the diseases. Current ongoing projects will be integrated systematicall, and will be applicable to develop innovative treatment of congenital endocrine disorder, including approaches using regenerative medicine.

### ● Nephrology Group

We are conducting researches to elucidate the mechanisms glomerulosclerosis and nephrotic syndrome: Elucidating the pathogenesis of glomerulosclerosis formation and the mechanisms in podocyte, research of infectivity in patients with refractory nephrotic syndrome, and revealing the mechanisms of immunological relevant to pediatric idiopathic nephrotic syndrome.

We are collaborating research with Division of Nephrology, Department of Internal Medicine, Juntendo University.

We participate in multi-institutional joint research of refractory nephrotic syndrome operated by Japanese Study Group of Kidney Disease in Children.

### ● Neonatology group

We are investigating a novel therapy with umbilical cord blood derived mesenchymal stem cells for treating periventricular leukomalacia using intrauterine infection model in cooperation with division of Cellular Physiological Chemistry and Nanomedicine (DNP) in TMDU.

### ● Allergy Group

One of our main project goals is to elucidate the immunological mechanisms of food allergy such as that against milk and eggs. Clinical and epidemiological study on food allergy is another major field in our study. We are conducting clinical studies of specific oral tolerance induction in food allergy in which the offending food is administered orally in order to achieve tolerance. Changing dietary habits in our country has led to an increase in allergies induced by uncommon food allergens, therefore we are analyzing the frequency and severity of immediate-type reactions induced by foods other than major food allergens such as hen eggs, cow's milk and wheat in early childhood.

In collaboration with the Japanese Society of Pediatric Allergy and Clinical Immunology, we are conducting several clinical studies to refine pharmacologic therapy listed in the Japanese pediatric guideline for the treatment and management of asthma.

## (3) Education

The new curriculum of education which was started on April, 2011 finally covered all graders from the 1st to 6th of the Medical Science in the School of Medicine. In fact, the 6th graders were first educated under the new curriculum.

The education of the 19 basic medical sciences was finished in the 2nd graders under the new curriculum, so the education of the clinical medicine was started from the first of the 3rd graders. The 3rd graders and the first two months of the 4th graders were proposed systematic lectures, which was called "Block Lecture" and performed together with Pediatrics, Obstetrics and Gynecology as "Reproduction and Development" block. The "Block Lecture" was composed of 25 lectures including introduction, laboratory examination, metabolism, emergency, nutrition, cardiology, gastroenterology, infection, allergy, endocrinology(2), development, hereditary disorder, neonatology(2), neurology(2), pediatric dentist, immunology, collagen disease, child health, hematology and oncology, nephrology, home healthcare and child abuse, four topics including fetus medicine, transitional medicine, advanced medicine and pediatric psychiatry, three cases including congenital heart disease, two hybrid with delivery and neonatology, and one and a half team based learning (TBL).

Moreover, we also took charge of several lectures in another blocks, for example five lectures and one case related to pediatric cardiology in "Cardiology" block, three lectures and one case related to pediatric oncology in "Oncology and Malignancy" block, one lecture related to pediatric pulmonology in "Pulmonology" block, and three lectures related to pediatric infection in "Infection and Clinics" block. Total 47 systematic lectures were almost produced by the staffs of Department of Pediatrics and Developmental Biology, and Department of Pediatrics, Perinatal and Maternal Medicine except five lectures by two another department staffs and three part-time lecturers.

Opportunity of training in scientific research, so-called project semester, was provided for the 4th graders during June to November. Three student was engaged in the pediatric research in 2016. Then the 5th graders were divided into the small groups, and started and continued for three months to learn the introduction of Clinical Clerkship, so-called Pre-clerkship. It was also performed together with Pediatrics, Obstetrics and Gynecology as "Reproduction and Development" block. The small group education chiefly for differential diagnosis was performed and divided into seven sessions, which was load test and mass screening in endocrine disorders, neurological evaluation for development, oncology, and immunology, renal function and fluid therapy, neonatal evaluation and diseases, congenital heart diseases, infection. The clinical reasoning, that is how to proceed the differential diagnosis, was very important for the clinicians and adopted in PCC since 2014.



After the OSCE and CBT was finished in the end of the 4th graders, clinical clerkship (CC) was started at the beginning of the 5th graders. One month practice in pediatric clinical training was provided for the 5th to 6th graders among 16 months, where every student belonged to one of the professional clinical teams (Hematology/Oncology/Immunology, Cardiology, Neurology, Endocrinology, Neonatology and Nephrology) in the University Hospital or some affiliated hospitals (Tsuchiura Kyodo General Hospital, Kawaguchi Municipal Medical Center or North Tokyo Medical Center), and studied clinical practice as one of the team members.

Our educational duty is not only for the students of medical school but for them of dental school and health science school. We provide lectures on general pediatrics for each of their students several times per year. Junior clinical fellows who are in the training course of pediatric practice under the supervision of senior staffs were also expected to supervise these medical students. The style of clinical training was maintained and the 1st year trainee as well as the 2nd year trainee could choose the training in the pediatric ward for two months. On the other hand, the 2nd year trainee was in general engaged in the basic training for one month in the pediatric ward in some affiliated hospitals (Musashino Red Cross Hospital, Soka Municipal Hospital or North Tokyo Medical Center). Depending on the individuals, they could select the advanced training at the pediatric ward in The University Hospital for two to eight months.

#### (4) Lectures & Courses

It is a goal of education for the 3rd and 4th graders (first half) of medical students to learn the whole picture of general pediatric diseases, and for the 4th graders (latter half, so-called project semester) to touch the basic research, get the fundamental way of thinking and skills of experiments. On the other hand, it is a goal for the 5th and 6th graders (so-called pre-Clerkship and Clinical Clerkship), to be in charge of each patient with pediatric staffs and experience the general steps under the clinical medicine, for example, the following steps how to interview the medical history, get the physical findings, plan the laboratory examinations, differentially diagnose by analyzing the personal data, describe the clinical records, and discuss about the treatment planning. Moreover, we educate the students of dentistry and health care sciences, who learn not only general pediatric diseases but the importance of pediatrics as playing roles of total coordination and mutual cooperation beyond specialty for children's care.

Junior clinical trainees, previously started to train the pediatrics from the 2nd year, became to be able to elect the pediatric training for two months from the 1st year, actually however, the fellows who desired to optionally choose the pediatric training did not necessarily perform it because of too many applicants. The 2nd year junior clinical trainees were divided two groups. Those only required pediatric training for one month were generally planned to experience the common pediatric diseases in the affiliated hospitals. On the other hand, those electively selected pediatrics were basically planned to train almost in university hospitals together with at the affiliated hospitals for one month. Senior clinical trainees were rotated among in the university hospitals and chief affiliated hospitals, planned to experience all kinds of pediatric diseases related to oncology, cardiology, neurology, infections and immunology, endocrinology and metabolic diseases, neonatology, nephrology, pulmonology, digestive diseases, and genomics.

#### (5) Clinical Services & Other Works

##### ● Hematology/Oncology/Immunology Group

Hematology/Oncology/Immunology Group treats children with primary immunodeficiency, hematological malignancies, hematological disorders, and malignant solid tumors. Our team consists of 9 staffs, including 5 senior with diplomate of board of pediatrics, hematology, and/or pediatric hematology/oncology and 4 junior staffs. We offer a team-based high-quality and evidence-based clinical care for both inpatients and outpatients. Additionally, we have a cooperative system for medical liaison with other professional facilities including St. Luke's International Hospital and Juntendo University Hospital; joint clinical conference and trainee exchange program has been ongoing..

1. Participation in multi-center cooperative clinical research group: In collaboration with national co-operative clinical research group, such as the Tokyo Children's Cancer Study Group (TCCSG) and Japanese Children's Cancer Study Group (JCCG), we offer our patients opportunities to participate in the latest clinical trials and contribute to establish both standard and novel therapies for childhood cancers and other non-malignant diseases.

2. Number of newly admitted patient was 37 (15 PID, 14 hematological malignancy and 2 solid tumor)  
Hematopoietic cell transplantation (HCT): In 2016, we performed HCT for 10 cases; related bone marrow transplantation (BMT) (n=2) (including 2 haploid identical or non sibling donor source), unrelated BMT (n=6),

unrelated peripheral blood stem cell transplantation (PBSCT) (n=1), unrelated cord blood transplantation (n=1). 6 cases of them were for PID patients. Our experience of HCT exceeds 172 cases including more than 65 cases with primary immunodeficiency diseases, so far. We are also working on novel HCT methods, such as transplantation with haplo-identical donor and killer inhibitory receptor (KIR) ligand mismatched donor, and use of reduced-intensity conditioning aiming for reduction of late effects in HSCT recipients.

3. Three Investigator oriented clinical trials were performed. Efficacy and safety of zoledronate for RALD. HCT for defective DNA damage response associated primary immunodeficiencies.

4. long-term follow-up for childhood cancer survivors (CSS): In cooperation with pediatric endocrinologists, CLS (child life specialist) and psychotherapists, we are taking care of cancer survivors and supporting their quality of life.

### ● Cardiology Group

The University Hospital has been certified as a training institute to produce Board Certified Pediatric Cardiologist recognized by Japanese Society of Pediatric Cardiology and Cardiac Surgery. In TMDU affiliated hospitals, there were 16 Board Certified Pediatric Cardiologists. In 2016 there were four full-time doctors, one Board Certified Pediatric Cardiologist (Doi S, MD, PhD) and three pre-Board Certified Pediatric Cardiologists (Komiya E, MD, Yamaguchi Y, MD, Maeda Y, MD) in The University Hospital, who were engaged in the diagnosis and treatment for every kind of heart disease patients both in the pediatric ward and the field for pediatric outpatients. Another Board Certified Pediatric Cardiologist (Izumida N, MD, PhD) helped to see the outpatients as a part-time doctor. Dr. Yamaguchi Y were belonged to be a staff of pediatric cardiovascular surgery.

The hospitalization number of patients was 102, which was a little bit decreased compared to the last year and the average length of hospital stay was 7.9 days, which was shorter than the last year. The diseases of admitted patients were 59 CHD, acquired heart diseases such as 12 PH, 14 cardiac arrhythmias, 10 Kawasaki diseases (KD), and seven another disease. Forty-five cardiac catheterizations were performed, which contained 31 CHD, 8 PH, 5 KD and 1 cardiac arrhythmias. Catheter interventions were performed on one patient who was ventricular tachycardia for the first time in pediatric cardiology group. Twenty CHD patients (9 VSDs, 9 ASDs, one TOF and one cAVSD) were surgically operated. Infants under 1 year old was 6 with 4 PAH. PA banding operation, which is classified in Risk category 3, was performed on cAVSD with Down syndrome in this year.

PH patients were admitted for diagnosis, evaluation of treatments or decision of treatment strategy. The most important thing is early diagnosis and early initiation of treatment for PH, which is nominated for difficult-cured and progressive disease. Therefore, we decided to positively treat by receiving up-front combination therapy (uCT) with three kinds of disease targeted drugs and inducing continuous venous infusion of epoprostenol. Four patients were treated with uCT and one patient was induced epoprostenol. As the result, we succeeded in decreasing pulmonary arterial pressure as well as increase in cardiac output and decrease in pulmonary vascular resistance. We also started to use a couple of new specific medications on PH such as subcutaneous treprostinil, oral macitentan and riociguat. Among them, effective subcutaneous trprostnil was induced for more two patients. As the result, three pediatric patients were induced subcutaneous trprostnil in TMDU which was 60% in Japan.

Out-patients for pediatric cardiology were up to 2,000 patients with the 1,500 examinations of echocardiogram. Moreover, Holter 24-hours ECG monitoring examination and Treadmill exercise tolerance examination were respectively performed on about 100 patients.

We have participated in the school heart screening program of Tokyo Metropolitan Institute for Preventive Medicine and Tokyo Medical Association, and checked 9,000 students ECG records in elementary, junior high and senior high schools. The students who were needed the third stage checkup visited The University Hospital, examined at out- or in-patients fields and finally decided the exercise restriction level in school life.

### ● Neurology Group

Child neurology group provides highly specialized diagnostic approach and medical care for neurological disorders such as epilepsy, neuromuscular disorders, infection of nervous system, neurodegenerative diseases and genetic syndromes. In particular, in cooperation with the department of neurosurgery, we evaluate the indication for surgical treatment and then perform surgical operation such as focal brain resection to the patient of intractable epilepsy.

### ● Endocrinology Group

We provide highly specific diagnostic approach and therapy for pediatric endocrine disorders, such as growth retardation, hypogonadism, thyroid diseases, disorder of sex development (DSD), disorder of Ca-P-PTH metabolism,



type1 diabetes mellitus. In collaborating with the satellite hospitals, we are following more than a thousand patients, and the annual number of inpatients with endocrine disorder of our university is more than 100.

Senior physician of our group is an adviser of Tokyo Health Service Association, and supervising the newborn screening of congenital adrenal hyperplasia in Tokyo.

Among many pediatric endocrine disorders, we are directing our effort at the disorders of adrenal gland and sex development (DSD), and looking at establishing the clinical center for those patients with pediatric-urologist and other co-medical staffs.

#### ● Nephrology Group

Nephrology Group provides diagnosis and treatment for patients with various kidney disease: acute and chronic glomerular diseases, nephrotic syndrome, chronic kidney disease, congenital abnormality of kidney and urinary tract, and acute kidney injury that requires blood purification. We perform kidney biopsy and imaging examination for diagnosis in our hospital. We willingly participate in urinary analysis screening for school children. This year, we treated children with congenital nephrotic syndrome, refractory nephrotic syndrome, IgA nephropathy, acute kidney injury, chronic kidney disease, vesicoureteral reflux, and so on. We performed peritoneal dialysis for low-body-weight children and provided acute hemodialysis for children who developed acute kidney injury. We performed kidney biopsy about 40 cases a year. Group conference is held on 4th Thursday every month for lecture and discussion about the cases we experienced. Graduate students present their research at the conference to share research progress. We participate to some conferences that pediatric nephrologists from other institutions gather, that give us the valuable opportunities to discuss the critical cases with other specialists.

Some members of our group receive training for pediatric nephrologists at National Research Institute for Child Health to improve their skills.

We present case reports of our patients and research reports in several major conferences such as the meeting of Japanese society of nephrology and the meeting of Japanese society of pediatric nephrology.

#### ● Neonatology group

1) Our NICU (Neonatal Intensive Care Unit) was established on April 2012 with 6 beds, and provide intensive care for preterm infants (> 28 weeks of gestation and/or > 1000g of birth weights). We also take care of critically ill newborns, those with congenital heart disease, hematological disorder, etc., in cooperation with other pediatric subspecialty groups.

2) As a designated Perinatal Cooperation Hospital in Tokyo, we accept newborn patients from various areas in Tokyo.

#### ● Allergy Group

The qualified allergists of the group attend both inpatient and outpatient care units for allergic diseases in affiliated hospitals of our university, where not only the standard medical services following clinical guidelines for allergic diseases are provided, but also highly advanced treatment such as oral immunotherapy for food allergy as well.

We conduct public educational activities about allergic diseases, organizing specific lecture meetings in cooperation with local public health center and/or medical societies.

### ( 6 ) Clinical Performances

#### ● Hematology-Oncology/ Immunology Group

Hematology-Oncology/ Immunology Group provides diagnosis, treatment and pathological analysis of hematological malignancies and primary immunodeficiency diseases. We perform hematopoietic stem cell transplantation for refractory diseases. Especially, we treat the largest number of primary immunodeficiency disease patients in Japan. We participate in multi-center cooperative clinical research to establish both standard and novel therapies for childhood cancers, and also participate in industry-based clinical trials for drug, such as anticancer drug, approval.

#### ● Cardiology Group

Cardiology group perform diagnosis, evaluation of treatment or decision of treatment strategy for PH patients. We positively treat by up-front combination therapy (uCT) with three kinds of disease targeted drugs and continuous venous infusion of epoprostenol. Worthy of special mention, surgical operation in children with congenital heart diseases was restarted after about 30 years blank.

### ● Neurology Group

Neurology group provide highly specialized diagnostic approach and medical care for neurological disorders such as epilepsy, neuromuscular disorders, nervous system infections, neurodegenerative diseases and genetic syndromes.

### ● Endocrinology Group

The leader of our endocrinology group is a supervisor of congenital adrenal hyperplasia (CAH) newborn screening in Tokyo. We treat many CAH (21-OHD) patients and performed couples of clinical studies. We also focus on disorder of sex development (DSD) and long-term follow-up for childhood cancer survivors (CSS). We are managing a Type 1 DM patients' association (Wakamatsu-kai) and organize the summer camp every year.

### ● Nephrology Group

We treat various pediatric kidney diseases, such as congenital nephrotic syndrome, refractory nephrotic syndrome, IgA nephropathy, etc. Kidney biopsy is performed to more than 40 patients. We provide acute hemodialysis treatment and peritoneal dialysis for low-body-weight patients (under 10kg) in cooperation with department of blood purification.

### ● Neonatology Group

Our NICU (Neonatal Intensive Care Unit) provides intensive care for preterm infants and critically ill newborns. As a designated Perinatal Cooperation Hospital in Tokyo, we accept newborn patients from various areas in Tokyo by collaborating with comprehensive reproductive medicine.

### ● Allergy Group

We focus on clinical care of severe and complicated allergic diseases such as food allergy-induced anaphylaxis, food-dependent exercise-induced anaphylaxis, food protein-induced enterocolitis syndrome and oral allergy syndrome induced by cross-reactivity among food, inhalant and contact allergens. We extensively perform food challenge tests not only for correct diagnosis of food allergy but for preparation of oral immunotherapy in cooperation with the affiliated hospitals.

## (7) Publications

### [Original Articles]

1. T Wada, Toma T, M Yasui, M Inoue, K Kawa, K Imai, T Morio, A Yachie. Different Clinical Phenotypes in 2 Siblings With X-Linked Severe Combined Immunodeficiency. *J Invest Allergol Clin Immunol.* 2016; 26(1); 63-65
2. Tomohiro Kohmoto, Atsumi Tsuji, Kei-Ichi Morita, Takuya Naruto, Kiyoshi Masuda, Kenichi Kashimada, Keisuke Enomoto, Tomohiro Morio, Hiroyuki Harada, Issei Imoto. A novel COL11A1 missense mutation in siblings with non-ocular Stickler syndrome. *Hum Genome Var.* 2016; 3; 16003
3. Kotaro Kai, Maki Sumida, Yaeko Motoyoshi, Yuichi Ogawa, Katsuyuki Miki, Kazuhiro Iwadoh, Akihito Sannomiya, Toru Murakami, Ichiro Koyama, Kumiko Kitajima, Ichiro Nakajima, Tomohiro Morio, Shohei Fuchinoue. Successful Long-term Graft Survival of a Renal Transplantation Patient with Wiskott-Aldrich Syndrome. *Intern. Med.* 2016; 55(13); 1761-1763
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5. Mami Miyado, Masafumi Inui, Maki Igarashi, Yuko Katoh-Fukui, Kei Takasawa, Akiko Hakoda, Junko Kanno, Kenichi Kashimada, Kenji Miyado, Moe Tamano, Tsutomu Ogata, Shuji Takada, Maki Fukami. The p.R92W variant of NR5A1/Nr5a1 induces testicular development of 46,XX gonads in humans, but not in mice: phenotypic comparison of human patients and mutation-induced mice. *Biol Sex Differ.* 2016; 7; 56
6. Yuki Aoki, Reiji Miyawaki, Kohsuke Imai, Masatoshi Takagi, Michiko Kajiwarra, Yasuyoshi Ishiwata, Masato Yasuhara, Tomohiro Morio, Shuki Mizutani, Daisuke Tomizawa. Haploidentical Bone Marrow Transplantation With Clofarabine and Busulfan Conditioning for a Child With Multiple Recurrent Acute Lymphoblastic Leukemia. *J. Pediatr. Hematol. Oncol.* 2016.01; 38(1); 39-41

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8. Laura Gámez-Díaz, Dietrich August, Polina Stepensky, Shoshana Revel-Vilk, Markus G Seidel, Mitsuiki Noriko, Tomohiro Morio, Austen J J Worth, Jacob Blessing, Frank Van de Veerdonk, Tobias Feuchtinger, Maria Kanariou, Annette Schmitt-Graeff, Sophie Jung, Suranjith Seneviratne, Siobhan Burns, Bernd H Belohradsky, Nima Rezaei, Shahrzad Bakhtiar, Carsten Speckmann, Michael Jordan, Bodo Grimbacher. The extended phenotype of LPS-responsive beige-like anchor protein (LRBA) deficiency. *J. Allergy Clin. Immunol.* 2016.01; 137(1); 223-230
9. T Muto, Y Takeda, S Tsukamoto, S Sakai, N Mimura, C Ohwada, M Takeuchi, E Sakaida, S Ota, T Iseki, N Shimizu, T Morio, C Nakaseko. Successful treatment of cytomegalovirus enteritis after unrelated allogeneic stem cell transplantation by the infusion of ex vivo-expanded CD4(+) lymphocytes derived from the recipient's peripheral blood donor cells. *Transpl Infect Dis.* 2016.02; 18(1); 93-97
10. Kei Takasawa, Sayaka Takeda, Masato Nishioka, Hiroshi Sakuma, Tomohiro Morio, Masayuki Shimohira. Steroid-responsive Status Epilepticus Caused by Human Parvovirus B19 Encephalitis. *Pediatr. Infect. Dis. J.* 2016.02; 35(2); 227-228
11. Yumiko Nakano, Takeshi Hayashi, Kentaro Deguchi, Kota Sato, Nozomi Hishikawa, Toru Yamashita, Yasuyuki Ohta, Yoshiki Takao, Tomohiro Morio, Koji Abe. Two young stroke patients associated with regular intravenous immunoglobulin (IVIg) therapy. *J. Neurol. Sci.* 2016.02; 361; 9-12
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14. Amit Rawat, Kohsuke Imai, Deepti Suri, Anju Gupta, Swapnil Bhisikar, Biman Saikia, Ranjana W Minz, Shobha Sehgal, Surjit Singh. Ataxia Telangiectasia Masquerading as Hyper IgM Syndrome. *Indian J Pediatr.* 2016.03; 83(3); 270-271
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16. Hiroshi Moritake, Masatoshi Takagi, Mariko Kinoshita, Osamu Ohara, Shojiro Yamamoto, Sayaka Moriguchi, Hiroyuki Nunoi. Autoimmunity Including Intestinal Behçet Disease Bearing the KRAS Mutation in Lymphocytes: A Case Report. *Pediatrics.* 2016.03; 137(3); 1-5
17. Masakatsu Yanagimachi, Takashi Ohya, Tomoko Yokosuka, Ryosuke Kajiwara, Fumiko Tanaka, Hiroaki Goto, Takehiro Takashima, Tomohiro Morio, Shumpei Yokota. The Potential and Limits of Hematopoietic Stem Cell Transplantation for the Treatment of Autosomal Dominant Hyper-IgE Syndrome. *J. Clin. Immunol.* 2016.04; 36(5); 511-516
18. Julie Toubiana, Satoshi Okada, Julia Hiller, Matias Oleastro, Macarena Lagos Gomez, Juan Carlos Al-dave Becerra, Marie Ouachée-Chardin, Fanny Fouyssac, Katta Mohan Girisha, Amos Etzioni, Joris Van Montfrans, Yildiz Camcioglu, Leigh Ann Kerns, Bernd Belohradsky, Stéphane Blanche, Aziz Bousfiha, Carlos Rodriguez-Gallego, Isabelle Meyts, Kai Kisand, Janine Reichenbach, Ellen D Renner, Sergio Rosenzweig, Bodo Grimbacher, Frank L van de Veerdonk, Claudia Traidl-Hoffmann, Capucine Picard, Laszlo Marodi, Tomohiro Morio, Masao Kobayashi, Desa Lilic, Joshua D Milner, Steven Holland, Jean-Laurent Casanova, Anne Puel. Heterozygous STAT1 gain-of-function mutations underlie an unexpectedly broad clinical phenotype: an international survey of 274 patients from 167 kindreds. *Blood.* 2016.04; 127(25); 3154-3164

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24. Shigeru Takishima, Keisuke Nakajima, Risa Nomura, Atsumi Tsuji-Hosokawa, Nozomi Matsuda, Yohei Matsubara, Makoto Ono, Kentaro Miyai, Kei Takasawa, Tomohiro Morio, Yukihiro Hasegawa, Kenichi Kashimada. Lower body weight and BMI at birth were associated with early adiposity rebound in 21-hydroxylase deficiency patients. Endocr. J.. 2016.08; 63(11); 983-990
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#### [Misc]

1. Masatoshi Takagi, Kevin Urayama. Inherited genetic variants associated with childhood lymphoblastic leukemia risk. *The Japanese Journal of Clinical Hematology.* 2016.07; 57(7); 891-899

#### [Conference Activities & Talks]

1. Mikhail Rojavin, Hirokazu Kanegane, Michael Borte, Imai k , Alphonse P. Hubsch, Helena Soop, Stephen R. Jolles. Pooled Analysis of Patient Treatment Satisfaction from Five Hizentra Studies. 2016 AAAAI ANNUAL MEETING 2016.03.04 Los Angeles, USA
2. Imai K. HYPER-IGM SYNDREOMS DUE TO CSR DEFECTS-HOW TO TREAT ACCORDING TO GENETIC SUBTYPES?. ASPID Spring School 2016.04.27 HongKong, China



3. Imai K. PIDJ AND PIER-PID DATABASE IN JAPAN FOR DOCTORS AND PATIENTS-HOW IT FACILITATES CARE AND RESEARCH?. ASPID Spring School 2016.04.27 HongKong
4. Kanegane H. Use of Flow Cytometry in PID diagnosis. APSID Spring School 2016.04.28 Hong Kong
5. Kanegane H. Immunoglobulin Replacement for Agammaglobulinemia – Intravenous or Subcutaneous?. ASPID Spring School 2016.05.01 HongKong, China
6. Okano T, Imai K, Tsujita Y, Mitsuiki , Mitsui-Sekinaka K, Takashima T, Kanegane H, Nonoyama S. Broad Spectrum of Clinical Manifestations and Outcome of Hematopoietic Stem Cell Transplantation in Japanese Patients with Activated P13KD Syndrome Type1. ASPID Spring School 2016.05.01 Hong Kong
7. Akihiro Hoshino, Hirokazu Kanegane. ABNORMAL HEMATOPOIESIS AND AUTOIMMUNITY IN HUMANS WITH GERMLINE IKZF1 MUTATIONS. 2016.05.27
8. Doi S. Congenital Heart Disease associated with Pulmonary Arterial Hypertension.. Panal Discussion. Riociguat Meet the Experts 2016.05.27 Tokyo, Japan
9. Kengo Moriyama, Shinpei Baba, Kazue Kimura, Yuji Sugawara. Clinical consideration of six cases of Angelman syndrome. The 58th Annual Meeting of the Japanese Society of Child Neurology 2016.06.04 Tokyo, Japan
10. Influence of ABCB1 polymorphisms with drug-responsiveness to Japanese children with epilepsy. 2016.06.05
11. Masatoshi Takagi, Misa Yoshida, Yoshino Nemoto, Hiroyuki Tamaichi, Rika Tsuchida, Masafumi Seki, Kumiko Uryu, Noriko Hoshino, Rina Nishii, Satoshi Miyamoto, Masahiro Saito, Toshiaki Shimizu, Ryoji Hanada, Hideo Kaneko, Toshiyuki Fukao, Takatoshi Koyama, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Yusuke Sato Sato, Keisuke Kataoka, Yusuke Okuno, Kenichi Yoshida, Tomohiro Morio, Akira Oka, Miki Ohira, Yasuhide Hayashi, Akira Nakagawara, Seishi Ogawa, Shuki Mizutani, Junko Takita. Loss of ATM function confers risk for advanced stage neuroblastoma but provides a therapeutic target for poly-ADP ribose polymerase inhibitors. Advances in Neuroblastoma Research Congress 2016 2016.06.21 Queensland, Australia
12. Haruna Shibayama, Ken-ichi Imadome, Chizuko Sakashita, Ken Watanabe, Norio Shimizu, Takatoshi Koyama, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. In vitro and in vivo effects of proteasome inhibitor bortezomib on Epstein-Barr virus-positive T- or NK-cell lymphoproliferative diseases. 17th International Symposium on Epstein-Barr virus (EBV) and Associated Diseases 2016.08.10 Zurich
13. Type I interferon response induced by transfected self DNA. 2016.09.03
14. Schwab C, Gabrysch A, Hoshino M, Slatter M, Hayakawa S, Schubert D, Klemann C, Frede N, Salzer U, Speckmann C, Freiburger T, Lorenz H.M, Hauck F, Klobuch S, Zeissig S, Leichtner A, Van de Veerdonk F, Elemnto O, Giulino-Roth L, Duckers G, Niehues T, Alsina L, Deya-Martinez A, Kanderiva V, Fronkova E, Price C, Patino V, Blumberg R, Yesim Kucuk Z, Seneviratne S, Kanariou M, Lougaris V, Albert M, Giese T, Litzman J, Ehl S, Okada S, Imai K, Dybedal I, Tasken K, Wolff D, Warnatz K, Hambleton S, Arkwright P, Cant A, Kanegane H, Grimbacher B.. The Clinical Spectrum and Treatment Options of 82 Individuals with CTLA-4 Deficiency. 17th Biennial Meeting of the European Society for Immunodeficiency 2016.09.22 Barcelona, Spain
15. Mitsui-Sekinaka K, Imai K, Tsujita Y, Mitsuiki N, Asano T, Sekinaka Y, Kanegane H, Yoshida K, Miyano S, Kojima S, Ogawa S, Ohara O, Okada S, Kobayashi M, Takagi M, Morio T, Nonoyama S.. Activated PI3 Kinase Delta Syndrome (APDS)-Like Immunodeficiency Caused by PTEN Mutation. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Barcelona, Spain
16. Hoshino A, Okada S, Yoshida K, Nishida N, Yamashita M, Okano T, Tsumura M, Nishimura S, Sakata S, Takagi M, Imai K, Miyano S, Ogawa S, Kojima S, Nonoyama S, Morio T, Kanegane H. . Abnormal Hematopoiesis and Autoimmunity in Humans with Germline IKZF1 Mutations. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Barcelona, Spain
17. Leiding J, Okada S, Shcherbina A, Abinun M, Pulsipher M, Hagin D, Linemans C, Sullivan K, Bunin N, Kilic S, De La Calle-Martin O, Roiman C, Aldave J.C, Iguchi A, Imai K, Ohkawa T, Gennery A, Slatter M, Ochs H, Mori T, Torgerson T. Hematopoietic Stem cell Transplantation in Patients with Gain of Function STAT1 Mutation. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Barcelona, Spain

18. Sekinaka Y, Mitsuiki N, Imai K, Yabe M, Mitsui-Sekinaka K, Honma K, Arai A, Yoshida K, Miyano S, Seiji K, Hira A, Takata M, Ohara O, Ogawa S, Morio T, Nonoyama S. Common Variable Immunodeficiency Caused by Fanc Mutations. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Brcelona, Spain
19. S. Singh, A. Rawat, D. Suri, A. Gupta, R. Garg, B. Saikia, R. Minz, S. Sehga, K. Chan, Y. Lau, C. Kamae, K. Honma, N. Nakagawa, K. Imai, S. Nonoyama, K. Oshima, N. Mitsuiki, O. Ohara. SPECTRUM OF BTK GENE MUTATIONS IN A SINGLE-CENTRE COHORT OF X-LINKED AGAMMAGLOBULINEMIA FROM NORTH INDIA. 17th Biennial Meeting of the European Society for Immunodeficiency 2016.09.22 Barcelona Spain
20. L.A. Henderson, A.E. O'Connell, J.I. Chu, Y.N. Lee, S. Volpi, M. Armant, I.B. Barlan, A. Ozen, S. Baris, I.C. Hanson, J.M. Despotovic, A. Saitoh, T. Takachi, K. Imai, A. King, S. Arredondo, A. Galy, D.A. Williams, S.Y. Pai, L.D. Notarangelo. GENE THERAPY USING A SELF-INACTIVATING LENTIVIRAL VECTOR AMELIORATES T CELL RECEPTOR REPERTOIRE ABNORMALITIES IN PATIENTS WITH WISKOTT-ALDRICH SYNDROME. 17th Biennial Meeting of the European Society for Immunodeficiency 2016.09.22 Barcelona Spain
21. Okano T, Watanabe E, Takashima T, Nishikawa T, Kawano Y, Tomoda T, Tanaka-Kubota M, Miyamoto S, Yeh T, Yamashita M, Tanaka K, Mitusiki N, Ohara O, Takagi M, Imai K, Kanegane H, Morio T. IGG1 Gammopathy in X-SCID Caused by Maternal T and B cell Engraftment. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.23 Barcelona, Spain
22. Jolles S, Rojavin M, Nelson Jr. R, Wasserman R.L, Borte M, Kanegane H, Imai K. Efficacy and Safety of HIZENTRA in Patients with Primary Immunodeficiency in Japan, Europe, and the US. 17th Biennial Meeting of 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.23 Barcelona, Spain
23. Moriya K, Tanita K, Ohnishi H, Niizuma H, Rikiishi T, Nishikomori R, Ishige T, Imai K, Kanegane H, Sasahara Y, Arakawa H, Kure S, Morio T.  $I\kappa B-\alpha$  S32 Mutations Underly Ectodermal Dysplasia with Immunodeficiency Manifestations and Correlation with Immunological Parameters. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.23 Brcelona, Spain
24. Rojavin M, Kanegane H, Borte H, Imai K, Hubsch A, Jolles S. Analysis of Patient Treatment Satisfaction from Five Studies of HIZENTRA 20% Subcutaneous Immunoglobulin. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.23 Barcelona, Spain
25. T. Mizukami, M. Iwata-Okada, T. Nishimura, T. Kawai, M. Onodera, K. Imai, S. Nonoyama, O. Ohara, H. Nunoi. CLINICAL AND GENETIC PROFILES OF CHRONIC GRANULOMATOUS DISEASE IN JAPAN. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.23 Barucelona Spain
26. Ono S, Okano T, Hoshino A, Yanagimachi M, Takagi M, Imai K, Morio T, Kanegane H. Hematopoietic stem cell transplantation for XIAP deficiency. XLP-WAS 2016 Symposium-London 2016.09.26 London, UK
27. Kanegane H, Hoshino A, Takashima T, Yeh T-W, Okano T, Yamashita M, Imai K, Morio T. . Selective dysregulation of Epstein Barr virus infection in hypomorphic ZAP70 mutation. XLP-WAS 2016 Symposium-London 2016.09.26 London, UK
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32. Akihiro Hoshino, Satoshi Okada, Kenichi Yoshida, Naonori Nishida, Yusuke Okuno, Hiroo Ueno, Motoi Yamashita, Tsubasa Okano, Miyuki Tsumura, Shiho Nishimura, Sonoko Sakata, Masatoshi Takagi, Kohsuke Imai, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Seishi Ogawa, Seiji Kojima, Shigeaki Nonoyama, Tomohiro Morio, Hirokazu Kanegane. ABNORMAL HEMATOPOIESIS AND AUTOIMMUNITY IN HUMANS WITH GERMLINE IKZF1 MUTATIONS. 2016.10.21
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42. Risa Nomura, Maki Gau, Takeru Yamauchi, Akito Sutani, Atsumi Tsji-Hosokawa, Yohei Matsubara, Kentaro Miyai, Susumu Hosokawa, Gen Nishimura, Kenichi Kashimada. Myhre syndrome: a progressive connective tissue disorder with short stature. The 9th Biennial Scientific Meeting of the Asia Pacific Endocrine Society/ The 50th Annual Meeting of the Japanese Society for Pediatric Endocrinology 2016.11.17 Tokyo, Japan



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44. Yuichi Miyakwa, Akito Sutani, Atsumi Tsuji, Tomohiro Morio, Kenichi Kashimada. A case of Atypical Pubertal Development Caused by Dopamine Antagonist. The 9th Biennial Scientific Meeting of the Asia Pacific Endocrine Society/ The 50th Annual Meeting of the Japanese Society for Pediatric Endocrinology 2016.11.17 Tokyo, Japan

## Rheumatology

Professor	Hitoshi KOHSAKA
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	Tetsuo KUBOTA (2)
	Kazuki TAKADA (3)
	Ryuji KOIKE (2)
Associate Professor	Toshihiro MATSUI (1)
Junior Associate Professor	Hideyuki IWAI (5)
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Resident Physician	Wakako KAWASAKI, Yuriko YAGYU, Nao TANAKA, Yoichi IMAI, Motohiko SATO, Seiya OBA
Office Administrator	Kaori KONNO, Shoko AIBA, Minako WATANABE, Tomoko TAKAHASHI (1)
Technical Staff	Hidemi KASAHARA, Kazuko YAMAZAKI

(1) Department of Lifetime Clinical Immunology, (2) Medical Innovation Promotion Center,  
(3) Curricular Management Division, Institute of Education, (4) Clinical Research Center, (5) Faculty of Medicine

### (1) Research

Following studies have been extensively carried out in our laboratory with various biochemical, immunological, molecular biological and statistical techniques:

- 1) Investigation of mechanism and development of new therapeutics for the treatment of rheumatoid arthritis and dermato/polymyositis.
  - 2) Establishment of evidence-based treatment of rheumatic diseases by implementing several cohort studies.
- We collaborate with department of lifetime clinical immunology and pediatrics.

### (2) Education

We have provided medical students and graduates with the opportunity to obtain the ability to identify important clinical problems and to solve them by clinical reasoning through their active participation into the

diagnosis and management of various rheumatic diseases.

### ( 3 ) Clinical Services & Other Works

We have provided care to many patients with diverse rheumatic diseases. We have aimed to practice evidence-based medicine and to provide care that is in accordance with the global standard. We have contributed to the development of potential new drugs and treatments through participation into industry- as well as investigator-initiated clinical trials for chemical and biological agents. We have also contributed to the refinement of the care of rheumatic disease patients through the conduct of various pharmacovigilance studies.

We cooperate with department of lifetime clinical immunology and pediatrics.

### ( 4 ) Publications

#### [Original Articles]

1. Mineto Ota, Hideyuki Iwai, Kaori Imai, Mari Kamiya, Yoko Yoshihashi-Nakazato, Nobuyuki Miyasaka, Hitoshi Kohsaka. Acute Tubulointerstitial Nephritis Associated with Infliximab in a Patient with Crohn's Disease. *Intern. Med.*. 2016; 55(10); 1367-1370
2. Kohno S, Tamura K, Niki Y, Izumikawa K, Oka S, Ogawa K, Kadota J, Kamei K, Takata T, Takesue Y, Teruya K, Tokimatsu I, Fukuda T, Maesaki S, Makimura K, Mikamo H, Mitsutake K, Miyazaki Y, Mori M, Yasuoka A, Yano K, Yamanaka N, Yoshida M.. Executive summary of Japanese domestic guidelines for management of deep-seated mycosis. *Med Mycol J* . 2016; 57(4); 117-163
3. Kato H, Mori M, Oba M, Kawahara H, Kaneko T.. Persistence and Half-lives of Anti-measles and Anti-rubella Antibodies in Japanese Hospital Workers: A Longitudinal Study. *Intern Med.* 2016; 55(18); 2587-2594
4. Hirokazu Sasaki, Hayato Yamazaki, Hitoshi Kohsaka. A Case of ANCA-associated Large Vessel Vasculitis with Multiple Saccular Aneurysms. *J. Rheumatol.*. 2016.01; 43(1); 179
5. Hiroyuki Tomimitsu, Akiko Ohta, Masaki Nagai, Motoko Nishina, Shoichiro Ishihara, Hitoshi Kohsaka. Epidemiologic analysis of the clinical features of Japanese patients with polymyositis and dermatomyositis. *Mod Rheumatol.* 2016.01; 26(3); 398-402
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7. Matsuo Yusuke, Mizoguchi Fumitaka, Saito Tetsuya, Kawahata Kimito, Ueha Satoshi, Matsushima Kouji, Inagaki Yutaka, Miyasaka Nobuyuki, Kohsaka Hitoshi. Local fibroblast proliferation but not influx is responsible for synovial hyperplasia in a murine model of rheumatoid arthritis. *Biochem Biophys Res Commun.* 2016.02; 470(3); 504-509
8. Yokoyama K, Mori M, Yoshida A. Mycophenolate mofetil therapy for two cases of antiphospholipid antibody-associated chorea. *Mod Rheumatol.* 2016.02;
9. Aya Inaba, Yuko Hamasaki, Kenji Ishikura, Riku Hamada, Tomoyuki Sakai, Hiroshi Hataya, Fumiyo Komaki, Tetsuji Kaneko, Masaaki Mori, Masataka Honda. Long-term outcome of idiopathic steroid-resistant nephrotic syndrome in children. *Pediatr. Nephrol.*. 2016.03; 31(3); 425-434
10. Y Tagawa, T Saito, K Takada, K Kawahata, H Kohsaka. Successful treatment of severe refractory lupus hepatitis with mycophenolate mofetil. *Lupus.* 2016.04; 25(5); 543-546
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12. Ge X, Tsang K, He L, Garcia RA, Ermann J, Mizoguchi F, Zhang M, Zhou B, Zhou B, Aliprantis AO. NFAT restricts osteochondroma formation from enthesal progenitors *JCI Insight.* 2016.04; 1(4); e86254

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25. Nobuo Sakata, Sayuri Shimizu, Fumio Hirano, Kiyohide Fushimi. Epidemiological study of adult-onset Still's disease using a Japanese administrative database. *Rheumatol. Int.*. 2016.10; 36(10); 1399-1405
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#### [Misc]

1. Shigeru Kohno, Kazuo Tamura, Yoshihito Niki, Koichi Izumikawa, Shinichi Oka, Kenji Ogawa, Junichi Kadota, Katsuhiko Kamei, Yoshinobu Kanda, Tetsuya Kiuchi, Kazutoshi Shibuya, Syunji Takakura, Toru Takata, Yoshio Takesue, Katsuji Teruya, Issei Tokimatsu, Takahiro Fukuda, Shigefumi Maesaki, Koichi Makimura, Hiroshige Mikamo, Kotaro Mitsutake, Yoshitsugu Miyazaki, Masaaki Mori, Akira Yasuoka, Keiko Yano, Noboru Yamanaka, Minoru Yoshida. Executive Summary of Japanese Domestic Guidelines for Management of Deep-seated Mycosis 2014. *Med Mycol J*. 2016.04; 57(4); E117-E163

#### [Conference Activities & Talks]

1. Tsuyoshi Yamada, Hideyuki Iwai, Sayuri Nitta, Masakazu Nagahori, Masayoshi Harigai. Creating Medical Innovators – a Whole-brain Approach to Hea. the 13th Asia Pacific Medical Education Conference 2016.01.15 Singapore
2. Fumitaka Mizoguchi, Kamil Slowikowski, Nir Hacohen, Peter A Nigrovic, Soumya Raychaudhuri, Michael B Brenner. Identification of Synovial Fibroblast Subsets That Define Pathology in Rheumatoid Arthritis. Stromal cells in immunity, Keystone symposia 2016.02.09 Keystone, USA
3. Fumitaka Mizoguchi. Single cell and whole-tissue transcriptomics identify pathogenic fibroblast subsets in rheumatoid arthritis. Queen Elizabeth Hospital, University of Birmingham, UK 2016.03.03 Queen Elizabeth Hospital, University of Birmingham, UK
4. Tetuya Saito, Kimito Kawahata, Hitoshi Kohsaka. Pathogenic role of lysol oxidase-like 2 in rheumatoid arthritis. The 60th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2016.04 Yokohama
5. Hitoshi Kohsaka. Use of anti-myositis biological agents available and unavailable on the market. 2016 Annual Symposium in Rheumatism Research Institute 2016.06.18 Seoul, Korea
6. Fumitaka Mizoguchi, Kamil Slowikowski, Soumya Raychaudhuri, Michael B Brenner. . Single cell transcriptomics and protein expression analysis define disease-specific fibroblast subsets in rheumatoid arthritis joint tissue.. Second Osteoimmunology conference 2016.07.06 Okinawa
7. Hirokazu Sasaki, Akito Takamura, Kimito Kawahata, Kohsuke Imai, Tomohiro Morio, and Hitoshi Kohsaka. Altered peripheral lymphocyte subset repertoires that reflect clinical features of dermatomyositis and polymyositis. The 13th International Workshop on Autoantibodies and Autoimmunity 2016.10.11 Kyoto
8. Hirokazu Sasaki, Akito Takamura, Kimito Kawahata, Kohsuke Imai, Tomohiro Morio, and Hitoshi Kohsaka. Abnormal composition of circulating T and B cells in patients with polymyositis and dermatomyositis is more biased in those with interstitial lung diseases.. ACR/ARHP Annual Meeting 2016.11.13 Washington, DC

9. Fumitaka Mizoguchi, Hisanori Hasegawa, and Hitoshi Kohsaka. Functional Screening of MicroRNAs Using the Inhibitor Library Identified MicroRNAs to Regulate Expression of MMP-3 and IL-6 in Rheumatoid Arthritis Synovial Fibroblasts. 2016 American College of Rheumatology/ Association of Rheumatology Health Professionals Annual Meeting 2016.11.14 Washington DC, USA

## Dermatology

Professor: Hiroo YOKOZEKI

Associate Professor: Ken IGAWA

Junior Associate Professor: Takeshi NAMIKI, Takaaki HANAFUSA

Project Junior Associate Professor: Kaoru TAKAYAMA

Assistant Professor: Shoun TOKORO, Takashi HASHIMOTO, Kohei NOJIMA

Senior Resident: Sakiko CHIKAZAWA, Ai INAGE, Yumiko SONE, Keiko INUI, Michiko NAKAMURA

Resident: Chika OMIGAWA

Doctoral Student: Rie YU, Takichi MUNETSUGU, Minako INAZAWA, Chen YUE, Sayaka KIKUCHI,

Aiko FURUI, Kohei KATO, Sally ESHIBA, Rumi SUZUKI, Takahiro ISHIKAWA,

Al-Busani Hind Abdullah Ahmed, Yutaro HANDA

Technical Assistant: Chiyako MIYAGISHI, Yoshiko ITO

Staff Assistant: Masae SAKATA, Mayuko HAYASHI, Yu KAWAMURA

### ( 1 ) Outline

Dermatology is a department of medical science which educates students to make a diagnosis and treatment for skin diseases. Main objective of Dermatology in the graduate course is to provide students opportunity to study advanced Immunodermatology, physiology, pathology and allergology, and also to study making diagnosis of skin diseases and operation techniques. Students are also taught on skin oncology (melanoma, angiosarcoma) and its related laboratory technology depending on their research project.

### ( 2 ) Research

- 1) Mechanisms of contact hypersensitivity
- 2) Pathological etiology of atopic dermatitis
- 3) Mechanisms of eosinophil recruitment to the skin
- 4) Roles of basophils in human skin diseases
- 5) Functional roles of PGD2 and its receptors in allergic inflammation
- 6) Therapeutic approach for skin diseases by stable form of galectin-9
- 7) Analysis of pathological mechanisms of hyperhidrosis
- 8) Investigation of mediators for itch
- 9) Pathological etiology of chronic prurigo
- 10) Therapeutic approach for angiosarcoma with HVJ-E.
- 11) To establish the in vitro diseases model of dermatological disorders using human induced pluripotent stem cell
- 12) Murine food allergy model with transcutaneous sensitization

### ( 3 ) Clinical Performances

Dermatology clinic provides an advanced treatment for skin diseases; skin tumors, infectious diseases, skin allergy, collagen diseases and psoriasis. Recently, we established the gene therapies (STAT6 decoy ODN) for severe atopic dermatitis in the clinic.

**(4) Publications****[Original Articles]**

1. Yokozeki H.. New Pathologies of Skin Disorders Identified from the History of Perspiration Research. *Curr Probl Dermatol.* 2016; 51; 1-6
2. Suzuki R, Yikelamu A, Tanaka R, Igawa K, Yokozeki H, Yaguchi T.. Studies in Phylogeny, Development of Rapid Identification Methods, Antifungal Susceptibility, and Growth Rates of Clinical Strains of *Sporothrix schenckii* Complex in Japan. *Med Mycol J.* 2016; 57(3); e47-e57
3. Sone Y, Namiki T, Munetsugu T, Ueno M, Tokoro S, Nishizawa A, Takayama K, Yokozeki H. A case of subungual melanoma with bone invasion: Destructive local invasion and multiple skin metastases. *J Eur Acad Dermatol Venereol.* 2016.01; 30(6); 1049-1050
4. Yoshioka Y, Hanafusa T, Namiki T, Nojima K, Amano M, Tokoro S, Igawa K, Yokozeki H. . Drug-induced hypersensitivity syndrome by ethambutol: A case report. *J Dermatol.* 2016.02; 43(8); 971-972
5. Kondo M, Igawa K, Munetsugu T, Shibama S, Nishizawa A, Tokoro S, Yokozeki H.. Increasing Numbers of Mast Cells in Skin Lesions of Hyperpigmented Mycosis Fungoides with Large-Cell Transformation. *Ann Dermatol.* 2016.02; 28(1); 115-116
6. Hirohata A, Hanafusa T, Igawa K, Inoue-Nishimoto T, Mabuchi-Kiyohara E, Nishide M, Yokozeki H, Ikegami R.. Oral tacrolimus for the treatment of generalized morphea. *Eur J Dermatol.* . 2016.02; 26(1); 112-113
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8. Matsuura-Otsuki Y, Hanafusa T, Igawa K, Sato H, Nishizawa A, Yokozeki H.. Macrophage activation syndrome triggered by disseminated tuberculosis with tuberculous gumma in a patient with adult-onset Still's disease and Good's syndrome. *Eur J Dermatol.* 2016.03; 26(3); 309-311
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10. Namiki T, Arai M, Miura K, Yokozeki H.. A case of phakomatosis pigmentovascularis type II: port-wine stain and dermal melanocytosis with cutis marmorata telangiectatica congenita-like lesions. *Eur J Dermatol.* 2016.03; 26(3); 203-303
11. Hanafusa T, Kato K, Azukizawa H, Miyazaki J, Takeda J, Katayama I.. B-1 B cell progenitors transiently and partially express keratin 5 during differentiation in bone marrow. *J Dermatol Sci.* 2016.03; 81(3); 173-181
12. Suzuki R, Fukuyama K, Miyazaki Y, Namiki T. Contact urticaria syndrome and protein contact dermatitis caused by glycerin enema. *JAAD Case Reports* . 2016.03; 2(2); 108-110
13. Hirohata A, Hanafusa T, Igawa K, Inoue-Nishimoto T, Mabuchi-Kiyohara E, Nakai C, Kasugai T, Yokozeki H, Ikegami R.. Bullous erythema ab igne with cutaneous reactive angiomatosis. *Eur J Dermatol.* . 2016.04; 26(2); 191-192
14. Inui K, Hanafusa T, Namiki T, Ueno M, Igawa K, Yokozeki H.. Intractable Postoperative Wounds Caused by Self-Inflicted Trauma in a Patient with Cutaneous Munchausen Syndrome Presenting as a Pyoderma Gangrenosum-Like Lesion. *Case Rep Dermatol.* 2016.04; 8(1); 97-101
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#### [Books etc]

1. Yokozeiki H, Murota H, Katayama I.. Current Problems in Dermatology. Perspiration Research.. Karger,, 2016
2. Yokozeiki H.. Current Problems in Dermatology. New pathologies of skin disorders identified from the history of perspiration research. Perspiration Research.. Karger,, 2016
3. Inoue R. . Current Problems in Dermatology. New finding on the mechanism of perspiration including aquaporin-5 water channel. . Karger,, 2016
4. Nishizawa A.. Current Problems in Dermatology. Dyshidrotic Eczema and its Relationship to metal allergy.. Karger,, 2016
5. Fujimoto T.. Current Problems in Dermatology. Pathophysiology and treatment of Hyperhidrosis.. Karger,, 2016

#### [Conference Activities & Talks]

1. Namiki T.. Overexpression of NUA2 has a significant impact on the survival of acral melanoma patients. . 46th Annual ESDR Meeting 2016 2016.09
2. Hanafusa T.. Evaluation of endothelial cells derived from induced pluripotent stem cells from systemic sclerosis patients .. 46th Annual ESDR Meeting 2016 2016.09
3. Hashimoto T.. Implication of amphiregulin in basophil-dependent prurigo-like skin reactions.. 46th Annual ESDR Meeting 2016.09
4. Namiki T, Nojima K, Funazami M, Ishikawa M, Kaneko Y, Tanemura A, Katayama I, Mori T, Yamazaki N, Yokozeiki H, Hearing VJ. Over-expression of NUA2 has a significant impact on the survival of acral melanomas patients and a relevance with DNA copy number gain. The 27th Annual Meeting of the Japanese Society for Pigment Cell Research 2016.10
5. Hanafusa T, Namiki T, Amano M, Inui K, Chikazawa S, Nojima K, Ueno M, Igawa K, Yokozeiki H. . Two cases of adverse reactions with anti-PD-1 and anti-CTLA4 antibody therapies used for treating malignant melanoma manifesting as graft-versus-host-like reactions and autoimmune hypophysitis.. The 12th Meeting of the German-Japanese Society of Dermatology 2016.10
6. Hashimoto T, Satoh T, Yokozeiki H. . Deneralized pruritus in primary sclerosing cholangitis: implications of histamine release by lysophosphatidic acid.. The 12th Meeting of the German-Japanese Society of Dermatology 2016.10
7. Hashimoto T, Satoh T, Yokozeiki H.. Pruritus in scabies infestation: Implications of Th2 immunity and IL-31.. Montagna Symposium on Biology of Skin 2016.10
8. Chen Y, Yokozeiki H, Katagiri K. . Dysfunction of the corneum in an ovariectomized mice model of climacterium is associated with aberrant epidermal differentiation and decreased expression of desmoglein-1.. The 12th Meeting of the German-Japanese Society of Dermatology 2016.10
9. Funazumi M, Nojima K, Ishikawa M, Kaneko Y, Tanemura A, Katayama I, Mori T, Yamazaki N, Yokozeiki H, Hearling V.J.. The expression of NUA2 affects the prognosis of acral melanoma patients. . The 27th Annual Meeting of the Japanese Society For Pigment Cell Research,Gifu 2016.11
10. Omigawa C, Chikazawa S, Hashimoto T, Hanafusa T, Namiki T, Igawa K, Yokozeiki H.. Multiple fixed drug eruption caused by trimethoprim/sufamethoxazole in a patient with systemic lupus erythematosus and anti-laminin 332 mucous membranous pemphigoid,. The 4th Eastern Asia Dermatology 2016.11

11. Namiki T, Nojima K, Funazumi M, Ishikawa M, Kaneko Y, Tanemura A, Katayama I, Mori T, Yamazaki N, Yokozeki H, Hearing VJ. The significance of over-expression of NUA2 on the survival of patients with acral melanomas and its relevance with DNA copy number gain. The 41th Annual Meeting of the Japanese Society for Investigative Dermatology 2016.12

# NCCHD Child Health and Development

## 1. Stuffs and Students

Collaborative Professor	Akutsu, Hidenori
Collaborative Professor	Onodera, Masashi
Collaborative Professor	Fukami, Maki
Collaborative Professor	Hata, Kenichiro
Collaborative Professor	Takada, Shuji
Collaborative Professor	Matsumoto, Kenji

## 2. Purpose of Education

The goal of this course is to learn the developmental process of human life from the viewpoints of latest molecular biology and genetics. Medical science for child health and development is the study to comprehensively grasp various health problems related to “human life cycle” to begin with the fertilization and to continue to the next generation through generation and development. Students of this course are required to understand a role and a function of medical care for child health and development, to acquire ability to handle such health problems and support relevant person with specialized theory and technique.

## 3. Research Subjects

1) Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells  
Application studies for reproductive medicine and regenerative medicine  
(Akutsu, Hidenori; Center for Regenerative Medicine, National Institute for Child Health and Development)

Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells.  
Application studies for reproductive medicine and regenerative medicine.

2) Studying for cellular model in human severe disease by advancing flow cytometry  
(Onodera, Masashi; Dept. of Human Genetics, National Institute for Child Health and Development)

We aim to identify causative genes for child intractable hereditary diseases and analyze their functions to develop new gene-based therapeutic options. We also establish iPS cells from peripheral blood or skin fibroblasts obtained from patients with intractable hereditary diseases such as primary immunodeficiencies and congenital metabolic disorders.

3) Elucidation of genetic abnormality in congenital severe metabolic diseases using advanced genetic analysis  
(Fukami, Maki; Dept. of Molecular Endocrinology, National Institute for Child Health and Development)

Our objective is to clarify the molecular basis of congenital endocrine-related disorders and apply our findings to new innovations in clinical medicine. We investigate the molecular basis of single gene disorders, epigenetic/inprinting disorders, and multifactorial disorder.

4) Elucidating for molecular mechanism of perinatal abnormality using system biology  
(Hata, Kenichiro; Dept. of Maternal-Fetal Biology, National Institute for Child Health and Development)

We aim to clarify mechanisms underlying abnormalities in fetal development and placentation, and/or perinatal diseases with developmental defects. To identify the underlying mechanisms of perinatal diseases, we take advantage of post-genomic technologies and investigate etiologies using an integrated genomic and epigenomic approach.

5) Identification of target molecules in severe diseases and establishment of disease model mice by studying molecular mechanisms of genomic imprinting, gametogenesis and sexual differentiation  
(Takada, Shuji; Dept. of Systems Biomedicine, National Institute for Child Health and Development)

Our aim is to reveal the molecular mechanisms underlying embryonic development, cell differentiation and tissue formation and apply our findings to understand the causes of developmental diseases.

6) Elucidation for allergic disease mechanism and target molecules using molecular biology and ‘omics’ technology  
(Matsumoto, Kenji; Dept. of Allergy and Clinical Immunology, National Institute for Child Health and Development)

Our mission is to clarify the precise pathogenic mechanisms of various immunological and allergic diseases, such as Kawasaki disease, various allergic diseases, allogeneic immune tolerance, congenital viral infections and severe infectious diseases. To achieve this, we employ various experimental approaches, including epidemiology, clinical and basic research. Our ultimate aim is to develop better means of preventing, diagnosing and treating allergic and immunological and infectious diseases based on our research findings and cumulative knowledge.

# 4. Publications

## [Original Articles]

1. Fukuda A, Mitani A, Miyashita T, Sado T, Umezawa A, Akutsu H\*. Maintenance of Xist imprinting depends on chromatin condensation state and Rnf12 dosage in mice. *PLoS Genet* 2016; 12(10): e1006375.
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11. Shima H, Tanaka T, Kamimaki T, Dateki S, Muroya K, Horikawa R, Kanno J, Adachi M, Naiki Y, Tanaka H, Mabe H, Yagasaki H, Kure S, Matsubara Y, Tajima T, Kashimada K, Ishii T, Asakura Y, Fujiwara I, Soneda S, Nagasaki K, Hamajima T, Kanzaki S, Jinno T, Ogata T, Fukami M; Japanese SHOX study group. Systematic Molecular Analyses of SHOX in Japanese Patients with Idiopathic Short Stature and Leri-Weill Dyschondrosteosis. *J Hum Genet.* 61(7): 585–591, 2016
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## [Review Articles]

1. Fukami M, Seki A, Ogata T. SHOX Haploinsufficiency as a cause of syndromic and non-syndromic short stature. *Mol Syndromol* 7(1): 3–11, 2016
2. Fukami M, Shima H, Suzuki E, Ogata T, Matsubara K, Kamimaki T, Catastrophic Cellular Events Leading to Complex Chromosomal Rearrangements in the Germline. *Clin Genet* 2016 (in press)

## [Books]



# Human Pathology

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Laboratory Technician: Asuka FURUKAWA

Technical Assistant: Yuki ISHIGE

Graduate Students:

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Tomohisa OGAWA, Tomohito AYABE, Nobuyasu AWANO,

Tomoya KAKEGAWA, Yuji SEKINE, Kurara AKITA

Masahiro YAMAMOTO

(MD-PhD course) Yuriko WADA

(Master's Program) Daisuke SAKONISHI, Momoko SAKAGUCHI

Reserch Student: Yuka HIROTA

Secretary: Miho IWAMITSU, Mayako TOKUNAGA

## ( 1 ) Outline

Pathology in a medical department used to be the general study field about human disease. Later, Microbiology and Parasitology had been separated from the field of Pathology. Lately, interdisciplinary of traditional study field had been advanced and new specific academic disciplines are developed. Pathology is currently under the same trend. Basic divisions such as Experimental and Cell Biological pathology are becoming independent from the clinicopathological field. Thus, Human Pathology has become the main category of pathology.

The principles of Human Pathology are to educate clinical pathologists with accurate pathological diagnosis skills of human disease, to research theses that are directly related to human disease, and to educate pathological researchers with ability to perform such research.

## ( 2 ) Research

- 1) Endogenous infection (diseases caused by indigenous microorganisms in susceptible hosts)
- 2) Cancer research (histopathology, carcinogenesis, prognostic factors, and so on)

## ( 3 ) Education

In the course, they usually spend the first two years for anatomical pathology training, searching for their own research theme and another two years for researches and thesis-writing.

## ( 4 ) Lectures & Courses

Department of Human Pathology provides a graduate course for future pathologists to train the skills and knowledge of anatomical pathology and develop the abilities for medical researches. Graduate students are

educated to associate their researches with problems in diagnosis and treatment of diseases and etiologies of the diseases of unknown causes.

## ( 5 ) Clinical Performances

After the Meiji Era, the department of Human Pathology in medical faculty belonged under the basic medical sciences; however, Pathology in the existing hospitals is essentially the clinical medicine. Diagnosis of patients in each clinical department is done by taking the biopsy of diseased tissues or collecting the cell samples by either endoscope or surgery. Then, the lesions are analyzed with the microscope, and pathological diagnosis is reported to the clinical departments. The samples of organs and tissues taken from the surgery are used to study the spread of the lesion and its characteristics, and also to examine the adequacy of surgery. It is also used to determine future treatment policy. During the course of patients' treatments, sample tissues are taken periodically and are analyzed pathologically to see therapeutic effect. If a patient has unfortunately joined the majority, morbid anatomy is done by the pathologists along with the patient's attending physician. They study the resulting effects of laboratory findings and choice of treatment, and improve the future diagnosis and treatments. The department of Human Pathology and Surgical Pathology technically work as one although they are separated in this university's organizational structure. Human Pathology does not directly work with the patients; however, it is involved directly with the diagnosis as well as the treatments. Strong cooperation between clinicians and pathologists is essential for the best practice, and is required for the university hospital as an "advanced treatment hospital." Therefore, doctors of Human Pathology study, research and practice pathology to be the great pathologists so-called the "doctor of doctors."

## ( 6 ) Publications

### [Original Articles]

1. Wakaba Yamaguchi, Naofumi Yui, Toshikage Nagao, Gaku Oshikawa, Mariko Negi, Soichiro Iimori, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida. Bence-Jones Protein  $\lambda$ -type Multiple Myeloma Patient Withdrawn from Maintenance Hemodialysis after Long-term Bortezomib and Dexamethasone Therapy. *Intern. Med.*. 2016; 55(3); 263-268
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7. Tadahisa Numakura, Tsutomu Tamada, Masayuki Nara, Soshi Muramatsu, Koji Murakami, Toshiaki Kikuchi, Makoto Kobayashi, Miho Muroi, Tatsuma Okazaki, Sho Takagi, Yoshinobu Eishi, Masakazu Ichinose. Simultaneous development of sarcoidosis and cutaneous vasculitis in a patient with refractory Crohn's disease during infliximab therapy. *BMC Pulm Med*. 2016.02; 16; 30

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9. Atsuko Konta, Kouichi Ozaki, Yasuhiko Sakata, Atsushi Takahashi, Takashi Morizono, Shinichiro Suna, Yoshihiro Onouchi, Tatsuhiko Tsunoda, Michiaki Kubo, Issei Komuro, Yoshinobu Eishi, Toshihiro Tanaka. A functional SNP in FLT1 increases risk of coronary artery disease in a Japanese population. J. Hum. Genet.. 2016.05; 61(5); 435-441
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11. Ryohei Hayashi, Kiichiro Tsuchiya, Keita Fukushima, Nobukatsu Horita, Shuji Hibiya, Keisuke Kitagaki, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Eriko Okada, Akihiro Araki, Kazuo Ohtsuka, Shinji Fukuda, Hiroshi Ohno, Ryuichi Okamoto, Tetsuya Nakamura, Shinji Tanaka, Kazuaki Chayama, Mamoru Watanabe. Reduced Human  $\alpha$ -defensin 6 in Noninflamed Jejunal Tissue of Patients with Crohn's Disease. Inflamm. Bowel Dis. 2016.05; 22(5); 1119-1128
12. Nariaki Kokuho, Yasuhiro Terasaki, Hirokazu Urushiyama, Mika Terasaki, Shinobu Kunugi, Taisuke Morimoto, Arata Azuma, Jitsuo Usuda, Akihiko Gemma, Yoshinobu Eishi, Akira Shimizu. Pulmonary mucosa-associated lymphoid tissue lymphoma associated with pulmonary sarcoidosis: a case report and literature review. Hum. Pathol.. 2016.05; 51; 57-63
13. Teruko Nakamura, Asuka Furukawa, Keisuke Uchida, Tomohisa Ogawa, Tomoki Tamura, Daisuke Sakonishi, Yuriko Wada, Yoshimi Suzuki, Yuki Ishige, Junko Minami, Takumi Akashi, Yoshinobu Eishi. Autophagy Induced by Intracellular Infection of Propionibacterium acnes. PLoS ONE. 2016.05; 11(5); e0156298
14. Masahiro Asakawa, Takanobu Yoshimoto, Mitsutane Ota, Mitsuyuki Numasawa, Yuriko Sasahara, Takato Takeuchi, Yujiro Nakano, Norihiko Oohara, Masanori Murakami, Ryotaro Bouchi, Isao Minami, Kyochiro Tsuchiya, Koshi Hashimoto, Hajime Izumiyama, Naoko Kawamura, Kazunori Kihara, Mariko Negi, Takumi Akashi, Yoshinobu Eishi, Hironobu Sasano, Yoshihiro Ogawa. A Case of Cushing's Syndrome with Multiple Adrenocortical Adenomas Composed of Compact Cells and Clear Cells. Endocr. Pathol.. 2016.06; 27(2); 136-141
15. Eriko Katsuta, Atsushi Kudo, Takumi Akashi, Yusuke Mitsunori, Satoshi Matsumura, Arihiro Aihara, Daisuke Ban, Takanori Ochiai, Shinji Tanaka, Yoshinobu Eishi, Minoru Tanabe. Macroscopic morphology for estimation of malignant potential in pancreatic neuroendocrine neoplasm. J. Cancer Res. Clin. Oncol.. 2016.06; 142(6); 1299-1306
16. Sanae Shimamura, Naoto Yokogawa, Kengo Murata, Tetsuo Yamaguchi, Keisuke Uchida, Yoshinobu Eishi. Saddle nose with sarcoidosis: "A great imitator" of relapsing polychondritis. Mod Rheumatol. 2016.06; 1-5
17. Yamada I, Hikishima K, Miyasaka N, Kato K, Ito E, Kojima K, Kawano T, Kobayashi D, Eishi Y, Okano H. q-Space MR imaging of gastric carcinoma ex vivo: correlation with histopathologic findings. Magn Reson Med. 2016.08; 76(2); 602-612
18. Ryuichi Okamoto, Mariko Negi, Syohei Tomii, Yoshinobu Eishi, Mamoru Watanabe. Diagnosis and treatment of microscopic colitis. Clin J Gastroenterol. 2016.08; 9(4); 169-174
19. Nishikawaji T, Akiyama Y, Shimada S, Kojima K, Kawano T, Eishi Y, Yuasa Y, Tanaka S. Oncogenic roles of the SETDB2 histone methyltransferase in gastric cancer. Oncotarget. 2016.10; 7(41); 67251-67265
20. Saori R Yoshii, Akiko Kuma, Takumi Akashi, Taichi Hara, Atsushi Yamamoto, Yoshitaka Kurikawa, Eisuke Itakura, Satoshi Tsukamoto, Hiroshi Shitara, Yoshinobu Eishi, Noboru Mizushima. Systemic Analysis of Atg5-Null Mice Rescued from Neonatal Lethality by Transgenic ATG5 Expression in Neurons. Dev. Cell. 2016.10; 39(1); 116-130

# [Conference Activities & Talks]

1. Yoshinobu EISHI. ABC method clinical trial protocol. Thai gastric cancer society meeting 2016.08.22 Bangkok, Thailand

# Physiology and Cell Biology

Lecturer: Shingo Sato

Assistant professor: Hiroki Ochi

Assistant professor: Satoko Sunamura

## (1) Outline

Recent progress in molecular biology and genetics advanced our understanding of molecular basis of physiological function and pathophysiological mechanisms of various diseases. Besides, signal transduction system using intercellular, intersystem, and inter-organ networks has been shown to be essential for whole-body homeostatic function. In our department, we are studying on the inter-organ regulatory networks of metabolism, especially between bone and the other organs.

## (2) Research

1. Studies on the regulatory network of metabolism between bone and the other internal organs: It had been believed that bone is controlled by local environment through the action of hormones and cytokines, independently of the other organs. However, our discovery that leptin regulates bone formation through the central nervous system shed light on a new regulatory system of bone metabolism, i.e., neuronal control (Takeda S, Cell, 2002, Nature, 2005). In addition, we have also demonstrated that neuromedin U, an anorexigenic neuropeptide, regulates bone formation through the central nervous system (Sato S, Nat Med, 2007). Moreover, recent studies have revealed that FGF23 or osteocalcin, which is secreted by bone, regulates the metabolism of kidney or pancreas. Thus, bone is now considered as a major player for whole-body homeostasis, and forms a regulatory network of metabolism together with the other organs. We are now conducting further experiments to clarify a comprehensive network between bone and the other organs.

2. Studies on the regulation of bone metabolism by sensory nerves: We have recently revealed that sensory nerves inside bones have a crucial role in regulating bone mass, and that the penetration of sensory nerves into bones is necessary for normal bone development or fracture healing (Fukuda T, Nature, 2013). Based on these findings, we are now conducting further experiments to develop novel therapeutic approaches to osteoporosis.

3. Studies on the regulation of bone metabolism and bone metastasis by microRNA: microRNA (miRNA) is a small non-coding RNA molecule, and regulates various developmental and homeostatic events in vertebrates and invertebrates. Aberrant expression of miRNA has been implicated in numerous disease states, and miRNA-based therapies are under investigation. We have previously demonstrated the physiological role of miRNA in osteoblast differentiation (PNAS, 2009). We are now conducting further experiments to identify novel miRNAs regulating bone metabolism or bone metastasis.

4. Studies on the mechanical regulation of musculoskeletal system: In Japan, the number of patients with osteoporosis or sarcopenia have rapidly increased. Mechanical stress is known to be essential for the maintenance of bone volume or muscle strength. However, the mechanism of the mechanical regulation remains elusive. We are now elucidating the role of gravity on bone or muscle homeostasis as well as on neurovascular formation in bone or muscle tissues by utilizing a tail suspension mouse model.

5. Studies on the mechanism in the development of bone and soft tissue sarcomas: Sarcomas are malignancies

derived from mesenchymal tissues such as bone, muscle, fat, and cartilage. Molecular mechanisms in the occurrence and growth of sarcomas have yet to be elucidated. Even the cell of origin for most sarcomas still remains unclear. We have recently established a novel mouse model for osteosarcoma and also demonstrated that sarcomas could be derived from pericytes with mutations of crucial genes. Based on these findings, we are now conducting further experiments to elucidate the detailed mechanism of sarcoma development.

### ( 3 ) Education

We give lectures and laboratory teachings about physiology to sophomore medical students. We also teach experimental techniques to a lot of undergraduate students to develop young basic scientist. PhD students are required to join our research team and learn various experimental techniques including molecular biology, cellular biology, and physiology.

### ( 4 ) Lectures & Courses

All students are expected to understand the background of the research field and bring up relevant scientific questions to verify the hypothesis. They are also expected to develop their scientific thinking with effective questions and cultivate their abilities to analyze obtained results objectively, discuss them logically and scientifically, and present them effectively.

### ( 5 ) Publications

#### [Original Articles]

1. Yoshinori Asou, Munetaka Iwata, Hiroki Ochi, Maierhaba Ailixiding, Zulipiya Aibibula, Jinying Piao, Guangwen Jin, Yasushi Hara, Atsushi Okawa. Pleiotropic Functions of High Fat Diet in the Etiology of Osteoarthritis. PLoS ONE. 2016; 11(9); e0162794
2. Cheng Xu, Hiroki Ochi, Toru Fukuda, Shingo Sato, Satoko Sunamura, Takeshi Takarada, Eiichi Hinoi, Atsushi Okawa, Shu Takeda. Circadian clock regulates bone resorption in mice J. Bone Miner. Res.. 2016.02; 31(7); 1344-1355
3. Masanori Saito, Mieradili Mulati, S Zakiah A Talib, Philipp Kaldis, Shu Takeda, Atsushi Okawa, Hiroyuki Inose. The Indispensable Role of Cyclin-Dependent Kinase 1 in Skeletal Development. Sci Rep. 2016.02; 6; 20622
4. Yoichi Imai, Eri Ohta, Shu Takeda, Satoko Sunamura, Mariko Ishibashi, Hideto Tamura, Yan-Hua Wang, Atsuko Deguchi, Junji Tanaka, Yoshiro Maru, Toshiko Motoji. Histone deacetylase inhibitor panobinostat induces calcineurin degradation in multiple myeloma. JCI Insight. 2016.04; 1(5); e85061
5. Sato S, Tang YJ, Wei Q, Hirata M, Weng A, Han I, Okawa A, Takeda S, Whetstone H, Nadesan P, Kirsch DG, Wunder JS, Alman BA. Mesenchymal tumors can derive from Ng2/Cspg4-expressing pericytes with  $\beta$ -catenin modulating the neoplastic phenotype Cell Reports. 2016.07; 16(4); 917-927
6. Takashi Iezaki, Kakeru Ozaki, Kazuya Fukasawa, Makoto Inoue, Shigetaka Kitajima, Takeshi Muneta, Shu Takeda, Hiroyuki Fujita, Yuki Onishi, Tetsuhiro Horie, Yukio Yoneda, Takeshi Takarada, Eiichi Hinoi. ATF3 deficiency in chondrocytes alleviates osteoarthritis development. J. Pathol.. 2016.08; 239(4); 426-437
7. Takeshi Takarada, Cheng Xu, Hiroki Ochi, Ryota Nakazato, Daisuke Yamada, Saki Nakamura, Ayumi Kodama, Shigeki Shimba, Michihiro Mieda, Kazuya Fukasawa, Kakeru Ozaki, Takashi Iezaki, Koichi Fujikawa, Yukio Yoneda, Rika Numano, Akiko Hida, Hajime Tei, Shu Takeda, Eiichi Hinoi. Bone Resorption Is Regulated by Circadian Clock in Osteoblasts. J. Bone Miner. Res.. 2016.12;
8. Masahiro Niimura, Tsuyoshi Sato, Yuichiro Enoki, Masahiko Okubo, Shoichiro Kokabu, Shu Takeda, Tetsuya Yoda. Semaphorin 3A Promotes Dendrite Elongation of Osteocytes in Association with Down-regulation of CDK6. In Vivo. 30(3); 231-236

**[Misc]**

1. Shingo Sato, Shu Takeda. RANKL/RANK/OPG genetically engineered mice PharmaNavigator. 2016;
2. Toru Fukuda, Shu Takeda. Regulation of bone homeostasis by nerve system The medical frontline. 2016.02; 71(2); 223-229
3. Sato S, Takeda S. The regulation of various organs by osteoblasts Clinical Calcium. 2016.05; 26(5); 721-727

**[Conference Activities & Talks]**

1. Yukihiro Tamura, Setsuko Mise, Yasutaka Sugamori, Md. Zahirul Haq Bhuyan, Mariko Takahashi, Tomoki Uehara, Yuki Arai, Michiyo Miyashin, Noriyuki Wakabayashi, Kazuhiro Aoki. A pharmacological role of metallothionein in zinc-treated cartilage-progenitor cells. APFP 2016(The 13th Asia Pacific Federation of Pharmacologists Meeting) 2016.02.01 The Berkeley Hotel Pratunam,Bangkok (Thailand)
2. Shingo Sato. The cell of origin of bone and soft tissue sarcomas. 242th Kanto musculoskeletal tumor workshop 2016.03.08 Tokyo
3. Shingo Sato, Takashi Hirai, Dai Ukegawa, Seiichi Matsumoto, Shu Takeda, Atsushi Okawa. Reduction in the frequency of emergency surgery by medical and dental combined treatment system for bone metastasis. The 49th Annual Musculoskeletal Tumor Meeting of the Japanese Orthopaedic Association 2016.07.14 Tokyo
4. Shingo Sato, Benjamin Alman, Shu Takeda, Atsushi Okawa. The same cellular origin of musculoskeletal tumor and pituitary tumor. The 31st Annual Research Meeting of the Japanese Orthopaedic Association 2016.10.13 Fukuoka
5. Shingo Sato, Yuning J. Tang, Qingxia Wei, Makoto Hirata, Ilkyu Han, Shu Takeda, David G. Kirsch, Jay S. Wunder, Benjamin A. Alman. Mesenchymal tumors can derive from NG2-expressing pericytes with beta-catenin modulating the neoplastic phenotype. Connective Tissue Oncology Society Meeting 2016 2016.11.11 Lisbon, Portugal
6. Shingo Sato, Hiroki Ochi, Shu Takeda. Novel molecular regulation of postmenopausal osteoporosis by the inter-organ metabolic network. The 39th Annual Meeting of the Molecular Biology Society of Japan 2016.12.02 Yokohama
7. Shingo Sato, Hiroki Ochi, Shu Takeda. Regulation of whole body homeostasis by organ-network between bone and other organs. Cardiovascular and Metabolic Week (CVMW) 2016 2016.12.16 Tokyo

## Molecular Cellular Cardiology

Professor	Tetsushi Furukawa
Assistant professor	Kensuke Ihara
Post-doc (RPD)	Masami Kodama
Post-doc (PD)	Nozomi Hayashiji
Post-doc	Kentaro Takahashi
D4(Dept. Cardiovascular Medicine)	Masahiro Yamazoe
D4	Lian Liu
M2	Shun Fukuda
M2	Xiaoki Yang
M1	Shuhei Ishii
M1	Sun Yihan
Technician	Tomoko Ando
Technician	Reiko Kimura
Secretary	Kuniko Yamaguchi

### ( 1 ) Outline

This laboratory focuses on understanding pathogenesis of intractable and common cardiovascular diseases using multidisciplinary approach (patch-clamp, cell biology, optical recording, genetic analysis, and computational analysis). Our ultimate goal is to improve diagnosis and management of intractable and common cardiovascular diseases.

### ( 2 ) Research

#### 1. Pathogenesis of atrial fibrillation (AF)

Up to the present, we have carried 3 GWAS (genome-wide association study); 1st GWAS with 250K SNPs, 2nd GWAS with 610K SNPs, and 3rd GWAS with 1000K SNPs. The 1st GWAS gave us 2 AF-sensitive SNPs, the 2nd GWAS 13 AF-sensitive SNPs (Nat. Genet. 2012;44:670-675, Circulation 2014;130:1225-1235), and the 3rd GWAS 16 AF-sensitive SNPs (under revision). Using the SNPs identified in the 2nd GWAS, we constructed weighed genetic risk score (GRS), which could predict AF development with 60% sensitivity and 61% specificity (Can. Heart J. 2017 [ in press ] , J. Cardiol. 2017 [ in press ] ).

#### 2. Pannexin for ischemic preconditioning

Pannexin is a member of gap-junction channel, which is not involved in the formation of gap-junction channels between cells, but provides hemi-channels on the surface of the membrane. Pannexin functions as chloride channels in the basal condition and as ATP-release channels after mechanical stimuli. Being suffered from myocardial infarction, hearts with prior ischemic events (angina) develop reduced size infarcted size compared with those without prior ischemic events. The effect of prior ischemic events is referred as “ischemic pre-conditioning” . Though extracellular ATP is known to play an important role for ischemic pre-conditioning, the source of ATP is not known. Using pannexin-1 (a major isoform of pannexin in hearts) KO mouse, we found that ATP released during hypoxia was much lower in KO mice than in WT mice. Ischemic pre-conditioning reduced the infarcted area in WT mice, which was almost abolished in KO mice. Taken together, we conclude that hypoxia-activated pannexin provides extracellular ATP, which is required for the ischemic pre-conditioning.



### 3. Safety cardiac pharmacology and toxicology using iPS cells and mathematical modeling

We aim to contribute to assessments for drug-induced lethal arrhythmias which have been a major reason for drug withdrawal from market. Novel multidisciplinary approaches using *in silico* mathematical models (collaborating with Dr. Takashi Ashihara at Shiga University of Medical Science) and human iPS cells-derived cardiomyocytes (collaborating with Dr. Yasunari Kanda and Dr. Yuko Sekino at National Institute of Health Sciences) are developing in order to predict lethal drug-induced arrhythmias at pre-clinical safety pharmacological and toxicological tests. In this year, we developed a simulation model which can describe automaticity of electrical activity of human iPS cells-derived cardiomyocytes, and found that KCNJ2 expression is crucial for the automaticity (under revision).

### 4. Cardiac development and regeneration

The technologies for cardiomyocyte induction from human iPSCs gave us one of progressive tools for clinical application. However, the cardiomyocyte characters greatly vary by their differentiation time and their places. Even long-cultured cardiomyocytes from human iPSCs still keep immature characters with arrhythmia or tachycardia. To address this issue, we identified that a novel transcription factor, *Sall1* acts as a key player for heart induction via regulation of major cardiac genes such as *Islet1/Nkx2-5/Tbx5/Gata4/Mef2c* etc (Morita et al., JMCC 2016), and cooperatively functions with a cardiac gene for heart specification and its maturation (Morita et al., submitted 2017). We also found that these genes function during cardiac regeneration in mammals (Nakamura et al., Develop. Growth. Differ. 2016). In addition, to address the mechanisms of congenital heart defects and heart failure in adults, we found the evidence that some epigenetic genes from RNA-sequence between males and females in human/rodents might enhanced these symptoms more worse (Tsuji et al., revised 2017; Hori et al., submitted 2017).

## (3) Education

School of Medicine

2nd grade Introduction to Neurophysiology (2 units)

2nd grade Physiology (6 units)

3rd grade Cardiology (1 unit)

4th grade Project semester

School of Dentistry

3rd grade Pharmacology III(2 units)

3rd grade Practice for Pathophysiological Sciences (2 units)

School of Health Care Medicine

3rd/4th grade Cardiac physiology (8 units)

## (4) Publications

### [Original Articles]

1. Yuki Hasegawa, Satomi Hamada, Takuro Nishimura, Takeshi Sasaki, Yusuke Ebana, Mihoko Kawabata, Masahiko Goya, Mitsuaki Isobe, Takatoshi Koyama, Tetsushi Furukawa, Kenzo Hirao, Tetsuo Sasano. Novel Dielectric Coagulometer Identifies Hypercoagulability in Patients with a High CHADS2 Score without Atrial Fibrillation. PLoS ONE. 2016; 11(6); e0156557
2. Soichiro Yoshikawa, Takako Usami, Junichi Kikuta, Masaru Ishii, Tetsuo Sasano, Koji Sugiyama, Tetsushi Furukawa, Eiji Nakasho, Hiroshi Takayanagi, Thomas F Tedder, Hajime Karasuyama, Atsushi Miyawaki, Takahiro Adachi. Intravital imaging of Ca(2+) signals in lymphocytes of Ca(2+) biosensor transgenic mice: indication of autoimmune diseases before the pathological onset. Sci Rep. 2016.01; 6; 18738
3. Kentaro Takahashi, Tetsuo Sasano, Koji Sugiyama, Junko Kurokawa, Noriko Tamura, Yurie Soejima, Motoji Sawabe, Mitsuaki Isobe, Tetsushi Furukawa. High-fat diet increases vulnerability to atrial arrhythmia by conduction disturbance via miR-27b. J. Mol. Cell. Cardiol.. 2016.01; 90; 38-46
4. Lopez-Redondo F, Kurokawa J, Nomura F, Kaneko T, Hamada T, Furukawa T, Yasuda K.. A distribution analysis of action potential parameters obtained from patch-clamped human stem cell-derived cardiomyocytes. Journal Pharmacological Science. 2016.04; 8613(16); 30032-30039



5. Sugiyama K, Sasano T, Kurokawa J, Takahashi K, Okamura T, Kato N, Isobe M, Furukawa T. Oxidative Stress Induced Ventricular Arrhythmia and Impairment of Cardiac Function in Nos1ap Deleted Mice International Heart Journal. 2016.05; 57(3); 341-349
6. Yoichi Otaki, Yusuke Ebana, Shunji Yoshikawa, Mitsuaki Isobe. Dielectric permittivity change detects the process of blood coagulation: Comparative study of dielectric coagulometry with rotational thromboelastometry. Thromb. Res.. 2016.06; 145; 3-11
7. Hirokazu Ohigashi, Natsuko Tamura, Yusuke Ebana, Masayoshi Harigai, Yasuhiro Maejima, Takashi Ashikaga, Mitsuaki Isobe. Effects of immunosuppressive and biological agents on refractory Takayasu arteritis patients unresponsive to glucocorticoid treatment. J Cardiol. 2016.08;
8. Okata S, Yuasa S, Suzuki T, Ito S, Makita N, Yoshida T, Li M, Kurokawa J, Seki T, Egashira T, Aizawa Y, Kodaira M, Motoda C, Yozu G, Shimojima M, Hayashiji N, Hashimoto H, Kuroda Y, Tanaka A, Murata M, Aiba T, Shimizu W, Horie M, Kamiya K, Furukawa T, Fukuda K. Embryonic type Na<sup>+</sup>-channel -subunit, SCN3B masks the disease phenotype of Brugada syndrome Science Reports. 2016.09; 6; 34198
9. Lian Liu, Yusuke Ebana, Jun-Ichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Toshihiro Tanaka, Masatoshi Komura, Mitsuaki Isobe, Tetsushi Furukawa. Genetic Variants Associated With Susceptibility to Atrial Fibrillation in a Japanese Population. Can J Cardiol. 2016.11;

#### [Misc]

1. Kurokawa J, Kodama M, Clancy CE and Furukawa T. Sex hormonal regulation of cardiac ion channels in drug-induced QT syndromes Pharmacology & Therapeutics. 2016; 168; 23-28
2. Yamazoe M, Furukawa T. Long-Term Prognosis of Catecholaminergic Polymorphic Ventricular Tachycardia Patients With Ryanodine Receptor (RyR2) Mutations 2016.08; 80(9); 1892-1894
3. Yusuke Ebana. Ethics in Clinical Research Obstet. Gynecol.. 2016.10; 83(10); 1119-1123

#### [Conference Activities & Talks]

1. 1. Sasano T, Sugiyama K, Kurokawa J, Takahashi K, Okamura T, Kato N, Isobe M, Furukawa T. Genetic deletion of Nos1ap induced ventricular arrhythmia and impairment of cardiac function under oxidative stress condition. 5th International Conference of Cardiovascular Medicine 2016.03.05 Taichung, Taiwan
2. Takahashi K, Sasano T, Sugiyama K, Isobe M, Furukawa T. Contribution of pannexin-1 to cardioprotection and arrhythmogenicity induced by ischemia/reperfusion injury. The 80th Annual Scientific Meeting of the Japanese Circulation Society 2016.03.18 Sendai
3. Takahashi K, Sasano T, Sugiyama K, Orui Y, Isobe M, Furukawa T. Contribution of pannexin-1 to cardioprotection and arrhythmogenicity induced by preconditioning against ischemia/reperfusion injury. The 80th Annual Scientific Meeting of the Japanese Circulation Society 2016.03.18 Sendai
4. Hayashi Y, Nitta J, Iwasaki T, Lee K, Watanabe K, Hirao T, Kato N, Inamura Y, Suzuki M, Negi K, Satoh A, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Gohya M, Hirao K, Isobe M. The occurrence of ectopy from pulmonary veins in atrial fibrillation in middle-aged women. The 80th Annual Scientific Meeting of the Japanese Circulation Society 2016.03.19 Sendai
5. Ito S, Ebana Y, Furukawa T. Neurl, ubiquitin E3 ligase, contributes to the maintenance of sarcomere structure and the regulation of autophagy. The 80th Annual Scientific Meeting of the Japanese Circulation Society 2016.03.19 Sendai
6. Hayashi Y, Nitta J, Iwasaki T, Lee K, Watanabe K, Hirao T, Kato N, Inamura Y, Suzuki M, Negi K, Satoh A, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Gohya M, Hirao K, Isobe M. The genotype of SNPs related whether ectopy is from pulmonary vein or others in atrial fibrillation. The 80th Annual Scientific Meeting of the Japanese Circulation Society 2016.03.19 Sendai
7. Hamada S, Hasegawa Y, Nishimura T, Furukawa T, Isobe M, Hirao K, Sasano T. Novel dielectric blood coagulometry can evaluate factor Xa and thrombin activity individually. The 80th Annual Scientific Meeting of the Japanese Circulation Society 2016.03.20 Sendai

8. Yusuke Ebana Hiroko Kohbata, Sayako Takahashi, Masayuki Yoshida. Genetic counselling for a case with breast cancer who underwent a whole-exome sequencing in a private company. The 13th International Congress Society of Human Genetics 2016.04.06
9. Furukawa T, Liu L, Ebana Y, Nitta J, Takahashi Y, Miyazaki M, Isobe M, Tanaka T . Gene-Guided Therapy in AF. Heart Rhythm Society's 37th Annual Scientific Sessions 2016.05.06 San Francisco
10. Sasano T, Sugiyama K, Kurokawa J, Takahashi K, Okamura T, Kato N, Isobe M, Furukawa T. Oxidative Stress Induced Ventricular Arrhythmia and Impairment of Cardiac Function in Nos1ap Deleted Mice. The 9th international conference on the biology, chemistry, and therapeutic approach of Nitric Oxide 2016.05.22
11. Tetsushi Furukawa. Add-on type cardiac development and arrhythmias. Annual Meeting of the Japanese Heart Rhythm Society 2016 July 15, 2016 2016.07.15 Sapporo, Hokkaido
12. Tetsushi Furukawa. Mechanisms of arrhythmias in heart failure and new advances in its management. Annual Meeting of the Japanese Heart Rhythm Society 2016 2016.07.16 Sapporo, Hokkaido
13. Lian Liu, Yusuke Ebana, Jun-ichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Toshihiro Tanaka, Masatoshi Komura, Mitsuki Isobe, Tetsushi Furukawa. Common genetic variants indicate the risk of atrial fibrillation in Japanese population.. The 63th Annual Meeting of the Japanese Heart Rhythm Society 2016.07.16 Sapporo
14. Sasano T, Hamada S, Hasegawa Y, Nishimura T, Yoshitake T, Shiohira S, Sasaki T, Kawabata M, Goya M, Isobe M, Furukawa T, Hirao K. Individual evaluation of whole blood coagulability and factor Xa activity by novel dielectric blood coagulometry.. The 63th Annual Meeting of the Japanese Heart Rhythm Society 2016.07.17 Sapporo
15. Kurokawa J, Kanda Y, Kodama M, Sekino Y, Furukawa T. Effects of anticancer drugs on contractile behaviors of human- induced pluripotent stem cell-derived cardiomyocyte monolayers evaluated with an image-based analysis using motion field imaging technique. 2016 SPS/JSPS/CSPT 2016.09.19 Vancouver, Canada
16. Furukawa T, Okata S, Yuasa S, Suzuki T, Makita N, Kurokawa J, Egashira T, Yamakawa H, Seki T, Aizawa T, Hashimoto H, Kuroda Y, Tanaka A, Yae K, Murata M, Aiba T, Shimizu W, Horie M, Kodama I, Ogawa S, Fukuda K. Disease modeling using iPS cells. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
17. Sato Y, Satoh A, Nitta J, Honda Y, Kuroda S, Sekigawa M, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Impact of SNP on IL6R (rs7514452) for age at onset of atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
18. Sekigawa M, Satoh A, Nitta J, Sato Y, Honda Y, Kuroda S, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Effect of SNP on 9q22 (rs6479562) on the progression from paroxysmal atrial fibrillation to persistent atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

## Stem Cell Regulation

Professor Tetsuya TAGA  
Associate Professor Ikuo NOBUHISA  
Assistant Professor Kouichi TABU  
Technical Assistant/Administrative Assistant Kazuko INOUE

### ( 1 ) Outline

Research in this department has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. Particular attention is given to cell-external cues (such as cytokines) and cell-intrinsic programs (including epigenetic modification), taking cross-interactions of transcriptional regulatory signals into consideration.

### ( 2 ) Research

Research Subjects in this department are as follows:

- 1) Molecular basis for the maintenance of neural stem cells
- 2) Regulation of the neural stem cell fate
- 3) Characterization of hematopoietic stem cells in fetal hematopoietic organs
- 4) Characterization of cancer stem cells and their niche
- 5) Epigenetic regulation of neural development

### ( 3 ) Education

Our education has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. The projects have been performed, for instance by elucidation of stem cell characteristics, analysis of transcriptional regulatory signaling pathways, and identification of niche signals.

### ( 4 ) Lectures & Courses

Under our education program, students will learn the molecular basis of stem cell regulation in view of cell-extrinsic signals and cell intrinsic-programs during tissue development, maintenance, and regeneration from molecular to whole-body levels. Students will receive exposure to cutting edge concepts and research technologies, and study regulatory mechanisms in neural, hematopoietic, and cancer stem cells. With emphasis also on physiological and pathological conditions surrounding the stem cells, we aims to improve student's understanding of stem cells from multiple viewpoints.

**( 5 ) Publications****[Original Articles]**

1. Inagaki T, Kusunoki S, Tabu K, Okabe H, Yamada I, Taga T, Matsumoto A, Makino S, Takeda S, and Kato K. Up-regulation of lymphocyte antigen 6 complex expression in side-population cells derived from a human trophoblast cell line HTR-8/SVneo. *Hum Cell*. 2016.01; 29; 10-21
2. Sudo G, Kagawa T, Kokubu Y, Inazawa J, and Taga T. Increase of GFAP-positive astrocytes in histone demethylase GASC1/KDM4C/JMJD2C hypomorphic mutant mice. *Genes Cells*. 2016.03; 21; 218-225
3. Kokubu Y, Tabu K, Wang W, Muramatsu N, Murota Y, Nobuhisa I, Jinushi M, and Taga T. Induction of protumoral CD11c<sup>high</sup> macrophages by glioma cancer stem cells through GM-CSF. *Genes Cells*. 2016.03; 21; 241-251
4. Tabu K, Muramatsu N, Mangani C, Wu M, Zhang R, Kimura T, Terashima K, Bizen N, Kimura R, Wang W, Murota Y, Kokubu Y, Nobuhisa I, Kagawa T, Kitabayashi I, Bradley M, and Taga T. A synthetic polymer scaffold reveals the self-maintenance strategies of rat glioma stem cells by organization of the advantageous niche. *Stem Cells*. 2016.05; 34; 1151-1162
5. Kimura T, Wang L, Tabu K, Tsuda M, Tanino M, Maekawa A, Nishihara H, Hiraga H, Taga T, Oda Y, and Tanaka S. Identification and analysis of CXCR4-positive synovial sarcoma-initiating cells. *Oncogene*. 2016.07; 35; 3932-3943
6. Murota Y, Tabu K, and Taga T. Requirement of ABC transporter inhibition and Hoechst 33342 dye deprivation for the assessment of side population-defined C6 glioma stem cell metabolism using fluorescent probes. *BMC Cancer*. 2016.11; 16; 847
7. Wang W, Tabu K, Hagiya Y, Sugiyama Y, Kokubu Y, Murota Y, Ogura SI, and Taga T. Enhancement of 5-aminolevulinic acid-based fluorescence detection of side population-defined glioma stem cells by iron chelation. *Sci Rep*. 2016.12; In press

**[Conference Activities & Talks]**

1. Sudo G. Analysis of pathogenic mechanisms of neurodevelopmental disorder-like phenotype exhibited by histone demethylase Gasc1 hypomorphic mutant mice. The 9th Annual Meeting for Japanese Developmental Neuroscientists 2016.03.18 Tokyo Medical and Dental University, Tokyo
2. Saito K, Nobuhisa I, Anani M, Harada K, Takahashi S, and Taga T. Mechanism of maintaining hematopoietic stem and progenitor cell phenotype of intra-aortic cell clusters in the AGM region through the Sox17-Notch1-Hes1 axis. The 14th Stem Cell Symposium 2016.05.20 Awaji Yumebutai International Conference Center, Hyogo, Japan
3. Tabu K, Kokubu Y, Muramatsu N, Nomoto S, Wang W and Taga T. Adaptive response of rat C6 glioma stem cells to iron deprivation by which the development of tumor infiltrating macrophages is induced. The 14th Stem Cell Research Symposium 2016.05.20 Awaji Yumebutai International Conference Center, Awaji, Japan
4. Wang W, Tabu K, Sugiyama Y, Hagiya Y, Ogura S and Taga T. Resistance of glioma stem cells to 5-aminolevulinic acid (ALA)-based detection due to enhanced metabolic conversion of protoporphyrin IX. The 14th Stem Cell Research Symposium 2016.05.20 Awaji Yumebutai International Conference Center, Awaji, Japan
5. Murota Y, Tabu K and Taga T. C6 glioma stem cell-derived extracellular vesicles promote the development of macrophages. The 14th Stem Cell Research Symposium 2016.05.20 Awaji Yumebutai International Conference Center, Awaji, Japan
6. Tabu K, Wang W, Murota Y and Taga T. Adaptive response of C6 glioma stem cells to iron deprivation through macrophage induction. The 75th Annual Meeting of the Japanese Cancer Association 2016.10.06 Pacifico Yokohama, Yokohama, Japan
7. Wang W, Tabu K, Hagiya Y, Murota Y, Ogura S and Taga T. Enhancement of 5-aminolevulinic acid-based fluorescence detection of glioma stem cells by chelating iron. The 75th Annual Meeting of the Japanese Cancer Association 2016.10.06 Pacifico Yokohama, Yokohama, Japan

8. Saito K, Nobuhisa I, Anani M, Harada K, Takahashi S, Lickert H, Kanai M, Kanai Y, and Taga T. Maintenance of hematopoietic stem and progenitor cell phenotype of intra-aortic cell clusters in the AGM region through the Sox17-Notch1-Hes1 axis. The 39th Annual Meeting of the Molecular Biology Society of Japan 2016.12.01 Pacifico Yokohama, Yokohama, Japan
9. Takahashi S, Nobuhisa I, Saito K, and Taga T. Involvement of transcription factor Sox17-mediated expression of adhesion molecules in hematopoietic cell cluster formation in midgestation mouse dorsal aorta. The 39th Annual Meeting of the Molecular Biology Society of Japan 2016.12.01 Pacifico Yokohama, Yokohama, Japan
10. Kagawa T, Yamaguchi Y, Sudo G, Kokubu Y, Hattori S, Takao K, Miyakawa T, Inazawa J, and Taga T. Astroglial development is regulated by DNA and histone methylation: from molecular basis to behavioral abnormalities in gene-manipulated mice. Cold Spring Harbor Asia meeting on Novel Insights into Glia Function & Dysfunction 2016.12.06 Suzhou Industrial Park Conference Center, Suzhou, China

# Molecular Pharmacology

Professor: Masaki Noda, M.D., Ph.D.

Associate Professor: Yoichi Ezura, M.D., Ph.D.

Assistant Professor: Yayoi Izu, DVM, Ph.D.

Research Assistant Professor: Smriti Aryal A.C., DDS, Ph.D.

## ( 1 ) Outline

In order to contribute to the establishment of therapy and prevention for osteoporosis and the other calcium-related disorders, we are elucidating molecular mechanisms underlying regulation of calcium metabolism with emphases on bone formation and resorption. Skeletal system is the largest storage site for calcium in a living body and its metabolism is conducted by a complex cell society consisting of bone-forming osteoblasts and bone-resorbing osteoclasts as well as stromal cells and chondrocytes. In our department, we take molecular and cellular biological approaches to study the mechanisms underlying regulation of development, differentiation, and function of these cells.

## ( 2 ) Research

Bone is the major organ for calcium metabolism in our body. The regulation of bone metabolism is mediated by a balance between osteoblastic bone formation and osteoclastic bone resorption. These activities are maintained in balance and called bone remodeling. Imbalance of the remodeling results in development of bone disorders, such as osteoporosis. Osteoblasts are differentiated from mesenchymal stem cells. These cells are under the regulation by local and systematic factors, such as growth factors and hormones. These factors activate intracellular signaling, which promotes transcription factors thereby delineates cell differentiation. In our laboratory, we are studying the process from various aspects of bone cell regulation including transcription factors, cytokines and hormones. To promote our study, knockout and transgenic mice, gene introduction via virus, global analysis of gene expression, and genome database analysis are used. Our study will provide the basic understandings of bone homeostasis, which will contribute the development of measures for diagnosis and treatment of bone disorders.

## ( 3 ) Publications

### [Original Articles]

1. Sakie Katsumura, Yoichi Ezura, Yayoi Izu, Jumpei Shirakawa, Atsushi Miyawaki, Kiyoshi Harada, Masaki Noda. Beta Adrenergic Receptor Stimulation Suppresses Cell Migration in Association with Cell Cycle Transition in Osteoblasts-Live Imaging Analyses Based on FUCCI System. *J. Cell. Physiol.* 2016.02; 231(2); 496-504
2. Katsumura S, Ezura Y, Izu Y, Shirakawa J, Miyawaki A, Harada K, Noda M. Beta Adrenergic Receptor Stimulation Suppresses Cell Migration in Association with Cell Cycle Transition in Osteoblasts-Live Imaging Analyses Based on FUCCI System *J Cell Physiol.* 2016.02; 231(2); 496-504
3. Lin W, Ezura Y, Izu Y, Aryal SA, Kawasaki M, Chantida PN, Moriyama K, Noda M. Profilin Expression Is Regulated by Bone Morphogenetic Protein (BMP) in Osteoblastic Cells. *Journal of Cellular Biochemistry.* 2016.03; 117(3); 621-628

4. Shirakawa J, Harada H, Noda M, Ezura Y. PTH-Induced Osteoblast Proliferation Requires Upregulation of the Ubiquitin-Specific Peptidase 2 (Usp2) Expression Calcif Tissue Int. 2016.03; 98(3); 306-315
5. Lin W, Ezura Y, Izu Y, Aryal SA, Kawasaki M, Chantida PN, Moriyama K, Noda M. Profilin Expression Is Regulated by Bone Morphogenetic Protein (BMP) in Osteoblastic Cells J Cell Biochem. 2016.03; 117(3); 621-628

# Stem Cell Biology

Professor : Emi Nishimura, M.D., Ph.D.  
 Associate Professor: Daisuke Nanba, Ph.D.  
 Assistant Professor : Hiroyuki Matsumura, Ph.D.  
 Project Assistant Professor :Yasuaki Mohri, Ph.D.  
 Makoto Fukuda, Ph.D.  
 JSPS Research Fellow : Hironobu Morinaga, Ph.D.

## ( 1 ) Outline

Stem cell systems play fundamental roles in tissue turnover and homeostasis. Our goal is to understand the mechanisms of tissue homeostasis driven by stem cell systems and to apply the knowledge to better understand the mechanisms underlying specific tissue decline, cancer development and other diseases associated with aging. We further aim to apply this knowledge to regenerative medicine using somatic stem cells and the treatment of cancer as well as other age-associated diseases.

## ( 2 ) Research

### 1) Identification of stem cells in the skin

The skin is the largest organ in the body. Hair follicles in the skin constantly renew themselves by alternate phases of growth, regression and rest. During this process, mature melanocytes (pigment cells) in hair follicles are replaced by a new cell population every hair cycle. We previously identified the source of those melanocytes, “melanocyte stem cells” (McSC), which are located in the hair follicle bulge and supply mature melanocytes required for hair and skin pigmentation (Nishimura EK et al. Nature 2002). We currently identified McSCs in eccrine sweat glands in non-hair-bearing skin areas as well. Also we are currently searching for the prospective method for identification of epidermal keratinocyte stem cells in mouse and human skin.

### 2) Mechanisms of stem cell maintenance

The underlying mechanisms of stem cell maintenance is a fundamental issue in stem cell biology and medicine. We previously demonstrated that the niche microenvironment plays dominant role in melanocyte stem cell fate determination (Nishimura EK et al. 2002). We then revealed that hair follicle stem cells (HFSC), which surround McSCs in the hair follicle bulge-subbulge area, serve as a functional niche for McSC maintenance through transforming growth factor  $\beta$  (TGF- $\beta$ ) (Nishimura EK et al. Cell Stem Cell, 2010) (Tanimura S et al. Cell Stem Cell 2011). As intrinsic defects in stem cells such as caused by Mitf or Bcl2 deficiency also induces McSC depletion which leads to the progressive expression of hair graying phenotype, incomplete maintenance of McSCs either by defective signaling from the stem cell niche or by intrinsic defects in stem cells induces the progressive hair graying phenotype.

### 3) Mechanisms for stem cell aging and quality control of stem cell pools.

Physiological hair graying is the most obvious outward sign of aging in mammals, yet it has been unclear what causes the incomplete maintenance of MsSCs during the course of aging (Nishimura EK et al. Science 2005). We have found that genotoxic stress abrogates renewal of McSCs by triggering their differentiation without inducing stem cell apoptosis nor cellular senescence. Our findings indicated that a “stem cell renewal check-point” exists to maintain the quality of the melanocyte stem cell pool (Inomata K, Aoto T et al. Cell 2009). Interestingly, a similar mechanism actually underlies epithelial tissue aging (See Highlight).



#### 4) Development of skin regeneration technology with human skin stem cells

Human epidermal keratinocyte stem cells can be cultivated under suitable conditions, and generate a progeny large enough to entirely reconstitute the epidermis of an adult human. This has enabled the autologous transplantation of cultured epidermal sheets onto patients with extensive burns. However, the cultured keratinocytes can regenerate only the epidermis and cannot suppress dermal scarring. To develop novel skin regeneration technology, we have investigated human epidermal keratinocytes and dermal fibroblasts, and obtained the following results. 1) Human epidermal keratinocyte stem cells can be identified in situ by analyzing cell motion during their cultivation (Nanba et al., J. Cell Biol., 2015, Tate et al., J. Dermatol. Sci. 2015). The identification of keratinocyte stem cells by image analysis is a valid parameter for quality control of cultured keratinocytes for transplantation, and improves the clinical outcome of cell therapy and the efficiency of cell manufacturing for regenerative medicine. 2) Human dermal fibroblasts can be categorized at least two functional clonal types by comprehensive phenotypic and gene expression profiling (Hiraoka et al., J. Dermatol. Sci. in press). One is highly proliferative, while the other is less proliferative but has the ability to remodel the tissue architecture. The proliferative clones are predominant in infants, but decrease with physiological aging. These data have implications regarding the functional heterogeneity of dermal fibroblasts and skin repair and aging.

### (3) Publications

#### [Original Articles]

1. Hiroyuki Matsumura,\* Yasuaki Mohri,\* Nguyen Thanh Binh,\* Hironobu Morinaga, Makoto Fukuda, Mayumi Ito, Sotaro Kurata, Jan Hoeijmakers, Emi K. Nishimura. Hair follicle aging is driven by transepidermal elimination of stem cells via COL17A1 proteolysis Science. 2016.02; 351(6273); 575-589
2. Karigane D, Kobayashi H, Morikawa T, Ootomo Y, Sakaki M, Nagamatsu G, Kubota Y, Goda N, Matsumoto M, Nishimura EK, Soga T, Otsu K, Suematsu M, Okamoto S, Suda T, and Takubo K. P38  $\alpha$  Activates Purine Metabolism to Initiate Hematopoietic Stem/Progenitor Cell Cycling in Response to Stress Cell Stem Cell. 2016.08; 19(2); 192-204

#### [Conference Activities & Talks]

1. Emi Nishimura. Regulation of Tissue Stem Cells in Hair Follicle Regulation and Aging. The 89th Annual Meeting of the Japanese Pharmacological Society 2016.03.09
2. Emi Nishimura. stem cell aging: a clue to understand hair thinning and graying. 1st International Symposium on Stem Cell Aging and Disease 2016.06.29 Tokyo, Japan
3. Emi Nishimura. Mechanisms of hair follicle aging and hair loss. Cell Symposia: Aging and Metabolism 2016 2016.07.10 Melia Sitges, Spain
4. Emi Nishimura. New Insights in Stem Cell Research & Age-related Changes in Skin and Hair Pigmentation. 46th Annual ESDR Meeting 2016.09 Munich, Germany
5. Emi Nishimura. Melanocyte Stem Cells in eccrine sweat glands: a potential of acral melanoma. 12th Meeting of the German-Japanese Society of Dermatology 2016.10.13 Nagano, Japan

# Respiratory Medicine

Professor: Naohiko INASE

Junior Associate Professor: Kimitake TSUCHIYA

Assistant Professor: Toshihide FUJIE, Tomoya TATEISHI, Haruhiko FURUSAWA, Masahiro ISHIZUKA,

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Masahiro MASUO, Tsuyoshi SHIRAI, Makiko SUGIURA, Yuta ADACHI, Ken UCHIBORI,

Yu KUSAKA, Rie SAKAKIBARA, Manabu SEMA, Tomoko TERADA, Yoshihisa NUKUI, Takayuki HONDA,

Takahiro MITSUMURA, Sho SHIBATA, Yukihisa INOUE, Rie KURASHIGE, Hiroaki SAITOH, Satoshi HANZAWA

## ( 1 ) Outline

Respiratory Medicine deals with a variety of pulmonary diseases including tumors, infectious diseases, allergic diseases, non-allergic inflammatory diseases, and genetic disorders.

## ( 2 ) Research

- 1) Pathogenesis of hypersensitivity pneumonitis and detection of environmental causative antigen
- 2) Airway remodeling in bronchial asthma model
- 3) Acute exacerbation in pulmonary fibrosis
- 4) Proteomics of pulmonary fibrosis
- 5) Pathogenesis of pulmonary fibrosis and emphysema

## ( 3 ) Education

Main objective in the graduate course is to provide students to study specific diagnostic modalities as well as basic scientific findings regarding the pathogenesis of pulmonary diseases. Students are also taught on basic science and its related laboratory technology depending upon their research subject.

## ( 4 ) Lectures & Courses

Students should try to understand a variety of pulmonary diseases in terms of scientific aspect and make an appropriate plan to examine unsolved research questions.

## ( 5 ) Clinical Services & Other Works

Our clinic provides a full spectrum of diagnosis and treatment of a variety of pulmonary diseases. Consultant system is open to all departments in this hospital and daily clinical conference regarding inpatients is organized by professors of the department. In outpatient clinic, chemotherapy, home oxygen therapy, management of sleep apnea, and arrange of clinical studies are provided.

## ( 6 ) Clinical Performances

We have immunological tools to examine hypersensitivity pneumonitis including antigen inhalation challenge test, specific antibody against causative antigen, and lymphocyte proliferation test. Many patients with interstitial lung diseases in Japan are referred to our clinic.

## ( 7 ) Publications

### [Original Articles]

1. Chiba S, Tsuchiya K, Akashi T, Ishizuka M, Okamoto T, Furusawa H, Tateishi T, Kishino M, Miyazaki Y, Tateishi U, Takemura T, Inase N. Chronic hypersensitivity pneumonitis with a usual interstitial pneumonia (UIP)-like pattern: Correlation between histopathological and clinical findings. *CHEST*. 2016; 149; 1473-1481
2. Sakakibara Y, Ohtani Y, Jinta T, Fujie T, Miyazaki Y, Inase N, Saito R, Akaza M, Sasano T, Sumi Y. Concentration of immunoglobulin G antibodies against pertussis toxin does not decrease over a long period of time in Japan. *Internal Medicine*. 2016; 55; 3257-3263
3. Masuo M, Miyazaki Y, Suhara K, Ishizuka M, Fujie T, Inase N. Factors associated with positive inhalation provocation test results in subjects suspected of having chronic bird-related hypersensitivity pneumonitis. *Respir Investig*. 2016; 54; 454-461
4. Suhara K, Miyazaki Y, Okamoto T, Ishizuka M, Tsuchiya K, Inase N. Fragmented gelsolins are increased in rheumatoid arthritis-associated interstitial lung disease with usual interstitial pneumonia pattern. *Allergol Int*. 2016.01; 65(1); 88-95

### [Misc]

1. Miyazaki Y, Tsutsui T, Inase N. Treatment and monitoring of hypersensitivity pneumonitis. *Expert Rev Clin Immunol*.. 2016.09; 12(9); 953-962

### [Conference Activities & Talks]

1. Nukui, Y, Miyazaki Y, Inase N. Proteomics analysis of BALF in sarcoidosis associated pulmonary fibrosis. *ATS International Conference 2016.05.15 San Francisco*
2. Tateishi, Fujie T, Miyazaki Y, Inase N. Clinical characteristics of community-acquired pneumonia in the patients with pulmonary fibrosis. *ATS International Conference 2016.05.15 San Francisco*
3. Sema M, Sakashita H, Miyazaki Y, Inase N. Clinical characteristics of lung cancer diagnosed during follow-up of interstitial pneumonia. *ATS International Conference 2016.05.16 San Francisco*
4. Wakabayashi K, Adachi Y, Tateishi T, Inase N, Nakazawa K. Ventilator type and setting for patients with acute respiratory failure on chronic interstitial lung disease. *ATS International Conference 2016.05.17 San Francisco*
5. Masuo M, Miyazaki Y, Fujie T, Inase N, Nakamura M, Ohbo K. Human epididymis protein 4 is a novel biomarker for chronic fibrosing interstitial pneumonias. *ATS International Conference 2016.05.17 San Francisco*
6. Furusawa H, Sugiura M, Miyazaki Y, Inase N. The usefulness of direct hemoperfusion with polymyxin B-immobilized fiber (PMX-DHP) treatment on acute exacerbation of interstitial pneumonitis. *ATS International Conference 2016.05.17 San Francisco*
7. Jin Y, Shimada S, Yamauchi S, Matsubara O, Yamanaka K, Inase N. Myeloid-derived suppressor cell expression within the microenvironment of lung adenocarcinoma.. *IASLC 17th World Conference of Lung Cancer, Vienna 2016.11.04 AUSTRIA*

# Gastroenterology and Hepatology

Professor Mamoru WATANABE

Professor Yasuhiro ASAHINA (Department for Hepatitis Control)  
 Kazuo OHTSUKA (Department of Endoscopic Diagnosis and Therapeutics)  
 Ryuichi OKAMOTO (Center for Stem Cell and Regenerative Medicine)  
 Tetsuya NAKAMURA  
 (Department of Advanced Therapeutics in Gastrointestinal Diseases)

Associate Professor  
 Kiichiro TSUCHIYA  
 Shinya OOKA (Cancer Center)  
 Mina NAKAGAWA (Center for Interprofessional Education)  
 Akihiro ARAKI (Center for Personalized Medicine for Healthy Aging)

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Junior Associate Professor  
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 Yasuhiro ITSUI (Department of General Medicine)  
 Eriko OKADA (Department of Endoscopic Diagnosis and Therapeutics)  
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 Tomohiro MIZUTANI  
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 (Department of Advanced Therapeutics in Gastrointestinal Diseases)  
 Masayoshi FUKUDA (Department of Endoscopic Diagnosis and Therapeutics)  
 Miyako MURAKAWA (Clinical Laboratory)

Project Assistant Professor  
 Sayuri NITTA, Ryu NISHIMURA

Hospital Staff  
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 Tatsuo MURANO, Taichi MATSUMOTO, Masanori KOBAYASHI, Toru NAKATA,  
 Yoichi NIBE, Masato YAUCHI, Konomi KUWAHARA, Maiko KIMURA,  
 Fukiko KITAHATA, Kento TAKENAKA, Nobuhiro KATSUKURA

AMED Fellow  
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 Fumio GOTO, Taichi MATSUMOTO, Masanori KOBAYASHI, Toru NAKATA,  
 Youichi NIBE, Satoru FUJII, Kento TAKENAKA, Hiroko NAGATA,  
 Shun KANEKO, Chiaki MAEYASHIKI, Taro WATABE, Yuka MATSUMOTO,  
 Kohei SUZUKI, Akinori HOSOYA, Yu ASANO, Emi INOUE, Shintaro AKIYAMA,  
 Fumiaki ISHIBASHI, Ami KAWAMOTO, Masato MIYOSHI, Tomoyuki TSUNODA,  
 Yuria TAKEI, JOSE Nisha, Sho ANZAI, Tomoaki SHIRASAKI, Shohei TANAKA,  
 Reiko KUNO, Kana OTSUBO, Ayako Sato, Sho WARANABE, JOSE Nisha,  
 Arisa TOUKAI

## ( 1 ) Outline

Research project is selected from the clinical problems in the Gastroenterology and Hepatology to understand the research policy, as clinical science that the results of research project finally should be restored to clinical medicine.

The purpose of this course is the understanding the situation of inflammatory bowel disease (IBD) in Japan and the problems about the pathogenesis and intractable cause of IBD. In addition, the understanding the pathogenesis and problems about the liver diseases such as viral hepatitis, cirrhosis and hepatocellular carcinoma is the purpose of this course.

## ( 2 ) Research

Basic Research Projects

Systemic Organ Regulation

- Elucidating the pathophysiology of inflammatory bowel diseases and development of treatment by diseasespecific

immune-regulation.

- Development of novel therapeutics for inflammatory and allergic diseases based on gut-specific mucosal immune

regulation.

- Basic research and clinical application of regenerative medicine in gastrointestinal diseases.

- Analysis of interferon-resistant hepatitis C virus.

- Comprehensive analysis of susceptibility genes for various gastrointestinal diseases.

- Crosstalk of the signaling pathways in intestinal epithelial cells.

- Functional analysis of the intestine using primary cell culture in vitro.

## ( 3 ) Education

We believe that the central role of clinical departments in the graduate school is to establish basis for the innovative medicine / medical treatment in the next generation. Basic research lead by clinical concepts, and development of novel therapeutics established upon basic research are both critically required to achieve our mission. Therefore, our primary goal is set to train highly educated and experienced clinician-researchers in the field of gastroenterology and hepatology.

In the clinical area, we pursue development and application of highly advanced technologies, including novel endoscopic procedures, for sophisticated diagnosis and treatment of gastrointestinal and liver diseases. In basic research, our principle is to achieve "clinical science", a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice. Based on these principals, we are running research projects to 1) develop novel therapy for refractory inflammatory bowel diseases, 2) prevent progression of liver failure in chronic hepatitis patients and 3) improve anti-cancer therapy for the treatment of gastrointestinal malignancies, by expanding our distinct basic research findings in the area of mucosal immunology, liver immunology, regenerative medicine and virology, to various clinical settings. Moreover, we promote both intra- and inter-national exchanges of researchers, and provide good opportunities to study abroad. The final goal of our education is to promote students to become a well-developed clinician researcher, and also a leading expert in the field of gastroenterology and hepatology.

## ( 4 ) Lectures & Courses

Research Conference                      every Tuesday 18:00 19:30

Journal Club                                every Tuesday 18:00 19:30

## ( 5 ) Clinical Services & Other Works

Expert Areas in Clinical Practice

- Immune-regulation based treatment of inflammatory bowel diseases.

- Prevention of chronic hepatitis progression to hepatocellular cancer and liver failure, by virology-based treatment strategy.
- Clinical trial of innovative treatment for hepatocellular cancer.
- Diagnosis and treatment of small intestinal diseases by balloon enteroscopy and capsule enteroscopy.
- Advanced diagnosis and treatment of colonic diseases by colonoscopy.
- Development of minimally-invasive diagnostic modalities for gastrointestinal diseases (i.e. MR enteroclysis).
- Improved chemotherapy for gastric and pancreatic malignancies.

## (6) Clinical Performances

Therapeutics of inflammatory bowel diseases by corrections of immunological disfunctions.

Diagnostic and interventional gastrointestinal endoscopy

Antiviral therapies against chronic viral hepatitis and preventions of hepatic malignancy novel interventions of hepatic malignancy.

## (7) Publications

### [Original Articles]

1. Jun Itakura, Masayuki Kurosaki, Chitomi Hasebe, Yukio Osaki, Kouji Joko, Hitoshi Yagisawa, Shinya Sakita, Hiroaki Okushin, Takashi Satou, Hiroyuki Hisai, Takehiko Abe, Keiji Tsuji, Takashi Tamada, Haruhiko Kobashi, Akeri Mitsuda, Yasushi Ide, Chikara Ogawa, Syotaro Tsuruta, Kouichi Takaguchi, Miyako Murakawa, Yasuhiro Asahina, Nobuyuki Enomoto, Namiki Izumi. Complex Pattern of Resistance-Associated Substitutions of Hepatitis C Virus after Daclatasvir/Asunaprevir Treatment Failure. *PLoS ONE*. 2016; 11(10); e0165339
2. Takashi Nagaishi, Taro Watabe, Nisha Jose, Arisa Tokai, Toshimitsu Fujii, Katsuyoshi Matsuoka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Epithelial Nuclear Factor- $\kappa$  B Activation in Inflammatory Bowel Diseases and Colitis-Associated Carcinogenesis Digestion. 2016.01; 93(1); 40-46
3. Yasuhiro Asahina, Mamoru Watanabe. Need for appropriate programs for prevention of hepatitis B infection: Lessons from the latest nationwide survey in Japan. *J. Gastroenterol. Hepatol.* 2016.01; 31(1); 12-13
4. Satoshi Otani, Sei Kakinuma, Akihide Kamiya, Fumio Goto, Shun Kaneko, Masato Miyoshi, Tomoyuki Tsunoda, Yu Asano, Fukiko Kawai-Kitahata, Sayuri Nitta, Toru Nakata, Ryuichi Okamoto, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Yasuhiro Asahina, Tomoyuki Yamaguchi, Naohiko Koshikawa, Motoharu Seiki, Hiromitsu Nakauchi, Mamoru Watanabe. Matrix metalloproteinase-14 mediates formation of bile ducts and hepatic maturation of fetal hepatic progenitor cells. *Biochem. Biophys. Res. Commun.* 2016.01; 469(4); 1062-1068
5. Tetsuhide Ito, Hiroshi Ishiguro, Hirotaka Ohara, Terumi Kamisawa, Junichi Sakagami, Naohiro Sata, Yoshifumi Takeyama, Morihisa Hirota, Hiroyuki Miyakawa, Hisato Igarashi, Lingaku Lee, Takashi Fujiyama, Masayuki Hijioka, Keiji Ueda, Yuichi Tachibana, Yoshio Sogame, Hiroaki Yasuda, Ryusuke Kato, Keisho Kataoka, Keiko Shiratori, Masanori Sugiyama, Kazuichi Okazaki, Shigeyuki Kawa, Yusuke Tando, Yoshikazu Kinoshita, Mamoru Watanabe, Tooru Shimosegawa. Evidence-based clinical practice guidelines for chronic pancreatitis 2015. *J. Gastroenterol.* 2016.02; 51(2); 85-92
6. Yasuhiro Asahina, Namiki Izumi, Kumada Hiromitsu, Masayuki Kurosaki, Kazuhiko Koike, Fumitaka Suzuki, Hajime Takikawa, Atsushi Tanaka, Eiji Tanaka, Yasuhito Tanaka, Hirohito Tsubouchi, Norio Hayashi, Naoki Hiramatsu, Hiroshi Yotsuyanagi. JSH Guidelines for the Management of Hepatitis C Virus Infection: A 2016 update for genotype 1 and 2. *Hepatol. Res.* 2016.02; 46(2); 129-165
7. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shinji Tanaka, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Satoshi Otani, Miki Taniguchi, Fumio Goto, Hiroko Nagata, Shun Kaneko, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Mina Nakagawa, Minoru Tanabe, Shinichi Takano, Mitsuharu Fukasawa, Minoru Sakamoto, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma with clinicopathological features. *J. Gastroenterol.* 2016.03; 51(5); 473-486

8. Taku Kobayashi, Yasuo Suzuki, Satoshi Motoya, Fumihito Hirai, Haruhiko Ogata, Hiroaki Ito, Noriko Sato, Kunihiko Ozaki, Mamoru Watanabe, Toshifumi Hibi. First trough level of infliximab at week 2 predicts future outcomes of induction therapy in ulcerative colitis-results from a multicenter prospective randomized controlled trial and its post hoc analysis. *J. Gastroenterol.* 2016.03; 51(3); 241-251
9. Kengo Nozaki, Wakana Mochizuki, Yuka Matsumoto, Taichi Matsumoto, Masayoshi Fukuda, Tomohiro Mizutani, Mamoru Watanabe, Tetsuya Nakamura. Co-culture with intestinal epithelial organoids allows efficient expansion and motility analysis of intraepithelial lymphocytes. *J. Gastroenterol.* 2016.03; 51(3); 206-213
10. Miki Taniguchi, Megumi Tasaka-Fujita, Mina Nakagawa, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Fumio Goto, Hiroko Nagata, Shun Kaneko, Sayuri Nitta, Miyako Murakawa, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Kenichi Mori, Shintaro Yagi, Sei Kakinuma, Yasuhiro Asahina, Mamoru Watanabe. Evaluation of Interferon Resistance in Newly Established Genotype 1b Hepatitis C Virus Cell Culture System. *J Clin Transl Hepatol.* 2016.03; 4(1); 5-11
11. Seishin Azuma, Yasuhiro Asahina, Yuki Nishimura-Sakurai, Sei Kakinuma, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Ootani, Fukiko Kawai-Kitahata, Miki Taniguchi, Miyako Murakawa, Takako Watanabe, Megumi Tasaka-Fujita, Yasuhiro Itsui, Mina Nakagawa, Mamoru Watanabe. Efficacy of additional radiofrequency ablation after transcatheter arterial chemoembolization for intermediate hepatocellular carcinoma. *Hepatol Res.* 2016.04; 46(4); 312-319
12. Kazuo Ohtsuka, Kento Takenaka, Yoshio Kitazume, Toshimitsu Fujii, Katsuyoshi Matsuoka, Maiko Kimura, Takashi Nagaishi, Mamoru Watanabe. Magnetic resonance enterography for the evaluation of the deep small intestine in Crohn's disease. *Intest Res.* 2016.04; 14(2); 120-126
13. Shunsuke Komoto, Satoshi Motoya, Yuji Nishiwaki, Toshiyuki Matsui, Reiko Kunisaki, Katsuyoshi Matsuoka, Naoki Yoshimura, Takashi Kagaya, Makoto Naganuma, Nobuyuki Hida, Mamoru Watanabe, Toshifumi Hibi, Yasuo Suzuki, Soichiro Miura, Ryota Hokari, . Pregnancy outcome in women with inflammatory bowel disease treated with anti-tumor necrosis factor and/or thiopurine therapy: a multicenter study from Japan *Intest Res.* 2016.04; 14(2); 139-145
14. Ryuichi Okamoto, Mamoru Watanabe. Investigating cell therapy for inflammatory bowel disease. *Expert Opin Biol Ther.* 2016.04; 1-9
15. Ryohei Hayashi, Kiichiro Tsuchiya, Keita Fukushima, Nobukatsu Horita, Shuji Hibiya, Keisuke Kitagaki, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Eriko Okada, Akihiro Araki, Kazuo Ohtsuka, Shinji Fukuda, Hiroshi Ohno, Ryuichi Okamoto, Tetsuya Nakamura, Shinji Tanaka, Kazuaki Chayama, Mamoru Watanabe. Reduced Human  $\alpha$ -defensin 6 in Noninflamed Jejunal Tissue of Patients with Crohn's Disease. *Inflamm. Bowel Dis.* 2016.05; 22(5); 1119-1128
16. Emma Calabrese, Christian Maaser, Francesca Zorzi, Klaus Kannengiesser, Stephen B Hanauer, David H Bruining, Marietta Iacucci, Giovanni Maconi, Kerri L Novak, Remo Panaccione, Deike Strobel, Stephanie R Wilson, Mamoru Watanabe, Francesco Pallone, Subrata Ghosh. Bowel Ultrasonography in the Management of Crohn's Disease. A Review with Recommendations of an International Panel of Experts. *Inflamm. Bowel Dis.* 2016.05; 22(5); 1168-1183
17. Kara G Lassen, Craig I McKenzie, Muriel Mari, Tatsuro Murano, Jakob Begun, Leigh A Baxt, Gautam Goel, Eduardo J Villablanca, Szu-Yu Kuo, Hailiang Huang, Laurence Macia, Atul K Bhan, Marcel Batten, Mark J Daly, Fulvio Reggiori, Charles R Mackay, Ramnik J Xavier. Genetic Coding Variant in GPR65 Alters Lysosomal pH and Links Lysosomal Dysfunction with Colitis Risk. *Immunity.* 2016.06; 44(6); 1392-1405
18. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Hironori Nishitsuji, Saneyuki Ujino, Kunitada Shimotohno, Masashi Iwamoto, Koichi Watashi, Takaji Wakita, Mamoru Watanabe. Human induced pluripotent stem cell-derived hepatic cell lines as a new model for host interaction with hepatitis B virus. *Sci Rep.* 2016.07; 6; 29358
19. Hiroshi Fukui, Hidetsugu Saito, Yoshiyuki Ueno, Hirofumi Uto, Katsutoshi Obara, Isao Sakaida, Akitaka Shibuya, Masataka Seike, Sumiko Nagoshi, Makoto Segawa, Hirohito Tsubouchi, Hisataka Moriwaki,



- Akinobu Kato, Etsuko Hashimoto, Kojiro Michitaka, Toshikazu Murawaki, Kentaro Sugano, Mamoru Watanabe, Tooru Shimosegawa. Evidence-based clinical practice guidelines for liver cirrhosis 2015. *J. Gastroenterol.* 2016.07; 51(7); 629-650
20. Taichi Matsumoto, Wakana Mochizuki, Yoichi Nibe, Shintaro Akiyama, Yuka Matsumoto, Kengo Nozaki, Masayoshi Fukuda, Ayumi Hayashi, Tomohiro Mizutani, Shigeru Oshima, Mamoru Watanabe, Tetsuya Nakamura. Retinol Promotes In Vitro Growth of Proximal Colon Organoids through a Retinoic Acid-Independent Mechanism. *PLoS ONE.* 2016.08; 11(8); e0162049
  21. Ryuichi Okamoto, Mariko Negi, Syohei Tomii, Yoshinobu Eishi, Mamoru Watanabe. Diagnosis and treatment of microscopic colitis. *Clin J Gastroenterol.* 2016.08; 9(4); 169-174
  22. Katsuhiko Iwakiri, Yoshikazu Kinoshita, Yasuki Habu, Tadayuki Oshima, Noriaki Manabe, Yasuhiro Fujiwara, Akihito Nagahara, Osamu Kawamura, Ryuichi Iwakiri, Soji Ozawa, Kiyoshi Ashida, Shuichi Ohara, Hideyuki Kashiwagi, Kyoichi Adachi, Kazuhide Higuchi, Hiroto Miwa, Kazuma Fujimoto, Motoyasu Kusano, Yoshio Hoshihara, Tatsuyuki Kawano, Ken Haruma, Michio Hongo, Kentaro Sugano, Mamoru Watanabe, Tooru Shimosegawa. Evidence-based clinical practice guidelines for gastroesophageal reflux disease 2015. *J. Gastroenterol.* 2016.08; 51(8); 751-767
  23. Naoki Hosoe, Kenji Watanabe, Takako Miyazaki, Masaaki Shimatani, Takahiro Wakamatsu, Kazuichi Okazaki, Motohiro Esaki, Takayuki Matsumoto, Takayuki Abe, Takanori Kanai, Kazuo Ohtsuka, Mamoru Watanabe, Keiichi Ikeda, Hisao Tajiri, Naoki Ohmiya, Masanao Nakamura, Hidemi Goto, Tomoyuki Tsujikawa, Haruhiko Ogata. Evaluation of performance of the Omni mode for detecting video capsule endoscopy images: A multicenter randomized controlled trial. *Endosc Int Open.* 2016.08; 4(8); E878-E882
  24. Haruhiko Ogata, Mamoru Watanabe, Toshiyuki Matsui, Hidenori Hase, Motohiro Okayasu, Tsuyoshi Tsuchiya, Yasuhiko Shinmura, Toshifumi Hibi. Safety of Adalimumab and Predictors of Adverse Events in 1693 Japanese Patients with Crohn's Disease. *J Crohns Colitis.* 2016.09; 10(9); 1033-1041
  25. Masato Miyoshi, Sei Kakinuma, Yoko Tanabe, Koji Ishii, Tian-Cheng Li, Takaji Wakita, Yukio Tsuura, Hideki Watanabe, Yasuhiro Asahina, Mamoru Watanabe, Takaaki Ikeda. Chronic Hepatitis E Infection in a Persistently Immunosuppressed Patient Unable to Be Eliminated after Ribavirin Therapy. *Intern. Med.* 2016.10; 55(19); 2811-2817
  26. Sayuri Nitta, Yasuhiro Asahina, Mami Matsuda, Norie Yamada, Ryuichi Sugiyama, Takahiro Masaki, Ryosuke Suzuki, Nobuyuki Kato, Mamoru Watanabe, Takaji Wakita, Takanobu Kato. Effects of Resistance-Associated NS5A Mutations in Hepatitis C Virus on Viral Production and Susceptibility to Antiviral Reagents. *Sci Rep.* 2016.10; 6; 34652
  27. Yoshihito Kano, Jonathan D Cook, Jeffrey E Lee, Michael Ohh. New structural and functional insight into the regulation of Ras. *Semin. Cell Dev. Biol.* 2016.10; 58; 70-78
  28. Hiroko Nagata, Mina Nakagawa, Yuki Nishimura-Sakurai, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Fumio Goto, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Naoko Tojo, Shuji Tohda, Yasuhiro Asahina, Mamoru Watanabe. Serial measurement of Wisteria floribunda agglutinin positive Mac-2-binding protein is useful for predicting liver fibrosis and the development of hepatocellular carcinoma in chronic hepatitis C patients treated with IFN-based and IFN-free therapy. *Hepatol Int.* 2016.11; 10(6); 956-964
  29. Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Toru Nakata, Tatsuro Murano, Go Ito, Hiromichi Shimizu, Tomohiro Mizutani, Shigeru Oshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Akihiro Araki, Kazuo Ohtsuka, Ryuichi Okamoto, Mamoru Watanabe. PGE2 is a direct and robust mediator of anion/fluid secretion by human intestinal epithelial cells. *Sci Rep.* 2016.11; 6; 36795
  30. Masanori Kobayashi, Shigeru Oshima, Chiaki Maeyashiki, Yoichi Nibe, Kana Otsubo, Yu Matsuzawa, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. The ubiquitin hybrid gene UBA52 regulates ubiquitination of ribosome and sustains embryonic development. *Sci Rep.* 2016.11; 6; 36780
  31. Toshiyuki Kojima, Kiichiro Tsuchiya, Shinji Ikemizu, Soichiro Yoshikawa, Yoshinori Yamanishi, Mamoru Watanabe, Hajime Karasuyama. Novel CD200 homologues iSEC1 and iSEC2 are gastrointestinal secretory cell-specific ligands of inhibitory receptor CD200R. *Sci Rep.* 2016.11; 6; 36457



32. Hitomi Takada, Kaoru Tsuchiya, Yutaka Yasui, Natsuko Nakakuki, Nobuharu Tamaki, Shoko Suzuki, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Masayuki Kurosaki, Yasuhiro Asahina, Nobuyuki Enomoto, Namiki Izumi. Irregular vascular pattern by contrast-enhanced ultrasonography and high serum Lens culinaris agglutinin-reactive fraction of alpha-fetoprotein level predict poor outcome after successful radiofrequency ablation in patients with early-stage hepatocellular carcinoma. *Cancer Med.* 2016.11; 5(11); 3111-3120
33. Ryuichi Okamoto, Mamoru Watanabe. Functional relevance of intestinal epithelial cells in inflammatory bowel disease. *Nihon Rinsho Meneki Gakkai Kaishi.* 2016.11; 39(6); 522-527
34. Toshiaki Watanabe, Yoichi Ajioka, Keiichi Mitsuyama, Kenji Watanabe, Hiroyuki Hanai, Hiroshi Nakase, Reiko Kunisaki, Keiji Matsuda, Ryuichi Iwakiri, Nobuyuki Hida, Shinji Tanaka, Yoshiaki Takeuchi, Kazuo Ohtsuka, Kazunari Murakami, Kiyonori Kobayashi, Yasushi Iwao, Masakazu Nagahori, Bunei Iizuka, Keisuke Hata, Masahiro Igarashi, Ichiro Hirata, Shin-Ei Kudo, Takayuki Matsumoto, Fumiaki Ueno, Gen Watanabe, Masahiro Ikegami, Yoko Ito, Koji Oba, Eisuke Inoue, Naoki Tomotsugu, Toru Takebayashi, Kenichi Sugihara, Yasuo Suzuki, Mamoru Watanabe, Toshifumi Hibi. Comparison of Targeted vs Random Biopsies for Surveillance of Ulcerative Colitis-Associated Colorectal Cancer. *Gastroenterology.* 2016.12; 151(6); 1122-1130

#### [Misc]

1. Ryuichi Okamoto, Mamoru Watanabe. Role of epithelial cells in the pathogenesis and treatment of inflammatory bowel disease. *J. Gastroenterol.* 2016.01; 51(1); 11-21
2. Klionsky DJ, Oshima S, et al. (2387/1536) . Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy.* 2016.01; 12(1); 1-222

#### [Conference Activities & Talks]

1. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H, Goto F, Otani S, Kitahata F, Murakawa M , Itsui Y, Nakagawa M, Azuma S, Watanabe M. A Model for Interaction between HBV and Host Cells Derived from Human Induced Pluripotent Stem Cells. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
2. Asahina Y. 【HCV 2】 Chair . The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
3. Asahina Y. 【HCV 5】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
4. Nakagawa M. 【HCV 】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
5. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Otani S, Goto F, Nagata H, Kaneko S, Asano Y, Miyoshi M, Tsunoda T, Azuma S, Itsui Y, Nakagawa M, Tanabe M, Maekawa S, Enomoto N, Watanabe M. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
6. Nagata H, Sakurai Y, Nakagawa M, Kakinuma S, Azuma S, Murakawa M, Nitta S, Itsui Y, Asahina Y, Watanabe M. Serial changes in M2BPGi levels as predictors of fibrosis and HCC in chronic hepatitis C. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
7. Nitta S, Asahina Y, Wakita T, Kato T. In vitro characterization and drug sensitivity analysis for HCV NS5A resistance-associated variants. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
8. Nakagawa M. 【HCV 11】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.23 International Convention Center Pamir, Tokyo (JAPAN)

9. Nakagawa M. **【HCV 12】** Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.23 International Convention Center Pamir, Tokyo (JAPAN)
10. Matsumoto T, Motoya S, Watanabe K, Hisamatsu T, Nakase H, Yoshimura N, Ishida T, Kato S, Nakagawa T, Esaki M, Nagahori M, Matsui T, Naito Y, Kanai T, Suzuki Y, Nojima M, Watanabe M, Hibi T. Comparison of adalimumab monotherapy and a combination with azathioprine for patients with Crohn's Disease: A prospective, multicentre, open-labeled clinical trial (DIAMOND Study). 11th Congress of ECCO - European Crohn's and Colitis Organisation 2016.03.18 Amsterdam (Nederland)
11. Matsuoka K, Saito E, Fujii T, Takenaka K, Iwamoto F, Kimura M, Nagahori M, Ohtsuka K, Watanabe M. Efficacy and safety of sequential rescue therapy with infliximab and tacrolimus in patients with corticosteroid-refractory Ulcerative Colitis. 11th Congress of ECCO - European Crohn's and Colitis Organisation 2016.03.19 Amsterdam (Nederland)
12. Kobayashi T, Suzuki Y, Motoya S, Hirai F, Ogata H, Ito H, Sato N, Ozaki K, Watanabe M, Hibi T. Factors associated with the first trough level of infliximab at week 2 that predicts short- and long-term outcomes in Ulcerative Colitis. 11th Congress of ECCO - European Crohn's and Colitis Organisation 2016.03.19 Amsterdam (Nederland)
13. Watanabe M. Gut Microbiota, Epithelial Cells and Stem Cell Therapy in IBD. AGA/CSG IBD Symposium 2016.04.08 Baijing (China)
14. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H, Goto F, Otani S, Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A new model for studying interaction between hepatitis B virus and host cells derived from human induced pluripotent stem cells. EASL The International Liver Congress 2016 2016.04.14 Barcelona (Spain)
15. Takenaka K, Ohtsuka K, Kitazume Y, Nagahori M, Matsuoka K, Fujii T, Kimura M, Fujioka T, Watanabe M. Enteroscopic and MR findings of small intestine in Crohn's disease. The 7th APTC 2016.04.20 Tokyo (JAPAN)
16. Tetsuya Nakamura. **【Session 2: Gut homeostasis and IBD】** Intestinal stem cell transplantation and regenerative medicine. The 102nd JSGE-The 5th International Forum 2016.04.21 Tokyo (JAPAN)
17. Kazuo Ohtsuka, Kento Takenaka, Mamoru Watanabe. **【Session 3: Imaging for follow up of IBD】** Assessment of small intestinal lesions of Crohn's disease. The 102nd JSGE-The 5th International Forum 2016.04.21 Tokyo (JAPAN)
18. Ryuichi Okamoto, Mamoru Watanabe. **【Session 4: Novel therapeutic approaches and emerging issues in IBD】** Application of regenerative medicine for the treatment of inflammatory bowel disease. The 102nd JSGE-The 5th International Forum 2016.04.21 Tokyo (JAPAN)
19. Masanori Kobayashi, Shigeru Oshima, Yoishi Nibe, Chiaki Maeyashiki, Mamoru Watanabe. UBA52, ubiquitin hybrid protein, regulates NF  $\kappa$  B signaling. The 102nd JSGE-The 5th International Forum 2016.04.21 Tokyo (JAPAN)
20. Kentaro Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Masakazu Nagahori, Katsuyoshi Matsuoka, Toshimitsu Fujii, Maiko Kimura, Tomoyuki Fujioka Mamoru Watanabe. Magnetic resonance evaluation for deep small intestinal strictures in patients with Crohn's disease. The 102nd JSGE-The 5th International Forum 2016.04.21 Tokyo (JAPAN)
21. Mamoru Watanabe. Closing Remarks. The 102nd JSGE-The 5th International Forum 2016.04.22 Tokyo (JAPAN)
22. Kano Y, Jen Jen Yeh, Zhong-Yin Zhang, Ohh M. Novel treatment strategy for pancreatic cancer by targeting the 'undruggable' Ras oncoprotein. AACR Special Conference on Pancreatic Cancer 2016.05.14 Orlando (USA)
23. Shuji Hibiya, Kiichiro Tsuchiya, Tomoaki Shirasaki, Keita Fukushima, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Construction of in vitro model for inflammatory bowel disease using primary colonic organoid. DDW2016 2016.05.21 San Diego (USA)

24. Kohei Suzuki, Satoru Fujii, Ami Kawamoto, Fumiaki Ishibashi, Toru Nakata, Go Ito, Hiromichi Shimizu, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Otsuka, Ryuichi Okamoto, Mamoru Watanabe. Single-cell level analysis reveals heterogeneous expression of stem-cell specific genes in human small intestinal organoids. DDW2016 2016.05.21 San Diego (USA)
25. Takashi Nagaishi, Arisa Tokai, Taro Watabe, Nisha Jose, Akinori Hosoya, Motomi Yamazaki, Richard S.Blumberg, Mamoru Watanabe. CEACAM1 may regulate BCR signaling in the activated B cells. DDW2016 2016.05.21 San Diego (USA)
26. Taichi Matsumoto, Wakana Mochizuki, Yoichi Nibe, Shintaro Akiyama, Yuka Matsumoto, Kengo Nozaki, Tomohiro Mizutani, Shigeru Oshima, Mamoru Watanabe, Tetsuya Nakamura. Retinol stimulates proliferation of epithelial stem cells of the proximal colon through a retinoic acid-independent mechanism. DDW2016 2016.05.21 San Diego (USA)
27. Taku Kobayashi, Yasuo Suzuki, Satoshi Motoya, Fumihito Hirai, Haruhiko Ogata, Hiroaki Ito, Noriko Sato, Kunihiko Ozaki, Mamoru Watanabe, Toshifumi Hibi. Factors Associated With the First Trough Level of Infliximab at Week 2 That Predicts Short- and Long-Term Outcomes in Ulcerative Colitis. DDW2016 2016.05.21 San Diego (USA)
28. Emma Calabrese, Torsten Kucharzik, Christian Maaser, Giovanni Maconi, Deike Strobel, Stephanie Wilson, Francesca Zorzi, Kerri L. Novak, David H. Bruining, Marietta Iacucci, Mamoru Watanabe, Elisabetta Lolli, Carlo Chiaramonte, Stephen B. Hanauer, Remo Panaccione, Francesco Pallone, Subrata Ghosh. Inter-Observer Agreement in Bowel Ultrasonography for Diagnostic Assessment in Patients With Crohn's Disease. DDW2016 2016.05.21 San Diego (USA)
29. Toru Nakata, Go Ito, Hiromichi Shimizu, Satoru Fujii, Kohei Suzuki, Fumiaki Ishibashi, Ami Kawamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Katsuto Hozumi, Ryuichi Okamoto, Mamoru Watanabe. Jagged1 is indispensable for the maintenance of tumor stem cell niche in APC-Deficient intestinal adenomas. DDW2016 2016.05.22 San Diego (USA)
30. Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Toru Nakata, Go Ito, Hiromichi Shimizu, Tomohiro Mizutani, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Ohtsuka, Ryuichi Okamoto, Mamoru Watanabe. In Vitro organoid model reveals PGF2 as a Robust Mediator of chloride & water secretion bt human intestinal epithelial cells. DDW2016 2016.05.23 San Diego (USA)
31. Kazuo Ohtsuka, Kento Takenaka, Toshimitsu Fujii, Katsuyoshi Matsuoka, Masakazu Nagahori, Kengo Nozaki, Masayoshi Fukuda, Mamoru Watanabe. Mucosal Healing is important for better outcomes of endoscopic balloon dilatation for small intestinal stricture of Crohn's disease. DDW2016 2016.05.23 San Diego (USA)
32. Chiaki Maeyashiki, Shigeru Oshima, Yoichi Nibe, Masanori Kobayashi, Mamoru Watanabe. Identification of autophagic regulators as therapeutic targets in intestinal epithelial cells. DDW2016 2016.05.23 San Diego (USA)
33. Tetsuya Nakamura. 【Innovative Approaches to Curing Intestinal Failure: The Future of Cell and Tissue Therapy】 Therapeutic Transplantation of Human Intestinal Stem Cells. DDW2016 2016.05.23 San Diego (USA)
34. Katsuyoshi Matsuoka, Makoto Naganuma, Toshiyuki Matsui, Makoto Arai, Satoshi Tanida, Kazuya Kitamura, Noriyuki Horiki, Mikihiro Fujiya, Masaki Iimuro, Keiichi Mitsuyama, Masayuki Saruta, Takayuki Matsumoto, Hiroko Nebiki, Motohiro Esaki, Fukunori Kinjo, Kiyoshi Oketani, Seiichiro Hojo, Hideto Akama, Toshio Imai, Hirohito Tsubouchi, Toshifumi Hibi, Takanori Kanai. Safety, Tolerability and Efficacy of E6011, Anti-Human Fractalkine Monoclonal Antibody, in the First-in-Patient Study for Crohn's Disease. DDW2016 2016.05.23 San Diego (USA)
35. Kiichiro Tsuchiya, Shuji Hibiya, Keita Fukushima, Tomoaki Shirasaki, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. ATOH1 Protein stabilization in tumor acquires the morphological change to signet ring cell enrichment in colon cancer. DDW2016 2016.05.24 San Diego (USA)
36. Masanori Kobayashi, Shigeru Oshima, Yoichi Nibe, Chiaki Maeyashiki, Mamoru Watanabe. UBA52, ubiquitin hybrid ribosomal protein, regulates NF- $\kappa$ B signaling in colon cancer. DDW2016 2016.05.24 San Diego (USA)

37. Takayuki Matsumoto, Satoshi Motoya, Kenji Watanabe, Tadakazu Hisamatsu, Hiroshi Nakase, Naoki Yochimura, Tetsuya Ishida, Shingo Kato, Tomoo Nakagawa, Motohiro Esaki, Masakazu Nagahori, Toshifumi Matsui, Yuji Naito, Takanori Kanai, Yasuo Suzuki, Masanori Nojima, Mamoru Watanabe, Toshifumi Hibi. Comparison of abalimumab monotherapy and a combination with azathioprine for patients with crohn's disease: A prospective, multicenter, open-labeled clinical trial (DIAMOND Study). DDW2016 2016.05.24 San Diego (USA)
38. Asahina Y. Hepatocarcinogenesis after hepatitis C viral eradication.. The 10th APASL Single Topic Conference 2016.06.08 Kaoshiung (Taiwan)
39. Tokai A, Nagaishi T, Watabe T, Jose N, Hosoya A, Yamazaki M, Onizawa M, Richard S. Blumberg, Watanabe M . Activated B cell receptor signaling may be regulated by CEACAM1. FOCIS 2016 2016.06.23 Boston
40. Meng-Tzu Weng, Katsuyoshi Matsuoka, Mamoru Watanabe, JY Lee, Sang Hyoung Park, Suk-Kyun Yang, Shu-Chen Wei. Thromboembolic events associated with inflammatory bowel disease in Asia: incidence and possible risk factors analysis. AOCC2016 2016.07.07 Kyoto International Conference Center, Kyoto (JAPAN)
41. Shinta Mizuno, Kosaku Nanki, Katsuyoshi Matsuoka, Keiko Ono, Makoto Mutaguchi, Mari Arai, Shinya Sugimoto, Hiroki Kiyohara, Kozue Takeshita, Makoto Naganuma, Takanori Kanai. Efficacy and safety of fecal microbiota transplantation on ulcerative colitis. AOCC2016 2016.07.07 Kyoto International Conference Center, Kyoto (JAPAN)
42. Tetsuya Nakamura. Stem-Cell Based Therapies for Intestinal Diseases. AOCC 2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
43. Katsuyoshi Matsuoka, Naoki Yoshimura, Mamoru Watanabe, Satoshi Motoya, Keiichi Tominaga, Ryuichi Iwakiri, Kenji Watanabe, Toshifumi Hibi, For the AJM300 Study Group. AJM300, an oral  $\alpha$  4 integrin antagonist, as induction therapy for active ulcerative colitis: a randomized trial. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
44. Tomoaki Shirasaki, Kiichiro Tsuchiya, Shuji Hibiya, Ryu Nishimura, Keita Fukushima, Sho Watanabe, Ryuichi Okamoto, Tetsuya Nakamura and Mamoru Watanabe. Stimulation with the ligands of Toll like receptors in primary human organoids. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
45. Ami Kawamoto, Go Ito, Toru Nakata, Satoru Fujii, Kohei Suzuki, Fumiaki Ishibashi, Hiromichi Shimizu, Kiichiro Tsuchiya, Tetsuya Nakamura, Ryuichi Okamoto, Mamoru Watanabe. OLFM4 and UBD are up-regulated in the inflamed intestinal epithelia of IBD patients by synergy of Notch signaling and TNF- $\alpha$  . AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
46. Maiko Kimura, Katsuyoshi Matsuoka, Eiko Saito, Toshimitsu Fujii, Kento Takenaka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Salvage therapy for corticosteroid-refractory ulcerative colitis patients. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
47. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Masakazu Nagahori, Katsuyoshi Matsuoka, Toshimitsu Fujii, Maiko Kimura, Tomoyuki Fujioka, Mamoru Watanabe. Enteroscopic and MR findings of small bowel in Crohn's disease. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
48. Minami Hama, Ayumi Hayashi, Tomohiro Mizutani, Satoru Fujii, Tatsuro Murano, Kiichiro Tsuchiya, Tetsuya Nakamura, Ken Watanabe, Norio Shimizu, Ryuichi Okamoto, Mamoru Watanabe. Prevalence of viral DNA in the mucosal tissue and cultured organoids of inflammatory bowel disease patients. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
49. Toshifumi Hibi, Satoshi Motoya, Kori Wallace, Andreas Lazar, Yasuko Nishimura, Morio Ozawa, Roopal Thakkar, Anne M. Robinson, Mamoru Watanabe. Adalimumab 80 mg Every Other Week in Japanese Patients with Crohn's Disease Who Lost Response to Maintenance Therapy. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
50. Shuji Hibiya, Kiichiro Tsuchiya, Tomoaki Shirasaki, Keita Fukushima, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Mouse colonic organoid acquires wnt-independent survival property after long-term inflammation. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)

51. Taro Watabe, Takashi Nagaishi, Arisa Tokai, Akinori Hosoya, Nisha Jose, Yudai Kojima, Motomi Yamazaki, Richard S. Blumberg, Mamoru Watanabe. BCR signaling in the activated B cells may be regulated by CD66a. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
52. Toshimitsu Fujii, Kento Takenaka, Maiko Kimura, Katsuyoshi Matsuoka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. The evaluation for small bowel strictures on MR enterocolonography in patients with Crohn' s disease. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
53. Kiichiro Tsuchiya, Shuji Hibiya, Keita Fukushima, Tomoaki Shirasaki, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Atoh1 protein stabilization in colon tumor acquires the phenotype of signet ring cell carcinoma with cancer stem cell enrichment. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
54. Masakazu Nagahori. Anal fistula - Seton first or anti-TNF first : anti-TNF first. AOCC2016 2016.07.09 Kyoto International Conference Center, Kyoto (JAPAN)
55. Kazuo Ohtsuka, Kento Takenaka, Toshimitsu Fujii, Katsuyoshi Matsuoka, Masakazu Nagahori, Maiko Kimura, Masayoshi Fukuda, Nobuhiro Katsukura, Mamoru Watanabe. Mucosal healing improves prognosis of endoscopic balloon dilatation for small intestinal strictures of Crohn' s disease. AOCC2016 2016.07.09 Kyoto International Conference Center, Kyoto (JAPAN)
56. Kiichiro Tsuchiya. 【Poster Oral : Group 4】 Chair. AOCC2016 2016.07.09 Kyoto International Conference Center, Kyoto (JAPAN)
57. Nagaishi T, Tokai A, Watabe T, Jose N, Hosoya A, Yamazaki M, Blumberg RS, Watanabe M. BCR signaling in the activated B cells may be regulated by CEACAM1. Mucosal Immunology Course & Symposium (MICS) 2016 2016.07.29 Toronto (Canada)
58. Horita N, Demitrack ES, Gifford GB, Keeley TM, Siebel CW, Samuelson LC. Notch1 and Notch2 regulate epithelial cell proliferation in mouse and human gastric corpus. The 2016 Gordon Research Conference on Notch Signaling in Development, Regeneration & Disease 2016.08.01 Lewiston (USA)
59. Watanabe M. Stem Cell Replacement in Gut. FNM2016 2016.08.26 San Francisco (USA)
60. Watanabe M. Intestinal Epithelial Stem Cells for the Treatment of Colitis.. eMed Meeting 2016 2016.10.04 Germany
61. Watanabe M. Gut Microbiota, Epithelial Cells and Stem Cell Therapy in GI disease. Microbiome Science Days 2016.10.07 Germany
62. Tetsuya Nakamura. Therapeutic transplantation of intestinal stem cells. International Conference on Bio-fabrication and Bio-monitoring (ICBB 2016) 2016.10.14 National Taiwan University, Taipei (China)
63. Toshimitsu Fujii, Kento Takenaka, Maiko Kimura, Katsuyoshi Matsuoka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. MR enterocolonography evaluation for small bowel strictures in patients with Crohn' s disease: comparison with balloon enteroscopy. UEGW2016 2016.10.18 Vienna (Austria)
64. Hibiya S, Tsuchiya K, Watanabe S, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Construction of in vitro model of ulcerative colitis using mouse primary colonic organoid. UEGW2016 2016.10.18 Vienna (Austria)
65. Hosoya A, Nagaishi T, Tokai A, Watabe T, Jose N, Kojima Y, Yamazaki M, Richard S. Blumberg, Watanabe M. CEACAM1 regulation of BCR signaling in the activated B cells. UEGW2016 2016.10.19 VIENNA
66. Asahina Y. Recent progress in anti-HCV therapy and challenges toward HCC eradication.. Academic Forum of Liver Disease in Northeast China and the Annual Convention for the Study of Liver Diseases in Jilin Province in 2016. 2016.10.29 Changchun (China)
67. Watanabe M. 【Innovative Topics-L5】 Chair. APDW2016 2016.11.03 Kobe convention center, KOBE (JAPAN)
68. Watanabe M. 【Hands-on Seminar : Clinical Science】 Chair. APDW2016 2016.11.03 Kobe convention center, KOBE (JAPAN)



69. Asahina Y. 【International Session (Symposium) 1】 Genomics of hepatocellular carcinoma: Hepatitis virus infection and hepatocarcinogenesis. Chair . JDDW2016 2016.11.03 Kobe Convention Center (Kobe JAPAN)
70. Kiichiro Tsuchiya. 【Digital Poster : Lower GI "Cell/Molecular Biology/Pathology 1"】 Chair. APDW2016 2016.11.03 Kobe convention center, KOBE (JAPAN)
71. Tsuchiya K, Hibiya S, Fukushima K, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Atoh1 protein stabilization in colon tumor acquires the morphological change to signet ring cell carcinoma with cancer stem cell enrichment. APDW2016 2016.11.03 Kobe convention center, KOBE (JAPAN)
72. Fujii T, Takenaka K, Kitazume Y, Kimura M, Matsuoka K, Nagahori M, Ohtsuka K, Watanabe M. MR enterocolonography can detect small bowel strictures and predict surgery in patients with Crohn's disease: Comparison with balloon enteroscopy. APDW2016 2016.11.03 Kobe convention center, KOBE (JAPAN)
73. Watabe T, Nagaishi T, Suzuki M, Yamazaki M, Onizawa M, Jose N, Tokai A, Hosoya A, Kojima Y, Watanabe M. Type 2 TNF receptor signaling in colonic epithelia may be involved in the development of colitis-associated carcinogenesis. APDW 2016 2016.11.03 Kobe Convention Center (Kobe JAPAN)
74. Watabe T, Nagaishi T, Tokai A, Jose N, Hosoya A, Kojima Y, Yamazaki M, Richard S. Blumberg, Watanabe M. CD66a regulation of BCR signaling in the activated B cells . APDW 2016 2016.11.04 Kobe Convention Center (Kobe JAPAN)
75. Watanabe M. 【IBD Consensus Symposium: Asia Pacific Consensus on IBD Management】Chair. APDW2016 2016.11.05 Kobe convention center, KOBE (JAPAN)
76. Takenaka K, Ohtsuka K, Watanabe M. Magnetic resonance evaluation for small bowel strictures of Crohn's disease: comparison with balloon enteroscopy. APDW2016 2016.11.05 Kobe convention center, KOBE (JAPAN)
77. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Ayako Sato, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Mamoru Watanabe. Genetically modified human induced pluripotent stem cell-derived hepatic progenitor-like cell lines as a model for interaction between hepatitis B virus and host cells. AASLD The Liver meeting 2016 2016.11.11 Boston (USA)
78. Wai-Kay Seto , Yasuhiro Asahina , Cheng-Yuan Peng , Carol Stanciu , Djamal Abdurakhmanov , John F. Flaherty , Kyungpil Kim , Anuj Gaggar , Mani Subramanian, Fehmi Tabak, Tuan T. Nguyen, Henry Lik-Yuen Chan. Reduced Changes In Bone Mineral Density In CHB Patients Receiving Tenofovir Alafenamide (TAF) Compared With Tenofovir disoproxil fumarate. AASLD The Liver meeting 2016 2016.11.11 Boston (USA)
79. Tetsuya Nakamura. Stem cell-based therapies for intestinal diseases. International Conference on Recent Advances in Inflammation 2016 2016.11.11 National Cheng Kung University, Tainan (Taiwan)
80. Watanabe M. Inflammation-related Carcinogenesis in Intestine.. 2016 TMDU-TMU Joint Symposium 2016.11.12 Taipei Medical University, Taipei (China)
81. Kawamoto A, Nakata T, Fujii S, Suzuki K, Ishibashi F, Shimizu H, Tsuchiya K, Nakamura T, Okamoto R, Watanabe M. Notch signaling and TNF- $\alpha$  synergistically up-regulate stem cell-specific genes, OLFM4 and UBD, in the inflamed intestinal epithelia of IBD patients. 2016 Advances in Inflammatory Bowel Diseases, Crohn's & Colitis Foundation of America's Clinical & Research Conference (CCFA) 2016.12.10 Orlando, Florida

## Specialized Surgeries

< Division of Specialized Surgeries>

Professor: Hiroyuki UETAKE

Associate Professor: Yoshinori INOUE

Junior Associate Professor: Toshiaki ISHIKAWA, Tsuyoshi NAKAGAWA, Kentaro OKAMOTO

Assistant Professor: Takahiro TOYOHUKU, Goshi ODA

< Department of Professional Development>

Junior Associate Professor: Toshifumi KUDO

< Department of Translational Oncology>

Associate Professor: Megumi ISHIGURO

< Graduate School Student>

Kimihiro IGARI, Masato NISHIZAWA, Yohei YAMAMOTO,

Tsuyoshi ICHINOSE, Mio FUKUDA

### ( 1 ) Outline

Division of Specialized Surgeries have been launched in April 2015, which consists of 4 clinical departments in the Medical Hospital:

- Division of Chemotherapy and Oncosurgery
- Division of Vascular Surgery
- Division of Breast Surgery
- Division of Pediatric surgery

### ( 2 ) Research

Main themes of our research activities

- Identification of prognostic factors and the predictive factors for chemo-responsiveness in gastrointestinal and breast cancer, by molecular biological technique and immuno-histochemical approach
- Micro circulation in severe ischemic extremity
- Relation between vascular disease and periodontitis
- Development of new device for evaluating hemodynamics
- Development of safety central venous catheterization
- Establishment of telemedicine

### ( 3 ) Education

Main objective in the graduate course is to bring up the well-rounded surgeons who has international and scientific feelings.



**(4) Publications****[Original Articles]**

1. Masuda T, Ishikawa T, Mogushi K, Okazaki S, Ishiguro M, Iida S, Mizushima H, Tanaka H, Uetake H, Sugihara K.. Overexpression of the S100A2 protein as a prognostic marker for patients with stage II and III colorectal cancer. *Int J Oncol.* 2016; 48(3); 975-982
2. Ishikawa T, Uetake H, Murotani K, Kobunai T, Ishiguro M, Matsi S, Sugihara K.. Genome-wide DNA Copy-number Analysis in ACTS-CC Trial of Adjuvant Chemotherapy for Stage III Colonic Cancer. *Anticancer Research.* 2016; 36; 853-860
3. Baba H, Ishikawa T, Mogushi K, Ishiguro M, Uetake H, Tanaka H, Sugihara K.. Identification of SATB1 as a specific biomarker for lymph node metastasis in colorectal cancer. *Anticancer Research.* 2016; 36; 4069-4076
4. Matsusaka S, Cao S, Hanna DL, Sunakawa Y, Ueno M, Mizunuma N, Zhang W, Yang D, Ning Y, Stintzing S, Sebio A, Stremitzer S, Yamauchi S, Parekh A, Okazaki S, Berger MD, El-Khoueiry R, Mendez A, Ichikawa W, Loupakakis F, Lenz HJ.. CXCR4 polymorphism predicts progression-free survival in metastatic colorectal cancer patients treated with first-line bevacizumab-based chemotherapy. *Pharmacogenomics J.* 2016; [ Epub ahead of print]
5. Igari K, Inoue Y, Iwai T.. The epidemiologic and clinical findings of patients with Buerger disease. *Ann Vasc Surg.* 2016; 30; 263-269
6. Zainuer A, Inoue Y, Kudo T, Toyofuku T, Igari K, Kawano T.. Usefulness of the tranfer function index for diagnosing peripheral arterial disease in patients with arterial calcification. *J Med Dent Sci.* 2016; 63(1); 29-35
7. Igari K, Kudo T, Toyofuku T, Inoue Y.. A novel approach to infrainguinal arteries with chronic total occlusions using the high frequency vibrational device. *Int Angiol.* 2016; 35(2); 212-216
8. Igari K, Kudo T, Toyofuku T, Inoue Y.. The outcomes of endovascular aneurysm repair with the chimney technique for juxtarenal aneurysms. *Ann Throac Cardiovasc Surg.* 2016; 22(3); 174-180
9. Yamamoto Y, Igari K, Toyofuku T, Kudo T, Inoue Y.. Late stent graft infection after the emergency endovascular repair of a secondary iliac artery-enteric fistula treated with graft removal and in situ aortic reconstruction using femoral veins. *Ann Thorac Cardiovasc Surg.* 2016; [ Epub ahead of print]
10. Yamamoto Y, Kudo T, Igari K, Toyofuku T, Inoue Y.. Radial artery aneurysm in the anatomical snuff box: A case report and literature review. *Int J Surg Case Rep.* 2016; 27; 44-47
11. Igari K, Kudo T, Toyofuku T, Inoue Y.. Relationship of inflammatory biomarkers with severity of peripheral arterial disease. *Int J Vasc Med.* 2016; 6015701
12. Igari K, Kudo T, Toyofuku T, Inoue Y.. A case of successful coil embolization for a late-onset type Ia endoleak after endovascular aneurysm repair with the chimney technique. *Case Rep Vasc Med.* 2016; 5307416
13. Igari K, Kudo T, Toyofuku T, Inoue Y.. Endothelial dysfunction of patients with peripheral arterial disease measured by peripheral arterial tonometry. *Int J Vasc Med.* 2016; 3805380
14. Igari K, Kudo T, Toyofuku T, Inoue Y.. The relationship between endothelial dysfunction and endothelial cell markers in peripheral arterial disease. *PLoS ONE.* 2016; 11(11); e0166840
15. Igari K, Inoue Y, Iwai T.. An experimental model of peripheral vascular disease involving the travenous injection of oral bacteria. *Ann Vasc Dis.* 2016; 9(4); 267-271

**[Conference Activities & Talks]**

1. Okamoto K, Tani Y, Yamaguchi T, Ogino K, Tsuchioka T, Matsudera S, Watanabe S, Kato H.. A Case of Meckel's diverticulum torsion, correctly diagnosed by preoperative computed tomography.. 24th Asian Association Pediatric Surgeons 2016.05.24 Fukuoka (Japan)

2. Igari K, Kudo T, Toyofuku T, Inoue Y.. Relationship of inflammatory biomarkers, PTX3 with severity of peripheral arterial disease.. 84th European Atherosclerosis Society Congress 2016.05.31 Innsbruck (Austria)
3. Kajiwarra Y, Ishiguro M, Teramukai S, Matsuda C, Fujii S, Kinugasa Y, Nakamoto Y, Kotake M, Sakamoto Y, Kurachi K, Maeda A, Komori K, Tomita N, Simada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Sugihara K.. A randomized phase III trial of 1-year adjuvant chemotherapy with oral tegafur-uracil (UFT) vs. surgery alone in stage II colon cancer.. American Society of Clinical Oncology (ASCO) 2016 Annual Meeting 2016.06.04 Chicago (USA)
4. Miura T, Sunami E, Kusumoto T, Ota M, Yoshida K, Tomita N, Maeda A, Mochizuki I, Okabe M, Kunieda K, Yamauchi J, Itabashi M, Kotake K, Takahashi K, Baba H, Boku N, Aiba K, Ishiguro M, Morita S, Sugihara K.. Planned safety analysis of the ACTS-CC 02 trial: A randomized phase III trial of S-1/oxaliplatin (SOX) versus UFT/LV as adjuvant chemotherapy for high-risk stage III colon cancer.. American Society of Clinical Oncology (ASCO) 2016 Annual Meeting 2016.06.04 Chicago (USA)
5. Igari K, Kudo T, Toyofuku T, Inoue Y.. Total endovascular treatment for acute deep venous thrombosis by catheter-directed thrombolysis.. Asian Society for Vascular Surgery 2016 2016.10.21 Singapore
6. Ishiguro M.. Colorectal cancer database in Japan.. 68th Congress of the Korean Surgical Society. 2016.11.05 Seoul (Korea)
7. Yamamoto Y, Ichinose T, Nakamura M, Nishizawa M, Igari K, Toyofuku T, Kudo T, Inoue Y.. Multiple recurrent pseudoaneurysms after EVAR in a patient with Behçet' s disease.. The 13th Tokyo Shanghai International Symposium for Vascular Surgery 2016.11.13 Tokyo (Japan)

## Cardiovascular Medicine

Professor

Mitsuaki Isobe

Clinical Professor

Kenzo Hirao

Endowed Professor

Takashi Ashikaga

Associate Professor

Tetsuo Sasano (Graduate School of Health Care Sciences,  
Biofunctional Informatics)

Masahiko Goya Kiyoshi Nobori (Clinical Research Center )

Junior Associate Professor

Yasuhiro Maejima, Yusuke Ebana (Medical Research Institute  
Bio-informational Pharmacology)

Assistant Professor

Mihoko Kawabata, Ryoko Azuma, Shunji Yoshikawa Takeshi Sasaki,  
Yuji Konishi, Takanobu Yamamoto, Yu Hatano

Specially-Appointed Professor

Shingo Maeda, Kentaro Takahashi

Endowed Assistant Professor

Daisuke Ueshima

Joint Research Assistant Professor

Yasuhiro Shirai

Graduate Student

Yusuke Ito, Natsuko Tamura, Ryo Watabe, Tetsuo Ohmi, Tomoko Manno,  
Kei Takayama, Ryota Iwatsuka, Yoichi Otaki, Atsuhiko Yagishita,  
Tatsuya Fujinami, Tomoyo Sugiyama, Osamu Inaba, Masahito Suzuki,  
Naoyuki Miwa, Rena Nakamura, Tomoyuki Umemoto, Norifumi Murai, Riri Watanabe,  
Masahiro Yamazoe, Shunsuke Hirose, Tetsuo Yamaguchi, Hironori Sato, Maki Ohno,  
Keiichi Hishikari, Takashi Nakagawa, Hidetsugu Nomoto, Yasuaki Tanaka,  
Tetsumin Lee, Yukihiro Inamura, Mie Ochida, Tomomasa Takamiya Kensuke Hirasawa,  
Ohnishi Kentaro, Mituhisa Asano, Nobutaka Kato, Naohiko Kawaguchi,  
Shinsuke Iwai, Yuki Osaka, Nobuyuki Kagiya, Shunsuke Kuroda, Takuro Nisimura,  
Junji Matuda, Makoto Araki, Kusa Shigeki, Kazuya Yamao, Takamitsu Takagi,  
Yoshihisa Kanechi, Nagamine Shyo, Rei Masuda, Hidehiro Shirai, Naoko Kato,  
Takashi Nida

### (1) Research

The purposes of our investigation are to reveal the etiology and pathophysiology of cardiovascular diseases, thereby developing novel technologies for diagnosis and treatment. For that purpose we investigate clinical cases and experimental animal models. Our faculty members pursue a wide variety of basic research, ranging from investigations on the molecular mechanism of heart failure to the development of novel interventional devices for patients with angina pectoris. Current strengths of the program include innovation of the next-generation drug-eluting balloon for percutaneous coronary intervention by the Chief of this Department, Mitsuaki Isobe

MD, and molecular cardiology under Yasuhiro Maejima MD, PhD. We also actively investigate immunocardiology, the molecular mechanism of pulmonary hypertension and periodontitis-associated cardiovascular diseases.

- 1) Clinical study of gene therapy for coronary artery disease (Isobe)
- 2) Clinical study for treatment of acute coronary syndrome (Isobe, Ashikaga, Yoshikawa)
- 3) Molecular mechanism and treatment of myocardial ischemia and reperfusion injury (Isobe)
- 4) Molecular mechanism and treatment of coronary restenosis and vascular disease (Isobe)
- 5) Gene therapy of myocarditis and cardiac chronic rejection (Isobe, Suzuki)
- 6) Cardiac rejection and immunological tolerance (development of safe immunosuppressive therapy) (Isobe, Suzuki)
- 7) Treatment of heart failure and cardiomyopathy by myocardial regeneration (Isobe, Maejima)
- 8) Regulation of arteriosclerosis by targeting transcription factors (Isobe, Maejima)
- 9) Gene therapy of vascular disease (Isobe)
- 10) Diagnostic imaging of aortitis (Isobe)
- 11) Molecular mechanism and treatment of aortitis (Isobe, Maejima)
- 12) Assessment of vascular endothelial dysfunction in vasculitis, heart failure and arrhythmia (Isobe)
- 13) Application in gene therapy for heart failure and cardiomyopathy (Isobe, Maejima)
- 14) Molecular system of myocardial remodeling in heart failure and ventricular hypertrophy (Isobe)
- 15) Therapy of sleep apnea syndrome with heart failure (Isobe)
- 16) Assessment by imaging of coronary artery and cardiac function (Isobe, Tezuka)
- 17) System of origin with tachyarrhythmias (particularly supraventricular tachycardia) (Hirao)
- 18) Medical therapy and ablation for tachyarrhythmias (Hirao)
- 19) Research for the conduction of atrio-ventricular node (Hirao)
- 20) Research and Therapy for arrhythmia by using cardioendoscopy (Hirao)
- 21) Research of atrial fibrillation from origin of pulmonary vein (Hirao)
- 22) Research of genetic factor with atrial fibrillation (Hirao)
- 23) Research of ablation for atrial fibrillation (Hirao, Goya)

There are many fruitful collaborative efforts between our department and other departments with the TMDU, such as the Department of Bio-informational Pharmacology, Medical Research Institute. Collaborations with other institutions are also common. Especially, we closely collaborate with the Department of Advanced Clinical Science and Therapeutics, University of Tokyo (Junichi Suzuki MD, PhD). Our cardiologists continuously contribute to establish evidence-based cardiovascular medicine through clinical researches. So far, we are engaged in over ten clinical studies. The targets of our clinical research include heart failure, ischemic heart disease, arrhythmia, cardiac imaging and Takayasu arteritis.

## (2) Education

The Department of Cardiovascular Medicine at Tokyo Medical and Dental University (TMDU) primarily aims at offering patient-centered care for every person who suffer from cardiovascular diseases, including ischemic heart diseases, arrhythmia, heart failure, valvular disorders and vasculitis. Our cardiologists are experts in electrophysiology, interventional cardiology, heart failure, and cardiac imaging who make full use of state-of-the-art diagnostic tests and therapeutic procedures to provide high-quality care for every patient. We also actively engage in basic and clinical research to elucidate the mechanism of heart & vessel disorders for providing novel therapeutic strategies to the patients of cardiovascular diseases. In addition to high-quality patient care and innovative research, our faculty members are vigorously involved in the education and training to the young physicians and researchers specializing in cardiovascular medicine. Thus, we are continuously making every effort to serve the highest quality of patient care, education and innovative research of cardiovascular medicine.

## (3) Clinical Services & Other Works

Our clinical training program provides the trainee with outstanding skills in clinical cardiology. The trainees will develop their clinical knowledge, clinical judgment, procedural skills and interpersonal skills required as a specialist in cardiovascular diseases. The program provides clinical cardiology training not only at the University Hospital but also at our outstanding affiliate hospitals (N=22), including Kameda General Hospital, Musashino Red-Cross Hospital, Tsuchiura Kyodo Hospital and Yokosuka Kyosai Hospital. Our training program for re-

search emphasizes developing academic cardiologists who will become leaders in cardiovascular research. The program offers training of basic, clinical and translational researches not only at the Graduate School of our department but also at other departments with the TMDU and at other institutions described above.

#### (4) Publications

##### [Original Articles]

1. Yuki Hasegawa, Satomi Hamada, Takuro Nishimura, Takeshi Sasaki, Yusuke Ebana, Mihoko Kawabata, Masahiko Goya, Mitsuaki Isobe, Takatoshi Koyama, Tetsushi Furukawa, Kenzo Hirao, Tetsuo Sasano. Novel Dielectric Coagulometer Identifies Hypercoagulability in Patients with a High CHADS2 Score without Atrial Fibrillation. *PLoS ONE*. 2016; 11(6); e0156557
2. Kentaro Takahashi, Tetsuo Sasano, Koji Sugiyama, Junko Kurokawa, Noriko Tamura, Yurie Soejima, Motoji Sawabe, Mitsuaki Isobe, Tetsushi Furukawa. High-fat diet increases vulnerability to atrial arrhythmia by conduction disturbance via miR-27b. *J. Mol. Cell. Cardiol.* 2016.01; 90; 38-46
3. Hirofumi Zempo, Jun-Ichi Suzuki, Masahito Ogawa, Ryo Watanabe, Mitsuaki Isobe. A different role of angiotensin II type 1a receptor in the development and hypertrophy of plantaris muscle in mice. *J. Appl. Genet.* 2016.02; 57(1); 91-97
4. Shiheido Y, Maejima Y, Suzuki J, Aoyama N, Kaneko M, Watanabe R, Sakamaki Y, Wakayama K, Ikeda Y, Akazawa H, Ichinose S, Komuro I, Izumi Y, Isobe M. *Porphyromonas gingivalis*, a periodontal pathogen, enhances myocardial vulnerability, thereby promoting post-infarct cardiac rupture. *J. Mol. Cell. Cardiol.* 2016.04;
5. Yoichi Otaki, Yusuke Ebana, Shunji Yoshikawa, Mitsuaki Isobe. Dielectric permittivity change detects the process of blood coagulation: Comparative study of dielectric coagulometry with rotational thromboelastometry. *Thromb. Res.* 2016.06; 145; 3-11
6. Hirokazu Ohigashi, Natsuko Tamura, Yusuke Ebana, Masayoshi Harigai, Yasuhiro Maejima, Takashi Ashikaga, Mitsuaki Isobe. Effects of immunosuppressive and biological agents on refractory Takayasu arteritis patients unresponsive to glucocorticoid treatment. *J Cardiol*. 2016.08;
7. Lian Liu, Yusuke Ebana, Jun-Ichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Toshihiro Tanaka, Masatoshi Komura, Mitsuaki Isobe, Tetsushi Furukawa. Genetic Variants Associated With Susceptibility to Atrial Fibrillation in a Japanese Population. *Can J Cardiol*. 2016.11;
8. Hirofumi Zempo, Jun-Ichi Suzuki, Masahito Ogawa, Ryo Watanabe, Katsuhito Fujiu, Ichiro Manabe, Simon J Conway, Yoshiaki Taniyama, Ryuichi Morishita, Yasunobu Hirata, Mitsuaki Isobe, Ryoza Nagai. Influence of periostin-positive cell-specific Klf5 deletion on aortic thickening in DOCA-salt hypertensive mice. *Hypertens. Res.* 2016.11; 39(11); 764-768

##### [Misc]

1. Yasuhiro Maejima, Mitsuaki Isobe, Junichi Sadoshima. Regulation of autophagy by Beclin 1 in the heart. *J. Mol. Cell. Cardiol.* 2016.06; 95; 19-25
2. Yusuke Ebana. Ethics in Clinical Research *Obstet. Gynecol.* 2016.10; 83(10); 1119-1123

##### [Conference Activities & Talks]

1. Yusuke Ebana Hiroko Kohbata, Sayako Takahashi, Masayuki Yoshida. Genetic counselling for a case with breast cancer who underwent a whole-exome sequencing in a private company. The 13th International Congress Society of Human Genetics 2016.04.06
2. Kiyoshi Nobori. HOW TO BALANCE THE NEED FOR GLOBAL TRIALS AND THE NEED FOR REGIONAL DATA? : Dosing and PK matters. 13th Global CardioVascular Clinical Trials Forum 2016.12.01 Embassy of France, 4101 Reservoir Rd NW, Washington D.C. 20007, USA

## Anesthesiology

Professor: Koshi Makita  
Associate Professor: Tokujiro Uchida  
Junior Associate Professor: Jiro Kurata, Seiji Ishikawa,  
Satoshi Toyama  
Assistant Professor: Maiko Satomoto, Akio Masuda, Mamoru Yamamoto  
Takashi Hakusui, Yusuke Ito, Akihiro Haramo, Tetsuo Koyanagi,  
Akiko Kitajo, Izumi Ebana  
Staff: Sonomi Tanaka, Sayomi Nagai, Takeshi Kasuga, Manami Tanaka  
Yohei Tetsuyuki, Atsushi Ito  
Resident: Tsubasa Akune, Tomoe Tajiri  
Postgraduate Student: Fukami Nakajima, Yutaka Miura,  
Yuzuru Inatomi, Hiroyuki Ito, Hiroyuki Kobinata, Eri Ikeda,  
Tomoko Ishibashi, Hiroto Yamamoto, Yudai Yamamoto, Yu Qi,  
Zhang Shuo, ZhongLiang Sun  
Research Student: Tianjiao Li, Suet May Chan

### (1) Outline

A comprehensive understanding of research trends, research methods, and analysis of results by introducing the latest papers published in prestigious journals related to anesthesiology.

### (2) Research

- 1) Discovering most effective ventilation methods for injury lungs.
- 2) Therapeutic mechanism of mesenchymal stem cell for lung injury (rat and mouse model)
- 3) Studies on the central nervous system effects of general anesthetics by human electrocorticogram and functional neuroimaging.
- 4) Studies on the mechanisms of cerebral pain processing and pain chronification by human functional magnetic resonance imaging and positron emission tomography.
- 5) Studies on the effects of protective one-lung ventilation on ventilatory mechanics.
- 6) Epidemiologic studies to identify incidence of, and risk factors for postoperative acute kidney injury in patients undergoing liver resection.
- 7) Studies on the effect of anesthetics on the developing brain.

### (3) Publications

#### [Original Articles]

1. Mizue Hobo, Akihito Uezato, Mitsunori Nishiyama, Mayumi Suzuki, Jiro Kurata, Koshi Makita, Naoki Yamamoto, Toru Nishikawa. A case of malignant catatonia with idiopathic pulmonary arterial hypertension treated by electroconvulsive therapy. *BMC Psychiatry*. 2016; 16(1); 130
2. Emi Nakamura, Hiroyuki Kinoshita, Guo-Gang Feng, Hisaki Hayashi, Maiko Satomoto, Motohiko Sato, Yoshihiro Fujiwara. Sevoflurane Inhalation Accelerates the Long-Term Memory Consolidation via Small

- GTPase Overexpression in the Hippocampus of Mice in Adolescence. *PLoS ONE*. 2016; 11(9); e0163151
3. Maiko Satomoto, Zhongliang Sun, Yushi U Adachi, Koshi Makita. Sugammadex-Enhanced Neuronal Apoptosis following Neonatal Sevoflurane Exposure in Mice. *Anesthesiol Res Pract*. 2016; 2016; 9682703
  4. Yukako Obata, Yushi U Adachi, Katsumi Suzuki, Taiga Itagaki, Hiromi Kato, Maiko Satomoto, Yoshiki Nakajima. The Influence of Differences in Solvents and Concentration on the Efficacy of Propofol at Induction of Anesthesia. *Anesthesiol Res Pract*. 2016.01; 2016; 9178523
  5. Z Sun, M Satomoto, Y U Adachi, H Kinoshita, K Makita. Inhibiting NADPH oxidase protects against long-term memory impairment induced by neonatal sevoflurane exposure in mice. *Br J Anaesth*. 2016.05; 117(1); 80-86
  6. Kazawa M, Fukagawa A, Ito H, Toyama S, Makita K. Risk of difficult intubation may increase with age in pediatric patients with pycnodysostosis. *Pediatric Anesthesia*. 2016.05; 5; 567-568
  7. Maiko Satomoto, Zhongliang Sun, Yushi U Adachi, Koshi Makita. Neonatal Sevoflurane Exposure Induces Adulthood Fear-induced Learning Disability and Decreases Glutamatergic Neurons in the Basolateral Amygdala. *J Neurosurg Anesthesiol*. 2016.11;
  8. Yu Qi, Tokujiro Uchida, Mamoru Yamamoto, Yudai Yamamoto, Koji Kido, Hiroyuki Ito, Nagara Ohno, Miho Asahara, Yoshitsugu Yamada, Osamu Yamaguchi, Chieko Mitaka, Makoto Tomita, Koshi Makita. Perioperative Elevation in Cell-Free DNA Levels in Patients Undergoing Cardiac Surgery: Possible Contribution of Neutrophil Extracellular Traps to Perioperative Renal Dysfunction. *Anesthesiology Research and Practice*. 2016.11; 2794364

#### [Books etc]

1. Lohser J, Ishikawa S. Chapter 6, Clinical management of one-lung ventilation. Slinger P Ed., Principles and practice of anesthesia for thoracic surgery. Springer, 2011, pp 83-101..
2. Lohser J, Ishikawa S. Chapter 5, Physiology of the lateral decubitus position, open chest, and one-lung ventilation. Slinger P Ed., Principles and practice of anesthesia for thoracic surgery. Springer, 2011, pp 71-82..

#### [Misc]

1. Koichi Nakazawa, Ken Shinoda. An overview of incidence and outcome of perioperative pulmonary aspiration *The Japanese Journal of Anesthesiology* . 2016.01; 65(1); 4-12
2. Jiro Kurata. Pulse oximeter: Oxygenation and hemodynamics at a glance *The Japanese Journal of Acute Medicine*. 2016.01; 40(1); 5-8
3. Maiko Satomoto, Koshi Makita. Anesthesia-induced neurotoxicity in an animal model of the developing brain: mechanism and therapies. *Neural Regen Res*. 2016.09; 11(9); 1407-1408

#### [Conference Activities & Talks]

1. Induction and mechanism of cytotoxicity by long-term propofol treatment in human induced pluripotent stem cell-derived neurons. 2016.05.26
2. A retrospective survey on Combined Spinal Epidural Anesthesia for colectomy with cardio-pulmonary complications during past eleven years. 2016.09.03
3. Koji Kido, Hiroyuki Ito, Yudai Yamamoto, Tokujiro Uchida, Koshi Makita. Dose-dependent Cytotoxicity of Propofol in Cultured Human-induced Pluripotent Stem Cell-derived Neurons. *Anesthesiology* 2016 annual meeting 2016.10.23 Chicago
4. SUN Zhongliang, Maiko Satomoto, RI Shinnbinn, Koshi Makita. Sugammadex-enhanced neuronal apoptosis following neonatal sevoflurane exposure in mice. *The 36th Annual Meeting of the Japan Society for Clinical Anesthesia* 2016.11.03 Kochi



## Cardiovascular Surgery

Professor Hirokuni ARAI  
Associate Professor Tomohiro MIZUNO  
Junior Associate Professor Keiji OI  
Assistant Professor Masafumi YASHIMA, Tsuyoshi HACHIMARU, Eiki NAGAOKA, Tatsuki FUJIWARA,  
Masashi TAKESHITA  
Graduate Student Hidehito KUROKI, Tatsuki FUJIWARA, Dai TASAKI  
Hospital Staff 2

### ( 1 ) Research

- 1) Developing safe and high quality surgical strategy in coronary artery bypass grafting surgery.
- 2) Developing new surgical technique for ischemic heart disease
- 3) Developing new surgical technique for beating mitral valve surgery
- 4) Clinical research for artificial heart
- 5) Research for new regenerative therapy for failing heart to recover cardiac function

### ( 2 ) Education

Cardiovascular Surgery is a branch of surgery which deals with heart and vascular (mainly aortic) disease. Main objective of our department in the graduate course is to provide medical students an opportunity to study surgical anatomy, pathophysiology, pharmacology, and advanced surgical treatment for heart and aortic disease. Students are also taught basic research for the surgical treatment for heart and aortic disease. We also provide clinical training program for young surgeon to obtain Japanese cardiovascular surgical board.

### ( 3 ) Clinical Performances

Our department provides well-advanced surgical treatment of heart and aortic surgery. We perform off-pump coronary artery bypass grafting for more than 90% of patients with coronary artery disease, mitral valve repair, not valve replacement, for almost all patients with mitral valve regurgitation. New surgical reconstruction technique is provided for patients with functional mitral regurgitation due to severe heart failure. For elderly patients, we offer minimally invasive aortic surgery such as thoracic endovascular aortic repair (TEVAR) and hybrid aortic surgery without cardiopulmonary bypass for aortic arch and thoracoabdominal aortic disease.

### ( 4 ) Publications

#### [Original Articles]

1. Fujiwara T, Sakota D, Ouchi K, Endo S, Tahara T, Murashige T, Kosaka R, Oi K, Mizuno T, Maruyama O, Arai H.. Optical dynamic analysis of thrombus inside a centrifugal blood pump during extracorporeal mechanical circulatory support in a porcine model *Artif Organs*. 2016; In Press;

2. Daisuke Sakota, Tomotaka Murashige, Ryo Kosaka, Tatsuki Fujiwara, Katsuhiro Ouchi, Masahiro Nishida, Osamu Maruyama. Noninvasive optical imaging of thrombus formation in mechanical circulatory support devices *Journal of Biorheology*. 2016; 30; 6-12
3. Shioiri A, Kurumaji A, Takeuchi T, Nemoto K, Arai H, Nishikawa T. . A Decrease in the Volume of Gray Matter as a Risk Factor for Postoperative Delirium Revealed by an Atlas-based Method. *The American Journal of Geriatric Psychiatry*. 2016.07; 24(7); 528-536
4. Minoru Ono, Yoshiki Sawa, Takeshi Nakatani, Ryuji Tominaga, Yoshiro Matsui, Kenji Yamazaki, Yoshikatsu Saiki, Hiroshi Niinami, Goro Matsumiya, Hirokuni Arai, . Japanese Multicenter Outcomes With the Heart-Mate II Left Ventricular Assist Device in Patients With Small Body Surface Area. *Circ. J.*. 2016.08; 80(9); 1931-1936
5. Daisuke Sakota, Tatsuki Fujiwara, Katsuhiro Ouchi, Katsuyuki Kuwana, Hiroyuki Yamazaki, Osamu Maruyama. Development of an Optical Detector of Thrombus Formation on the Pivot Bearing of a Rotary Blood Pump. *Artificial Organs*. 2016.09; 40(9); 834-841
6. Tomomi Hasegawa, Munetaka Masuda, Meinoshin Okumura, Hirokuni Arai, Junjiro Kobayashi, Yoshikatsu Saiki, Kazuo Tanemoto, Hiroshi Nishida, Noboru Motomura. Trends and outcomes in neonatal cardiac surgery for congenital heart disease in Japan from 1996 to 2010. *Eur J Cardiothorac Surg*. 2016.10; 1-7
7. Tomohiro Mizuno, Koso Egi, Kenji Sakai, Keiji Oi, Tsuyoshi Hachimaru, Tohru Makita, Kiyotoshi Oishi, Hirokuni Arai. Minimally Circulatory-Assisted On-Pump Beating Coronary Artery Bypass Grafting for Patients With Complex Conditions for Off-Pump Surgery. *Artif Organs*. 2016.10;
8. Munetaka Masuda, Hiroyuki Kuwano, Meinoshin Okumura, Hirokuni Arai, Shunsuke Endo, Yuichiro Doki, Junjiro Kobayashi, Noboru Motomura, Hiroshi Nishida, Yoshikatsu Saiki, Fumihiro Tanaka, Kazuo Tanemoto, Yasushi Toh, Hiroyasu Yokomise. Erratum to: Thoracic and cardiovascular surgery in Japan during 2013 : Annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg*. 2016.12; 64; 496-500

#### [Books etc]

1. Mizuno T, Arai H.. Off-Pump Coronary Artery Bypass, Chapter 9: Exposure / Chapter 11: Securing the Distal Anastomosis Site: Coronary Artery Occlusion, Shunt, and Blower. Springer Japan, 2016

#### [Conference Activities & Talks]

1. Tasaki D., Mizuno T., Oi K., Hachimaru T., Nagaoka E., Kuroki H., Fujiwara T., Kinoshita R., Arai H.. Therapeutic Strategy of Malignant Cardiac Tumor. the 24th Annual meeting of Asian Society for Cardiovascular ant Thoracic Surgery (ASCVTS2016) 2016.04.07 Taipei,Taiwan
2. Eiki Nagaoka, Tomohiro Mizuno, Keiji Oi, Tsuyoshi Hachimaru, Hidehito Kuroki, Dai Tasaki, Tatsuki Fujiwara, Ryouji Kinoshita, Hirokuni Arai. The Effect of Papillary Muscle Relocation on Posterior Leaflet Tethering in Functional Mitral Regurgitation. the 24th Annual meeting of Asian Society for Cardiovascular ant Thoracic Surgery (ASCVTS2016) 2016.04.08 Taipei,Taiwan
3. Keji Oi, Tomohiro Mizuno, Tsuyoshi Hachimaru, Eiki Nagaoka, Hidehito Kuroki, Dai Tasaki, Tatsuki Fujiwara, Ryoji Kinoshita, Hirokuni Arai. LONG-TERM OUTCOME OF TOTAL ARTERIAL GRAFT CABG WITH SINGLE INTERNAL MAMMARY ARTERY AND OTHER ARTERIAL GRAFTS. the 24th Annual meeting of Asian Society for Cardiovascular ant Thoracic Surgery (ASCVTS2016) 2016.04.08 Taipei,Taiwan
4. Kinoshita R., Mizuno T., Hachimaru T., Arai H., Oi K., Nagaoka E., Kuroki H., Tasaki D., Fujiwara T., Yashima M., Takeshita M. . Multiple Inflammatory Aortic Aneurysms due to Vasculitis. AATS Aortic Symposium 2016 2016.05.12 New York,USA
5. Mizuno T., Hachimaru T., Oi K., Nagaoka E., Kuroki H., Tasaki D., Fujiwara T., Kinoshita R., Arai H.. Total Debranching TEVAR for Extended Thoracic Aortic Disease Including Aortic Arch. American Association for Thoracic Surgery 2016.05.12 New York, USA

6. K Ohuchi, T Mizuno, K Oi, M Yashima, T Hachimaru, E Nagaoka, T Fujiwara, H Kuroki, D Tasaki, M Takeshita, R Kinoshita, S Endo, M Kanai, S Suzuki, T Kimura, H Arai. Attempt for the Development of Cardiac Surgery Training Program Combined with Live Animal Surgery. The 63rd Annual Meeting of Japanese Association for Animal Science 2016.05.18
7. Mizuno T., Hachimaru T., Oi K., Yashima M., Nagaoka E., Kuroki H., Tasaki D., Fujiwara T., Takeshita M., Kinoshita R., Arai H.. Surgical Strategy to Balance less Invasiveness with Complete Aortic Repair and Less Neurologic and Aorta-Related Complications for Extended Thoracic Aortic Disease Including Aortic Arch. ISMICS(International Society for Minimally Invasive Cardiothoracic Surgery) 2016 Annual Scientific Meeting 2016.06.15 Montreal Quebec, Canada
8. Impact of Papillary Muscle Relocation on Prognosis of Patient with Functional Mitral Regurgitation. 2016.07.14 Fukuoka/Japan
9. Fujiwara T, Arai H, Mizuno T, Oi K, Yashima M, Hachimaru T, Nagaoka E, Kuroki H, Tasaki D, Takeshita M, Kinoshita R, Ohuchi K. Which is a better acute-phase circulatory support for cardiogenic shock patients in INTERMACS profile-1: a pulsatile VAD or a centrifugal pump?. 24th Annual Congress of the International Society for Rotary Blood Pumps 2016.09.21 Ibaraki
10. Ohuchi K, Mizuno T, Oi K, Yashima M, Hachimaru T, Nagaoka E, Fujiwara T, Kuroki H, Tasaki D, Takeshita M, Kinoshita R, Endo S, Kanai M, Kimura T, Arai H. Development of Heart Surgery Training Program Combined with Live Animal Surgery. 24th Congress of the International Society for Rotary Blood Pumps 2016.09.21
11. Fujiwara T, Arai H, Mizuno T, Oi K, Yashima M, Hachimaru T, Nagaoka E, Kuroki H, Tasaki D, Takeshita M, Kinoshita R, Ohuchi K. Which is a better acute-phase circulatory support for cardiogenic shock patients in INTERMACS Profile-1: A pulsatile VAD or a centrifugal pump?. 24th Congress of the International Society for Rotary Blood Pumps 2016.09.21
12. Sakota D, Fujiwara T, Ouchi K, Kuwana K, Yamazaki H, Arai H, Maruyama O. Development of an optical thrombus detector on the pivot bearing of a rotary blood pump. 24th Congress of the International Society for Rotary Blood Pumps 2016.09.22
13. Arai H.. (Panelist) Coronary Artery Bypass Graft: Minimally Invasive and Hybrid Revascularisation.. 30th European Association for Cardio-Thoracic Surgery 2016.10.04 Barcelona, Spain
14. Hirokuni Arai. (Moderator) Coronary Revascularization. ISMICS 2016 Winter Workshop 2016.10.28 Kyoto
15. Mizuno T.. Total debranching TEVAR. ISMICS 2016 Winter Workshop 2016.10.28 Kyoto
16. E Nagaoka, T Mizuno, K Oi, T Hachimaru, H Kuroki, D Tasaki, T Fujiwara, R Kinoshita, H Arai. On-pump Beating Heart Mitral Valve Repair without Aortic Cross-clamping: Tips and Tricks for Safe Practice. ISMICS 2016 Winter Workshop 2016.10.29 Kyoto
17. Arai H. Epi-aortic Ultrasound: Standard of Care. AATS International Coronary Congress 2016 2016.11.11 New Delhi, India
18. Arai H. (moderator) Parallel Session V: BITA Grafting: How to Harvest and Use BITA Grafts. AATS International Coronary Congress 2016 2016.11.11 New Delhi, India
19. Arai H. (moderator) Parallel Session X: Mini Debates, Hot Topics 2.. AATS International Coronary Congress 2016 2016.11.12 New Delhi, India
20. Arai H. (moderator) Parallel Session XVI: Management of Ischemic MR, Heart Failure and Unbypassable Targets. AATS International Coronary Congress 2016 2016.11.13 New Delhi, India
21. Keji Oi, Tomohiro Mizuno, Masafumi Yashima, Tsuyoshi Hachimaru, Eiki Nagaoka, Hidehito Kuroki, Dai Tasaki, Tatsuki Fujiwara, Masashi Takeshita, Ryoji Kinoshita, Hirokuni Arai. Elevated Preoperative Hemoglobin A1c Level and Adverse Longterm Outcomes After Coronary Artery Bypass Surgery in Patients With Renal Dysfunction and Diabetes. American Heart Association 2016 2016.11.14 NewOrleans,USA
22. Arai H. Posterior leaflet New Repair Technique. Medtronic Mitral Academy Japan 2016 2016.11.19 Tokyo

23. Arai H. Papillary Muscle Relocation in Functional MR cases. . Medtronic Mitral Academy Japan 2016 2016.11.20 Tokyo
24. Arai H. Innovation in Cardiac Surgery. the 30th Kalyanakit Kitiyakara Lecture 2016.11.28 Bangkok, Thailand
25. Arai H. How to improve the quality of modern CABG. Inter-hospital Conference 39 2016.12.17 Bangkok, Thailand
26. Arai H. Target vessels exposure, flow measurement and ultrasound imaging. 5th RAMA OPCAB Meeting 2016.12.19 Bangkok, Thailand
27. Arai H. My approach to reduce Neurological complication in CABG. 5th RAMA OPCAB Meeting 2016.12.20 Bangkok, Thailand

**[Patents]**

1. OSTEOSYNTHESIS MEMBER, Announcement Number : CN106137358A

## Nephrology

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### (1) Outline

The policy of the Department of Nephrology is to accomplish trustworthy medicine and to educate excellent academic scientists and nephrologists. Our department is one of the initial institutes that started the hemodialysis therapy in Japan, and thus, has a long experience of clinical practice of kidney diseases.

We are now investigating pathophysiological mechanisms of various kidney diseases including genetic renal diseases. Furthermore, we are taking a proactive stance in developing innovative therapy. We hope new young scientists and physicians join us for future science and nephrology.

## ( 2 ) Research

The theme of our study is "to investigate the mechanisms of maintaining blood pressure and body fluids homeostasis regulated by the kidney and to clear the pathophysiology caused by their failure, and to develop novel strategies for their treatment." This would lead to the development of kidney disease therapy itself and would also lead to studying for multiple organ failure caused by chronic kidney disease (CKD).

In 2016, our 17 presentations, including 2 oral presentations, were adopted in the annual meeting of American society of nephrology (ASN KIDNEY WEEK). Moreover, the articles written by Fumiaki Ando and Wakana Shoda, were accepted by Nature Communication (IF: 11.33) and Kidney International (IF: 7.68) respectively. Both of them were presented in "press release".

In addition to them, a lot of our members have got prizes in various medical meetings regardless of whether they are in or out of the country. Further, comprehensive diagnosis of inherited kidney diseases using next generation sequencer (NGS) and clinical studies on genome information are now on track and is contributing to various genetic diagnosis of many patients. CKD-ROUTE study, which is the clinical cohort study with 1,000 subjects we take the initiative have been finished the observation period of 3 years, and useful knowledge would be expected to be obtained.

## ( 3 ) Education

"Undergraduate education"

(Systematic lecture)

For third grade medical students, we are conducting lectures organized in a three-week 'block form' together with urology and pathology sections. Under the name of "Body Fluid Regulation and Urology" Block, the students can learn intensively about kidney and urologic diseases during a period of three weeks. In this lecture, we incorporate PBL (problem-based learning) lectures and lectures held by actual patients, so that the students will be able to study independently and bi-directionally.

(Project semester)

We accept several students every year in the project semester, in which they are expected to participate in the forefront research with the assistance of graduate students.

(Clinical clerkship)

For fifth grade students who finished the systematic lectures and project semester, we provide the pre-clinical clerkship (PCC) lectures for ten weeks, which are more practical and comprehensive than that the previous lectures held in the classroom. After PCC, the students will undergo clinical clerkship (CC), in which they will actually take charge of patients in the hospital ward, and study about kidney diseases while developing their clinical skills. They will be in charge of one new inpatient each week, make a presentation about their patient at the medical conference every week, and are expected to learn about the pathophysiology of various kidney diseases in depth.

"Postgraduate education"

After the two-year initial training after graduation, postgraduate doctors will be engaged in clinical training as nephrologists either in the University Hospital or affiliated hospitals as senior trainees, and during this period, we teach them so that they can be aware about unsolved clinical problems. We are planning to bring them up as "academic doctors".

Research activities in the graduate school are quite active, and by carrying out the state-of-the-art research as described above, we are training doctors to be able to excel in both basic and clinical works.

## ( 4 ) Clinical Services & Other Works

Our department is one of the initial institutes that started the hemodialysis therapy in Japan, and thus, has a long experience of clinical practice of kidney diseases. We have close coordination with affiliated hospitals, and are performing CKD-ROUTE clinical cohort study stated above in cooperation with 15 of hospitals and we are coping with revealing the pathophysiology of CKD patients. We have been actively adopting the "educational admission" for CKD patients and it has been showing the significant inhibitory effect on progression of kidney

disease. For end-stage renal disease patients, vascular access surgery, peritoneal dialysis-related surgery, and induction of dialysis are consistently carried out in our department.

Our hemopurification center is one of the biggest institutions among 42 hospitals belonging to national universities. In 2015, the number of newly started dialysis patients was in 1st place, the number of plasma exchange was 1st place, the number of hemodialysis was 2nd place, and total number of hemopurification therapy was within 2nd place. Furthermore, we developed diagnostic panel of hereditary diseases like nephrogenic diabetes insipidus, pseudohypoaldosteronism type II, and Liddle syndrome, and then we receive requests of genetic tests from all over the country.

## (5) Publications

### [Original Articles]

1. Takeshi Kusuda, Tadashi Hosoya, Takayasu Mori, Katsuhito Ihara, Hidenori Nishida, Motoko Chiga, Eisei Sohara, Tatemitsu Rai, Ryuji Koike, Shinichi Uchida, Hitoshi Kohsaka. Acquired Gitelman Syndrome in an Anti-SSA Antibody-positive Patient with a SLC12A3 Heterozygous Mutation. *Intern. Med.* 2016; 55(21); 3201-3204
2. Wakaba Yamaguchi, Naofumi Yui, Toshikage Nagao, Gaku Oshikawa, Mariko Negi, Soichiro Iimori, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida. Bence-Jones Protein  $\lambda$ -type Multiple Myeloma Patient Withdrawn from Maintenance Hemodialysis after Long-term Bortezomib and Dexamethasone Therapy. *Intern. Med.* 2016; 55(3); 263-268
3. Hiroaki Kikuchi, Eiichiro Kanda, Shintaro Mandai, Masanobu Akazawa, Soichiro Iimori, Katsuyuki Oi, Shotaro Naito, Yumi Noda, Takayuki Toda, Teiichi Tamura, Sei Sasaki, Eisei Sohara, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida. Combination of low body mass index and serum albumin level is associated with chronic kidney disease progression: the chronic kidney disease-research of outcomes in treatment and epidemiology (CKD-ROUTE) study. *Clin. Exp. Nephrol.* 2016.02;
4. Shintaro Mandai, Eiichiro Kanda, Soichiro Iimori, Shotaro Naito, Yumi Noda, Hiroaki Kikuchi, Masanobu Akazawa, Katsuyuki Oi, Takayuki Toda, Eisei Sohara, Tomokazu Okado, Sei Sasaki, Tatemitsu Rai, Shinichi Uchida. Association of serum chloride level with mortality and cardiovascular events in chronic kidney disease: the CKD-ROUTE study. *Clin. Exp. Nephrol.* 2016.04;
5. Rahman Asadur, Kittikulsuth Wararat, Fujisawa Yoshihide, Sufiun Abu, Rafiq Kazi, Hitomi Hirofumi, Nakano Daisuke, Sohara Eisei, Uchida Shinichi, Nishiyama Akira. Effects of diuretics on sodium-dependent glucose cotransporter 2 inhibitor-induced changes in blood pressure in obese rats suffering from the metabolic syndrome. *J Hypertens.* 2016.05; 34(5); 893-906
6. Arai Yohei, Kanda Eiichiro, Iimori Soichiro, Naito Shotaro, Noda Yumi, Kawasaki Tomoki, Sato Hidehiko, Ando Ryoichi, Sasaki Sei, Sohara Eisei, Okado Tomokazu, Rai Tatemitsu, Uchida Shinichi. The use of vitamin D analogs is independently associated with the favorable renal prognosis in chronic kidney disease stages 4-5: the CKD-ROUTE study. *Clin Exp Nephrol.* 2016.06;
7. Imai Eri, Kaneko Shuzo, Mori Takayasu, Okado Tomokazu, Uchida Shinichi, Tsukamoto Yusuke. A novel heterozygous mutation in the ATP6V0A4 gene encoding the V-ATPase a4 subunit in an adult patient with incomplete distal renal tubular acidosis. *Clin Kidney J.* 2016.06; 9(3); 424-428
8. Ohkubo Atsushi, Okado Tomokazu, Miyamoto Satoko, Goto Keigo, Yamamoto Motoki, Maeda Takuma, Itagaki Ayako, Seshima Hiroshi, Kurashima Naoki, Sohara Eisei, Uchida Shinichi, Rai Tatemitsu. Removal Characteristics of Immunoabsorption With the Immusorba TR-350 Column Using Conventional and Selective Plasma Separators. *Ther Apher Dial.* 2016.08; 20(4); 360-367
9. Miyamoto Satoko, Ohkubo Atsushi, Seshima Hiroshi, Maeda Takuma, Itagaki Ayako, Kurashima Naoki, Iimori Soichiro, Naito Shotaro, Sohara Eisei, Rai Tatemitsu, Uchida Shinichi, Okado Tomokazu. Removal Dynamics of Immunoglobulin and Fibrinogen by Conventional Plasma Exchange, Selective Plasma Exchange, and a Combination of the Two. *Ther Apher Dial.* 2016.08; 20(4); 342-347
10. Mitani Marie, Furuichi Munehiro, Narumi Satoshi, Hasegawa Tomonobu, Chiga Motoko, Uchida Shinichi, Sato Seiji. A patient with pseudohypoaldosteronism type II complicated by congenital hypopituitarism carrying a KLHL3 mutation. *Clin Pediatr Endocrinol.* 2016.10; 25(4); 127-134



11. Cheung W Pui, Nomura Naohiro, Nair V Anil, Pathomthongtaweethai Nutthapoom, Ueberdiek Lars, Lu Hua A Jenny, Brown Dennis, Bouley Richard . EGF Receptor Inhibition by Erlotinib Increases Aquaporin 2-Mediated Renal Water Reabsorption. *J. Am. Soc. Nephrol.* 2016.10; 27(10); 3105-3116
12. Wakana Shoda, Naohiro Nomura, Fumiaki Ando, Yutaro Mor, Takayasu Mori, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Calcineurin inhibitors block sodium-chloride cotransporter dephosphorylation in response to high potassium intake *Kidney International* . 2016.10; 91; 402-411
13. Ando Fumiaki, Sohara Eisei, Morimoto Tetsuji, Yui Naofumi, Nomura Naohiro, Kikuchi Eriko, Takahashi Daiei, Mori Takayasu, Vandewalle Alain, Rai Tatemitsu, Sasaki Sei, Kondo Yoshiaki, Uchida Shinichi. Wnt5a induces renal AQP2 expression by activating calcineurin signalling pathway. *Nat Commun.* 2016.11; 7; 13636
14. Imai Eri, Kaneko Shuzo, Mori Takayasu, Okado Tomokazu, Uchida Shinichi, Tsukamoto Yusuke. Erratum: A novel heterozygous mutation in the ATP6V0A4 gene encoding the V-ATPase a4 subunit in an adult patient with incomplete distal renal tubular acidosis. *Clin Kidney J.* 2016.12; 9(6); 871

### [Misc]

1. Yuki Yoshizaki, Shinichi Uchida. Renal tubular acidosis(Fanconi syndrome included) *JMEDJ.* 2016.04;

### [Conference Activities & Talks]

1. Sohara E. WNK signaling and KLHL3/Cullin3 ubiquitin ligase complex in salt-sensitive hypertension. The 89th Annual Meeting of the Japanese Pharmacological Society 2016.02.09
2. Arai Yohei, Sohara Eisei, Takahashi Daiei, Oda Mayumi, Ko Shigeru, Ko Minoru, Rai Tatemitsu, Uchida Shinichi. CaMk1g phosphorylates WNK4 S1190. The 59th Annual Meeting of the Japanese Society of Nephrology 2016.06.18 Yokohama
3. Wakana Shoda, Naohiro Nomura, Fumiaki Ando, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. High potassium intake promotes urinary potassium excretion by activation of calcineurin and dephosphorylation of Na-Cl cotransporter(NCC). The 59th Annual Meeting of the Japanese Society of Nephrology 2016.06.18 Yokohama
4. Emi Sasaki, Eisei Sohara, Koichiro Susa, Takayasu Mori, Kiyoshi Isobe, Yuya Araki, Yuichi Inoue, Tatemitsu Rai, Shinichi Uchida,. Generation and analysis of KLHL3 knockout mice. The 59th Annual meeting of Japanese Society of Nephrology 2016.06.18 Yokohama
5. Yuanlong Wnang, Eisei Sohara, Moko Zeniya, Yutaro Mori, Daiei Takahashi, Shotaro Naito, Tatemitsu Rai, Shinichi Uchida. High Potassium Regulates Vascular Tonus through KLHL2 Protein and WNK3-SPAK-NKCC1 Phosphorylation Cascade. The 59th Annual Meeting of the Japanese Society of Nephrology 2016.06.18
6. Taisuke Furusho, Noriyuki Toshima, Takashi Miyazaki, Itaru Yasuda, Shotaro Takakuwa, Makiko Konishi, Minami Toda, Yatsuka Saito, Suguru Hirasawa, Noriyoshi Toki, Takaie Kuki, Hiromi Kihira, Manabu Haneda, Yasuhide Nishio. Relationship between arterial and interstitial lesions in IgA nephropathy. The 59th Annual Meeting of the Japanese Society of Nephrology 2016.06.19 Yokohama
7. Yuki Yoshizaki, Eisei Sohara, Takayasu Mori, Daiei Takahashi, Moko Zeniya, Yutaro Mori, Yuya Araki, Fumiaki Ando, Tatemitsu Rai, Shinichi Uchida. Drug Repositioning Screening for Keap1-Nrf2 Binding Inhibitors by Using Fluorescent Correlation Spectroscopy. The 59th Annual Meeting of the Japanese Society of Nephrology 2016.06.19 Yokohama
8. Ando F, Sohara E, Yui N, Nomura N, Kikuchi E, Takahashi D, Mori T, Rai T, Sasaki S, and Uchida S.. Calcineurin is a target for the treatment of nephrogenic diabetes insipidus. . 3rd Next Generation Kidney Research Meeting. 2016.08 Tokyo
9. Soichiro Suzuki, et al.. Two cases of Hypercalcemia leading to End Stage Kidney Disease. The 46th Eastern Regional Meeting of the Japanese Society of Nephrology 2016.10.08
10. Wakana Shoda, Naohiro Nomura, Fumiaki Ando, Yutaro Mori, Takayasu Mori, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Calcineurin rapidly dephosphorylates sodium-chloride cotransporter in response to high potassium intake. The 26th Ochanomizu Jin Kenkyukai 2016.10.27 Tokyo

11. Eriko Takehara, Daiei Takahashi, Yujiro Nakano, Koichiro Susa, Moko Zeniya, Hidehiko Sato, Soichiro Iimori, Naohiro Nomura, Shotaro Naito, Eisei Sohara, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida. Severe alkalosis and hypokalemia in a patient with pancreatic neuroendocrine tumor. *Rinsho Taieki* 2016.10.29
12. Zeniya M, Mori T, Yui N, Nomura N, Chiga M, Sohara E, Rai T, Uchida S.. The proteasome inhibitor bortezomib attenuates renal fibrosis in mice.. The 49th Annual Meeting of American Society of Nephrology 2016.11 Chicago
13. Hiroaki Kikuchi, Naohiro Nomura, Yoji Andrew Minamishima, Tatemitsu Rai, Shinichi Uchida and Eisei Sohara.. Targeted Metabolomic Analysis of Kidney from the Subtotal Nephrectomy Mouse Model of Chronic Kidney Disease. The 49th Annual Meeting of American Society of Nephrology. 2016.11.15 Chicago.
14. Yutaro Mori, Shintaro Mandai, Takayasu Mori, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Generation of p62/SQSTM1 (p62) KO Cell Lines Using CRISPR/Cas9 -The Role of p62 on WNK1 Regulation by Changes of Extracellular Potassium Concentration-. The 49th Annual Meeting of the American Society of Nephrology 2016.11.17 Chicago
15. Emi Sasaki, Koichiro Susa, Takayasu Mori, Kiyoshi Isobe, Yuya Araki, Yuichi Inoue, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. Generation and Analysis of KLHL3 Knockout Mice. The 49th Annual Meeting of American Society of nephrology 2016.11.18 Chicago
16. Naofumi Yui, Sei Sasaki, Shinichi Uchida. Regulated Ser-261 Dephosphorylation Combined with Ser-256 and Ser-269 Phosphorylation in the C-terminus of Aquaporin-2 Water Channel. American Society of Nephrology 2016.11.18 Chicago
17. Yohei Arai, Eiichiro Kanda, Soichiro Iimori, Shotaro Naito, Yumi Noda, Sei Sasaki, Eisei Sohara, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida. Low White Blood Cell Count Is Independently Associated with the Progression of Chronic Kidney Disease in the Elderly: The CKD-ROUTE Study. The 49th Annual Meeting of American Society of Nephrology 2016.11.18 Chicago
18. Wakana Shoda, Naohiro Nomura, Fumiaki Ando, Yutaro Mori, Takayasu Mori, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Calcineurin Rapidly Dephosphorylates Sodium-Chloride Cotransporter in Response to High Potassium Intake. The 49th Annual Meeting of American Society of nephrology. 2016.11.18 Chicago
19. Yuki Yoshizaki, Eisei Sohara, Takayasu Mori, Eriko Kikuchi, Daiei Takahashi, Moko Zeniya, Yuya Araki, Yutaro Mori, Fumiaki Ando, Tatemitsu Rai, Shinichi Uchida.. Drug Repositioning Screening for Keap1-Nrf2 Binding Inhibitors by Using Fluorescent Correlation Spectroscopy. The 49th Annual Meeting of American Society of Nephrology 2016.11.18 Chicago
20. Takuya Fujimaru, Takayasu Mori, Shintaro Mandai, Motoko Chiga, Hiroaki Kikuchi, Fumiaki Ando, Yutaro Mori, Naohiro Nomura, Shotaro Naito, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. Development of a Customized Diagnostic Panel for Targeted Exome Sequencing of Polycystic Kidney Diseases. *Kidney Week 2016* 2016.11.19 Chicago, IL
21. Daiei Takahashi, Takayasu Mori, Eisei Sohara, Motoko Chiga, Yuichi Inoue, Naohiro Nomura, Moko Zeniya, Tatemitsu Rai, and Shinichi Uchida. WNK4 regulates adipocyte differentiation in 3T3-L1 cells. The 47th Annual Meeting of American Society of Nephrology 2016.11.19 Chicago, IL.
22. Yuya Araki, Tatemitsu Rai, Eisei Sohara, Takayasu Mori, Yuichi Inoue, Yutaro Mori, Shinichi Uchida. The Pseudohypoaldosteronism Type II-Causing Mutant Cul3 Protein Forms Dimer with KLHL3 and Inhibits the Degradation of WNK4 with a Dominant-Negative Effect. The 49th Annual Meeting of American Society of Nephrology. 2016.11.19 Chicago

# Comprehensive Reproductive Medicine

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Junior Associate Professor : Naoyuki YOSHIKI, Tatsuya HARADA

Project Associate Professor : Masakazu TERAUCHI

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Takashi NAKASUJI, Kazuki SAITO, Akiko FURUSAWA, Takuto MATSUURA, Rie OI,

Takayuki TATSUMI, Masaki SEKIGUCHI, Tamami ODAI, Kenta TAKAHASHI, Mayumi KOBAYASHI,

Ayumi YAMAGUCHI, Yuri SUKENOBE, Nozomi UTIDA

## (1) Research

Research divisions :

- 1) Research in physiology, endocrinology and metabolism in the reproductive medicine
- 2) Research of female physical and mental change with aging
- 3) Pathophysiological examination of gynecological malignant tumor
- 4) Clinical research and basic research in perinatal medicine

Available scientific procedures :

- 1, Cell culture technique of ovarian granulosa cells, endometrial cells, malignant cells, osteoblast and so on.
- 2, Determination of intracellular calcium (by Fura 2 method and patch clamp )
- 3, Measurement of intra-cellular IP3
- 4, Hormonal assay in plasma, urine, follicular fluid (RIA & EIA)
- 5, Immunohistochemistry with ABC method
- 6, Analysis of micro-structure with electrical microscopy
- 7, Determination with molecular biological technique.
- 8, Physiological determination with isometric tension change
- 9, Determination of cerebral blood flow with MRI in cerebral infarction
- 10, Analysis of protein expression with flow cytometry

## ( 2 ) Education

CRM (OB/GY) department has an obligation to offer medical services, education, research as one of the clinical departments in national graduate school, and has duty on making a mutual cooperation with local gynecological institutions.

Our main objectives are

- 1, Investigation for a new progress in treatment technique
- 2, Acquisition of medical knowledge and procedure
- 3, Providing systemic lecture about women's physiological and pathological change during adolescence through senescence.

Aims of research works are focusing on reproductive medicine, perinatal medicine and oncology.

Educational intention in medical doctor course and nursing course includes systemic lectures, clinical conferences and special lecture by many extramural speakers. During Bed-Side Learning period, students should be treated as one of medical stuffs, attend all of deliveries and be present at gynecological procedure. Several OB/GY institutions will be provided as an extramural drills.

## ( 3 ) Clinical Performances

For intractable sterilization, satisfactory results are obtained with endoscopic examinations and IVF-ET methods. Health care unit for menopausal women was established, where inspections for atherosclerosis, osteoporosis (DEXA), autonomic nervous system are performed, and postmenopausal managements are provided including HRT, mental care and counseling.

After construction of LDR(labor, delivery, recovery) unit, cure for complicated pregnancies is now carried out, and cases of deliveries are rising now.

Malignant gynecological tumor is also an important aim of this department, for which surgery, chemotherapy and radiotherapy with complete cure are applied to patients. For benign tumor and endometriosis, laparoscopic operations are aggressively performed, whose number is now increasing.

## ( 4 ) Publications

### [Original Articles]

1. Asuka Hirose, Masakazu Terauchi, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Depressive symptoms are associated with oxidative stress in middle-aged women: a cross-sectional study. *Biopsychosoc Med.* 2016; 10; 12
2. Tatsumi T, S.C. Jwa, Kuwahara A, Irahara M, Kubota T, Saito H. No increased risk of major congenital anomalies or adverse pregnancy or neonatal outcomes following letrozole use in assisted reproductive technology *Human Reproduction.* 2016;
3. Yamada I, Hikishima K, Miyasaka N, Kato K, Kojima K, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H. Gastric carcinoma: evaluation with diffusion-tensor MR imaging and tractography ex vivo. *Magn Reson Imaging.* 2016.02; 34(2); 144-151
4. Asuka Hirose, Masakazu Terauchi, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Low-dose isoflavone aglycone alleviates psychological symptoms of menopause in Japanese women: a randomized, double-blind, placebo-controlled study. *Arch. Gynecol. Obstet..* 2016.03; 293(3); 609-615
5. Saito K, Matsuzaki T, Iwasa T, Miyado M, Saito H, Kubota T, Irahara M, Ogata T, Fukami M.. Blood allopregnanolone levels in women with polycystic ovary syndrome. *Clinical Endocrinology.* 2016.04;
6. Saito K, Matsuzaki T, Iwasa T, Miyado M, Saito H, Hasegawa T, Homma K, Inoue E, Miyashiro Y, Kubota T, Irahara M, Ogata T, Fukami M. Steroidogenic pathways involved in androgen biosynthesis in eumenorrheic women and patients with polycystic ovary syndrome *Journal of Steroid Biochemistry and Molecular Biology.* 2016.04; 158; 31-37
7. Kon M, Saito K, Mitsui T, Miyado M, Igarashi M, Moriya K, Nonomura K, Shinohara N, Ogata T, Fukami M.. Copy-number Variations of the Azoospermia Factor Region or SRY Are Not Associated with the Risk of Hypospadias. *Sexual Development.* 2016.04;

8. Haruka Maneyama, Naoyuki Miyasaka, Kimio Wakana, Megumi Nakamura, Yoshio Kitazume, Toshiro Kubota. Vanishing intravenous leiomyomatosis after hysterectomy: Assessment of the need to perform complete resection. *J. Obstet. Gynaecol. Res.*. 2016.04;
9. Takahashi K, Yoshida H. Watanabe R, Ishikawa M, Ikeda SI, Kato T. Metastasis of extra-ampullary duodenal adenocarcinoma to the uterine cervix *Malaysian Journal of Pathology Malays J Pathol.* 2016.04; 38 (1); 45-48
10. Makiko Egawa, Naoyuki Miyasaka, Takuyuki Kubo, Miho Naitou, Takashi Ito, Toshiro Kubota. A case of puerperal group a streptococcal sepsis complicated by ovarian vein thrombosis. *J Obstet Gynaecol.* 2016.05; 1-5
11. Ikeda Y, Furusawa A, Kitagawa R, Tokinaga A, Ito F, Ukita M, Nomura H, Yamagami W, Tanabe H, Mikami M, Takeshima N, Yaegashi N. Practice patterns of adjuvant therapy for intermediate/high recurrence risk cervical cancer patients in Japan *J Gynecol Oncol.* 2016.05; 27(3);
12. Yoshiki N, Kubota T. Two-port laparoscopic ovarian cystectomy using 3-mm instruments. *Gynecol Minim Invasive Ther.* 2016.05; 5(2); 78-80
13. Yoshiki N. Single-incision laparoscopic myomectomy: A review of the literature and available evidence *Gynecol Minim Invasive Ther.* 2016.05; 5(2); 54-63
14. Makoto Iizuka, Naoyuki Miyasaka, Yuki Hirose, Mikayo Toba, Shuichi Sakamoto, Toshiro Kubota. Is there a differential impact of parity on factors regulating maternal peripheral resistance? *Hypertens. Res.*. 2016.06;
15. A Hirose, M Terauchi, M Akiyoshi, Y Owa, K Kato, T Kubota. Subjective insomnia is associated with low sleep efficiency and fatigue in middle-aged women. *Climacteric.* 2016.08; 19(4); 369-374
16. Yamada I, Hikishima K, Miyasaka N, Kato K, Ito E, Kojima K, Kawano T, Kobayashi D, Eishi Y, Okano H. q-Space MR imaging of gastric carcinoma ex vivo: correlation with histopathologic findings. *Magn Reson Med.* 2016.08; 76(2); 602-612
17. Dolmans MM and Iwahara Y, Donnez J, Soares M, Vaerman JL , Amorim CA, Poirel H. Evaluation of minimal disseminated disease in cryopreserved ovarian tissue from bone and soft tissue sarcoma patients *Human Reproduction.* 2016.09; 31; 2292-2302
18. Kihara A, Wakana K, Kubota T, Kitagawa M. SLUG expression is an indicator of tumour recurrence in high-grade endometrial carcinomas *Histopathology.* 2016.09; 69(3); 374-382
19. Miyasaka N, Egawa M, Isobe M, Inoue Y, Kubota T. Obstetrical management of patients with extra-anatomic vascular bypass grafts due to takayasu arteritis *Obstet Gynaecol Res.* 2016.10; 42(12); 1864-1869
20. Yoshii SR, Kuma A, Akashi T, Hara T, Yamamoto A, Kurikawa Y, Itakura E, Tsukamoto S, Shitara H, Eishi Y, Mizushima N. Systemic Analysis of Atg5-Null Mice Rescued from Neonatal Lethality by Transgenic ATG5Expression in Neurons *Dev Cell.* . 2016.10; 10;39(1); 116-130
21. Matsuura T, Otsuka I. Effectiveness of Carboplatin plus Taxane Chemotherapy for Advanced or Recurrent Uterine Serous Carcinoma *Gan To Kagaku Ryoho.* 2016.11; 43(11); 1401-1404
22. Yuji Komaki, Keigo Hikishima, Shinsuke Shibata, Tsunehiko Konomi, Fumiko Seki, Masayuki Yamada, Naoyuki Miyasaka, Kanehiro Fujiyoshi, Hirotaka J Okano, Masaya Nakamura, Hideyuki Okano. Functional brain mapping using specific sensory-circuit stimulation and a theoretical graph network analysis in mice with neuropathic allodynia. *Sci Rep.* 2016.11; 6; 3782
23. Miyasaka N, Miura O, Kawaguchi T, Arima N, Morishita E, Usuki K, Morita Y, Nishiwaki K, Ninomiya H, Gotoh A, Imashuku S, Urabe A, Shichishima T, Nishimura J, Kanakura Y. . Pregnancy outcomes of patients with paroxysmal nocturnal hemoglobinuria treated with eculizumab: A Japanese experience and updated review. *Int. j. hematol.* .
24. Sekiguchi M, Mioyazaki O, Wada S, Nosaka S, Sago H. Prenatal diagnosis of Pfeiffer syndrome type II using ultralow dose CT {Online}

**[Books etc]**

1. Miyasaka N, Miura O. Pregnancy in Paroxysmal Nocturnal Hemoglobinuria. Paroxysmal Nocturnal Hemoglobinuria, 2016

**[Misc]**

1. Masakazu Terauchi. Menopausal symptoms and the Kampo medicine: Tokishakuyakusan, Kamishoyosan, and Keishibukuryogan Recent Progress in Kampo Medicine in Obstetrics and Gynecology. 2016.04; 33; 23-30

**[Conference Activities & Talks]**

1. Oi R, Yamashita T, Takeda Y, Nakayama S, Hatakeyama M, Maruyama T, Sakamoto H, Adachi T, Okai T, Kubota T, Nakabayashi M. Indication and detective rate of amniocentesis changed by the adoption of non-invasive prenatal genetic testing. 13th International Congress of Human Genetics 2016.04.04 Kyoto
2. Hiraoka K, Hayashi N, Kaji T, Yamaguchi K, Ichihashi A, Suhara T, Ohtsuka Y, Kidera N, Ishikawa T, Ohuchi K, Takagi K. Can Piezo-ICSI improve the fertilization rates of junior embryologists and how many procedures are needed?. . The 6th Congress of the Asia Pacific Initiative on Reproduction 2016.04.09
3. Masakazu Terauchi. Palpitation in middle-aged women is associated with anxiety. 68th Annual Congress of Japan Society of Obstetrics and Gynecology 2016.04.22
4. Ishikawa T, Kubota T. 27-hydroxycholesterol promotes estrogen receptor positive breast cancer. 68th Annual Congress of Japan Society of Obstetrics and Gynecology, Tokyo 2016.04.22
5. Kuwahara A, Ishikawa T, Ishihara O, Kugu K, Sawa R, Banno K, Saito H, Irahara M. Assisted Reproductive Technology (ART) in Japan 2013. Annual report of Japan ART registry. 68th Annual Congress of Japan Society of Obstetrics and Gynecology 2016.04.22 Tokyo
6. Akihiko Ueda, Makoto Akiyama, Takashi Nakasuji, Shota Nii. Cesarean section in Japan : Epidemiology, trends, and surgical procedures. 68th Annual Congress of Japan Society of Obstetrics and Gynecology 2016.04.23 Tokyo
7. Nakasuji T, Sakumoto T, Araki R, Kuwahara A, Kubota T. Saito H. The Incidence of Monozygotic Twinning in Assisted Reproductive Technology in Japan. 2016ACOG Annual Clinical and Scientific Meeting 2016.05 Washington DC, USA
8. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Toshiro Kubota. Palpitation in Middle-aged Women Is Associated with Anxiety. 18th International Society of Psychosomatic Obstetrics and Gynecology Congress 2016.05.12 Malaga, Spain
9. Asuka Hirose, Masakazu Terauchi, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Subjective insomnia is associated with low sleep efficiency and feeling of fatigue in middle-aged women.. 18th International Society of Psychosomatic Obstetrics and Gynecology Congress 2016.05.13
10. Furusawa A, Inoue J, Miyasaka N, Inazawa J. Differential requirement of amino acids on cell survival of ovarian cancer cells . 3rd Annual Meeting of the International Ovarian Cancer Consortium in conjunction with the International Symposium of Tumor Microenvironment and Therapy Resistance 2016.08.29
11. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Makoto Iizuka, Naoyuki Miyasaka, Toshiro Kubota. Palpitation in middle-aged women is associated with anxiety. 15th World Congress on the Menopause 2016.09.30 Prague, Czech Republic
12. Yamaguchi A, Iizuka M, Ohkura Y, Obayashi S. Functional change in rat tail artery by Gamma-Oryzanol. The North American Menopause Society 2016.10.07
13. Oshima N, Fusegi A, Furusawa A, Toba M, Wakana K, Wakabayashi A, Obayashi S. Adjuvant Therapy After Radical Hysterectomy for Cervical Cancer. Biennial Meeting of the International Gynecologic Cancer Society 2016.10.30



14. Takahashi K, Kato T, Kobayshi M , Takehara Y, Tsukada T, Tate K, Shimizu H, Uehara T, Ishikawa M, Ikeda S . Oncologic outcome and adverse events after para-aortic lymphadenectomy for FIGO stage IIIC endometrioid adenocarcinoma of the uterine body. 16th Biennial meeting of the International Gynecologic Cancer Society, 2016.10.30
15. Kazuki Saito, Toshiya Matsuzaki, Mami Miyado, Momori Katsumi, Shigeru Nakamura, Minoru Irahara, Tsutomu Ogata, Maki Fukami. Androgen measurement in women with polycystic ovary syndrome: Comparison between immunoassays and liquid chromatography-tandem mass spectrometry. APPES-JESPE joint meeting 2016.11.18 Tokyo
16. Kawai K, Ohuchi K, Nara K, Miyagawa T, Kidera N, Iwahara Y, Yamamoto A, Ishikawa T, Kawahara M, Teraoka K, Harada T. Efficacy of Random-start Controlled Ovarian Stimulation in Breast Cancer Patients Asian Society for Fertility Preservation.. The 1st Asia congress on fertility preservation 2016.11.19
17. Ishikawa T, Nonaka M, Murakata S, Kidera N, Yamamoto A, Iwahara Y, Miyasaka N. Fertility preservation at Tokyo Medical and Dental University: Our 1year experience Asian Society for Fertility Preservation. The 1st Asia congress on fertility preservation 2016.11.24



## Urology

Professor and Chairman: Kazunori Kihara (-March), Yasuhisa Fujii (August-)  
Associate Professor: Yasuhisa Fujii (-July)  
Junior Associate Professor: Kazutaka Saito,  
Noboru Numao (-February Department of Insured Medical Care Management),  
Yoh Matsuoka, Junichiro Ishioka (-February, March- Department of Insured Medical Care Management)  
Assistant Professor: Minato Yokoyama, Soichiro Yoshida, Toshiki Kijima (March-), Masaya Ito,  
Masaharu Inoue  
Hospital Staff: Naoko Kawamura, Hajime Tanaka, Takayuki Nakayama, Shingo Moriyama (-March),  
Yuma Waseda, Yuki Nakamura (-October), Motohiro Fujiwara (-June), Shugo Yajima (November-),  
Keita Izumi (April-)  
Graduate Student: Naoko Kawamura (-March), Sachi Kitayama, Toshihiro Kanda (-March), Saori Araki,  
Yosuke Yasuda, Sho Uehara, Yuma Waseda, Hiroshi Fukushima, Shingo Moriyama (April-)  
Project professor: Kazunori Kihara (April-)

### (1) Outline

Our mission is to establish and provide the best urological care to all patients in the super aging society which all over the world is facing.

Besides offering urological practices of the international standard, we are making a continuous effort to improve daily practices based on the evidences of the clinical and translational research which we commit under the concept of “Bed to Bench, Feedback to Bed” .

To realize the mission, we have been developing various procedures.

1. Gasless Single-Port RoboSurgeon urological surgery which can be applied to most of patients with urological tumors is a safe and educational minimally invasive surgery satisfying no CO<sub>2</sub> gas insufflation, no peritoneal injury, no multiple ports, and no high cost.
2. Bladder sparing treatment consisting of transurethral resection of bladder tumor, low-dose chemoradiotherapy and Gasless Single-Port RoboSurgeon partial cystectomy with pelvic lymph node dissection can preserve urinary and sexual function without compromising curability in carefully selected patients with muscle-invasive bladder cancer for which radical cystectomy with urinary diversion is the standard treatment.
3. Gasless Single-Port RoboSurgeon clampless partial nephrectomy for kidney cancer potentially preserves maximal renal function with minimal invasiveness especially in patients with single kidney or impaired renal function.
4. Focal brachytherapy for localized prostate cancer precisely diagnosed by MRI and meticulous biopsy can provide cure without deteriorating urinary and sexual function.

The continuous commitment to clinical and translational research is reflected to publications in international journals, presentations at international meetings and awards.

### (2) Research

Clinical Research

- 1) Innovation and establishment of a minimally invasive surgery, Gasless Single-Port RoboSurgeon urological surgery
- 2) Development of optimal MRI-ultrasonography fusion prostate needle biopsy

- 3) Sequential combination therapy to prolong survival of advanced prostate cancer patients
- 4) Development and establishment of curative and minimally invasive bladder preservation using low-dose chemoradiotherapy plus Gasless Single-Port RoboSurgeon partial cystectomy against muscle-invasive bladder cancer
- 5) Development and establishment of Gasless Single-Port RoboSurgeon clampless partial nephrectomy against kidney cancer
- 6) Development and establishment of focal brachytherapy against localized prostate cancer
- 7) Sequential combination therapy to prolong survival of advanced kidney cancer patients, starting with immunotherapy combined with multiple molecular targeted agents
- 8) Application of diffusion-weighted MRI to diagnosis, assessment of therapeutic effects and monitoring of relapse in urological cancer
- 9) Application of serum C-reactive protein as a prognostic biomarker of urological malignancies and as a marker for surgical invasiveness
- 10) Development of prognostic prediction model for non-muscle-invasive bladder cancer

#### Translational Research

- 1) Development of differentiation-inducing therapy against hormone-resistant prostate carcinomas
- 2) Investigation on molecular mechanisms, in particular deregulation of the NO system, underlying voiding and erectile dysfunction to develop rational therapy
- 3) Overcoming therapeutic resistance to chemo- and/or radiotherapy against urological malignancies using novel molecular targeted agents
- 4) Investigation on functional roles of p63 protein in urothelial carcinomas

### (3) Lectures & Courses

Our top priority is to establish the best urological practice in the super aging society which all over the world is facing. We are committed to offering educational programs to facilitate the development of outstanding academic urologists of the next generation. We believe that one of our missions is to educate students, residents and fellows in the art and science of urology and thereby to train the future leaders in the field. The continuous commitment to clinical and translational research is reflected to publications in international journals, presentations at international meetings and awards.

### (4) Clinical Performances

Our mission is to provide the best urological care to all patients. Besides offering urological practices of the international standard, we are making a continuous effort to improve daily practices. The Gasless Single-Port RoboSurgeon urological surgery, which we have innovated its concept and developed surgical techniques specific to all urological organs, has been officially approved as medical services provided by the Japanese Governmental Health Insurance System in April 2008. These minimally invasive surgical techniques can be fundamentally applied to all patients having urological malignancies, even those having locally advanced disease and previous histories of abdominal surgery.

### (5) Publications

#### [Original Articles]

1. Madoka Kataoka, Hiroshi Fukushima, Yasukazu Nakanishi, Minato Yokoyama, Nobuaki Funata, Toru Motoi, Ken-Ichi Tobisu, Fumitaka Koga. Retroperitoneal Teratoma in an Adult: A Potential Pitfall in the Differential Diagnosis of Adrenal Myelolipoma. *Case Rep Urol.* 2016; 2016; 5141769
2. Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Hiroshi Tanaka, Jiro Kumagai, Soichiro Yoshida, Junichiro Ishioka, Fumitaka Koga, Hitoshi Masuda, Satoru Kawakami, Yasuhisa Fujii, Kazunori Kihara. Candidate selection for quadrant-based focal ablation through a combination of diffusion-weighted magnetic resonance imaging and prostate biopsy. *BJU Int.* 2016.01; 117(1); 94-101
3. Hajime Tanaka, Soichiro Yoshida, Yoshinobu Komai, Yasuyuki Sakai, Shinji Urakami, Takeshi Yuasa, Shinya Yamamoto, Hitoshi Masuda, Mitsuru Koizumi, Atsushi Kohno, Iwao Fukui, Junji Yonese, Ya-

suhisa Fujii, Kazunori Kihara. Clinical Value of 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Upper Tract Urothelial Carcinoma: Impact on Detection of Metastases and Patient Management. *Urol. Int.*. 2016.01; 96(1); 65-72

4. Takayuki Nakayama, Noboru Numao, Soichiro Yoshida, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. A novel interactive educational system in the operating room—the IE system. *BMC Med Educ.* 2016.02; 16; 44
5. Naoko Kawamura, Minato Yokoyama, Yasuhisa Fujii, Junichiro Ishioka, Noboru Numao, Yoh Matsuoka, Kazutaka Saito, Chizuru Arisawa, Tetsuo Okuno, Akira Noro, Shinji Morimoto, Kazunori Kihara. Recovery of renal function after radical nephrectomy and risk factors for postoperative severe renal impairment: A Japanese multicenter longitudinal study. *Int. J. Urol.*. 2016.03; 23(3); 219-223
6. Masanori Murakami, Takanobu Yoshimoto, Yujiro Nakano, Kyoichiro Tsuchiya, Isao Minami, Ryotaro Bouchi, Yasuhisa Fujii, Kazuhiko Nakabayashi, Koshi Hashimoto, Ken-Ichiro Hata, Kazunori Kihara, Yoshihiro Ogawa. Expression of inflammation-related genes in aldosterone-producing adenomas with KCNJ5 mutation. *Biochem. Biophys. Res. Commun.*. 2016.08; 476(4); 614-619
7. Toshihiro Kanda, Syohei Fukuda, Naotaka Fukui, Yu Ohkubo, Tomoko Kazumoto, Yoshihiro Saito, Ayataka Ishikawa, Masafumi Kurosumi, Yukio Kageyama, Yasuhisa Fujii, Kazunori Kihara. Favorable outcome of intraoperative radiotherapy to the primary site in patients with metastatic prostate cancer. *Int. J. Clin. Oncol.*. 2016.08; 21(4); 764-772
8. Kawano S, Komai Y, Ishioka J, Sakai Y, Fuse N, Ito M, Kihara K, Saito N.. Development of prognostic model for predicting survival after retrograde placement of ureteral stent in advanced gastrointestinal cancer patients and its evaluation by decision curve analysis. *MINERVA UROLOGICA E NEFROLOGICA.* 2016.10; 68(5); 437-443
9. Mutsushi Yamasaki, Takeshi Yuasa, Sho Uehara, Yasuhisa Fujii, Shinya Yamamoto, Hitoshi Masuda, Iwao Fukui, Junji Yonese. Improvement of renal function by changing the bone-modifying agent from zoledronic acid to denosumab. *Int. J. Clin. Oncol.*. 2016.12; 21(6); 1191-1195

## [Misc]

1. Kazutaka Saito. Words of Wisdom. Re: Nephron-sparing Techniques Independently Decrease the Risk of Cardiovascular Events Relative to Radical Nephrectomy in Patients with a T1a-T1b Renal Mass and Normal Preoperative Renal Function. *Eur. Urol.*. 2016.03; 69(3); 538
2. Kazutaka Saito. Words of Wisdom. Re: Evaluation of Functional Outcomes After Laparoscopic Partial Nephrectomy Using Renal Scintigraphy: Clamped vs. Clampless Technique. *Eur. Urol.*. 2016.04; 69(4); 753
3. Minato Yokoyama. Editorial Comment to Outcomes of artificial urinary sphincter placement in octogenarians. *Int. J. Urol.*. 2016.05; 23(5); 423-424
4. Kazutaka Saito. Local Treatment of the Prostate in Metastatic Prostate Cancer: Need to Change the Concept? *Eur. Urol.*. 2016.06;
5. Matsuoka Y, Inoue M, Ito M, Yoshida S, Yokoyama M, Ishioka J, Numao N, Saito K, Fujii Y, Kihara K. Gassless single-port RoboSurgeon radical prostatectomy using an endoscopic manipulator robot 2016.07; 8(1); 31-35
6. Matsuoka Y, Inoue M, Ito M, Yoshida S, Yokoyama M, Ishioka J, Numao N, Saito K, Fujii Y, Kihara K. Gassless single-port RoboSurgeon radical prostatectomy using an endoscopic manipulator robot 2016.07; 8(1); 31-35
7. Kazutaka Saito. Reply to Umberto Capitanio, Paolo Dell'Oglio, Alessandro Larcher, and Francesco Montorsi's Reply to Kazutaka Saito's Words of Wisdom re: Nephron-sparing Techniques Independently Decrease the Risk of Cardiovascular Events Relative to Radical Nephrectomy in Patients with a T1a-T1b Renal Mass and Normal Preoperative Renal Function. *Eur Urol.* 2016;69:538. *Eur. Urol.*. 2016.10; 70(4); e99

**[Conference Activities & Talks]**

1. Saito K. Focal Brachytherapy for Localized Prostate Cancer . 5th Metropolitan Urology Seminar 2016.01.23 Tokyo, Japan
2. Yoshida S et al. . Potential utility of standardized apparent diffusion coefficient value as a biomarker predicting clinical aggressiveness of bladder cancer with various MRI protocols at various institutions. .European Association of Urology annual congress 2016.03.12 Munich, Germany
3. Tanaka H et al. Novel stepwise algorithm using CT and MRI for differential diagnosis of fat-poor angiomyolipoma in small renal masses: Development and external validation. . European Association of Urology annual congress 2016.03.12 Munich, Germany
4. Ishioka J et al. When should patients undergo prostate biopsy? Decision analysis using differences in the health-related quality-of-life between pre-biopsy healthy men and patients with castration-resistant prostate cancer. .European Association of Urology annual congress 2016.03.12 Munich, Germany
5. Fujiwara M et al.. Antibiotic prophylaxis is avoidable in minimally invasive clean surgery for renal or adrenal tumors: A prospective study of 678 cases. Munich, Germany 2016.03.12 Munich, Germany
6. 1.Fujii Y, Kihara K, Tanaka H, Saito K., Yoshida S, Yokoyama M., Ishioka J, Matsuoka Y, Numao N. . Bladder-sparing protocol consisting of low-dose chemoradiotherapy and consolidative partial cystectomy against muscle-invasive bladder cancer: Oncological and functional outcome in elderly patients.. European Association of Urology annual congress 2016.03.13 Germany
7. 5.Yokoyama M, Kawamura N, Fujii Y, Inoue M, Ishioka J, Numao N, Matsuoka Y, Saito K, Arisawa C, Okuno T, Noro A, Morimoto S, Kihara K. . Longitudinal changes in renal function after radical nephrectomy and risk factors for postoperative severe renal impairment: A Japanese multicenter study using a linear mixed model analysis. European Association of Urology annual congress 2016.03.13 Germany
8. Moriyama S et al. A new quantitative method for characterizing small renal masses: MRI intensity ratio curve analysis. European Association of Urology annual congress 2016.03.13 Munich, Germany
9. Waseda Y. et al.. Elevation of urinary metanephrine/normetanephrine and impairment of glucose tolerance predict the development of hypoglycemia after resection of pheochromocytoma. European Association of Urology annual congress 2016.03.13
10. Nakamura Y et al. Renal dysfunction manifestation in patients with adrenal Cushing's syndrome after adrenalectomy. European Association of Urology annual congress 2016.03.13 Munich, Germany
11. Masaharu Inoue, Fumitaka Koga, Soichiro Yoshida, Hajime Tanaka, Shuichiro Kobayashi, Masaya Ito, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Prediction of therapeutic resistance using ERBB2 expression status and Ki-67 labeling index in muscle-invasive bladder cancer patients treated with chemoradiation-based selective bladder-sparing approach. the 31st Annual EAU Congress 2016.03.14
12. 4.Kawamura N, Yokoyama M, Fujii Y, Inoue M, Ito M, Yoshida S, Ishioka J, Numao N, Matsuoka Y, Saito K, Kihara K.. Longitudinal preservation of renal function after clamp-less partial nephrectomy: An analysis of patients with chronic kidney disease.. European Association of Urology annual congress 2016.03.14 Germany
13. 14.Yasuda Y, Saito K, Kawamura N, Yuasa T, Yokoyama M, Matsuoka Y, Ishioka J, Numao N, Okuno T, Yamamoto S, Takahashi S, Yonese J, Fujii Y, Kihara K. Prognostic significance of early CRP response for metastatic renal cell carcinoma treated with tyrosine kinase inhibitor. European Association of Urology annual congress 2016.03.14 Germany
14. Matsuoka Y, Ishioka J, Tanaka H, inoue M, Ito M, Yoshida S, Yokoyama M, Numao N, Saito K, Fujii Y, Kihara K. Impact of PI-RADS version 2 on MRI diagnosis for extracapsular extension of prostate cancer: A multireader study. European Association of Urology annual congress 2016.03.14 Munich, Germany

15. Yoshida S et al. The utility of diffusion-weighted MRI as an imaging biomarker of upper urinary tract cancer: A preoperative prognostic indicator reflecting histological grade. . European Association of Urology annual congress 2016.03.14 Munich, Germany
16. Inoue M et al. . Prediction of therapeutic resistance using ERBB2 expression status and Ki-67 labelling index in muscle-invasive bladder cancer patients treated with chemoradiation-based selective bladder-sparing approach. . European Association of Urology annual congress 2016.03.14 Munich, Germany
17. Matsuoka Y, Numao N, Saito K, Tanaka H, Inoue M, Ito M, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Kihara K. Applicability analysis of focal therapy to intermediate- and high-risk prostate cancer. . annual meeting of the American Urological Association 2016.05.06 San Diego, USA
18. Waseda Y et al. Impact of elevated urinary metanephrine/normetanephrine and impaired glucose tolerance test on the development of hypoglycemia following removal of pheochromocytoma. annual meeting of the American Urological Association 2016.05.06 San diego
19. Numao N et al. Optimal combination of MRI-targeted biopsy and systematic biopsy for men with suspicion of prostate cancer. . annual meeting of the American Urological Association 2016.05.06 San diego, USA
20. Ishioka J et al.. The incidence of late bladder tumor recurrence of upper tract urothelial carcinoma and optimal cystoscopic follow-up: A multicenter study.. annual meeting of the American Urological Association 2016.05.06 San diego, USA
21. Ishioka J et al. Prognostic impact of C-reactive protein kinetics on survival of patients with advanced urothelial carcinoma. A multicenter study. . annual meeting of the American Urological Association 2016.05.06 San diego, USA
22. Nakamura Y et al.. Masked renal dysfunction in patients with adrenal Cushing's syndrome manifested by adrenalectomy. annual meeting of the American Urological Association 2016.05.06 San diego, USA
23. Nakamura Y et al. . High specificity of diffusion-weighted MRI in differentiating residual bladder cancer from postoperative changes. annual meeting of the American Urological Association 2016.05.06 San diego, USA
24. 21.Nakanishi Y, Fukushima H, Yokoyama M, Kataoka M, Tobisu K, Koga F. Can systematic biopsy be safely omitted in the era of MRI/TRUS-fusion targeted prostate biopsy?. annual meeting of the American Urological Association 2016.05.06 San diego, USA
25. Yoshida S et al. . Apparent diffusion coefficient as a prognostic biomarker of upper urinary tract cancer..annual meeting of the American Urological Association 2016.05.07 San diego, USA
26. Tanaka H et al. Development and validation of a novel stepwise algorithm using CT and MRI for diagnosis of fat-poor angiomyolipoma in small renal masses. . annual meeting of the American Urological Association 2016.05.07
27. Ito M et al. Likelihood of underlying Lynch syndrome in Japanese upper tract urothelial carcinoma patients. annual meeting of the American Urological Association 2016.05.07 San diego, USA,
28. Ito M et al. Likelihood of underlying Lynch syndrome in Japanese upper tract urothelial carcinoma patients. . San diego, USA 2016.05.07
29. Kobayashi M et al. Maximum standardized uptake value of 18F-FDG PET/CT predicts survival of patients with advanced urothelial carcinoma. annual meeting of the American Urological Association 2016.05.07 San diego, USA
30. Fujiwara M et al.. Feasibility of non-use of antimicrobial prophylaxis in minimally invasive. annual meeting of the American Urological Association 2016.05.07 San diego, USA

31. Fukushima H, Nakanishi Y, Kataoka M, Tobisu K, Koga F. Prognostic significance of postoperative skeletal muscle mass recovery in metastatic renal cell carcinoma patients who underwent cytoreductive nephrectomy. annual meeting of the American Urological Association 2016.05.07 San diego, USA
32. Fujii Y et al.. Bladder-sparing protocol consisting of low-dose chemoradiotherapy and consolidative partial cystectomy against muscle-invasive bladder cancer: Comparison of oncological and functional outcomes between older and younger patients. annual meeting of the American Urological Association 2016.05.08 USA
33. Matsuoka Y, Ishioka J, Tanaka H, Nakayama T, Inoue M, Ito M, Yoshida S, Yokoyama M, Numao N, Saito K, Fujii Y, Kihara K. Impact of prebiopsy magnetic resonance imaging (MRI) on preoperative risk stratification for biochemical recurrence after radical prostatectomy. . annual meeting of the American Urological Association 2016.05.08 San Diego, USA
34. Ishioka J et al. Prognostic impact of C-reactive protein kinetics on survival of patients with advanced urothelial carcinoma. A multicenter study. . annual meeting of the American Urological Association 2016.05.08 San diego, USA
35. 8.Ishioka J et al. Yokoyama M., Kawamura N., Fujii Y., Inoue M., Ishioka J., Numao N., Matsuoka Y., Saito K., Arisawa C., Okuno T., Noro A., Morimoto S., Kihara K.. Longitudinal renal function recovery after radical nephrectomy and risk factors for postoperative severe renal impairment: a Japanese multicenter study.. annual meeting of the American Urological Association 2016.05.08 San diego, USA
36. Matsuoka Y, Ishioka J, Tanaka H, Inoue M, Ito M, Yoshida S, Yokoyama M, Numao N, Saito K, Fujii Y, Kihara K. Impact of the Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) on the assessment of extracapsular extension in prostate cancer: A multireader study.. annual meeting of the American Urological Association 2016.05.09 San Diego, USA
37. Moriyama S et al. MRI intensity ratio curve analysis: a new objective method for characterizing small renal masses.. annual meeting of the American Urological Association 2016.05.09 San diego, USA
38. 13.Nakayama T, Kazutaka S, Fujii Y, Waseda Y, Moriyama S, Tanaka H, Kawamura N, Inoue M, Ito M, Yoshida, S, Yokoyama M, Matsuoka Y, Numao N, Kihara K. Association of M2 macrophage invasion with C-reactive protein in renal cell carcinoma.. annual meeting of the American Urological Association 2016.05.09 San diego, USA
39. Masaharu Inoue, Fumitaka Koga, Soichiro Yoshida, Hajime Tanaka, Shuichiro Kobayashi, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Predictive model for therapeutic resistance using ERBB2 expression status and Ki-67 labeling index in muscle-invasive bladder cancer patients treated with chemoradiotherapy-based bladder-sparing protocol. AUA2016 Annual Meeting 2016.05.09 San Diego, USA
40. S. Yoshida, F. Koga, H. Tanaka, H. Fukushima, Y. Nakanishi, M. Yokoyama, J. Ishioka, Y. Matsuoka, N. Numao, K. Saito, Y. Fujii, K. Kihara.. Apparent diffusion coefficient ratio as a potential inter-institutional marker for histological grade of bladder cancer. 24th International Society of Magnetic Resonance in Medicine (ISMRM) 2016.05.12 Singapore
41. Matsuoka Y, Saito K, Numao N, Tanaka H, Inoue M, Ito M, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Kihara K. Risk assessment for undertreatment in focal therapy and its applicability to intermediate- and high-risk prostate cancer. 9th International Symposium on Focal Therapy and Imaging in prostate & kidney cancer 2016.06.23 Durham, USA
42. Saito K, Matsuoka Y, Numao N, Hayashi K, Toda K, Ito M, Inoue M, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Yoshimura R, Kihara K. Hemi-gland brachytherapy for localized prostate cancer. 9th International Symposium on Focal Therapy and Imaging in prostate & kidney cancer 2016.06.23 Durham, USA
43. Ito M et al.. Likelihood of underlying Lynch syndrome in Japanese upper tract urothelial carcinoma patients. . annual meeting of the American Urological Association San diego, USA

**[Awards & Honors]**

1. Best Poster Presentation, The 31th Annual Congress of the European Association of Urology, European Association of Urology, 2016.03
2. Best Poster Presentation, The 31th Annual Congress of the European Association of Urology, European Association of Urology, 2016.03
3. Best Poster Presentation, The 31th Annual Congress of the European Association of Urology, European Association of Urology, 2016.03
4. Best Poster Presentation, 110th annual meeting of the American Urological Association, American Urological Association , 2016.05



## Gastrointestinal Surgery

Professor

Project Professor

Masahiro TSUBAKI

Associate Professor

Masamichi YASHUNO, Mikito INOKUCHI, Yasuaki NAKAJIMA

Junior Associate Professor

Kenro KAWADA, Takuya OKADA

Assistant Professor

Yutaka TOKAIRIN, Akifumi KIKUCHI, Toshiro TANIOKA

Akihiro HOSHINO, Shinichi YAMAUCHI

Graduate Student

Yasunori SOMENO, Masafumi OKUDA, Taichi OGOU,

Michiyo TOKURA, Marie HANAOKA, Yuichiro KUME,

Yutaka NAKAJIMA, Toshihiro MATSUI, Tomoki ABURATANI,

Chiharu TOMII, Keisuke OKUNO, Kentaro GOKITA,

Fukuichiro ORITA, Yudai KAWAMURA, Tomiyuki MIURA,

Kazuya YAMAGUCHI, Megumi SASAKI, Rei GHO, Mora ANDRES

### (1) Research

- 1) Development of esophageal surgery.
- 2) Development of gastric surgery.
- 3) Development of colorectal surgery.

### (2) Education

The history of the department started as both the Department of Esophageal and General Surgery and the Department of Surgical Oncology of TMDU, and many surgeons and researchers in various specialties have gathered and have been keeping a high level of activities. Our main purposes of education are to make the post-graduate physicians grown up to excellent surgeons and to contribute in development of medical/surgical sciences. Surgeons with high-level medical knowledge and techniques are expected to grow up in this department. Moreover, making surgeons with matured humanity is one of the purposes. The department has a peaceful atmosphere and stands for active work in solving difficult problems.

### (3) Clinical Performances

Main clinical services are diagnosis and treatment for esophageal, gastric and colorectal diseases. Post-graduate students learn and study general surgery and sub-specialty, e.g. esophageal surgery, gastric surgery and colorectal surgery. The territory of clinics is wide and the department provides a full spectrum of standard and special technologies such as minimally invasive surgery and extended radical surgery for malignancies.

#### (4) Publications

##### [Original Articles]

1. Okada T, Tanaka K, Kawachi H, Ito T, Nishikage T, Odagaki T, Zárate AJ, Kronberg U, López-Köstner F, Karelovic S, Flores S, Estela R, Tsubaki M, Uetake H, Eishi Y, Kawano T. International collaboration between japan and chile to improve detection rates in colorectal cancer screening. *Cancer*. 2016; 1(122); 71-77
2. Miyawaki Y, Nakajima Y, Kawada K, Okada T, Tokairin Y, Kawano T.. Efficacy of docetaxel, cisplatin, and 5-fluorouracil chemotherapy for superficial esophageal squamous cell carcinoma. *Dis Esophagus*. 2016;
3. Ishibashi T, Ishikawa S, Suzuki A, Miyawaki Y, Kawano T, Makita K.. Successful Anesthesia Management for 2-Stage Surgical Procedure of a Refractory Tracheogastric Tube Fistula After Esophagectomy. *A A Case Rep*. 2016; 6(4); 84-87
4. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Toru Kawamura, Tatsuyuki Kawano and Akira Nalashima. An evaluation of the diagnostic potential of CT scans and herniography for inguinal hernias *Int Surg*. 2016;
5. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Akihiro Hoshino, Kagami Nagai and Tatsuyuki Kawano. The usefulness of a long forceps technique in single-incision laparoscopic surgery for totally extraperitoneal repair of inguinal hernia *Int Surg*. 2016;
6. Kumagai Y, Takubo K, Kawada K, Higashi M, Ishiguro T, Sobajima J, Fukuchi M, Ishibashi K, Mochiki E, Aida J, Kawano T, Ishida H.. Endocytoscopic observation of various types of esophagitis *Esophagus*. 2016; 13; 200-207
7. Kumagai Y, Sobajima J, Higashi M, Ishiguro T, Fukuchi M, Ishibashi K, Mochiki E, Yakabi K, Kawano T, Tamaru j, Ishida H. Tumor-associated macrophages and angiogenesis in early stage esophageal squamous cell carcinoma *Esophagus*. 2016; 13; 245-253
8. Nakajima Y, Kawada K, Tokairin Y, Miyawaki Y, Okada T, Miyake S, Kawano T.. Retrospective Analyses of Esophageal Bypass Surgery for Patients with Esophagorespiratory Fistulas Caused by Esophageal Carcinomas. *World J Surg*. 2016; 40(5); 1158-1164
9. Nakajima Y, Kawada K, Tokairin Y, Tomita T, Satoshi M, Kawano T.. Prognostic factors for post-recurrence survival in patients with thoracic esophageal squamous cell carcinoma after curative resection. *Dig Surg*. 2016; 33(2); 136-145
10. Nakajima Y, Kawada K, Tokairin Y, Hoshino A, Miyawaki Y, Okada T, Miyake S, Kawano T.. “Larynx-preserving surgery” for cervical esophageal carcinoma can preserve the vocal function and improve the clinical outcome. *Esophagus*. 2016;
11. Nishikawaji T, Akiyama Y, Shimada S, Kojima K, Kawano T, Eishi Y, Yuasa Y, Tanaka S. . Onco-genic roles of the SETDB2 histone methyltransferase in gastric cancer. *Oncotarget*. 2016; 7(41); 67251-67265
12. Ishihara R, Oyama T, Abe S, Takahashi H, Ono H, Fujisaki J, Kaise M, Goda K, Kawada K, Koike T, Takeuchi M, Matsuda R, Hirasawa D, Yamada M, Kodaira J, Tanaka M, Omae M, Matsui A, Kanesaka T, Takahashi A, Hirooka S, Saito M, Tsuji Y, Maeda Y, Yamashita H, Oda J, Tomita Y, Matsunaga T, Terai S, Ozawa S, Kawano T, Seto Y. Risk of metastasis in adenocarcinoma of the esophagus a multicenter retrospective study in a Japanese population *J Gastroenterol*. 2016;
13. Takashi Ito, Hiroshi Kawachi, Paulina Peñaloza, Alejandro José Zárate, Alejandra Ponce, Maki Kobayashi, Takuya Okada, Tomoyuki Odagaki, Koji Tanaka, Tetsuro Nishikage, Udo Kronberg, Masahiro Tsubaki, Yoshinobu Eishi, Tatsuyuki Kawano, Francisco López-Köstner. Protocolo Estandarizado de Anatomía Patológica de lesiones polipoideas en Proyecto de Prevención de Neoplasias Colorrectales (PRENEC) en Chile. *Gastroenterol. Latinoam*. 2016; 27; 37-46

14. Takashi Ito, Hiroshi Kawachi, Paulina Peñaloza, Alejandro José Zárate, Alejandra Ponce, Maki Kobayashi, Takuya Okada, Tomoyuki Odagaki, Koji Tanaka, Tetsuro Nishikage, Udo Kronberg, Masahiro Tsubaki, Yoshinobu Eishi, Tatsuyuki Kawano, Francisco López-Köstner. Protocolo Estandarizado de Anatomía Patológica de lesiones polipoideas en Proyecto de Prevención de Neoplasias Colorrectales (PRENEC) en Chile. *Gastroenterol. Latinoam.* 2016; 27; 37-46
15. T Muramatsu, K-i Kozaki, S Imoto, R Yamaguchi, H Tsuda, T Kawano, N Fujiwara, M Morishita, S Miyano and J Inazawa. The hypusine cascade promotes cancer progression and metastasis through the regulation of RhoA in squamous cell carcinoma *Oncogene* (2016), 1–13 *Oncogene advance online publication.* 2016;
16. Nakajima Y, Kawada K, Tokairin Y, Tomita M, Miyake S, Kawano T. Prognostic Factors for Post-Recurrence Survival in Patients with Thoracic Esophageal Squamous Cell Carcinoma after Curative Resection. *Dig Surg* (Epub ahead of print).
17. Nakajima Y, Kawada K, Tokairin Y, Miyawaki Y, Okada T, Satoshi Miyake, Kawano T. Retrospective Analyses of Esophageal Bypass Surgery for Patients with Esophagorespiratory Fistulas Caused by Esophageal Carcinomas. *World J Surg* (Epub ahead of print).

### [Conference Activities & Talks]

1. Nakajima Y, Kawada K, Tokairin Y, Chiba T, Hoshino A, Miyawaki Y, Okada T, Kawano T.. Super-high larynx-preserving surgery for cervical esophageal carcinoma.. 51st Congress of the European Society for Surgical Research 2016.05.28 Prague
2. Nakajima Y, Kawada K, Tokairin Y, Hoshino A, Okada T, Ogo T, Okuda M, Kawamura Y, Yamaguchi K, Kawano T. A pilot trial of S-1 and paclitaxel in relapsed or refractory esophageal squamous cell carcinoma pre-treated by docetaxel, cisplatin and 5-fluorouracil chemotherapy.. 26th World Congress of the International Association of Surgeons, Gastroenterologists and Oncologists 2016.09.10 Seoul
3. Nakajima Y, Kawada K, Tokairin Y, Chiba T, Hoshino A, Okada T, Okuda M, Ogo T, Nakajima Y, Matsui T, Kawano T.. Larynx-preserving surgery for cervical esophageal carcinoma extending around the esophageal orifice.. 15th WORLD CONGRESS International Society for Diseases of the Esophagus (ISDE) 2016.09.19 Singapore
4. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Tetsuma Chiba, Akihiro Hoshino, Takuya Okada, Naoto Fujiwara, Yutaka Nakajima, Hisashi Fujiwara, Taichi Ogo, Masafumi Okuda, Yuichiro Kume, Toshihiro Matsui, Kagami Nagai, Keiichi Akita, Tatsuyuki Kawano.. Anatomical feature during upper mediastinal lymph nodes dissection using a trans-bicervical approach under the pneumomediastinum.. 15th WORLD CONGRESS International Society for Diseases of the Esophagus (ISDE) 2016.09.20 Singapore
5. Kenro Kawada. Long-term prognosis of esophageal squamous cell carcinoma invading muscularis mucosae: comparison between ER and radical surgery. 15th WORLD CONGRESS International Society for Diseases of the Esophagus (ISDE) 2016.09.20 Singapore
6. Masafumi Okuda.. Mucoepidermoid carcinoma of the esophagus detected in minimal lesion.. 15th WORLD CONGRESS International Society for Diseases of the Esophagus (ISDE) 2016.09.20 Singapore
7. Akihiro Hoshino.. The optimal wavelength for low-concentration iodine staining with flexible spectral imaging color enhancement for esophageal cancer screening.. 15th WORLD CONGRESS International Society for Diseases of the Esophagus (ISDE) 2016.09.20 Singapore
8. Taichi Ogo, Kenro Kawada, Yasuaki Nakajima, Yutaka Tokairin, Tetsuma Chiba, Akihiro Hoshino, Takuya Okada, Masafumi Okuda, Yutaka Nakajima, Toshihiro Matsui, Cho, Mora, Yudai Kawamura, Kazuya Yamaguchi, Takashi Ito, Tatsuyuki Kawano. Analysis of avascular area of superficial esophageal cancers with magnifying endoscopy after formalin fixation.. 15th WORLD CONGRESS International Society for Diseases of the Esophagus (ISDE) 2016.09.20 Singapore
9. Yutaka Tokairin. Mediastinoscopic approach with bilateral cervico-hiatal pneumomediastinum in radical esophagectomy.. 40th World Congress of the International College of Surgeons 2016.10.25 Kyoto

10. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Masafumi Okuda, Taichi Ogo, Katsumasa Saito, Naoto Fujiwara, Tairou Ryoutokuji, Takuya Okada, Yutaka Miyawaki, Youichi Kumagai, Kagami Nagai, Tatsuyuki Kawano. . Efficacy of endoscopy for evaluating esophago-gastric anastomosis on post-esophagectomy day 1. . 14th World Congress of the International Society for Diseases of the Esophagus

# Thoracic Surgery

Professor Kenichi Okubo  
 Junior Associate Professor Hironori Ishibashi  
 Assistant Professor Masashi Kobayashi  
 Hospital assistant professor Chihiro Takasaki  
 Graduate Student Sachiko Imai  
 Graduate Student Akiko Sugawara  
 Graduate Student Ken Takahashi  
 Graduate Student Katsutoshi Seto  
 Graduate Student Ryo Wakejima  
 Graduate Student Syunichi Baba  
 Graduate Student Yasuhiro Nakashima

## ( 1 ) Outline

Department of Thoracic Surgery deal with clinical management, basic and clinical research, and education of thoracic surgery, which includes surgical diagnosis and treatment of respiratory diseases.

## ( 2 ) Research

- Minimally invasive surgery for lung cancer
- Multimodal treatments for thoracic malignancies
- Surgery for metastatic lung tumors
- Clinico-pathological studies on lung cancer

## ( 3 ) Education

Department of Thoracic Surgery has a mission to educate medical post-graduates for expert thoracic surgeons. Thoracic surgeon requires the Board of Surgery and the Board of Thoracic Surgery to perform clinical cares as a specialist. We provide clinical specialty course for thoracic surgery and graduate course for thoracic surgery, and support to obtain the boards.

## ( 4 ) Clinical Services & Other Works

Out-patient Clinic: Tuesday, Thursday, Friday  
 Operative Day: Monday, Wednesday, Thursday, Friday  
 Clinical Conference: Monday  
 Chest Conference : Monday  
 Clinico-pathological Conference: Wednesday  
 Medical Round: every morning  
 Professor's Round: Tuesday  
 Journal Club: Tuesday (every other week)  
 Mortality & Morbidity Conference: Tuesday (every other week)  
 Lab Meeting: Tuesday (monthly)

Scientific Meeting: Japan Surgical Society, Japanese Association for Chest Surgery, Japanese Association for Thoracic Surgery, Japan Lung Cancer Society, Japan Society for Respiratory Endoscopy

## ( 5 ) Clinical Performances

Thoracic Surgery deal with surgical treatment for lung, mediastinum, pleura and chest wall. We provide high-grade medical care as a university hospital. We offer less invasive surgery for early-stage lung cancers or benign diseases, and multimodality treatment for locally advanced thoracic malignancies.

## ( 6 ) Publications

### [Original Articles]

1. Iwata T, Yoshino I, Yoshida S, Ikeda N, Tsuboi M, Asato Y, Katakami N, Sakamoto K, Yamashita Y, Okami J, Mitsudomi T, Yamashita M, Yokouchi H, Okubo K, Okada M, Takenoyama M, Chida M, Tomii K, Matsuura M, Azuma A, Iwasawa T, Kuwano K, Sakai S, Hiroshima K, Fukuoka J, Yoshimura K, Tada H, Nakagawa K, Nakanishi Y; West Japan Oncology Group. A phase II trial evaluating the efficacy and safety of perioperative pirfenidone for prevention of acute exacerbation of idiopathic pulmonary fibrosis in lung cancer patients undergoing pulmonary resection West Japan Oncology Group 6711 L (PEOPLE Study). *Respir Res.* 2016.07; 17(1); 90
2. Hironori Ishibashi, Masashi Kobayashi, Chihiro Takasaki, Seiji Ishikawa, Yutaka Miura, Koshi Makita, Kenichi Okubo. Efficacy of Supraglottic Airway for Preventing Lung Injury Associated with Coughing at Extubation after Pulmonary Lobectomy. *World Journal of Surgery.* 2016.08; 40(8); 1892-1898
3. Chihiro Takasaki, Masashi Kobayashi, Hironori Ishibashi, Takumi Akashi, Kenichi Okubo. Expression of hypoxia-inducible factor-1 affects tumor proliferation and antiapoptosis in surgically resected lung cancer *Molecular and Clinical Oncology.* 2016.08; 5(2); 295-300
4. Kobayashi M, Huang C. L., Sonobe M, Kikuchi R, & Date H. Ad-shWnt2b Vector Therapy Demonstrates Antitumor Activity in Orthotopic Intrapleural Models as Monitored with the In Vitro Imaging System (IVIS). *Anticancer Research.* 2016.11; 36(11); 5887-5893
5. Sachiko K,Hironori Ishibashi,Ken Takahashi, Kenichi Okubo,. Transcervical excision of thymoma and video-assisted thoracoscopic extended thymectomy (VATET) for ectopic cervical thymoma with myasthenia gravis: report of a case *General Thoracic and Cardiovascular Surgery .* 2016.12; 64(12); 752-751
6. Tomii S, Akashi T, Ando N, Tamura T, Sakurai A, Terada A, Furukawa A, Suzuki Y, Kayamori K, Sakamoto K, Ishibashi H, Eishi Y.. Cortical Actin Alteration at the Matrix-Side Cytoplasm in Lung Adenocarcinoma Cells and Its Significance in Invasion. *Pathobiology.*(in print). 2016.12;

### [Others]

1. Successful excision of a massive bleeding schwannoma by thoracoscopic surgery., 2016.04  
*Asian Cardiovascular & Thoracic Annals*2016, Vol. 24(5) 484-486. Hironori Ishibashi, Chihiro Takasaki and Kenichi Okubo
2. Preservation of the lung after 4-year compression by fibrous tumors of pleura, 2016.06  
*Asian Cardiovascular & Thoracic Annals* 2016, Vol. 24(7)718-721  
Hironori Ishibashi, Ken Takahashi, Sachiko Kumazawa and Kenichi Okubo.

## Igakuken Disease-oriented Molecular Biology

Visiting Professor    Takahiko Hara  
 Visiting Professor    Masanari Itokawa  
 Visiting Professor    Masato Hasegawa  
 Visiting Professor    Haruo Okado  
 Graduate Student    Mai   Kanokoda,   Marino  
 Nakajima, Rena   Takahashi, Natsumi Yokote,  
 Narumi Ikeda (April~), Risa   Kanda (April~),  
 Kasumi Kori (April~), Riichi Okuda (April~)

### (1) Research

[Takahiko Hara]    We attempt to elucidate how tissue stem cells (hematopoietic stem cells, skeletal muscle stem cells, etc.) are developed in embryos and maintained in adults by utilizing *in vitro* differentiation systems of ES/iPS cells and conditional KO mouse strains. In addition, we advance the molecular biology of CXCL14, which is involved in obesity-induced diabetes, carcinogenesis, feeding behavior, etc.

[Masanari Itokawa]    Our research focuses on unraveling the pathophysiology of mental illnesses using molecular biology tools. Our ultimate goal is to identify new disease mechanisms, leading to the development of novel and more efficacious therapies. We perform genetic association studies, as well as metabolomics studies using samples from patients with mental disorders. Any abnormalities identified from patient samples are investigated further, using *in vitro* and *in vivo* systems, such as, cell culture assays to highlight functional alterations and behavioral studies in gene knockout mouse models.

[Masato Hasegawa]    We investigate the molecular pathogenesis and progression of neurodegenerative diseases including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. We use biochemistry, immunohistochemistry and molecular biology in all our work of *in vitro*, cellular and animal models to find effective ways for clinical therapy.

[Haruo Okado]    To discover the fundamental cause of various nervous diseases, e.g., brain tumors, brain malformations, and neurodevelopmental disorders, we will study the molecular mechanisms for the regulation of neural development in the cerebral cortex using gene-targeted mice, primary cultures, viral vectors, *in-utero*



electroporation, real-time imaging of slice culture, immunohistochemistry, and transcription analysis.

## (2) Education

We will educate students for the purpose that they could investigate molecular mechanisms of life-threatening diseases such as cancer, diabetes, schizophrenia, amyotrophic lateral sclerosis, and brain malformations. Trained students will eventually help us to develop novel therapeutic strategies against them. In addition, they must learn the importance of good animal models (including genetically engineered mice), which faithfully reproduce symptom and progression of the diseases.

## (3) Publications

### [Original Articles]

1. M. Kawaguchi, K. Kitajima, M. Kanokoda, H. Suzuki, K. Miyashita, M. Nakajima, H. Nuriya, K. Kasahara, and T. Hara. Efficient production of platelets from mouse embryonic stem cells by enforced expression of Gata2 in late hemogenic endothelial cells. *Biochem. Biophys. Res. Commun.*, 474: 462-468, 2016.
2. K. Tamura, H. Naraba, T. Hara, K. Nakamura, M. Yoshie, H. Kogo, and E. Tachikawa. A positive feedback loop between progesterone and microsomal prostaglandin E synthase-1-mediated PGE2 promotes production of both in mouse granulosa cells. *Prostaglandins Other Lipid Mediat.*, 123: 56-62, 2016.
3. T. Suzuki, Y. Kazuki, M. Oshimura, and T. Hara. Highly efficient transfer of chromosomes to a broad range of target cells using Chinese hamster ovary cells expressing murine leukemia virus-derived envelope proteins. *PLoS ONE*, 11: e0157187, 2016.
4. K. Tanegashima, Y. Sato-Miyata, M. Funakoshi, Y. Nishito, T. Aigaki, and T. Hara. Epigenetic regulation of the glucose transporter gene *Slc2a1* by b-hydroxybutyrate underlies preferential glucose supply to the brain of fasted mice. *Genes Cells*, 22: 71-83, 2017.
5. H. Ohtsuka, T. Iguchi, M. Hayashi, M. Kaneda, K. Iida, M. Shimonaka, T. Hara, M. Arai, Y. Koike, N. Yamamoto, and K. Kasahara. SDF-1 $\alpha$ /CXCR4 signaling in lipid rafts induces platelet aggregation via PI3 kinase-dependent Akt phosphorylation. *PLoS ONE*, 12: e0169609, 2017.
6. R. Mizutani, R. Saiga, S. Takekoshi, C. Inomoto, N. Nakamura, M. Itokawa, M.

- Arai, K. Oshima, A. Takeuchi, K. Uesugi, Y. Terada, and Y. Suzuki. A method for estimating spatial resolution of real image in the Fourier domain. *J Microsc.*, 261: 57-66. 2016.
7. I. Kushima, B. Aleksic, M. Nakatochi, T. Shimamura, T. Shiino, A. Yoshimi, H. Kimura, Y. Takasaki, C. Wang, J. Xing, K. Ishizuka, T. Oya-Ito, Y. Nakamura, Y. Arioka, T. Maeda, M. Yamamoto, M. Yoshida, H. Noma, S. Hamada, M. Morikawa, Y. Uno, T. Okada, T. Iidaka, S. Iritani, T. Yamamoto, M. Miyashita, A. Kobori, M. Arai, M. Itokawa, M.-C. Cheng, Y.-A. Chuang, C.-H. Chen, M. Suzuki, T. Yoshikawa, S. Numata, T. Ohmori, S. Kunitomo, D. Mori, N. Iwata, and N. Ozaki. High-resolution copy number variation analysis of schizophrenia in Japan. *Molecular Psychiatry*, doi:10.1038/mp.2016.88 published online 2016.
  8. M. Miyashita, T. Watanabe, T. Ichikawa, K. Toriumi, Y. Horiuchi, A. Kobori, I. Kushima, R. Hashimoto, M. Fukumoto, S. Koike, H. Ujike, T. Arinami, Y. Tatebayashi, K. Kasai, M. Takeda, N. Ozaki, Y. Okazaki, T. Yoshikawa, N. Amano, S. Washizuka, H. Yamamoto, T. Miyata, M. Itokawa, Y. Yamamoto, and M. Arai. The regulation of soluble receptor for AGEs contributes to carbonyl stress in schizophrenia. *Biochem. Biophys. Res. Commun.*, 479: 447-452, 2016.
  9. D. Abe, M. Arai, and M. Itokawa. Music-evoked emotions in schizophrenia. *Schizophr Res.*, doi.org/10.1016/j.schres.2016.12.013 published on line 2016.
  10. A. Tarutani, G. Suzuki, A. Shimozaawa, T. Nonaka, H. Akiyama, S.-I. Hisanaga, and M. Hasegawa. The Effect of Fragmented Pathogenic  $\alpha$ -Synuclein Seeds on Prion-like Propagation. *J. Biol. Chem.*, 291: 18675-18688, 2016.
  11. T. Oikawa, T. Nonaka, M. Terada, A. Tamaoka, S.-I. Hisanaga, and M. Hasegawa.  $\alpha$ -Synuclein Fibrils Exhibit Gain of Toxic Function, Promoting Tau Aggregation and Inhibiting Microtubule Assembly. *J. Biol. Chem.*, 291: 15046-15056, 2016.
  12. F. Kametani, T. Obi, T. Shishido, H. Akatsu, S. Murayama, Y. Saito, M. Yoshida, and M. Hasegawa. Mass spectrometric analysis of accumulated TDP-43 in amyotrophic lateral sclerosis brains. *Sci. Rep.*, 6: 23281, 2016.
  13. S. Shimonaka, T. Nonaka, G. Suzuki, S.-I. Hisanaga, and M. Hasegawa M. Templated aggregation of TDP-43 by seeding with TDP-43 peptide fibrils. *J. Biol. Chem.* 291: 8896-8907, 2016.
  14. Y. Tanaka, T. Nonaka, G. Suzuki, F. Kametani, and M. Hasegawa. Gain-of-function profilin 1 mutations linked to familial amyotrophic lateral sclerosis cause seed-dependent intracellular TDP-43 aggregation. *Hum. Mol. Genet.*, 25: 1420-1433, 2016.
  15. T. Nonaka, G. Suzuki, Y. Tanaka, F. Kametani, S. Hirai, H. Okado, T. Miyashita, M.

- Saitoe, H. Akiyama, H. Masai, and M. Hasegawa. Phosphorylation of TAR DNA-binding Protein of 43 kDa (TDP-43) by Truncated Casein Kinase 1 $\delta$  Triggers Mislocalization and Accumulation of TDP-43. *J. Biol. Chem.* 291: 5473-5483, 2016.
16. S. Taniguchi Watanabe, T. Arai, F. Kametani, T. Nonaka, M. Masuda Suzukake, A. Tarutani, S. Murayama, Y. Saito, K. Arima, M. Yoshida. H. Akiyama, A. Robinson, D. Mann, T. Iwatsubo, and M. Hasegawa. Biochemical classification of tauopathies by immunoblot, protein sequence and mass spectrometric analyses of sarkosyl-insoluble and trypsin-resistant tau. *Acta Neuropathol.* 131: 267-280, 2016.

#### [Review Articles]

1. R. Saiga, R. Mizutani, C. Inomoto, S. Takekoshi, N. Nakamura, A. Tsuboi, M. Osawa, M. Arai, K. Oshima, M. Itokawa, K. Uesugi, A. Takeuchi, Y. Terada, and Y. Suzuki. Three-dimensional structure of brain tissue at submicrometer resolution. *AIP Conference Proceedings.*, 1696, 2016.
2. M. Hasegawa, T. Nonaka, and M. Masuda-Suzukake. Prion-like mechanisms and potential therapeutic targets in neurodegenerative disorders. *Pharmacol Ther*, pii: S0163-7258(16) 30236-4, 2016.
3. M. Hasegawa. Molecular Mechanisms in the Pathogenesis of Alzheimer's disease and Tauopathies-Prion-Like Seeded Aggregation and Phosphorylation. *Biomolecules*, 6, 2016.
4. Y. Tanaka, and M. Hasegawa. Profilin 1 mutants form aggregates that induce accumulation of prion-like TDP-43. *Prion* 10: 283-9, 2016.

#### [Books]

1. M. Hasegawa. Molecular Biology of Dementia with Lewy Bodies, *Dementia with Lewy Bodies*, Chapter 4: P41-58, Springer, Edited by Kenji Kosaka.
2. M. Hasegawa, T. Nonaka, and M. Masuda-Suzukake.  $\alpha$ -Synuclein: Experimental pathology. *Cold Spring Harb. Perspect. Med.* 1; 6(9), 2016.

#### [Conference Activities & Talks]

1. K. Kitajima, K. Kitajima and T. Hara. *In vitro* differentiation of pluripotent stem cells to hematopoietic stem cell-like cells (Oral presentation). 14<sup>th</sup> IGAKUKEN International Symposium-IGAKUKEN Summit for Japan and Korea Science Leaders 2016, 2016.6.30-7.1, Kamikitazawa.
2. T. Hara, K. Tanegashima, R. Takahashi, H. Nuriya, N. Naruse, K. Tsuji, A. Shigenaga, and A. Otaka. A Novel Function of a CXC-type Chemokine CXCL14 as

- a Specific Carrier of CpG DNA into Dendritic Cells for Activating Toll-like Receptor 9-mediated Adaptive Immunity. 58<sup>th</sup> American Society of Hematology Annual Meeting and Exposition, 2016.12.3-6, San Diego.
3. M. Hasegawa. Molecular mechanisms of TDP-43 aggregation. Brain Protein Aging and Dementia Control International Workshop, 2016.9.9, Nagoya.
  4. H. Okado. Regulation of brain development by transcription repressor RP58 12<sup>th</sup> IGAKUKEN International Symposium IGAKUKEN Summit for Japan and Korea Science Leaders 2016, 2016.7.29, Tokyo.

## Clinical Anatomy

Professor Keiichi AKITA

Associate Professor Akimoto NIMURA (Exercise machinery and tools ability morphology lecture)

Junior Associate Professor Kumiko YAMAGUCHI

(Department of Professional Development in Health Science)

Assistant Professor Masayo HARADA, Hisayo NASU

Takashi MIYAMOTO (Exercise machinery and tools ability morphology lecture)

Research Technician Kiyomi SAIKAWA, Masahiro TSUTSUMI

Parttime lecturer Kenji IBUKURO, Itsuko OKUDA,

Sachiyuki TSUKADA

Graduate Student Hitomi FUJISHIRO (~March), Tatsuya TAMAKI (~March), Yasuo NAKAJIMA,

Kazuhito SEKIZAWA, Keiko OKUMURA, Ryuhei OKADA, Eichirou KAGAWA,

Motoki TANAKA, Kotaro EGUCHI, Nobuaki KAWAI, Saya HORIUCHI,

Pawaree NONTHASAEN, Natnicha KAMPAN, Kentaro AMAHA,

Yusuke UEDA, Yasunori TATARA, Shota HOSHIKA, Phichaya BARAMEE,

Atsuhiko OCHI (April~), Souichi HATTORI (April~), Kou Miwa (April~),

Satoru MURO (April~), Suriyut JANARUK (April~)

Research Student Hirokazu SAKAMOTO, Mamiko SUZUKI, Masataka NAKAZAWA

### (1) Outline

Department of Clinical Anatomy supports clinical medicine through formulation of human anatomical and developmental biological bases of diagnoses and surgical procedures. We handle the whole body in human anatomical researches. We think it is classic but important to represent human morphology for exactly what they are based on meticulous observations of human body structures regardless of diagnostic technics and surgical procedures. Our researches are aimed to share languages among all clinicians based on clinical anatomy by describing the results of observations in an accessible way for clinicians. In addition, we perform analyses using experimental embryological approaches and developmental biological approaches, because we think it is important to consider how human structures are constructed.

### (2) Research

- 1) Clinical anatomic study of the shoulder joint and rotator cuff.
- 2) Clinical anatomic study of the anal region for the rectoanal surgery.
- 3) Cadaveric study of the female pelvis for the gynecologic oncology and colposcopy.
- 4) Analyses of the lamination in the masticatory muscles with special reference of nerve supply.
- 5) Embryological study of the differentiation of cloaca and surrounding muscles.

### (3) Education

Clinical anatomy is generally considered as the practical application of anatomical knowledge to diagnosis and treatment, however we think that this course is a part of pure anatomical science based on the findings of the morphological observations of the human bodies. Main objective of Clinical anatomy in the graduate course is to

make detailed anatomical data to answer the questions developed from clinical fields especially by surgeons and radiologists. We collaborate with many clinicians: ENT, orthopedics, gynecology, thoracic surgery, radiology and so on, and our projects have been broad areas. Students are expected to get fine dissection techniques of human bodies and also learn techniques of histology and embryological experiments. By using these techniques, we study the spatial relationships of organs, vessels nerves, and also try to examine their developmental processes in various projects.

#### ( 4 ) Lectures & Courses

Theories and hypotheses of morphogenesis derived from descriptive anatomy and descriptive biology have been confirmed and modified by experimental biology. Furthermore, progresses of developmental biology identified molecules and signaling pathways involved in the morphogenesis. Progresses in the developmental biology also verified morphological hypotheses, and added revisions to the morphological models. The postulates of the morphological models which are currently investigated were built and completed by Anatomy. However, we find Anatomy is still not completed and has many obscure issues through careful dissection of human body. It might be thought that everything was done and there could be no new finding in the human anatomical field anymore because the anatomy employs the classic procedures such as the gross anatomy. However, there are still a lot of unclear anatomical topics, because they had not been focused and not investigated with their clinical significances.

#### ( 5 ) Publications

##### [Original Articles]

1. Tomomi Sakaguchi-Kuma, Nao Hayashi, Hitomi Fujishiro, Kumiko Yamaguchi, Kazuo Shimazaki, Takashi Ono, Keiichi Akita. An anatomic study of the attachments on the condylar process of the mandible: muscle bundles from the temporalis Surg Radiol Anat. 2016.05; 38(4); 461-467
2. Yuichiro Tsukada, Masaaki Ito, Kentaro Watanabe, Kumiko Yamaguchi, Motohiro Kojima, Ryuichi Hayashi, Keiichi Akita, Norio Saito. Topographic Anatomy of the Anal Sphincter Complex and Levator Ani Muscle as It Relates to Intersphincteric Resection for Very Low Rectal Disease. Dis Colon Rectum. 2016.05; 59(5); 426-433
3. Haruhiko Shimura, Akimoto Nimura, Hisayo Nasu, Hitomi Fujishiro, Junya Imatani, Atsushi Okawa, Keiichi Akita. Joint capsule attachment to the coronoid process of the ulna: an anatomic study with implications regarding the type 1 fractures of the coronoid process of the O'Driscoll classification. J Shoulder Elbow Surg. 2016.09; 25(9); 1517-1522
4. Masataka Nakazawa, Akimoto Nimura, Tomoyuki Mochizuki, Masahiro Koizumi, Tatsuo Sato, Keiichi Akita. The Orientation and Variation of the Acromioclavicular Ligament: An Anatomic Study. Am J Sports Med. 2016.10; 44(10); 2690-2695
5. Kenji Ibukuro, Takaya Takeguchi, Hozumi Fukuda, Shoko Abe, Kimiko Tobe. Spatial anatomy of the round ligament, gallbladder, and intrahepatic vessels in patients with right-sided round ligament of the liver Surg Radiol Anat. 2016.11; 38(9); 1061-1067

##### [Books etc]

1. Akimoto Nimura, Hisayo Nasu, Tomoyuki Mochizuki, Keiichi Akita. Advances in Shoulder Surgery. Springer, 2016 (ISBN : 978-4-431-55986-3)
2. Keiichi Akita, Akimoto Nimura. Bergman's Comprehensive Encyclopedia of Human Anatomic Variation. Wiley, 2016 (ISBN : 978-1-1184-30354)

##### [Conference Activities & Talks]

1. Yusuke Ueda, Hiroyuki Sugaya, Norimasa Takahashi, Keisuke Matsuki, Morihito Tokai, Kazutomo Onishi, Shota Hoshika. Difference in Site of PASTA Lesion between Shoulders with Recurrent Anterior Instability and Throwing Injuries. 2016 Annual Meeting 2016.03.02 Florida

2. Mari Uomizu, Hideya Yoshimura, Akimoto Nimura, Takashi Miyamoto, Tomoyuki Mochizuki. Return to Sports Activity after Arthroscopic Rotator Cuff Repair on the Middle-aged and Senior Patients. The 13th International Congress of Shoulder and Elbow Surgery 2016.05.18 Korea
3. Daisuke Ban, Keiichi Akita, Kumiko Yamaguchi, Hiroki Ueda, Minoru Tanabe. ANATOMICAL STUDY OF THE UNCUS OF THE PANCREAS FOR THE SURGERY IN PANCREATODUODENECTOMY. 50th ANNUAL MEETING OF THE PANCREAS CLUB 2016.05.20 San Diego
4. Tatsuo Sato, Masashi Ito, Hirokazu Sakamoto. Two Major Lymphatic Pathways from the Gallbladder to the Para-aortic Lymph Nodes(DVD). 33rd Annual Meeting American Association of Clinical Anatomists 2016.06.13 California
5. Keiichi Akita, Satoru Muro, Kumiko Yamaguchi, Hisayo Nasu, Phichaya Baramée, Janyaruk Suriyut. Mutual Relationships among Perineal Muscles Based on Anatomic and Histologic Findings. 33rd Annual Meeting American Association of Clinical Anatomists 2016.06.15 California
6. Itsuko Okuda, Keiichi Akita, Yasuo Nakajima. Magnetic Resonance-Thoracic and Ductography:Thoracic Duct Variations and Contribution for the Thoracic Surgery. 33rd Annual Meeting American Association of Clinical Anatomists 2016.06.15 California
7. Ryuhei Okada, Taro Sugimoto, Takuro Sumi, Taro Fujikawa, Yusuke Kiyokawa, Fuminori Nomura, Akihisa Tasaki, Tomoaki Asamori, Seiji Kishimoto, Takahiro Asakage. Chemotherapy and followed endoscopic laryngo-pharyngeal surgery (ELPS) is useful for recurrence of pharyngeal carcinoma: a case report. AHNS 9TH International Conference on Head and Neck Cancer 2016.07.16 Washington
8. Keiichi Akita. Recent progresses of Clinical Anatomy of Shoulder joint with special reference to Rotator cuff muscles. Asian Association of Clinical anatomy 2016.08.06 China
9. Keiichi Akita. Research Application in Surgical Anatomy. Research Month for Surgical Resident Course 2016.08.25 Thailand
10. Satoru Muro, Phichaya Baramée, Janyaruk Suriyut, Hisayo Nasu, Masayo Harada, Kumiko Yamaguchi, Keiichi Akita. Structural analysis of the anterior and posterior regions of the external anal sphincter; the spatial relationship with the bulbospongiosus and the coccyx. 8th ISCAA, 2016.08.31 Hungary
11. Kumiko Yamaguchi, Satoru Muro, Keiichi Akita. Anatomy of Treitz's muscle of anal canal. 8th ISCAA 2016.08.31 Hungary
12. Natnicha Kampan, Itsuko Okuda, Hisayo Nasu, Kumiko Yamaguchi, Keiichi Akita. The Transitional Muscle of Eyes and Its Complex Relations with Neighboring Muscles. The 8th International Symposium of Clinical and Applied Anatomy; ISCAA 2016 2016.08.31 Hungary
13. Pawaree Nonthasaen, Hisayo Nasu, Eiichirou Kagawa, Akimoto Nimura, Keiichi Akita. The morphology study of the extraforaminal ligaments in cervical and thoracic levels. 8th ISCAA 2016.08.31 Hungary
14. Keiko Okumura. Female sexual wellness; application of products. World meeting on sexual medicine 2016.09.22 China
15. Keiichi Akita. Trends in Anatomy Teaching for Clinical Education. International symposium of Medical Education 2016.10.08 Taiwan
16. Pawaree Nonthasaen, Hisayo Nasu, Eiichirou Kagawa, Akimoto Nimura and Keiichi Akita. Changes of morphological features of the extraforaminal ligaments of the spinal nerve roots in cervico-thoracic transitional zone. The 4th International Anatomical Sciences and Cell Biology Conference; IASCBC 2016 2016.12.04 Hong Kong
17. Natnicha Kampan, Itsuko Okuda, Hisayo Nasu, Kumiko Yamaguchi, Keiichi Akita. The Transition of Complex Periorbital Muscle Bundles with Their Adjacent Muscles. The 4th International Anatomical Sciences and Cell Biology Conference; IASCBC 2016 2016.12.06 HongKong
18. Keiichi Akita. Recent progresses of Clinical Anatomy of Shoulder joint with special reference to Rotator cuff muscles. Seminar in Department of Anatomy, Semmelweis University, Faculty of Medicine 2016.12.13 Poland



## Systems BioMedicine

Professor Hiroshi ASAHARA  
 Junior Associate Professor Masahiro SHINOHARA  
 Project Junior Associate Professor Masaki MORI  
 Tenure track Assistant Professor Yoshiaki ITO  
 Assistant Professor Satoshi YAMASHITA  
 Project Assistant Professor Tomoki CHIBA, Takahide MATSUSHIMA  
 Project Researcher Yoko TANAKA  
 Graduate Students  
 Takeshi SAITO, Kensuke KATAOKA, Shoya KITADA, Soichi FURUKAWA,  
 Naoki KODA, Hidetsugu SUZUKI, Takashi NAKASUJI, Hiroto YAMAMOTO,  
 Takahiro MITSUMURA, Ryo NAKAMICHI, Tomohiro KAYAMA, Masashi NAITO,  
 Yusuke MOCHIZUKI, Rin OKUMURA

### ( 1 ) Research

We revealed that A to I RNA editing altered target genes of microRNAs using a reporter library.  
 The function and regulatory mechanisms of eIF2 gamma will be examined.  
 Search for novel regulator of microRNA by high throughput screening.  
 Established novel strategies for the osteoporosis by targeting molecules critical for the bone homeostasis.  
 Revealed the molecular mechanism by which osteocytes regulate bone homeostasis.  
 Analyzed the bone phenotype of spaceflight mice.  
 Analyzed molecular mechanisms by which the bone tissue regulates the energy metabolism.  
 The Screening of novel Damage-associated molecular patterns proteins  
 Protein localization analysis by High-throughput microscope system  
 MiRNA which regulates cartilage homeostasis was identified.  
 We developed screening system for miRNA target genes using reporter vector library.  
 MicroRNA KO mice were generated using CRISPR/Cas9 system, and its function in skeletal pattern formation was analyzed.  
 Molecular mechanisms and in vivo roles of RNA-binding proteins and long non-coding RNAs in the context of inflammatory response

### ( 2 ) Education

Under Graduate:  
 Conducting “Molecular Genetics” , which is a series of lectures to understand the gene expression machinery and human genetics and their application to current medicine and biology. Under graduate students can join the lab works to learn the skills for molecular biology and pathology.  
 Graduate School:  
 Organizing “Development and Regeneration” lecture series to understand the basis for regenerative medicine and reproduction at the level of molecular genetics.  
 Students can join the Lab to perform researches using various experimental techniques, such as microarray, cell-based high throughput screening etc. Using these techniques, core molecular network for tissue development

and inflammatory diseases will be examined, which forms the basis of systems biomedicine.

### (3) Publications

#### [Original Articles]

1. Masamichi Doiguchi, Takeya Nakagawa, Yuko Imamura, Mitsuhiro Yoneda, Miki Higashi, Kazuishi Kubota, Satoshi Yamashita, Hiroshi Asahara, Midori Iida, Satoshi Fujii, Tsuyoshi Ikura, Ziyang Liu, Tulip Nandu, W Lee Kraus, Hitoshi Ueda, Takashi Ito. SMARCAD1 is an ATP-dependent stimulator of nucleosomal H2A acetylation via CBP, resulting in transcriptional regulation. *Sci Rep.* 2016; 6; 20179
2. Shimbo M, Kudo T, Hamada M, Jeon H, Imamura Y, Asano K, Okada R, Tsunakawa Y, Mizuno S, Yagami KI, Ishikawa C, Li H, Shiga T, Ishida J, Hamada J, Murata K, Ishimaru T, Hashimoto M, Fukamizu A, Yamane M, Ikawa M, Morita H, Shinohara M, Asahara H, Akiyama T, Akiyama N, Sasanuma H, Yoshida N, Zhou R, Wang YY, Ito T, Kokubu Y, Noguchi TK, Ishimine H, Kurisaki A, Shiba D, Mizuno H, Shirakawa M, Ito N, Takeda S, Takahashi S.. Ground-based assessment of JAXA mouse habitat cage unit by mouse phenotypic studies. *Experimental Animals.* 2016;
3. Kayama T, Mori M, Ito Y, Matsushima T, Nakamichi R, Suzuki H, Ichinose S, Saito M, Marumo K, Asahara H.. Gtf2ird1-dependent Mohawk (Mkx) expression regulates mechanosensing properties of tendon. *Mol Cell Biol.* 2016.02;
4. Doiguchi M, Nakagawa T, Imamura Y, Yoneda M, Higashi M, Kubota K, Yamashita S, Asahara H, Iida M, Fujii S, Ikura T, Liu Z, Nandu T, Kraus WL, Ueda H, Ito T. SMARCAD1 is an ATP-dependent stimulator of nucleosomal H2A acetylation via CBP, resulting in transcriptional regulation *Sci Rep.* 2016.02;
5. Tomohiro Kayama, Masaki Mori, Yoshiaki Ito, Takahide Matsushima, Ryo Nakamichi, Hidetsugu Suzuki, Shizuko Ichinose, Mitsuru Saito, Keishi Marumo, Hiroshi Asahara. Gtf2ird1-dependent Mohawk (Mkx) expression regulates mechanosensing properties of tendon. *Mol. Cell. Biol.* 2016.02;
6. Otero M, Peng H, El Hachem K, Culley KL, Wondimu EB, Quinn J, Asahara H, Tsuchimochi K, Hashimoto K, Goldring MB.. ELF3 modulates type II collagen gene (COL2A1) transcription in chondrocytes by inhibiting SOX9-CBP/p300-driven histone acetyltransferase activity. *Connect Tissue Res.* 2016.06;
7. Suzuki H, Ito Y, Shinohara M, Yamashita S, Ichinose S, Kishida A, Oyaizu T, Kayama T, Nakamichi R, Koda N, Yagishita K, Lotz MK, Okawa A, Asahara H.. Gene targeting of the transcription factor Mohawk in rats causes heterotopic ossification of Achilles tendon via failed tenogenesis. *Proceedings of the National Academy of Sciences of the United States of America.* 2016.07; 113(28); 7840-7845
8. Naito M, Mori M, Inagawa M, Miyata K, Hashimoto N, Tanaka S, Asahara H.. Dnmt3a Regulates Proliferation of Muscle Satellite Cells via p57Kip2. *PLoS Genetics.* . 2016.07; 12(7); e1006167
9. Ryo Nakamichi, Yoshiaki Ito, Masafumi Inui, Naoko Onizuka, Tomohiro Kayama, Kensuke Kataoka, Hidetsugu Suzuki, Masaki Mori, Masayo Inagawa, Shizuko Ichinose, Martin K Lotz, Daisuke Sakai, Koichi Masuda, Toshifumi Ozaki, Hiroshi Asahara. Mohawk promotes the maintenance and regeneration of the outer annulus fibrosus of intervertebral discs. *Nat Commun.* 2016.08; 7; 12503
10. Asahara H\*.. Current Status and Strategy of microRNA Research for Cartilage Development and Osteoarthritis Pathogenesis. *J Bone Metab.* . 2016.08; 23(3); 121-127
11. Saito T, Hara S, Tamano M, Asahara H, Takada S.. Deletion of conserved sequences in IG-DMR at Dlk1-Gtl2 locus suggests their involvement in expression of paternally expressed genes in mice. *J Reprod Dev.* 2016.12;
12. Hironori Nakagami, Mariana Kiomy Osako, Yoichi Takami, Rie Hanayama, Hiroshi Koriyama, Masaki Mori, Hiroki Hayashi, Hideo Shimizu, Ryuichi Morishita. Differential response of vascular hepatocyte growth factor concentration and lipid accumulation between telmisartan and losartan in ApoE-deficient mice. *Mol Med Rep.* 1(5); 657-661
13. Suzuki H, Ito Y, Shinohara M, Yamashita S, Ichinose S, Kishida A, Oyaizu T, Kayama T, Nakamichi R, Koda N, Yagishita K, Lotz MK, Okawa A, Asahara H. Gene targeting of the transcription factor Mohawk in rats causes heterotropic ossification of Achilles tendon via failed tenogenesis. *Proc Natl Acad Sci USA.* 113; 7840-7845

14. Koda N, Sato T, Shinohara M, Ichinose S, Ito Y, Nakamichi R, Kayama T, Kataoka K, Suzuki H, Moriyama K, Asahara H. Mohawk transcription factor regulates homeostasis of the periodontal ligament. *Development*. 144; 313-320
15. Ohmae S, Noma N, Toyomoto M, Shinohara M, Takeiri M, Fuji H, Takemoto K, Iwaisako K, Fujita T, Takeda N, Kawatani M, Aoyama M, Hagiwara M, Ishihama Y, Asagiri M. Actin-binding protein coronin 1A controls osteoclastic bone resorption by regulating lysosomal secretion of cathepsin K *Sci Rep*. in press;

#### [Books etc]

1. Y. Ito, H. Asahara. non-coding miRNA. 2016.06
2. Y. Ito, S.Mokuda, K.Miyata, T. Matsushima, H. Asahara. *Chronic Inflammation*. Springer, 2016.11
3. Ito Y, Mokuda S, Miyata K, Matsushima T, Asahara H\*. . *Chronic Inflammation (Chapter 6)*. Springer, 2016.11

#### [Misc]

1. T. Chiba, Y. Ito, H. Asahara.. *Post-Transcriptional Gene Regulation by MicroRNA and RNA-Binding Protein Biomedical Sciences*. 2016;
2. Gene targeting of the transcription factor Mohawk in rats causes heterotopic ossification of Achilles tendon via failed tenogenesis 2016.12;

#### [Conference Activities & Talks]

1. Koda N, Shinohara M, et al.. Roles of transcription factor Mohawk in periodontal ligament. *International Bone and Mineral Society Herbert Fleisch Workshop 2016* 2016.02
2. Elucidating The Transcriptional Network of Mechanosensitive Tendon Master Gene Mohawk (Mkx). 2016.03
3. Tomohiro Kayama,Masaki Mori,Yoshiaki Ito,Ryo Nakamichi,Takahide Matsushima,Shizuko Ichinose,Mitsuru saito,Keishi Marumo,Hiroshi Asahara. Elucidating The Transcriptional Network Of Mechanosensitive Tendon Master Gene Mohawk(Mkx). *Orthopaedic Research Society Annual meeting 2016 Orlando* 2016.03.06 Florida
4. Hidetsugu Suzuki. Mohawk Knock-Out Rats Revealed Early Heterotopic Ossification of Achilles Tendon Through Failed Tenogenesis. *Orthopaedic Research Society Annual meeting 2016 Orlando* 2016.03.07 Florida
5. Yoko Tanaka-Watanabe, et al.. MicroRNA-381 ameliorates arthritis by controlling functions of fibroblast-like synoviocytes, which are affected by A to I RNA editing.. *Annual European Congress of Rheumatology 2016* 2016.06.08 London, UK
6. Hiroshi Asahara. Gene targeting of the transcription factor Mohawk in rats causes heterotopic ossification of Achilles tendon via failed tenogenesis. *Stem Cell, Growth Factor Signaling and Bone Biology 2016*.07.25 Hangzhou
7. Yoko Tanaka, et al.. Regulation of arthritis by microRNA-381. 2016.10.14 Tokyo, Japan
8. Kensuke Kataoka, Ysoshiaki ITO,Tomoki CHIBA,Ryo NAKAMICHI,HiroshiASAHAHA. Tendon Regeneration and Development by Transcription Factor Mkx. *Visual-JW 2016* 2016.10.17
9. Takahide MATSUSHIMA,Naoki GOSHIMA,Hiroshi ASAHARA. The High-Throughput Microscopy Screening System with Genome-Wide cDNA Expression Libraries. *Visual-JW 2016* 2016.10.17
10. Yoko Tanaka-Watanabe, et al.. MicroRNA-381 mimic resulted in a therapeutic effect on arthritis by controlling several functions of fibroblast-like synoviocytes.. *Cold Spring Harbor Asia conference on Bone & Cartilage: From Development to Human Diseases 2016*.10.25 Suzhou, China
11. Yoko Tanaka-Watanabe, . A to I RNA editing of microRNA-381 dysregulates proliferation of fibroblast-like synoviocytes. *Cell Symposia: Functional RNAs*. *Cell Symposia: Functional RNAs 2016*.11.07

12. Yoko Tanaka, et al.. Function of microRNA-381 in arthritis. 2016.11.30 yokohama, Japan
13. Koda N, Shinohara M, et al.. Roles of transcription factor Mohawk in periodontal ligament. International Association for Dental Research 2016 2016.12
14. Y.Ito, A. Inoue, T. Seers, Y. Hato, A. Igarashi, T. Toyama, H. Asahara. Identification of targets of microRNA-34a using a reporter library system. The 39th Annual Meeting of the Molecular Biology Society of Japan 2016.12.02

**[Awards & Honors]**

1. Pediatric Academic Societies (PAS) and Asian Society for Pediatric Research (ASPR) Joint Meeting 2014, Travel Award North America

# Comprehensive Pathology

Professor Masanobu KITAGAWA  
 Junior associate Professor Morito KURATA  
 Assistant Professor Kouhei YAMAMOTO, Iichiro ONISHI  
 Laboratory Technician Miori INOUE  
 Technical Assistant Sachiko ISHIBASHI, Masumi IKEDA,  
 Graduate Students Xiao Hai JIN, Yuko KINOWAKI,  
 Atsushi KIHARA, GULINISHA Aihemaiti  
 Masae Yanai, Mariko Muto,  
 Ryoko KATO, Naoko OZAWA  
 Norikazu MIYAMOTO, Masafumi INOUE,  
 Keiichi KINOWAKI, Naoko Tsuyama,  
 Yusuke FURUKAWA, Risa Hou,  
 Sumito Shingaki, Masanori Matsuda,  
 Tan Wang, Akiko YAMAMOTO,  
 Miyaka Umemori, Momoko Yamada,  
 Takuya Maeda, Miu Katsuyama,  
 Tatsunori Mineo, Vilayvong Sulideyh,  
 Luangxay Thitsamay,  
 Abudushalamu Muyashaer,

## ( 1 ) Outline

Main objective of comprehensive pathology in the graduate course is to acquire the technique of clinical and basic pathology. This course provides students opportunity to study clinical pathology (for example, histological and cytological diagnosis, autopsy, clinico-pathologic conference) and also basic pathology (molecular pathology and molecular biology).

## ( 2 ) Research

- 1) Clinico-pathological study by morphological findings, immunohistochemistry, and electron microscope, etc.
- 2) Molecular analysis of leukomogenesis induced by Friend leukemia virus (FLV)
- 3) Enhancement of apoptosis by virus-derived protein and development of apoptosis-induction cancer therapy
- 4) Molecular pathology of the myelodysplastic syndromes (MDS)
- 5) Clarification of drug resistance mechanism for hematopoietic malignancies
- 6) Comprehensive research for aging focus on the decreased immune competence
- 7) Molecular biology of the cancer progression and metastasis

## ( 3 ) Education

Main objective of comprehensive pathology in the graduate course is to acquire the techniques of clinical and basic pathology. This course provides students opportunities to study clinical pathology (for example, histological and cytological diagnosis, autopsy, clinico-pathologic conference) and also basic pathology (molecular pathology and molecular biology).

#### (4) Publications

##### [Original Articles]

1. Yusuke F, Kentaro T, Katsuhide I, Maky IO, Kenichi A, Satoshi K, Masanobu K, Jun K. Learning and Memory Deficits in Male Adult Mice Treated with a Benzodiazepine Sleep-Inducing Drug during the Juvenile Period *Front. Neurosci.* 2016; 10; 3389
2. Susumu Kirimura, Morito Kurata, Yasunori Nakagawa, Iichiroh Onishi, Shiho Abe-Suzuki, Shinya Abe, Kouhei Yamamoto, Masanobu Kitagawa. Role of microRNA-29b in myelodysplastic syndromes during transformation to overt leukaemia. *Pathology.* 2016.04; 48(3); 233-241
3. Kazuhito Suzuki, Kouhei Yamamoto, Yasuhiro Arakawa, Hisashi Yamada, Keisuke Aiba, Masanobu Kitagawa. Antimyeloma activity of bromodomain inhibitors on the human myeloma cell line U266 by down-regulation of MYCL. *Anticancer Drugs.* 2016.09; 27(8); 756-765
4. Shunichiro Yasuda, Keisuke Tanaka, Ayako Ichikawa, Ken Watanabe, Emi Uchida, Masahide Yamamoto, Kouhei Yamamoto, Daisuke Mizuchi, Osamu Miura, Tetsuya Fukuda. Aggressive TAFRO syndrome with reversible cardiomyopathy successfully treated with combination chemotherapy. *Int. J. Hematol.* 2016.10; 104(4); 512-518
5. Sumito Shingaki, Yumiko Yoshiki, Kouhei Yamamoto, Yasunori Ota, Kenshi Suzuki. Coexistent adrenal diffuse large B cell lymphoma in a patient with Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma. *Ann. Hematol.* 2016.10; 95(10); 1723-1724
6. Jin XH, Yamamoto K, Abe S, Onishi I, Kirimura S, Aihemaiti G, Kinowaki Y and Kitagawa M. Prognostic Impact of Cancer Stem Cell-Like Phenotypes in Pancreatic Ductal Adenocarcinoma *Journal of Clinical and Experimental Pathology* . 2016.10; 6(295);
7. Morito Kurata, Susan K Rathe, Natashay J Bailey, Natalie K Aumann, Justine M Jones, G Willemijn Veldhuijzen, Branden S Moriarity, David A Largaespada. Using genome-wide CRISPR library screening with library resistant DCK to find new sources of Ara-C drug resistance in AML. *Sci Rep.* 2016.11; 6; 36199

##### [Misc]

1. Kouhei Yamamoto, Yukako Miwa, Shiho Abe-Suzuki, Shinya Abe, Susumu Kirimura, Iichiroh Onishi, Masanobu Kitagawa, Morito Kurata. Extramedullary hematopoiesis: Elucidating the function of the hematopoietic stem cell niche (Review). *Mol Med Rep.* 2016.01; 13(1); 587-591

# Molecular Oncology

Professor: Shinji TANAKA  
 Associate Professor: Yoshimitsu AKIYAMA  
 Associate Professor: Hiroshi FUKAMACHI  
 Assistant Professor: Shu SHIMADA  
 Laboratory Technician: Hiromi NAGASAKI  
 Graduate Student: Ayuna SAKAMOTO  
 Graduate Student: Taketo NISHIKAWAJI

## ( 1 ) Outline

To understand the molecular mechanisms underlying carcinogenesis and malignant progression for clinical application of cancer prevention, diagnosis and treatment.

## ( 2 ) Research

1. Molecular analysis of refractory malignancies including liver, pancreatic and scirrhus gastric cancers
2. Development of molecularly targeted therapy for refractory malignancies
3. Cancer epigenetics/epigenomics and clinical application in refractory malignancies
4. Research of cancer stem cells and targeted therapy
5. Development of regenerative medicine using stem cell research

## ( 3 ) Education

Hygiene is our charge. The undergraduate curriculum of hygiene includes lectures, and laboratory studies. Topics of lectures consist of environmental pollution and human health, world-wide environmental problems, carcinogen and occupational cancer, smoking-related diseases, infectious diseases including AIDS and hepatitis, food poisoning, anoxia and heat-related diseases.

## ( 4 ) Lectures & Courses

The graduate students pursue their own projects associated with one of researches being in progress in the division. Every student can learn the basic scientific techniques, such as genetic engineering, cell culture and biochemical procedures. There are also many special lectures on cancer, gene, cell biology and biochemistry for the graduate students. On weekly seminars, the students present their own research data and introduce important papers from newly-arrived journals. Once the students get new findings, they are encouraged to present them at the domestic or international meeting and write manuscripts.

## ( 5 ) Publications

### [Original Articles]

1. Ito H, Tanaka S, Akiyama Y, Shimada S, Adikrisna R, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Arie S, Yamaoka S, Tanabe M. Dominant Expression of DCLK1 in Human Pancreatic



- Cancer Stem Cells Accelerates Tumor Invasion and Metastasis. PLoS ONE. 2016.01; 11(1); e0146564
2. Akiyama Y, Koda Y, Byeon SJ, Shimada S, Nishikawaji T, Sakamoto A, Chen Y, Kojima K, Kawano T, Eishi Y, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. *Oncotarget*. 2016.01; 7(4); 3966-3983
3. Katsuta E, Tanaka S, Mogushi K, Shimada S, Akiyama Y, Aihara A, Matsumura S, Mitsunori Y, Ban D, Ochiai T, Kudo A, Fukamachi H, Tanaka H, Nakayama K, Arii S, Tanabe M. . CD73 as a therapeutic target for pancreatic neuroendocrine tumor stem cells. *International Journal of Oncology* . 2016.02; 48; 657-669
4. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shinji Tanaka, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Satoshi Otani, Miki Taniguchi, Fumio Goto, Hiroko Nagata, Shun Kaneko, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Mina Nakagawa, Minoru Tanabe, Shinichi Takano, Mitsuharu Fukasawa, Minoru Sakamoto, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma with clinicopathological features. *J. Gastroenterol*. 2016.03; 51(5); 473-486
5. Lentjes MH, Niessen HE, Akiyama Y, de Bruïne AP, Melotte V, van Engeland M. The emerging role of GATA transcription factors in development and disease. *Expert Rev Mol Med*. 2016.03; 18; e3
6. Furuyama T, Tanaka S, Shimada S, Akiyama Y, Matsumura S, Mitsunori Y, Aihara A, Ban D, Ochiai T, Kudo A, Fukamachi H, Arii S, Kawaguchi Y, Tanabe M. Proteasome activity is required for the initiation of precancerous pancreatic lesions. *Sci Rep*. 2016.05; 6; 27044
7. Eriko Katsuta, Atsushi Kudo, Takumi Akashi, Yusuke Mitsunori, Satoshi Matsumura, Arihiro Aihara, Daisuke Ban, Takanori Ochiai, Shinji Tanaka, Yoshinobu Eishi, Minoru Tanabe. Macroscopic morphology for estimation of malignant potential in pancreatic neuroendocrine neoplasm. *J. Cancer Res. Clin. Oncol.* 2016.06; 142(6); 1299-1306
8. Akahoshi K, Tanaka S, Mogushi K, Shimada S, Matsumura S, Akiyama Y, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, AriiS, Tanabe M. Expression of connective tissue growth factor in the livers of non-viral hepatocellular carcinoma patients with metabolic risk factors. *J. Gastroenterol.* 2016.09; 51(9); 910-922
9. Ojima F, Saito Y, Tsuchiya Y, Kayo D, Taniuchi S, Ogoshi M, Fukamachi H, Takeuchi S, Takahashi S. Runx3 transcription factor regulates ovarian functions and ovulation in female mice *J Reprod Dev*. 2016.10; 62(5); 479-486
10. Nishikawaji T, Akiyama Y, Shimada S, Kojima K, Kawano T, Eishi Y, Yuasa Y, Tanaka S. Oncogenic roles of the SETDB2 histone methyltransferase in gastric cancer. *Oncotarget*. 2016.10; 7(41); 67251-67265
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15. Oba A, Shimada S, Akiyama Y, Nishikawaji T, Mogushi K, Ito H, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Asahara H, Kaida A, Miura M, Tanabe M, Tanaka S . ARID2 modulates DNA damage response in human hepatocellular carcinoma cells *Journal of Hepatology*, in press.
16. Ueda H, Ban D, Akahoshi K, Mitsunori Y, Matsumura S, Ochiai T, Kudo A, Tanaka S, Tanabe M. Refractory long-term cholangitis after pancreaticoduodenectomy: a retrospective study *World Journal of Surgery*, in press.
17. Oba A, Ban D, Kirimura S, Akahoshi K, Mitsunori Y, Matsumura S, Ochiai T, Kudo A, Tanaka S, Tanabe M. . Clinical application of the biomarkers for the selection of adjuvant chemotherapy in pancreatic ductal adenocarcinoma. *J Hepatobiliary Pancreat Sci.*, in press.
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#### [Books etc]

1. Tanaka S. Cancer stem cells as therapeutic targets. in *Human Stem Cell Toxicity*, ed. Sherley JL. (Royal Society of Chemistry, London), 2016
2. Fukamachi H. *Encyclopedia of Cancer*, 4th ed. Springer, 2016.01

#### [Misc]

1. Tanaka S.. Molecular pathogenesis and targeted therapy of pancreatic cancer. *Annals of Surgical Oncology*. 2016.02; Suppl (2); 197-205
2. Tanaka S. Molecular analysis for therapeutic targets of pancreatic cancer. in *Molecular diagnosis and targeting for thoracic and gastrointestinal malignancy*, eds. Shimada Y, Yanaga K. (Springer), in press.

#### [Conference Activities & Talks]

1. Shimada S, Akiyama Y, Fukamachi H, Yuasa Y, Tanaka S. Identification of selective inhibitors of diffuse-type gastric cancer cells by screening annotated compounds. *AACR Annual Meeting 2016* 2016.04.18 New Orleans, LA
2. Akiyama Y, Nishikawaji T, Shimada S, Yuasa Y, Tanaka S. Expression changes of the histone methyltransferase genes, SETDB2, in gastric cancers. *26th Seoul International Cancer Symposium* 2016.06.17 Seoul, Korea
3. Fukamachi H, Nishikawaji T, Shimada S, Akiyama Y, Yuasa Y, Tsuchiya K, Tanaka S. Characteristics of diffuse-type gastric cancer stem cells. *26th Seoul International Cancer Symposium* 2016.06.17 Seoul, Korea
4. Akiyama Y, Nishikawaji T, Shimada S, Sakamoto A, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Reduced expression and its function of SET7/9, a histone methyltransferase gene, in gastric cancer. *The 35th Sapporo International Cancer Symposium* 2016.06.24 Sapporo
5. Tanaka S, Ito H, Furuyama T, Aihara A, Matsumura S, Mitsunori Y, Ban D, Ochiai T, Kudo A, Tanabe M. Personalized medicine to target the cancer stemness of hepato-biliary-pancreatic malignancies (Symposium).. *The 72th Annual Meeting of the Japanese Society of Gastroenterological Surgery* 2016.07.15 Tokushima
6. Nishikawaji T, Akiyama Y, Shimada S, Yuasa Y, Tanaka S. SETDB2 contributes to gastric cancer progression by deregulating the expression of tumor suppressor genes. *The 75th Annual Meeting of the Japanese Cancer Association* 2016.10.06 Yokohama
7. Tanaka S, Shimada S, Akiyama Y. Epigenetic target of stemness for metastasis and therapeutic resistance in patients with pancreatic and liver cancers. *The 75th Annual Meeting of the Japanese Cancer Association* 2016.10.06 Yokohama

8. Fukamachi H, Nishikawaji T, Shimada S, Akiyama Y, Yuasa Y, Tanaka S. Identification of MTDs that suppress the growth of PDX-derived diffuse-type gastric tumor-initiating cells. The 75th Annual Meeting of the Japanese Cancer Association 2016.10.06 Yokohama
9. Akiyama Y, Nishikawaji T, Shimada S, Sakamoto A, Yuasa Y, Tanaka S. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. The 75th Annual Meeting of the Japanese Cancer Association 2016.10.07 Yokohama
10. Shimada S, Akiyama Y, Fukamachi H, Yuasa Y, Tanaka S. Identification of selective inhibitors of diffuse-type gastric cancer cells by screening of annotated compounds. The 75th Annual Meeting of the Japanese Cancer Association 2016.10.07 Yokohama
11. Akiyama Y, Nishikawaji T, Shimada S, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Expression changes of the histone H3 lysine methyltransferase genes and their function in gastric cancer. 5th International Cancer Epigenetics Meeting 2016.10.22 Beijing, China

#### **[Patents]**

1. Dominant negative mutants of IRS-1 and uses there of (Tanaka S, Wands JR), Patent Number : United States Patent 6,528,479
2. Compositions and methods for detection and treatment of hepatocellular carcinoma (Tanaka S, MacDonald G), Application Number : US 61/811,360

# Surgical Pathology

Professor : Yoshinobu EISHI

Associate Professor : Takumi AKASHI, Masanobu KITAGAWA

Assistant Professor : Emiko SUGAWARA, Susumu KIRIMURA,  
Shohei TOMII, Atsuko KONTA

Hospital Staff Doctor : Keiko MIURA

Secretary : Ayako UENO

## ( 1 ) Outline

Missions of diagnostic pathology are summarized to following 4 items. 1) participation to the medical treatment of the patients through anatomical diagnosis 2) assessment of medical treatment through autopsy examination 3) training of diagnostic pathologists 4) development of diagnostic methods by anatomical, immunohistochemical, microbiological and molecular technologies.

In cooperation with departments of human pathology and comprehensive pathology, department of surgical pathology provides 1. diagnostic pathology services for the clinicians of the affiliated hospital 2. education of medical students and post-graduate students through both lectures and medical practice 3. development of new methods in diagnostic pathology.

## ( 2 ) Research

1) Analysis of the pathophysiology of the disease, especially invasion mechanism of lung and gastrointestinal cancers by molecular biological technology.

2) Identification of epithelial neoplasms with chromosome translocation

3) Carcinogenesis of prostatic cancer in view of microbiology

## ( 3 ) Education

Main object of surgical pathology in the course of graduate school is to provide medical students opportunity to study pathophysiology and diagnosis of core diseases, both neoplastic and non-neoplastic, through biopsy, surgical and autopsy cases. Another important mission is a training of pathology specialist in the post-graduate school through diagnostic services of surgical pathology, cytopathology and autopsy.

## ( 4 ) Lectures & Courses

The initial purpose of this program is to acquire how to morphologically diagnose both neoplastic and non-neoplastic diseases. In addition, it is also very important to recognize the limitations and problems of morphological diagnosis and to learn the morphological and molecular methods which are necessary for the resolution of the problems. The ultimate purpose is to develop a new diagnostic method which can resolve the problems of morphological diagnosis.

**( 5 ) Clinical Services & Other Works**

In cooperation with departments of human pathology and comprehensive pathology, department of surgical pathology provides autopsy services (38 case in a year), cytopathology services (9,957 cases in a year) and surgical pathology (11,574 cases in a year) for the clinicians of the affiliated hospital. Diagnosis is mostly done by the organ-subspecialized staffs. Clinico-pathological conferences have been held about two hundred times in 2014.

**( 6 ) Clinical Performances**

Department of diagnostic pathology participates in the medical treatment of the patients through anatomical diagnosis. In the era of molecule-targeted therapy, specialized information has been requested in the field of pathological diagnosis. In order to appropriately respond to a latest request of clinicians, we practice pathological diagnosis in cooperation with departments of human pathology and comprehensive pathology with latest techniques, such as immunohistochemistry, electron microscopy, and FISH.

**( 7 ) Publications****[Original Articles]**

1. Kou Kayamori, Ken-Ichi Katsube, Kei Sakamoto, Yoshio Ohyama, Hideaki Hirai, Akane Yukimori, Yae Ohata, Takumi Akashi, Masao Saitoh, Kiyoshi Harada, Hiroyuki Harada, Akira Yamaguchi. NOTCH3 Is Induced in Cancer-Associated Fibroblasts and Promotes Angiogenesis in Oral Squamous Cell Carcinoma. PLoS ONE. 2016; 11(4); e0154112
2. Teruko Nakamura, Asuka Furukawa, Keisuke Uchida, Tomohisa Ogawa, Tomoki Tamura, Daisuke Sakonishi, Yuriko Wada, Yoshimi Suzuki, Yuki Ishige, Junko Minami, Takumi Akashi, Yoshinobu Eishi. Autophagy Induced by Intracellular Infection of *Propionibacterium acnes*. PLoS ONE. 2016; 11(5); e0156298
3. Akiyama Y, Koda Y, Byeon SJ, Shimada S, Nishikawaji T, Sakamoto A, Chen Y, Kojima K, Kawano T, Eishi Y, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. Oncotarget. 2016.01; 7(4); 3966-3983
4. Okada T, Tanaka K, Kawachi H, Ito T, Nishikage T, Odagaki T, Zárate AJ, Kronberg U, López-Köstner F, Karelovic S, Flores S, Estela R, Tsubaki M, Uetake H, Eishi Y, Kawano T. International collaboration between japan and chile to improve detection rates in colorectal cancer screening. Cancer. 2016.01; 122(1); 71-77
5. Atsuko Konta, Kouichi Ozaki, Yasuhiko Sakata, Atsushi Takahashi, Takashi Morizono, Shinichiro Suna, Yoshihiro Onouchi, Tatsuhiko Tsunoda, Michiaki Kubo, Issei Komuro, Yoshinobu Eishi, Toshihiro Tanaka. A functional SNP in FLT1 increases risk of coronary artery disease in a Japanese population. J. Hum. Genet.. 2016.01;
6. Nobuo Sanjo, Satoko Kina, Yukiko Shishido-Hara, Yurie Nose, Satoru Ishibashi, Tetsuya Fukuda, Taketoshi Maehata, Yoshinobu Eishi, Hidehiro Mizusawa, Takanori Yokota. A Case of Progressive Multifocal Leukoencephalopathy with Balanced CD4/CD8 T-Cell Infiltration and Good Response to Mefloquine Treatment. Internal Medicine. 2016.01; 55(12); 1631-1635
7. Yamada I, Hikishima K, Miyasaka N, Kato K, Kojima K, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H. Gastric carcinoma: evaluation with diffusion-tensor MR imaging and tractography ex vivo. Magn Reson Imaging. 2016.02; 34(2); 144-151
8. Tadahisa Numakura, Tsutomu Tamada, Masayuki Nara, Soshi Muramatsu, Koji Murakami, Toshiaki Kikuchi, Makoto Kobayashi, Miho Muroi, Tatsuma Okazaki, Sho Takagi, Yoshinobu Eishi, Masakazu Ichinose. Simultaneous development of sarcoidosis and cutaneous vasculitis in a patient with refractory Crohn's disease during infliximab therapy. BMC Pulm Med. 2016.02; 16; 30
9. Ryohei Hayashi, Kiichiro Tsuchiya, Keita Fukushima, Nobukatsu Horita, Shuji Hibiya, Keisuke Kitagaki, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Eriko Okada, Akihiro Araki, Kazuo Ohtsuka, Shinji Fukuda, Hiroshi Ohno, Ryuichi Okamoto, Tetsuya Nakamura, Shinji Tanaka, Kazuaki Chayama,

- Mamoru Watanabe. Reduced Human  $\alpha$ -defensin 6 in Noninflamed Jejunal Tissue of Patients with Crohn's Disease. *Inflamm. Bowel Dis.* 2016.05; 22(5); 1119-1128
10. Nariaki Kokuho, Yasuhiro Terasaki, Hirokazu Urushiyama, Mika Terasaki, Shinobu Kunugi, Taisuke Morimoto, Arata Azuma, Jitsuo Usuda, Akihiko Gemma, Yoshinobu Eishi, Akira Shimizu. Pulmonary mucosa-associated lymphoid tissue lymphoma associated with pulmonary sarcoidosis: a case report and literature review. *Hum. Pathol.* 2016.05; 51; 57-63
  11. Masahiro Asakawa, Takanobu Yoshimoto, Mitsutane Ota, Mitsuyuki Numasawa, Yuriko Sasahara, Takato Takeuchi, Yujiro Nakano, Norihiko Oohara, Masanori Murakami, Ryotaro Bouchi, Isao Minami, Ky-oichiro Tsuchiya, Koshi Hashimoto, Hajime Izumiyama, Naoko Kawamura, Kazunori Kihara, Mariko Negi, Takumi Akashi, Yoshinobu Eishi, Hironobu Sasano, Yoshihiro Ogawa. A Case of Cushing's Syndrome with Multiple Adrenocortical Adenomas Composed of Compact Cells and Clear Cells. *Endocr. Pathol.* 2016.06; 27(2); 136-141
  12. Sanae Shimamura, Naoto Yokogawa, Kengo Murata, Tetsuo Yamaguchi, Keisuke Uchida, Yoshinobu Eishi. Saddle nose with sarcoidosis: "A great imitator" of relapsing polychondritis. *Mod Rheumatol.* 2016.06; 1-5
  13. Eriko Katsuta, Atsushi Kudo, Takumi Akashi, Yusuke Mitsunori, Satoshi Matsumura, Arihiro Aihara, Daisuke Ban, Takanori Ochiai, Shinji Tanaka, Yoshinobu Eishi, Minoru Tanabe. Macroscopic morphology for estimation of malignant potential in pancreatic neuroendocrine neoplasm. *J. Cancer Res. Clin. Oncol.* 2016.06; 142(6); 1299-1306
  14. Sahoko Chiba, Kimitake Tsuchiya, Takumi Akashi, Masahiro Ishizuka, Tsukasa Okamoto, Haruhiko Furusawa, Tomoya Tateishi, Mitsuhiro Kishino, Yasunari Miyazaki, Ukihide Tateishi, Tamiko Takemura, Naohiko Inase. Chronic Hypersensitivity Pneumonitis With a Usual Interstitial Pneumonia-Like Pattern: Correlation Between Histopathologic and Clinical Findings. *Chest.* 2016.06; 149(6); 1473-1481
  15. Yamada I, Hikishima K, Miyasaka N, Kato K, Ito E, Kojima K, Kawano T, Kobayashi D, Eishi Y, Okano H. q-Space MR imaging of gastric carcinoma ex vivo: correlation with histopathologic findings. *Magn Reson Med.* 2016.08; 76(2); 602-612
  16. Ryuichi Okamoto, Mariko Negi, Syohei Tomii, Yoshinobu Eishi, Mamoru Watanabe. Diagnosis and treatment of microscopic colitis. *Clin J Gastroenterol.* 2016.08; 9(4); 169-174
  17. Chihiro Takasaki, Masashi Kobayashi, Hironori Ishibashi, Takumi Akashi, Kenichi Okubo. Expression of hypoxia-inducible factor-1  $\alpha$  affects tumor proliferation and antiapoptosis in surgically resected lung cancer. *Mol Clin Oncol.* 2016.08; 5(2); 295-300
  18. Nishikawaji T, Akiyama Y, Shimada S, Kojima K, Kawano T, Eishi Y, Yuasa Y, Tanaka S. Oncogenic roles of the SETDB2 histone methyltransferase in gastric cancer. *Oncotarget.* 2016.10; 7(41); 67251-67265
  19. Saori R Yoshii, Akiko Kuma, Takumi Akashi, Taichi Hara, Atsushi Yamamoto, Yoshitaka Kurikawa, Eisuke Itakura, Satoshi Tsukamoto, Hiroshi Shitara, Yoshinobu Eishi, Noboru Mizushima. Systemic Analysis of Atg5-Null Mice Rescued from Neonatal Lethality by Transgenic ATG5 Expression in Neurons. *Dev. Cell.* 2016.10; 39(1); 116-130
  20. Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Shuji Hibiya, Nobukatsu Horita, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Satoshi Motoya, Yoshiaki Takeuchi, Reiko Kunisaki, Ken Fukunaga, Shiro Nakamura, Naoki Yoshimura, Masakazu Takazoe, Bunei Iizuka, Yasuo Suzuki, Masakazu Nagahori, Mamoru Watanabe. CDX2 expression induced by leukocytapheresis might be associated with mucosal healing in ulcerative colitis. *J. Gastroenterol. Hepatol.* 2016.11;
  21. Jiro Akimoto, Kenta Nagai, Daisuke Ogasawara, Yujiro Tanaka, Hitoshi Izawa, Michihiro Kohno, Keisuke Uchida, Yoshinobu Eishi. Solitary tentorial sarcoid granuloma associated with *Propionibacterium acnes* infection: case report. *J. Neurosurg.* 2016.11; 1-4
  22. Shohei Tomii, Takumi Akashi, Noboru Ando, Tomoki Tamura, Akira Sakurai, Asami Terada, Asuka Furukawa, Yoshimi Suzuki, Kou Kayamori, Kei Sakamoto, Hironori Ishibashi, Yoshinobu Eishi. Cortical Actin Alteration at the Matrix-Side Cytoplasm in Lung Adenocarcinoma Cells and Its Significance in Invasion. *Pathobiology.* 2016.12;

23. Nobuyasu Awano, Minoru Inomata, Soichiro Ikushima, Daisuke Yamada, Masatoshi Hotta, Shunji Tsukuda, Toshio Kumasaka, Tamiko Takemura, Yoshinobu Eishi. Histological analysis of vasculopathy associated with pulmonary hypertension in combined pulmonary fibrosis and emphysema: comparison with idiopathic pulmonary fibrosis or emphysema alone. *Histopathology*. 2016.12;

**[Conference Activities & Talks]**

1. Yoshinobu EISHI. ABC method clinical trial protocol. Thai gastric cancer society meeting 2016.08.22 Bangkok, Thailand



# Experimental Animal Model for Human Disease

Professor  
Junior Associate Professor  
Assistant Professor  
Assistant Professor  
Assistant Professor

Masami Kanai-Azuma  
Yoshikazu Hirate  
Shu Endo  
Hitomi Suzuki  
Hinako M Takase

## ( 1 ) Research

- 1)Molecular biological analysis of organ formation using knockout mice and knockout ES cells.
- 2)Application of Sox17 mutant mice as the animal model for human disease.
- 3)Analysis of molecular mechanisms using mice with implantaion defects.
- 4)Analysis of folliculogenesis using disease-model mouse for premature ovarian insufficiency.
- 5)Study of the molecular events involved in the regulation of spermatogonial stem cells.

## ( 2 ) Publications

### [Original Articles]

1. Hirate Yoshikazu, Suzuki Hitomi, Kawasumi Miyuri, Takase Hinako M, Igarashi Hitomi, Naquet Philippe, Kanai Yoshiakira, Kanai-Azuma Masami. Mouse Sox17 haploinsufficiency leads to female subfertility due to impaired implantation. Sci Rep. 2016; 6; 24171
2. Uchida Aya, Kishi Kasane, Aiyama Yoshimi, Miura Kento, Takase Hinako M, Suzuki Hitomi, Kanai-Azuma Masami, Iwamori Tokuko, Kurohmaru Masamichi, Tsunekawa Naoki, Kanai Yoshiakira. In vivo dynamics of GFRalpha1-positive spermatogonia stimulated by GDNF signals using a bead transplantation assay. Biochem Biophys Res Commun. 2016.05;

## Signal Gene Regulation

Professor NAKAMURA Masataka  
Associate Professor FUNATO Noriko  
Assistant Professor MIZUGUCHI Mariko

### ( 1 ) Research

- 1) Molecular mechanism of tumorigenesis by human T-cell leukemia virus type I (HTLV-I).
- 2) Roles of transcription factors in cell differentiation.
- 3) Implication of prostaglandin D2 receptor (CRTH2) in allergy reactions.

### ( 2 ) Lectures & Courses

The aim of Human Gene Sciences Center is to provide laboratory equipment, room and information for researches in advanced molecular and cellular biology. In educational objectives in the graduate school, our Center gives lecture, seminar, training course and individual assistance in research fields of molecular genetics, immunology and virology.

### ( 3 ) Publications

#### [Original Articles]

1. Yosuke Motai, Masahiko Takahashi, Takayuki Takachi, Masaya Higuchi, Toshifumi Hara, Mariko Mizuguchi, Yutaka Aoyagi, Shuji Terai, Yuetsu Tanaka, Masahiro Fujii. Human T-cell leukemia virus type 1 (HTLV-1) Tax1 oncoprotein but not HTLV-2 Tax2 induces the expression of OX40 ligand by interacting with p52/p100 and RelB. *Virus Genes*. 2016.02; 52(1); 4-13
2. Mariko Mizuguchi, Yuka Sasaki, Toshifumi Hara, Masaya Higuchi, Yuetsu Tanaka, Noriko Funato, Nobuyuki Tanaka, Masahiro Fujii, Masataka Nakamura. Induction of Cell Death in Growing Human T-Cells and Cell Survival in Resting Cells in Response to the Human T-Cell Leukemia Virus Type 1 Tax. *PLoS ONE*. 2016.02; 11(2); e0148217
3. Tomoaki Kumagai, Nozomi Yamaguchi, Hiroyuki Hirai, Shigeyuki Kojima, Yoshiko Kodani, Akihiko Hashiguchi, Michiko Haida, Masataka Nakamura. Loxoprofen sodium induces the production of complement C5a in human serum. *Int. Immunopharmacol.* 2016.02; 33; 55-62
4. Lindsay E Laurie, Hiroki Kokubo, Masataka Nakamura, Yumiko Saga, Noriko Funato. The transcription factor Hand1 is involved in Runx2-Ihh-regulated endochondral ossification *PLoS ONE*. 2016.02; 11(2); e0150263
5. Noriko Funato, Hiroki Kokubo, Masataka Nakamura, Hiromi Yanagisawa, Yumiko Saga. Specification of jaw identity by the Hand2 transcription factor. *Sci Rep*. 2016.06; 6; 28405
6. Noriko Funato, Hiroki Kokubo, Yumiko Saga. Transcriptomic analyses of Hand2 transgenic embryos. *Genom Data*. 2016.09; 9; 60-62

7. Deping Kong, Yujun Shen, Guizhu Liu, Shengkai Zuo, Yong Ji, Ankang Lu, Masataka Nakamura, Michael Lazarus, Constantine A Stratakis, Richard M Breyer, Ying Yu. PKA regulatory II  $\alpha$  subunit is essential for PGD2-mediated resolution of inflammation. *J. Exp. Med.*. 2016.09; 213(10); 2209-2226
8. Yusuke Onaka, Norihito Shintani, Takanobu Nakazawa, Takuya Kanoh, Yukio Ago, Toshio Matsuda, Ryota Hashimoto, Kazutaka Ohi, Hiroyuki Hirai, Kin-Ya Nagata, Masataka Nakamura, Atsushi Kasai, Atsuko Hayata-Takano, Kazuki Nagayasu, Kazuhiro Takuma, Asao Ogawa, Akemichi Baba, Hitoshi Hashimoto. Prostaglandin D2 signaling mediated by the CRTH2 receptor is involved in MK-801-induced cognitive dysfunction. *Behav. Brain Res.*. 2016.11; 314; 77-86

#### **[Conference Activities & Talks]**

1. Funato N. The role of transcription factors in bone development. Nippi Research Institute of Biomatrix 2016.07.11
2. Mariko Mizuguchi, Toshifumi Hara, Manami Yoshita-Takahashi, Yuetsu Tanaka, Takuya Fukushima, Masataka Nakamura. DNA methylation of the human telomerase reverse transcriptase (hTERT) promoter in human T-cell leukemia virus type-1 (HTLV-1) infected T-cells. The 5th JCA-AACR special joint conference 2016.07.13
3. Funato N. Hand2 transforms upper jaw to lower jaw by regulating the expression of homeobox transcription factors. The 58th Annual Meeting of Japanese Association for Oral Biology 2016.08.25

# Material Biofunctions

Akiko Nagai (Associate Professor)  
Kosuke Nozaki (Assistant Professor)

## (1) Outline

### 1. Reaction mechanism between materials and living tissues

Development of standard evaluation process for the safety, biocompatibility, and biofunction of biomedical materials and devices, based on interfacial reactions between the materials and living tissue.

### 2. Effects of medical materials and devices on human health

Systematization of influences of biofunctional materials and artificial organs on the human body from the viewpoint of medicine.

### 3. Development of functional materials accelerating bone formation

Development of new surface modification processes of bioimplants to accelerate bone formation.

### 4. Development of evaluation methods for studying interaction of materials with biological function

Development of new intravital observation methods for evaluating biological effects of physical and chemical factors.

## (2) Education

The objective and principle of this graduate course is to educate students with materials knowledge demanded to medical and dental doctors who are leading medical professionals and bioscientists who are capable of carrying out their own research at an international level in the area of their special fields of science, respectively.

## (3) Publications

### [Original Articles]

1. Hattori T, Igarashi K, Miyazaki H, Aizawa M, Katayama K, Yamashita K, Nagai A. An electrostatic field on a bioceramic growth surface suppressed leiomyosarcoma cell proliferation but accelerated differentiation International Journal of Metallurgical & Materials Engineering. 2016; 2; 127
2. Norio Wada, Naohiro Horiuchi, Kastuyuki Mukougawa, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Toshinori Okura, and Kimihiro Yamashita. Electrostatic induction power generator using hydroxyapatite ceramic electrets Materials Research Bulletin. 2016.02; 74; 50-56
3. Naohiro Horiuchi, Norio Wada, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, and Kimihiro Yamashita. Dielectric relaxation in monoclinic hydroxyapatite: Observation of hydroxide ion dipoles Journal of Applied Physics. 2016.02; 119(8); 084903-6
4. Chen P, Nagai A, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Differences in the calcification of preosteoblast cultured on sputter-deposited titanium, zirconium, and gold J Biomed Mater Res A. 2016.03; 104(3); 639-651

5. Fukuhara Y, Kyuzo M, Tsutsumi Y, Nagai A, Chen P, Hanawa, T. Phospholipid polymer electrodeposited on titanium inhibits platelet adhesion J. Biomed. Mater. Res. B Appl. Biomater.. 2016.04; 104(3); 554-560
6. Ana Milheiro, Kosuke Nozaki, Cornelis J Kleverlaan, Joris Muris, Hiroyuki Miura, Albert J Feilzer. In vitro cytotoxicity of metallic ions released from dental alloys. Odontology. 2016.05; 104(2); 136-142

#### [Books etc]

1. N. Horiuchi, N. Wada, M. Nakamura, A. Nagai and K. Yamashita. Handbook of Solid State Chemistry. Wiley, 2016

#### [Conference Activities & Talks]

1. Iwata N, Nozaki K, Miura H, Yamashita K, Nagai A. Surface modification of Ti implant with controlled micro/nano-structured topography. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
2. Risa Yamada, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita and Akiko Nagai. Antimicrobial activity of silver nanoparticle-coated yttria-stabilized zirconia. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
3. Minamifuchi.M, Nemoto.R, Inagaki.T, Uraba.A, Nozaki.K and Miura.H. Influence of framework design on shear stress distribution . AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
4. Uraba A, Inagaki T, Nemoto R, Minamifuchi M, Nozaki K, Miura H. The shear stress distribution of two different cantilever RBFPDs. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
5. Fujita K, Nozaki K, Yamashita K, Miura H, and Nagai A. Differentiation of periodontal ligament cell on hydroxyl- and carbonated-apatites. AADR/CADR Annual Meeting & Exhibition 2016.03.19 Los Angeles, CA, USA
6. Nozaki K, Fujita K, Miura H, Yamashita K, Nagai A. Bone remodeling-optimization of carbonated apatite for guided bone regeneration. AADR/CADR Annual Meeting & Exhibition 2016.03.19 Los Angeles, CA, USA
7. Akiko Nagai, Takaaki Masutani, Kosuke Nozaki, Kimihiro Yamashita. Electric stimulation induced by polarized hydroxyapatite regulates osteoblast proliferation through ERK activation. 10th World Biomaterials Congress 2016.05.18
8. Kosuke Nozaki, Kazuhisa Fujita, Naohiro Horiuchi, Miho Nakamura, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. In vivo evaluation of the role of carbonate ion in hydroxyapatite for bone remodeling. 10th World Biomaterials Congress 2016.05.20
9. Fabrication and evaluation of yttria-stabilized zirconia with antimicrobial properties. 2016.07.09
10. Osteoblast behavior on controlled micro/nano structured titanium surface. 2016.07.09
11. Alkaline Phosphatase Activity of Periodontal Ligament Cell on Collagen-coated Hydroxyl-Apatites. 2016.07.09
12. In vivo evaluation of calcium phosphate with optimized osteoconductivity and solubility by carbonate ion. 2016.07.10
13. Fabrication of antibacterial yttria-stabilized zirconia using silver nanoparticle . 2016.09.09
14. Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Phase transition in calcium hydroxyapatite observed by thermally stimulated current method. The 9th International Symposium on Inorganic Phosphate Materials (ISIPM-9) 2016.09.26 Tokyo Metropolitan University, Tokyo, Japan

15. Kosuke Nozaki, Risa Yamada, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. Antibacterial activity of silver nanoparticles coating on zirconia against oral bacteria. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development 2016.10.17
16. Naohiro Horiuchi, Norio Wada, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, and Kimihiro Yamashita. Surface charges on hydroxyapatite electrets studied by Kelvin probe method. The 28th Annual Meeting of the International Society for Ceramics in Medicine (Bioceramics 28) 2016.10.20 Charlotte, North Carolina, USA
17. Akiko Nagai. Carbonate Substitution in Hydroxyapatite Influences on Macrophage Differentiation. K-J Ceramics 33 2016.11.17 Daejeon, Korea

# Genetic Regulation

Professor Akinori KIMURA  
 Associate Professor Takeharu HAYASHI  
 Assistant Professor Jianbo AN  
 Research Associate Taeko K. NARUSE

## (1) Outline

Research and Education in the Department of Genetic Regulation are carried out by staff members of the Department of Molecular Pathogenesis, Medical Research institute.

The main purpose of this Department is to decipher the genetic regulation involved in the pathogenesis of intractable diseases, including hereditary cardiovascular diseases such as hypertrophic cardiomyopathy, dilated cardiomyopathy and hereditary arrhythmia, autoimmune diseases such as rheumatoid arthritis, type I diabetes mellitus, autoimmune thyroid diseases (Graves disease and Hashimoto thyroiditis), inflammatory bowel diseases (Crohn disease and ulcerative colitis) and SLE, as well as infectious diseases including HIV/AIDS. We also investigate molecular pathogenesis of coronary heart disease (atherosclerosis) and intractable vascular diseases (Takayasu arteritis and Buerger disease).

## (2) Research

- 1) Identification and functional analysis of disease-related genes for cardiovascular diseases including hereditary cardiomyopathy and arrhythmia
- 2) Identification and functional analysis of disease-related genes for autoimmune diseases including autoimmune thyroiditis and inflammatory bowel disease
- 3) Identification and functional analysis of disease-related genes for infectious diseases including HIV-1 infection
- 4) Structural, functional and evolutionary analyses of MHC and immune-related genes
- 5) Evolutionary medicine for human diseases

## (3) Education

Structural and functional diversity of human genome, are involved in the etiology and pathogenesis of human diseases. Main objective of Genetic Regulation is to identify the gene mutations or polymorphisms and to decipher the molecular mechanisms involved in the etiology and pathogenesis of intractable diseases, in order to develop new strategies for diagnosis, treatment and/or prevention of the diseases. Current research is focused on the intractable cardiovascular diseases (e.g. idiopathic cardiomyopathy, idiopathic arrhythmia, and coronary heart disease), autoimmune diseases (e.g. Burger disease, Graves disease, and rheumatoid arthritis) and infectious diseases (e.g. HIV/AIDS). In addition, genome diversity in immune-related genes is investigated from the view-point of primate evolution.

## (4) Lectures & Courses

Main purpose is to understand the molecular pathogenesis of various intractable diseases by methodologies in the fields of Human Genetics, Genome Medicine, Biochemistry and Cell Biology.



## ( 5 ) Publications

### [Original Articles]

1. Taeko K Naruse, Daisuke Sakurai, Hitoshi Ohtani, Gaurav Sharma, Surendra K Sharma, Madhu Vajpayee, Narinder K Mehra, Gurbinder Kaur, Akinori Kimura. APOBEC3H polymorphisms and susceptibility to HIV-1 infection in an Indian population. *J. Hum. Genet.*. 2016.03; 61(3); 263-265
2. Masayoshi Oikawa, Nobuo Sakamoto, Atsushi Kobayashi, Satoshi Suzuki, Akiomi Yoshihisa, Takayoshi Yamaki, Kazuhiko Nakazato, Hitoshi Suzuki, Shu-Ichi Saitoh, Yuichirou Kiko, Hajime Nakano, Takeharu Hayashi, Akinori Kimura, Yasuchika Takeishi. Familial hypertrophic obstructive cardiomyopathy with the GLA E66Q mutation and zebra body. *BMC Cardiovasc Disord.* 2016.05; 16; 83
3. Sumire Iseda, Naofumi Takahashi, Hugo Poplimont, Takushi Nomura, Sayuri Seki, Taku Nakane, Midori Nakamura, Shoi Shi, Hiroshi Ishii, Shota Furukawa, Shigeyoshi Harada, Taeko K Naruse, Akinori Kimura, Tetsuro Matano, Hiroyuki Yamamoto. Biphasic CD8+ T-Cell Defense in Simian Immunodeficiency Virus Control by Acute-Phase Passive Neutralizing Antibody Immunization. *J. Virol.*. 2016.07; 90(14); 6276-6290
4. Hideki Kawai, Shin-Ichiro Morimoto, Yoko Takakuwa, Akihiro Ueda, Ken-Ichi Inada, Masayoshi Sarai, Takuro Arimura, Tatsuro Mutoh, Akinori Kimura, Yukio Ozaki. Hypertrophic Cardiomyopathy Accompanied by Spinocerebellar Atrophy With a Novel Mutation in Troponin I Gene. *Int Heart J.* 2016.07; 57(4); 507-510
5. Hiroshi Ishii, Saori Matsuoka, Takushi Nomura, Midori Nakamura, Teiichiro Shiino, Yuko Sato, Naoko Iwata-Yoshikawa, Hideki Hasegawa, Kazuta Mizuta, Hiromi Sakawaki, Tomoyuki Miura, Yoshio Koyanagi, Taeko K Naruse, Akinori Kimura, Tetsuro Matano. Association of lymph-node antigens with lower Gag-specific central-memory and higher Env-specific effector-memory CD8(+) T-cell frequencies in a macaque AIDS model. *Sci Rep.* 2016.07; 6; 30153
6. John M Gregson, Daniel F Freitag, Praveen Surendran, Nathan O Stitzel, Rajiv Chowdhury, Stephen Burgess, Stephen Kaptoge, Pei Gao, James R Staley, Peter Willeit, Sune F Nielsen, Muriel Caslake, Stella Trompet, Linda M Polfus, Kari Kuulasmaa, Jukka Kontto, Markus Perola, Stefan Blankenberg, Giovanni Veronesi, Francesco Gianfagna, Satu Männistö, Akinori Kimura, Honghuang Lin, Dermot F Reilly, Mathias Gorski, Vladan Mijatovic, , Patricia B Munroe, Georg B Ehret, , Alex Thompson, Maria Uria-Nickelsen, Anders Malarstig, Abbas Dehghan, , Thomas F Vogt, Taishi Sasaoka, Fumihiko Takeuchi, Norihiro Kato, Yoshiji Yamada, Frank Kee, Martina Müller-Nurasyid, Jean Ferrières, Dominique Arveiler, Philippe Amouyel, Veikko Salomaa, Eric Boerwinkle, Simon G Thompson, Ian Ford, J Wouter Jukema, Naveed Sattar, Chris J Packard, Abdulla Al Shafi Majumder, Dewan S Alam, Panos Deloukas, Heribert Schunkert, Nilesh J Samani, Sekar Kathiresan, , Børge G Nordestgaard, Danish Saleheen, Joanna M Howson, Emanuele Di Angelantonio, Adam S Butterworth, John Danesh, . Genetic invalidation of Lp-PLA2 as a therapeutic target: Large-scale study of five functional Lp-PLA2-lowering alleles. *Eur J Prev Cardiol.* 2016.12;

### [Misc]

1. Toshihiro Tanaka, Akinori Kimura. Cardiovascular genetics. *J. Hum. Genet.*. 2016.01; 61(1); 1

### [Conference Activities & Talks]

1. Akinori Kimura, Taeko K. Naruse, Daisuke Sakurai, Jianbo An, Hiroshi Terunuma, Emi E. Nakayama, Tatsuo Shioda, Gaurav Sharma, Narinder Mehra, Gurbinder Kaur. IkBL regulates susceptibility to HIV-1 infection. The 13th International Congress of Human Genetics 2016.04.04 Kyoto, Japan
2. Taeko K. Naruse, Daisuke Sakurai, Hitoshi Ohtani, Hiroshi Terunuma, Yasumasa Iwatani, Wataru Sugiura, Gaurav Sharma, Narinder Mehra, Gurbinder Kaur, Akinori Kimura. APOBEC3H polymorphisms are associated with susceptibility to HIV-1 infection and development of AIDS in Asian populations. The 13th international Congress of Human Genetics 2016.04.04 Kyoto, Japan

# Applied Gene Medicine

Professor Yoshio MIKI  
 Associate Professor Akira NAKANISHI  
 Assistant professor Miho TAKAOKA  
 Project Assistant Professor Ken MIYAGUCHI  
 Graduate Student Konuskan Ucar AYSE,  
 Shun ITO,  
 Maiko UMEGAKI,  
 Gen SATO  
 Naoko Otsuka

## ( 1 ) Outline

Since 1981, cancer has been a top leading cause of death in our country and a novel action is an urgent social challenge. In Department of Molecular Genetics, we aim to study a basic biology underlying cancer and establish novel diagnostic and therapeutic modalities based on findings from the fundamental researches. We have largely focused on three major research directions to understand the molecular mechanisms of breast cancer development: 1) Uncovering DNA damage repair function and genome stabilization mechanism, 2) Uncovering hormone-dependent cellular proliferation, and 3) Determining how the tumor microenvironment contributes to cancer development and progression. Utilizing a wide variety of approaches in genomics, molecular biology, biochemistry and informatics, we are addressing an integrative understanding of multidisciplinary analyses.

## ( 2 ) Research

1. Molecular Mechanisms of Breast Cancer Progression
  - ◆ Understanding Molecular Mechanisms of Metastasis, Invasion, Recurrence in Cancer
  - ◆ Uncovering Molecular functions of hereditary breast cancer genes, BRCA1 and BRCA2
2. Cancer Genomics Research
  - ◆ Cancer Genomics Research with Next-Generation Sequencing
  - ◆ Identification of Genes Involved in Human Cancer Using Genome-Wide Association Studies
3. Cell Death Signaling in Cancer
4. DNA Damage Repair and Genome Instability in Cancer
5. Hormone-Dependent Breast Cancer Cell Growth
6. Cancer Microenvironment

## ( 3 ) Education

Our research is directed at understanding the molecular mechanism of carcinogenesis, based on basic molecular cell biology and molecular genetics. We have applied new findings and information obtained by basic research to develop the new diagnosis, treatment, and prevention of cancer. Our objective in the graduate course is to provide students opportunity to study basic science and applied genome science for cancer research.

**(4) Publications**

**[Original Articles]**

1. Samir Kumar Pal, Chi Thi Kim Nguyen, Kei-Ichi Morita, Yoshio Miki, Kou Kayamori, Akira Yamaguchi, Kei Sakamoto. THBS1 is induced by TGFB1 in the cancer stroma and promotes invasion of oral squamous cell carcinoma. *J. Oral Pathol. Med.*. 2016.02;
2. Junhui Wang, Qianshan Ding, Hiroaki Fujimori, Akira Motegi, Yoshio Miki, Mitsuko Masutani. Loss of CtIP disturbs homologous recombination repair and sensitizes breast cancer cells to PARP inhibitors. *Oncotarget*. 2016.02; 7(7); 7701-7714
3. Hiroki Osumi, Eiji Shinozaki, Mitsukuni Suenaga, Satoshi Matsusaka, Tsuyoshi Konishi, Takashi Akiyoshi, Yoshiya Fujimoto, Satoshi Nagayama, Yosuke Fukunaga, Masashi Ueno, Yoshihiro Mise, Takeaki Ishizawa, Yosuke Inoue, Yu Takahashi, Akio Saiura, Hirohumi Uehara, Mingyon Mun, Sakae Okumura, Nobuyuki Mizunuma, Yoshio Miki, Toshiharu Yamaguchi. RAS mutation is a prognostic biomarker in colorectal cancer patients with metastasectomy. *Int. J. Cancer*. 2016.03;

**[Conference Activities & Talks]**

1. Hiroko Saito, Miho Takaoka, Akira Nakanishi, Yoshio Miki. Loss of BRCA2 enhances microtubules more stabilization with PTX treatment. Tenth AACR-JCA Joint Conference 2016.02.16 USA

# Molecular Cytogenetics

Professor Johji Inazawa M.D., Ph.D.

Lecturer Jun Inoue Ph.D.

Assistant Professor Tomoki Muramatsu Ph.D.

Assistant Professor Yasuyuki Gen M.D., Ph.D.

## ( 1 ) Research

1. Identification of genes responsible for intractable diseases including cancer and genomic disorders through integrative genomics and epigenomics.
2. Discovery of molecular mechanisms of cancer-related genes, including microRNAs, in the multistep processes of carcinogenesis and cancer progression, such as cancer stem cell, epithelial-mesenchymal transition (EMT), invasion and metastasis using systems biology.
3. Establishment of autophagy-based diagnosis and therapy in human cancers by understanding cellular context-dependent role of autophagy.
4. Multiple genomic analyses of genetic disorders of unknown etiology, e.g. mental retardation or epilepsy, to detect causative genes and clarify the etiology. Also, an array chip for diagnosis of known congenital disorders, 'Genome Disorder Array', was developed and released for a practical use at 2009.
5. Development of innovative techniques for genomics and epigenomics in medical science.
6. Development of practically useful tools for molecular diagnosis of intractable diseases.

## ( 2 ) Lectures & Courses

The principal aim of the Department of Molecular Cytogenetics(MCG) is to understand the molecular mechanism underlying intractable diseases, such as cancer and uncharacterized genetic diseases. Main objective of MCG in the graduate course is to provide students opportunity to study molecular cytogenetic approach for intractable diseases, identify genes responsible for those diseases, and develop innovative techniques/ practically useful tools for detection of genomic and epigenomic aberrations in those diseases. It is our goal to bridge the gap between basic and clinical research for the benefit of each of the patients.

## ( 3 ) Publications

### [Original Articles]

1. Okada Yukinori, Muramatsu Tomoki, Suita Naomasa, Kanai Masahiro, Kawakami Eiryo, Iotchkova Valentina, Soranzo Nicole, Inazawa Johji, Tanaka Toshihiro. Significant impact of miRNA-target gene networks on genetics of human complex traits. *Sci Rep.* 2016; 6: 22223
2. Maki Morishita, Tomoki Muramatsu, Yumiko Suto, Momoki Hirai, Teruaki Konishi, Shin Hayashi, Daichi Shigemizu, Tatsuhiko Tsunoda, Keiji Moriyama, Johji Inazawa. Chromothripsis-like chromosomal rearrangements induced by ionizing radiation using proton microbeam irradiation system. *Oncotarget.* 2016.03; 7(9); 10182-10192

3. Genki Sudo, Tetsushi Kagawa, Yasuhiro Kokubu, Johji Inazawa, Tetsuya Taga. Increase in GFAP-positive astrocytes in histone demethylase GASC1/KDM4C/JMJD2C hypomorphic mutant mice. *Genes Cells*. 2016.03; 21(3); 218-225
4. Daniela Tiaki Uehara, Shin Hayashi, Nobuhiko Okamoto, Seiji Mizuno, Yasutsugu Chinen, Rika Kosaki, Tomoki Kosho, Kenji Kurosawa, Hiroshi Matsumoto, Hiroshi Mitsubuchi, Hironao Numabe, Shinji Saitoh, Yoshio Makita, Akira Hata, Issei Imoto, Johji Inazawa. SNP array screening of cryptic genomic imbalances in 450 Japanese subjects with intellectual disability and multiple congenital anomalies previously negative for large rearrangements. *J. Hum. Genet.* 2016.04; 61(4); 335-343
5. T Muramatsu, K-I Kozaki, S Imoto, R Yamaguchi, H Tsuda, T Kawano, N Fujiwara, M Morishita, S Miyano, J Inazawa. The hypusine cascade promotes cancer progression and metastasis through the regulation of RhoA in squamous cell carcinoma. *Oncogene*. 2016.04;
6. Michelle Nuylan, Tatsuyuki Kawano, Johji Inazawa, Jun Inoue. Down-regulation of LAPTM5 in human cancer cells. *Oncotarget*. 2016.04;
7. Tumurkhuu T, Fujiwara T, Komazaki Y, Kawaguchi Y, Tanaka T, Inazawa J, Ganburged G, Bazar A, Ogawa T, Moriyama K. Association between maternal education and malocclusion in Mongolian adolescents: a cross-sectional study. *BMJ Open*. 2016.11; 6(11); e012283

### [Conference Activities & Talks]

1. Morita K, Naruto T, Tanimoto K, Yasukawa C, Oikawa Y, Masuda K, Imoto I, Inazawa J. Simultaneous detection of both single nucleotide variations and copy number alterations by nextgeneration sequencing in Gorlin syndrome.. ICHG2016 2016.04 Kyoto, Japan
2. Kanai M, Okada Y, Muramatsu T, Suita N, Kawakami E, Iotchkova V, Soranzo N, Inazawa J, Tanaka T. Significant impact of miRNA-target gene networks on genetics of human complex traits. ICHG2016 2016.04 Kyoto, Japan
3. Uehara D.T, S Hayashi, Makita Y, Hata A, Imoto I, Inazawa J. Screening of copy number variants in 450 Japanese subjects presenting with intellectual disability (ID) and multiple congenital anomalies (MCA) by SNP array unveiling rare small variants and PPFIA2 as a novel candidate gene for ID. ICHG2016 2016.04.05 Kyoto, Japan
4. Inoue J. MicroRNA-based diagnosis and therapy in NRF2-stabilized tumor. 107th annual meeting of American Association for Cancer Research 2016 2016.04.18 New Orleans, USA.
5. Muramatsu T, Tanimoto K, Inazawa J. Exploring target genes of eukaryotic initiation factor 5A in cancer using RNA sequence analysis. 107th annual meeting of American Association for Cancer Research 2016 2016.04.18 New Orleans, USA.
6. Inoue J, Fujiwara N, Yamamoto S, Kawano T, Inazawa J. MicroRNA-based diagnosis and therapy in NRF2-stabilized tumor. 107th annual meeting of American Association for Cancer Research 2016 2016.04.18 New Orleans, USA.

# Hematology

Professor Osamu Miura

Professor( Immunotherapy for Hematopoietic Disorders) Norihiko Kawamata

Junior Associate Professor Ayako Arai

Assistant Professor Tetsuya Fukuda, Masahide Yamamoto, Ken Watanabe, Ayako Nogami

Project Assistant Professor Chizuko Sakashita

Senior Resident Tomoko Yamashitai, Tatsuya Saito, Kota Yoshifuji  
Graduate Student Yoshihiro Umezawa, Hiroki Akiyama, Shinya Ishida,  
Keigo Okada, Emi Uchida, Daisuke Watabae,  
Koji Sasaki, Shuhei Fujita

## ( 1 ) Outline

The Department of Hematology is responsible for clinical services at our University Hospital with treatment of patients with various hematological disorders including leukemias, lymphomas, anemia, and hemorrhagic diseases by chemotherapies, immunotherapies, molecularly-targeted therapies, and hematopoietic cell transplantation. Our department is also responsible for teaching undergraduate students with the lecture course in hematology as well as the clinical clerkship and for training junior and senior residents. Our department is also actively involved, with doctoral course students, in basic and clinical researches aiming to elucidate the molecular and cellular mechanisms involved in pathogenesis of hematological malignancies as well as in acquisition of therapy resistance to develop novel efficient therapies against these diseases.

## ( 2 ) Research

The research interests and activities of the Department of Hematology are diverse, and the following projects among others are currently under way. 1. Elucidation of the molecular mechanisms involved in acquisition of resistance against chemotherapies and molecularly-targeted therapies by leukemic cells from chronic myeloid leukemia, acute myeloid leukemia, and various myeloproliferative neoplasms expressing aberrant tyrosine kinases, including BCR/ABL, FLT3-ITD, and Jak2-V617F, aiming to develop novel therapeutic strategies to overcome the resistance. 2. Elucidation of the regulation mechanisms for immune responses to indolent lymphoid neoplasms, including chronic lymphocytic leukemia, for developing novel immunotherapies. 3. Elucidation of the pathogenesis of chronic active EB virus infection and development of effective therapeutic modalities. 4. Signal transduction mechanisms from cytokine/growth factor receptors regulating proliferation, survival, and adhesion of hematopoietic cells including leukemia and lymphoma cells. The Department is also actively involved in a variety of clinical studies for treatment of various leukemias, lymphomas, and multiple myeloma.

## ( 3 ) Education

The Department of hematology is responsible for teaching basic and clinical hematology to the 3rd and 4th grade students in the integrated hematology course and the hematology and oncology united block course. The

Department is also responsible for teaching the 5th and 6th grade students in clinical clerkship to obtain basic knowledge and problem-solving abilities in hematology as well as general internal medicine. The Department is also actively involved in training about 24 junior residents every year to acquire clinical skills in hematology and internal medicine and about 4 senior residents to practice diagnosis and treatment of various hematological disorders and to obtain the certificate for hematology specialist. As a division in the Graduate School of Medical and Dental Sciences, the Department is actively involved in education of 6 to 8 graduate students, who participate in the research projects listed above, to obtain the Ph. D. degree in medicine.

#### ( 4 ) Lectures & Courses

The major objective of the course is to understand the pathophysiology of blood cells, blood cell-forming organs, and hemostasis to provide a basis for rational diagnosis and treatment of their disorders.

#### ( 5 ) Clinical Services & Other Works

The Department of Hematology provides diagnosis and treatment for hematological diseases, such as leukemia, malignant lymphoma, anemia, and thrombocythemia, with chemotherapeutics, molecularly-targeted drugs, immunosuppressive agents, and hematopoietic cell trans-plantation.

#### ( 6 ) Clinical Performances

We provide the highest quality of patient care for a wide spectrum of blood diseases and cancers.

#### ( 7 ) Publications

##### [Original Articles]

1. Yui S, Yamaguchi H, Imadome K, Arai A, Takahashi M, Ohashi R, Asayama T, Kondo A, Moriya K, Nakayama K, Dan K, Shimizu S, Inokuchi K.. Epstein-Barr virus positive T cell lymphoproliferative disease following cord blood transplantation for acute myelogenous leukemia The Journal of Nippon Medical School. 2016;
2. Nobuo Sanjo,Satoko Kina,Yukiko Shishido-Hara,Yurie Nose,Satoru Ishibashi,Tetsuya Fukuda,Taketoshi Maehara,Yoshinobu Eishi,Hidehiro Mizusawa,Takanori Yokota. A Case of Progressive Multifocal Leukoencephalopathy with Balanced CD4/CD8 T-Cell Infiltration and Good Response to Mefloquine Treatment. Internal Medicine. 2016.01; 55(12); 1631-1635
3. Uchida Emi, Watanabe Ken, Oshikawa Gaku, Sakasita Chizuko, Kurosu Tetsuya, Fukuda Tetsuya, Arai Ayako, Murakami Naoki, Miura Osamu, Yamamoto Masahide. Refractory primary myeloid sarcoma of the breast with MLL-AF9 rearrangement. The Japanese Journal of Clinical Hematology. 2016.01; 57(1);
4. Arai A, Sakashita C, Hirose C, Imadome K, Yamamoto M, Jinta M, Fujiwara S, Tomita M, Shimizu N, Morio T, and Miura O.. Hematopoietic stem cell transplantation for adults with EBV-positive T- or NK-cell lymphoproliferative disorders: efficacy and predictive markers Bone Marrow Transplantation. 2016.02;
5. Naoyuki Miyasaka, Osamu Miura, Tatsuya Kawaguchi, Nobuyoshi Arima, Eriko Morishita, Kensuke Usuki, Yasuyoshi Morita, Kaichi Nishiwaki, Haruhiko Ninomiya, Akihiko Gotoh, Shinsaku Imashuku, Akio Urabe, Tsutomu Shichishima, Jun-Ichi Nishimura, Yuzuru Kanakura. Pregnancy outcomes of patients with paroxysmal nocturnal hemoglobinuria treated with eculizumab: a Japanese experience and updated review. Int. J. Hematol.. 2016.02;
6. Shunsuke Yui, Hiroki Yamaguchi, Ken-ichi Imadome, Ayako Arai, Mikiko Takahashi, Ryuji Ohashi, Hayato Tamai, Keiichi Moriya, Kazutaka Nakayama, Akira Shimizu, Koiti Inokuchi. Epstein-Barr Virus-positive T-cell Lymphoproliferative Disease Following Umbilical Cord Blood Transplantation for Acute Myeloid Leukemia. J Nippon Med Sch. 2016.02; 83(1); 35-42



7. Megumi Akiyama, Kota Yoshifuji, Tetsuya Fukuda, Shuji Tohda, Tohru Miki, Osamu Miura, Masahide Yamamoto. Fulminant visceral disseminated varicella-zoster virus infection without skin involvement in a patient with autoimmune hemolytic anemia on prednisolone therapy. *Rinsho Ketsueki*. 2016.04; 57(4); 467-471
8. Shunichiro Yasuda, Masahide Yamamoto, Tetsuya Fukuda, Yasufumi Ohtsuka, Osamu Miura. Postoperative Atypical Hemolytic Uremic Syndrome Treated Successfully with Eculizumab. *Intern. Med.*. 2016.05; 55(9); 1171-1175
9. Masahide Yamamoto, Kazuteru Ohashi, Kazuhiko Kakihana, Yuichi Nakamura, Takuya Komeno, Hiroshi Kojima, Satoshi Morita, Hisashi Sakamaki. A multicenter clinical study to determine the feasible initial dose of lenalidomide for maintenance therapy in patients with multiple myeloma following autologous peripheral blood stem-cell transplantation. *Mol Clin Oncol*. 2016.06; 4(6); 965-970
10. Yoshihiro Umezawa, Tetsuya Kurosu, Hiroki Akiyama, Nang Wu, Ayako Nogami, Toshikage Nagao, Osamu Miura. Down regulation of Chk1 by p53 plays a role in synergistic induction of apoptosis by chemotherapeutics and inhibitors for Jak2 or BCR/ABL in hematopoietic cells. *Oncotarget*. 2016.06;
11. Yuki Shirai, Mitsunori Miyashita, Masako Kawa, Toru Motokura, Fumiaki Sano, Tetsuya Fukuda, Kazuo Oshimi, Keiko Kazuma. Evaluation of care for leukemia and lymphoma patients during their last hospitalization from the perspective of the bereaved family. *Leuk. Res.*. 2016.08; 47; 93-99
12. Hiroki Akiyama, Hiroshi Takase, Fumito Kubo, Tohru Miki, Masahide Yamamoto, Makoto Tomita, Manabu Mochizuki, Osamu Miura, Ayako Arai. High-dose methotrexate following intravitreal methotrexate administration in preventing central nervous system involvement of primary intraocular lymphoma. *Cancer Science*. 2016.10; 107(10); 1458-1464
13. Shunichiro Yasuda, Keisuke Tanaka, Ayako Ichikawa, Ken Watanabe, Emi Uchida, Masahide Yamamoto, Kouhei Yamamoto, Daisuke Mizuchi, Osamu Miura, Tetsuya Fukuda. Aggressive TAFRO syndrome with reversible cardiomyopathy successfully treated with combination chemotherapy. *Int. J. Hematol.*. 2016.10; 104(4); 512-518
14. Koichi Miyamura, Toshihiro Miyamoto, Mitsune Tanimoto, Kazuhito Yamamoto, Shinya Kimura, Tatsuya Kawaguchi, Itaru Matsumura, Tomoko Hata, Hisashi Tsurumi, Shigeki Saito, Masayuki Hino, Seiji Tadokoro, Kuniaki Meguro, Hideo Hyodo, Masahide Yamamoto, Kohmei Kubo, Junichi Tsukada, Midori Kondo, Makoto Aoki, Hikaru Okada, Masamitsu Yanada, Kazuma Ohyashiki, Masafumi Taniwaki. Switching to nilotinib in patients with chronic myeloid leukemia in chronic phase with molecular suboptimal response to frontline imatinib: SENSOR final results and BIM polymorphism substudy. *Leuk. Res.*. 2016.12; 51; 11-18

#### [Misc]

1. Ayako Arai. The issues of chronic active Epstein-Barr virus infection 2016.09; 73(3); 400-404

#### [Conference Activities & Talks]

1. The impact of 2nd autologous stem cell transplantation (ASCT) in patients with multiple myeloma who relapsed after 1st ASCT. The 38th Annual Meeting of the Japan Society for Hematopoietic Cell Transplantation 2016.03.05
2. Haruna Shibayama, Ken-ichi Imadome, Chizuko Sakashita, Ken Watanabe, Norio Shimizu, Takatoshi Koyama, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. In vitro and in vivo effects of proteasome inhibitor bortezomib on Epstein-Barr virus-positive T- or NK-cell lymphoproliferative diseases. 17th International Symposium on Epstein-Barr virus (EBV) and Associated Diseases 2016.08.10 Zurich
3. Yujin Sekinaka, Noriko Mitsui, Kohsuke Imai, Miharuru Yabe, Hiromasa Yabe, Masatoshi Takagi, Ayako Arai, Kenichi Yoshida, Yusuke Okuno, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Seiji Kojima, Asuka Hira, Minoru Takata, Osamu Ohara, Seishi Ogawa, Tomohiro Morio, and Shigeaki Nonoyama. Common variable immunodeficiency caused by FANCD1 mutations. 17th Biennial Meeting of European Society for Immunodeficiency. 2016.09 Barcelona

4. Ayako Nogami, Keigo Okada, Gaku Oshikawa, Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Tet-suya Kurosu, Osamu Miura. FLT3-ITD Confers Resistance to Bortezomib by Protecting the mTOR Pathway via the Pim Kinases in AML. The 78th Annual Meeting of the Japanese Society of Hematology 2016.10.13
5. Yoshihiro Umezawa, Hiroki Akiyama, Keigo Okada, Shinya Ishida, Ayako Nogami, Gaku Oshikawa, Tet-suya Kurosu, Osamu Miura. PECAM-1 enhances SDF-1-induced chemotaxis mediated through activation of the PI3K/Akt/mTORC1 pathway. The 78th annual meeting of the Japanese society of hematology 2016.10.14 Yokohama, Japan
6. Haruna Shibayama, Ken-ichi Imadome, Chizuko Sakashita, Ken Watanabe, Fuyuko Kawano, Norio Shimizu, Takatoshi Koyama, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. In vitro and in vivo effects of bortezomib on EBV-T/NK-LPDs. The 78th Annual Meeting of the Japanese Society of Hematology 2016.10.14 Yokohama
7. Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Shinya Ishida, Ayako Nogami, Gaku Oshikawa, Osamu Miura. Deubiquitinase inhibitor WP1130 blocks JAK2-V617F and FLT3-ITD to induce apoptosis in leukemic cells. The 78th Annual Meeting of the Japanese Society of Hematology 2016.10.15 Yokohama

# Molecular Endocrinology and Metabolism

Professor: Yoshihiro Ogawa

Associate Professor: Takanobu Yoshimoto, Hajime Izumiyama

Assistant Professor: Isao Minami, Kyoichiro Tsuchiya, Ryotaro Bouchi

Clinical Fellow: Eri Ueda, Yusuke Matsuda, Hideyuki Okuma, Yoshihiro Niitsu

Resident: Seizaburo Matsuda, Asuka Shinmei

Project Assistant Professor: Misa Saijo, Masanori Murakami, Takeru Sakai, Xunmei Yuan<sup>1</sup>, Michiko Shirakawa<sup>1</sup>, Ibuki Shirakawa<sup>1</sup>

Graduate Students (Doctor's course): Kazutaka Tsujimoto, Yasutaka Miyachi, Kumiko Shiba, Kenichi Kawahori, Maki Kawasaki, Toshihiro Goto, Takuya Ohmura, Megumi Hatano, Yujiro Nakano, Takato Takeuchi, Masahiro Asakawa, Nozomi Hanzawa, Kentaro Mori, Tatsuya Fukuda

Project Associate Professor: Koshi Hashimoto<sup>2</sup>, Kyoko Shirakabe<sup>1</sup>

<sup>1</sup>Department of Organ Network and Metabolism, <sup>2</sup>Department of Preemptive Medicine and Metabolism

## (1) Outline

### 1. Purpose of Education

Our training program enables postdoctoral trainees to prepare for the future academic careers and the clinical practice in the broad discipline of endocrinology and metabolism. The research program provides mentor-based training in experimental design, laboratory and clinical research techniques and methodology, and interpretation and analysis of the results obtained from cellular and molecular biology, physiology, clinical physiology, clinical therapeutics, and health sciences. This training program is designed to educate and establish 'physician-scientist' in the field of endocrinology and metabolism.

### 2. Research Subjects

- 1) Role of adipose tissue inflammation in the metabolic syndrome
- 2) Molecular mechanisms of saturated fatty acid-induced chronic inflammation
- 3) Molecular mechanism of vascular injury in diabetes, endocrine and metabolic diseases
- 4) Role of epigenetic regulation in metabolism
- 5) Mechanism of pathogenesis in endocrine tumors
- 6) Development of novel diagnostic and therapeutic tools in endocrine and metabolic diseases

### 3. Clinical Services

Comprehensive inpatient and outpatient services in the area of endocrine and metabolic disorders, including:

- 1) diseases of the thyroid, pituitary and adrenal glands.
- 2) diabetes mellitus, diabetic complications, metabolic syndrome, and obesity
- 3) primary and secondary hypertension
- 4) disorders of calcium metabolism

**(2) Publications****[Original Articles]**

1. Ryotaro Bouchi, Masahiro Asakawa, Norihiko Ohara, Yujiro Nakano, Takato Takeuchi, Masanori Murakami, Yuriko Sasahara, Mitsuyuki Numasawa, Isao Minami, Hajime Izumiyama, Koshi Hashimoto, Takanobu Yoshimoto, Yoshihiro Ogawa. Indirect measure of visceral adiposity 'A Body Shape Index' (ABSI) is associated with arterial stiffness in patients with type 2 diabetes. *BMJ Open Diabetes Res Care*. 2016; 4(1); e000188
2. Chikara Komiya, Kyoichiro Tsuchiya, Kumiko Shiba, Yasutaka Miyachi, Shunsaku Furuue, Noriko Shimazu, Shinobu Yamaguchi, Kazuo Kanno, Yoshihiro Ogawa. Ipragliflozin Improves Hepatic Steatosis in Obese Mice and Liver Dysfunction in Type 2 Diabetic Patients Irrespective of Body Weight Reduction. *PLoS ONE*. 2016; 11(3); e0151511
3. Koshi Hashimoto, Tetsuya Tagami, Hajime Yamakage, Kazuya Muranaka, Masashi Tanaka, Shinji Odori, Shigeo Kono, Akira Shimatsu, Yoshihiro Ogawa, Noriko Satoh-Asahara. Serum free thyroxine levels are associated with the efficacy of weight reduction therapy in obese female patients. *Endocr. J.* 2016; 63(3); 221-229
4. Ryotaro Bouchi, Norihiko Ohara, Masahiro Asakawa, Yujiro Nakano, Takato Takeuchi, Masanori Murakami, Yuriko Sasahara, Mitsuyuki Numasawa, Isao Minami, Hajime Izumiyama, Koshi Hashimoto, Takanobu Yoshimoto, Yoshihiro Ogawa. Is visceral adiposity a modifier for the impact of blood pressure on arterial stiffness and albuminuria in patients with type 2 diabetes? *Cardiovasc Diabetol*. 2016.01; 15; 10
5. Sumiyo Morita, Kazuhiko Nakabayashi, Tomoko Kawai, Keiko Hayashi, Takuro Horii, Mika Kimura, Yasutomi Kamei, Yoshihiro Ogawa, Kenichiro Hata, Izuho Hatada. Gene expression profiling of white adipose tissue reveals paternal transmission of proneness to obesity. *Sci Rep*. 2016.02; 6; 21693
6. Ryotaro Bouchi, Yujiro Nakano, Norihiko Ohara, Takato Takeuchi, Masanori Murakami, Masahiro Asakawa, Yuriko Sasahara, Mitsuyuki Numasawa, Isao Minami, Hajime Izumiyama, Koshi Hashimoto, Takanobu Yoshimoto, Yoshihiro Ogawa. Clinical relevance of dual-energy X-ray absorptiometry (DXA) as a simultaneous evaluation of fatty liver disease and atherosclerosis in patients with type 2 diabetes. *Cardiovasc Diabetol*. 2016.04; 15; 64
7. Tatsuya Fukuda, Ryotaro Bouchi, Isao Minami, Norihiko Ohara, Yujiro Nakano, Rie Nishitani, Masanori Murakami, Takato Takeuchi, Momoko Akihisa, Masamichi Fujita, Hajime Izumiyama, Koshi Hashimoto, Takanobu Yoshimoto, Yoshihiro Ogawa. Retrograde pyelonephritis and lumbar spondylitis as a result of *Salmonella typhi* in a type 2 diabetes patient with neurogenic bladder. *J Diabetes Investig*. 2016.05; 7(3); 436-439
8. Rumi Hachiya, Takuya Shiihashi, Ibuki Shirakawa, Yorihiro Iwasaki, Yoshihiro Matsumura, Yumiko Oishi, Yukiteru Nakayama, Yoshihiro Miyamoto, Ichiro Manabe, Kozue Ochi, Miyako Tanaka, Nobuhito Goda, Juro Sakai, Takayoshi Suganami, Yoshihiro Ogawa. The H3K9 methyltransferase Setdb1 regulates TLR4-mediated inflammatory responses in macrophages. *Sci Rep*. 2016.06; 6; 28845
9. Takanori Chiba, Erika Ishihara, Norio Miyamura, Rika Narumi, Mihoko Kajita, Yasuyuki Fujita, Akira Suzuki, Yoshihiro Ogawa, Hiroshi Nishina. MDCK cells expressing constitutively active Yes-associated protein (YAP) undergo apical extrusion depending on neighboring cell status. *Sci Rep*. 2016.06; 6; 28383
10. Masahiro Asakawa, Takanobu Yoshimoto, Mitsutane Ota, Mitsuyuki Numasawa, Yuriko Sasahara, Takato Takeuchi, Yujiro Nakano, Norihiko Ohara, Masanori Murakami, Ryotaro Bouchi, Isao Minami, Kyoichiro Tsuchiya, Koshi Hashimoto, Hajime Izumiyama, Naoko Kawamura, Kazunori Kihara, Mariko Negi, Takumi Akashi, Yoshinobu Eishi, Hironobu Sasano, Yoshihiro Ogawa. A Case of Cushing's Syndrome with Multiple Adrenocortical Adenomas Composed of Compact Cells and Clear Cells. *Endocr. Pathol.* 2016.06; 27(2); 136-141
11. Ryotaro Bouchi, Takato Takeuchi, Momoko Akihisa, Norihiko Ohara, Yujiro Nakano, Rie Nishitani, Masanori Murakami, Tatsuya Fukuda, Masamichi Fujita, Isao Minami, Masatomo Mihara, Takanobu Yoshimoto, Yoshihiro Ogawa. Increased visceral adiposity with normal weight is associated with the prevalence of non-alcoholic fatty liver disease in Japanese patients with type 2 diabetes. *J Diabetes Investig*. 2016.07; 7(4); 607-614

12. Masanori Murakami, Takanobu Yoshimoto, Yujiro Nakano, Kyoichiro Tsuchiya, Isao Minami, Ryotaro Bouchi, Yasuhisa Fujii, Kazuhiko Nakabayashi, Koshi Hashimoto, Ken-Ichiro Hata, Kazunori Kihara, Yoshihiro Ogawa. Expression of inflammation-related genes in aldosterone-producing adenomas with KCNJ5 mutation. *Biochem. Biophys. Res. Commun.*. 2016.08; 476(4); 614-619
13. Richard Thomas Jennings, Erdenezaya Odkhuu, Akina Nakashima, Naoko Morita, Toshihiko Kobayashi, Ikuko Yamai, Miyako Tanaka, Takayoshi Suganami, Sanae Haga, Michitaka Ozaki, Yasuharu Watanabe, Yoshinori Nagai, Kiyoshi Takatsu, Takane Kikuchi-Ueda, Isao Ichimonji, Yoshihiro Ogawa, Hidekazu Takagi, Tatsuya Yamazaki, Kensuke Miyake, Sachiko Akashi-Takamura. Inflammatory responses increase secretion of MD-1 protein. *Int. Immunol.*. 2016.10; 28(10); 503-512
14. Megumi Hatano, Toshiro Migita, Tomokazu Ohishi, Yuichi Shima, Yoshihiro Ogawa, Ken-Ichirou Morohashi, Yukihiro Hasegawa, Futoshi Shibasaki. SF-1 deficiency causes lipid accumulation in Leydig cells via suppression of STAR and CYP11A1. *Endocrine*. 2016.11; 54(2); 484-496

## Hepatobiliary and Pancreatic Surgery

Director & Professor

Minoru Tanabe MD, PhD

Lecturer

Atsushi Kudo MD, PhD

Assistant Professor

Takanori Ochiai MD, PhD

Daisuke Ban MD, PhD

Arihiro Aihara MD, PhD (until September)

Hiroaki Ono MD, PhD (since March)

Satoshi Matsumura MD, PhD

Yusuke Mitsunori MD, PhD

Satoshi Matsumura MD, PhD

Hiromitsu Ito MD (until March)

Keiichi Akakhoshi MD, PhD (since October)

Yasuhito Iwao MD, PhD (since April)

Graduate School Students

Keiichi Akakhoshi MD (until March)

Yasuhito Iwao MD (until March)

Hiroki Ueda MD (until September)

Yoshiteru Ohata MD (until March)

Atsushi Oba MD (until March)

Taku Sato MD

Yuki Mizuno MD

Norimichi Chiyonobu MD

Haku Liu MD

Shuichi Watanabe MD

Yoshiya Ishikawa MD

Daisuke Asano MD (joining April)

Jun Yoshino MD (joining April)

### ( 1 ) Outline

The department of Hepato-Biliary-Pancreatic Surgery at Tokyo Medical and Dental University focus on the liver, biliary tract and pancreas with benign and malignant disorders. We constantly strive to provide the highest level of complex and innovative surgical care, comprehensive surgical training for tomorrow's leaders as well as groundbreaking basic science and clinical research.

### ( 2 ) Research

We conduct medical research in both clinical and laboratory settings and develop novel ideas in research which impact patient outcomes, teaching, and clinical care.

Our research programs encompass:

- Biomolecular mechanisms of carcinogenesis, cancer growth, invasion and metastasis

- Molecular target therapy for malignant diseases
- Cancer stem cell
- Extended indication for hepatectomy
- The system of liver microcirculation
- Laparoscopic surgery for hepatobiliary pancreatic diseases
- Liver transplantation and organ preservation
- Treatments for neuroendocrine tumor
- Innovation of imaging modality for hepatobiliary pancreatic diseases

### (3) Education

Medical students program:

We conduct the various experiences of hepatobiliary pancreatic diseases, diagnosis and management, through lectures, pre-clinical clerkship and clinical clerkship. Clinical clerkship exposes students to the surgical patients and basic surgical techniques. It also provides opportunities to participate in peri-operative care as well as operative procedures. Students learn interpersonal and communication skills that result in the effective exchange of information and teaming with patients, their families, and professional associates.

Surgical training program:

The aim of our surgical training program cultivates not only training for certified board surgeons, but also the future surgical leaders, through experiences from the academic, the operative, and the outpatient aspects of management in university hospital and affiliated hospitals. Clinically, the trainees receive training and experience in the preoperative, operative, and post-operative care of patients and basic science and clinical research in our training programs strive to help young surgeons develop both technical and cognitive expertise.

### (4) Clinical Performances

Our highly experienced surgeons offer state-of-the-art diagnosis and treatment, such as the multidisciplinary treatments (based on radical surgery) for advanced malignant diseases, minimally invasive procedures (including reduced port surgery).

Annually, 255 operations (hepatectomy: 96 cases, pancreatectomy: 73 cases) were performed in 2014, placing one of the top high volume medical centers in the country for hepatobiliary pancreatic surgery.

The 325 patients with neuroendocrine tumors were treated in 2016. We have treated the largest number of the patients with NENs in Japan.

### (5) Publications

#### [Original Articles]

1. E. Soeda, K. Hoshino, Y. Izawa, C. Takaoka, C. Isobe, A. Takahashi, N. Takahashi, Y. Yamada, N. Shimojima, A. Fujino, M. Shinoda, Y. Kitagawa, M. Tanabe, S. Nakamura, N. Taki, A. Sekiguchi, Y. Nakazawa, T. Turukawa, and T. Kuroda. A report on the Positive Response to an Outdoor Nature Challenge of a Snow Camp for Young Liver Transplantation Patients Transplant Proceedings. 2016.01; 49; 115-120
2. M. Shimazu, Y. Kato, S. Kawachi, M. Tanabe, K. Hoshino, G. Wakabayashi, Y. Kitagawa, and M. Kitajima. Impact of Portal Hemodynamic Changes in Partial Liver Grafts on Short-Term Graft Regeneration in Living Donor Liver Transplantation Transplant Proceedings. 2016.01; 48; 2747-2755
3. Masaki Kaibori , Hiroyuki Nitta , Michihiro Hayashi , Shigekazu Takemura , Hiroaki Nagano , Kosuke Matsui , Hisashi Ikoma , Takuya Nakai , Masafumi Yasunaga , Masahiro Kido , Takeshi Aoki , Toshiki Rikiyama , Keiji Sano , Atsushi Kudo , Satoshi Katagiri , Yuichiro Otsuka , Tamotsu Kuroki , Takeo Nomi , Koichi Yano , Itaru Endo , Masaki Ueno , Akishige Kanazawa , Hiroaki Terajima , Saiho Ko , Goro Honda , Yasuji Seyama , Hiroki Sunagawa , Tsukasa Aibara. Questionnaire survey on work motivations of gastrointestinal and hepatobiliary pancreatic surgeons enrolled in a Japanese national interdisciplinary program J Hepatobiliary Pancreat Sci . 2016.01; 23; 697-702



4. Katsuta E, Tanaka S, Mogushi K, Shimada S, Akiyama Y, Aihara A, Matsumura S, Mitsunori Y, Ban D, Ochiai T, Kudo A, Fukamachi H, Tanaka H, Nakayama K, Arie S, Tanabe M.. CD73 as a therapeutic target for pancreatic neuroendocrine tumor stem cells. *Int J Oncol.* . 2016.02; 48(2); 657-669
5. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shinji Tanaka, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Satoshi Otani, Miki Taniguchi, Fumio Goto, Hiroko Nagata, Shun Kaneko, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Mina Nakagawa, Minoru Tanabe, Shinichi Takano, Mitsuharu Fukasawa, Minoru Sakamoto, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma with clinicopathological features. *J. Gastroenterol.* 2016.03; 51(5); 473-486
6. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Watanabe T, Otani S, Taniguchi M, Goto F, Nagata H, Kaneko S, Tasaka-Fujita M, Nishimura-Sakurai Y, Azuma S, Itsui Y, Nakagawa M, Tanabe M, Takano S, Fukasawa M, Sakamoto M, Maekawa S, Enomoto N, Watanabe M.. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma with clinicopathological features. *J Gastroenterol.* . 2016.05; 51(5); 473-486
7. Iwasa Y, Kitazume Y, Tateishi U, Saida Y, Ban D, Tanabe M, Takemoto A.. Hepatocellular Carcinoma Histological Grade Prediction: A Quantitative Comparison of Diffusion-Weighted, T2-Weighted, and Hepatobiliary-Phase Magnetic Resonance Imaging. *J Comput Assist Tomogr.* . 2016.05; 40(3); 463-470
8. Eriko Katsuta, Atsushi Kudo, Takumi Akashi, Yusuke Mitsunori, Satoshi Matsumura, Arihiro Aihara, Daisuke Ban, Takanori Ochiai, Shinji Tanaka, Yoshinobu Eishi, Minoru Tanabe. Macroscopic morphology for estimation of malignant potential in pancreatic neuroendocrine neoplasm *J Cancer Res Clin Oncol.* . 2016.06; 142; 1299-1306
9. Yamada Y, Hoshino K, Irie R, Tomita H, Kato M, Shimojima N, Fujino A, Hibi T, Shinoda M, Obara H, Itano O, Kawachi S, Tanabe M, Sakamoto M, Kitagawa Y, Kuroda T.. The optimal immunosuppressive protocol for the portal vein infusion of PGE1 and methylprednisolone in pediatric liver transplantation for fulminant hepatic failure of unknown etiology. *Pediatr Transplant.* 2016.08; 20(5); 640-646
10. Oba A, Ban D, Kirimura S, Akahoshi K, Mitsunori Y, Matsumura S, Ochiai T, Kudo A, Tanaka S, Minoru T.. Clinical application of the biomarkers for the selection of adjuvant chemotherapy in pancreatic ductal adenocarcinoma. *J Hepatobiliary Pancreat Sci.* . 2016.08; 23(8); 480-488
11. Akahoshi K, Tanaka S, Mogushi K, Shimada S, Matsumura S, Akiyama Y, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Arie S, Tanabe M.. Expression of connective tissue growth factor in the livers of non-viral hepatocellular carcinoma patients with metabolic risk factors. *J Gastroenterol.* . 2016.09; 51(9); 910-922
12. Yuichiro Watanabe, Shinya Honda, Akimitsu Konishi, Satoko Arakawa, Michiko Murohashi, Hirofumi Yamaguchi, Satoru Torii, Minoru Tanabe, Shinji Tanaka, Eiji Warabi, Shigeomi Shimizu. Autophagy controls centrosome number by degrading Cep63. *Nat Commun.* 2016.11; 7; 13508
13. Furuyama T, Kudo A, Matsumura S, Mitsunori Y, Aihara A, Ban D, Ochiai T, Tanaka S, Tanabe M.. Pre-operative direct bilirubin to prothrombin time ratio index to prevent liver failure after minor hepatectomy. *J Hepatobiliary Pancreat Sci.* . 2016.12; 23(12); 763-770
14. Norihiro Kishida, Masahiro Shinoda, Osamu Itano, Hideaki Obara, Minoru Kitago, Taizo Hibi, Hiroshi Yagi, Yuta Abe, Kentaro Matsubara, Masanori Odaira, Minoru Tanabe, Motohide Shimazu, Yuko Kitagawa. Increased Incidence of Thrombotic Microangiopathy After ABO-Incompatible Living Donor Liver Transplantation. *Ann. Transplant.* 2016.12; 21; 755-764

#### [Conference Activities & Talks]

1. Akahoshi K, Ochiai T, Ito H, Matsumura S, Mitsunori Y, Aihara A, Ban D, Kudo A, Tanaka S, Tanabe M. Evaluation of POSSUM score for predicting morbidity after hepatectomy for hepatocellular carcinoma. 11th Annual Academic surgical Congress 2016.02.04 Florida
2. Itou H, Ochiai T, Matsumura S, Mitsunori Y, Aihara A, Ban D, Kudo A, Tanabe M. The consensus and controversial points of new IPMN guideline. 11th Annual Academic surgical Congress 2016.02.04 Florida

3. Ochiai T, Miura T, Tanaka S, Yamazaki S, Kudo A, Noguchi N, Irie T, Ban D, Aihara A, Matsumura S, Mitsunori Y, Ito H, Akahoshi K, Tanabe M. Is papillectomy for early ampullary carcinoma justified? -Analysis of 65 resected cases - . 11th Annual Academic surgical Congress 2016.02.04 Florida
4. Akahoshi K, Kudo A, Tanabe M. Ischemic Reperfusion Injury by Selective Hepatic Artery Clampig Iduced the Sinusoidal Flow Increase in Rat. Proceedings of the Second International Symposium 2016.02.11 Aichi
5. Tanabe M. State of the Art in radiofrequency, micro-wave, and cryoablation. ASIA IRCAD Advanced Course in Hepatobiliary and Pancreatic surgery 2016.02.26 Taiwan
6. Tanabe M. A difficulty scoring system for resection for hepatocellular carcinoma located in segments of the liver. ASIA IRCAD Advanced Course in Hepatobiliary and Pancreatic surgery 2016.02.26 Taiwan
7. Tanabe M. Technical points: Anatomy around the SMA in pancreatic surgery. ASIA IRCAD Advanced Course in Hepatobiliary and Pancreatic surgery 2016.02.26 Taiwan
8. Kudo A, Tanaka S, Tanabe M. Parametric Imaging to estimate HCC malignancy. Ultrasonic Week 2016 2016.05.28 Kyoto
9. Ban D, Iwao Y, Matsumura S, Ono h, Aihara A, Mitsunori Y, Kudo A, Tanabe M. The optimal pancreatic stump closure method of a laparoscopic distal pancreatectomy: wrapping and fibrin capping technique.. Second Triangle Symposium of the Poland-Hungary-Japan Surgical Society 2016.06.20 Lublin, Poland
10. Oba A, Ban D, Kirimura S, Akahoshi K, Kudo A, Ito H, Matsumura S, Mitsunori Y, Aihara A, Ochiai T, Tanaka S, Tanabe M. Impact of the Biomarkers for the Selection of Gemcitabine and S-1 Adjuvant Chemotherapy in Pancreatic Ductal Adenocarcinoma. IAP&JPS&AOPA2016 2016.08.04 Sendai
11. Ban D, Iwao Y, Ishikawa Y, Watanabe S, Mizuno Y, Chiyonobu N, Ueda H, Ohata Y, Sato T, Mitsunori Y, Matsumura S, Aihara A, Ochiai T, Kudo A, Tanaka S, Tanabe M. The role of local treatment for the recurrence of pancreatic cancer after pancreatectomy. IAP&JPS&AOPA2016 2016.08.04 Sendai
12. Kudo A, Tanaka S, Tanabe M. Hormonal map determines the indication of regional therapy for patients with functional pancreatic neuroendocrine tumor. IAP&JPS&AOPA2016 2016.08.05 Sendai
13. Iwao Y, Ban D, Ishikawa Y, Watanabe S, Ishikawa Y, Mizuno Y, Chiyonobu N, Ueda H, Ohata Y, Oba A, Sato T, Akahoshi K, Ito H, Mitsunori Y, Matsumura S, Aihara A, Ochiai T, Kudo A, Tanaka S, Tanabe M. analysis of the image findings around superior mesenteric artery of invasive ductal carcinoma in the pancreas head. IAP&JPS&AOPA2016 2016.08.06 Sendai
14. Tanabe M. Necessity of a systematic preoperative imaging before laparoscopic cholecystomy ? -Eastern experience. Ircad France 2016 2016.08.21 Strasbourg
15. Tanabe M. Controversies – One port cholesystectomy ; pro side. Ircad France 2016 2016.08.22 Strasbourg
16. Tanabe M. SILS Laparoscopic cholecystectomy Prerecorded LIVE case : Single Port Laparoscopic cholecystectomy. Ircad France 2016 2016.08.22 Strasbourg
17. Tanabe M. Experimental Laboratory - Practice on Live Tissue. Ircad France 2016 2016.08.24 Strasbourg
18. Iwao Y, Ojima H, Tanabe M. Mechanism of Liver Atrophy due to Portal vein Embolization - Association with Autophagy and Apoptosis - . UEGweek 2016 2016.10.17 Vienna,Austria
19. Sato T, Ochiai T, Iwao Y, Ono H, Mitsunori Y, Matsumura S, Aihara A, Ban D, Kudo A, Tanaka S, Tanabe. Prognosis and Therapy for Ruptured Hepatocellular Carcinoma: A single Hospital Experiences. 40th World Congress of the International College of Surgeons 2016.10.25 Kyoto
20. Ochiai T, Yoshino J, Asano D, Watanabe S, Ishikawa Y, Mizuno Y, Chiyonobu N, Ueda H, Sato T, Iwao Y, Ono H, Mitsunori Y, Matsumura S, Aihara A, Ban D, Kudo A, Tanaka S, Tanabe M. The impact of Neo-adjuvant and Adjuvant Hepatic Arterial Infusion Chemotherapy Combined with Hepatectomy for Patients with Advanced Hepatocellular Carcinoma. 40th World Congress of the International College of Surgeons 2016.10.25 Kyoto
21. Ban D. Intraoperative Bleeding Control. WCES & ELSA & CSLES 2016.11.10 Shanghai
22. Tanabe M. Special Lectures. Japan-Taiwan Medical Spectroscopy International Symposium (JTMSIS) 2016.12.07 Awaji Island,Japan

**[Patents]**

1. ORGAN FUNCTION MAINTAINING AND AMELIORATING SOLUTION, Patent Number:PCT/JP2006/304269

**[Awards & Honors]**

1. the Basis Science Travel Grant award of the United European Gastroenterology Week 2016, United European Gastroenterology(UEG), 2016.10

## Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa

Associate Professor: Toshitaka Yoshii

Assistant Professor: Hiroyuki Inose, Yuko Segawa, Koji Fujita, Takashi Hirai, Yoto Oh, Tsuyoshi Yamada

Department of Orthopaedic Research and Development

Associate Professor: Shinichi Sotome, Yoshinori Asou

Joint Research Department of Advanced Medical Technology

Specially Appointed Professor: Shigenori Kawabata

### ( 1 ) Outline

Members of our section and Orthopaedic Joint Sugery section work together in a clinic and OR. Through these practices we train to make the clinical diagnosis and to plan the adequate surgery. We study findings of clinical problem of the locomotorium lesion such as joints, spine and spinal cord, peripheral nerve disorders, aging, injury, tumorigenesis mechanism, and image findings. To solve a lot of clinical question and develop new methodology to treat patients having severe orthopaedic problems, we especcially research spinal cord function, bone regeneration, and pain perception mechanism at dorsal root ganglion.

### ( 2 ) Research

Research themes:

Bone and cartilage metabolism

Development and evaluation of biomaterials for clinical application

Mechanism of spinal ligament ossification

Development of measuring device for spinal cord magnetic signals

Research of bone and spinal metastatic tumors

We collaborate with other sections in our university such as the Clinical Anatomy, the Neurology, and the Physiology and Cell Biology.

### ( 3 ) Education

Our department has several regular program such as "Bedside Professor Round" at Monday 14:30-16:30, "Clinical Conference" at Monday 7:30-9:00, and "Jounal Clubb or Research Progress meeting" at 7:30-8:00 of Tuesday, Thursday, and Friday.

Graduate students in our department can acquire the basic techniques of orthopaedic research and can learn a up-dated knowledge of clinical medicaine through regularly-held journal clubs and research meetings.

#### (4) Lectures & Courses

Japanese orthopaedic research is characterised by the fact that orthopaedic surgeon himself participates experiments while he is working as a clinician. A lot of new knowledge concerning bone, cartilage and nerve were discovered by this so-called "surgeon scientist".

We have already taken a new artificial bone developed in our section to the market and have been preparing a revolutionary measuring device for spinal magnetic signals. We think it very important that research by a surgeon should be based on clinical problems even when methodology of molecular biology is used.

Our graduate students learn basic technique of orthopaedic research and also acquire the ability of life-continuing attitude for clinical studies.

#### (5) Clinical Services & Other Works

Our orthopaedic department consists of two graduate school sections, the Orthopaedic and Spinal Surgery and the Joint Surgery and Sports Medicine. We deal with all kinds of orthopaedic diseases such as spine, hand, hip, knee, and musculo-skeletal tumor. More than twenty registered orthopaedic surgeons belong to our department.

Our anterior cervical operation for OPLL results in a good clinical outcome. We also organize many spinal surgeons who are members of a nation-wide research organization for spinal ligament ossification supported by the Ministry of Health, Labour and Welfare.

#### (6) Clinical Performances

We aim to provide safer surgery to the patients with intractable spinal disease using many kinds of modality as navigation, microscopic surgery, spinal cord monitoring, and intraoperative CAT scan. Treatments of adult spinal deformity and osteoporotic vertebral fracture are our other interest. We have also developed an original artificial bone composed of hydroxyapatite and collagen, now promoting to use aggressively to fill large bone defect.

#### (7) Publications

##### [Original Articles]

1. Yoshinori Asou, Munetaka Iwata, Hiroki Ochi, Maierhaba Ailixiding, Zulipiya Aibibula, Jinying Piao, Guangwen Jin, Yasushi Hara, Atsushi Okawa. Pleiotropic Functions of High Fat Diet in the Etiology of Osteoarthritis. PLoS ONE. 2016; 11(9); e0162794
2. Takashi Hirai, Toshitaka Yoshii, Akio Iwanami, Kazuhiro Takeuchi, Kanji Mori, Tsuyoshi Yamada, Kanichiro Wada, Masao Koda, Yukihiro Matsuyama, Katsushi Takeshita, Masahiko Abematsu, Hiro-taka Haro, Masahiko Watanabe, Kei Watanabe, Hiroshi Ozawa, Haruo Kanno, Shiro Imagama, Shun-suke Fujibayashi, Masashi Yamazaki, Morio Matsumoto, Masaya Nakamura, Atsushi Okawa, Yoshiharu Kawaguchi. Prevalence and Distribution of Ossified Lesions in the Whole Spine of Patients with Cervical Ossification of the Posterior Longitudinal Ligament A Multicenter Study (JOSL CT study). PLoS ONE. 2016; 11(8); e0160117
3. Tomokazu Masaoka, Toshitaka Yoshii, Masato Yuasa, Tsuyoshi Yamada, Takashi Taniyama, Ichiro Tori-goe, Kenichi Shinomiya, Atsushi Okawa, Sadao Morita, Shinichi Sotome. Bone Defect Regeneration by a Combination of a  $\beta$ -Tricalcium Phosphate Scaffold and Bone Marrow Stromal Cells in a Non-Human Primate Model. Open Biomed Eng J. 2016; 10; 2-11
4. Takada R, Jinno T, Tsutsumi Y, Doi H, Muneta T, Okawa A. Inhibitory Effect of Zirconium Coating to Bone Bonding of Titanium Implants in Rat Femur Mater Trans. 2016;
5. Tsuyoshi Yamada, Toshitaka Yoshii, Hiroaki Yasuda, Atsushi Okawa, and Shinichi Sotome. Dexametha-sone Regulates EphA5, a Potential Inhibitory Factor with Osteogenic Capability of Human Bone Marrow Stromal Cells Stem Cells International. 2016.01; 2016;
6. Yamada T, Yoshii T, Egawa S, Takada R, Hirai T, Inose H, Kato T, Jinno T, Okawa A.. Drain Tip Culture is Not Prognostic for Surgical Site Infection in Spinal Surgery Under Prophylactic Use of Antibiotics. Spine (Phila Pa 1976). 2016.02;

7. Sakie Katsumura, Yoichi Ezura, Yayoi Izu, Junpei Shirakawa, Atsushi Miyawaki, Kiyoshi Harada, Masaki Noda. Beta Adrenergic Receptor Stimulation Suppresses Cell Migration in Association with Cell Cycle Transition in Osteoblasts-Live Imaging Analyses Based on Fucci System. *J. Cell. Physiol.*. 2016.02; 231(2); 496-504
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#### [Conference Activities & Talks]

1. Tsuyoshi Yamada, Hideyuki Iwai, Sayuri Nitta, Masakazu Nagahori, Masayoshi Harigai. Creating Medical Innovators – a Whole-brain Approach to Healthcare. 13TH ASIA PACIFIC MEDICAL EDUCATION CONFERENCE (APMEC) 2016 2016.01.15



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5. Gaku Koyano, Tetsuya Jinno, Daisuke Koga, Takeshi Muneta, Atsushi Okawa. Bilateral Comparison of Hip Joint Morphology between the Hips with and without Herniation Pit. Orthopaedic Research Society 2016 Annual Meeting 2016.03.05 Orlando, USA
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8. T. Hirai, T Yoshii, A Iwanami, K Takeuchi, K Mori, T Yamada, S Nishimura, M Matsumoto, M Nakamura, A Okawa, Y Kawaguchi.. Incidence and Distribution of Ossified Lesions in the Whole Spine of Patients with Cervical Ossification of the Posterior Longitudinal Ligament – A Multicenter Study . CSRS-AP2016 2016.04.21 seoul, Korea
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10. Mari Uomizu, Hideya Yoshimura, Akimoto Nimura, Takashi Miyamoto, Tomoyuki Mochizuki. Return to Sports Activity after Arthroscopic Rotator Cuff Repair on the Middle-aged and Senior Patients. The 13th International Congress of Shoulder and Elbow Surgery 2016.05.18 Korea
11. Atsuhiko Tano, Yoto Oh, Yoshiro Kurosa, Atsushi Okawa . “Tangential view” for percutaneous screw fixation of pelvic ring fractures: preoperative calibration of computed tomographic image . 3rd AOTAP Scientific Congress & TK Experts’ Symposium 2016.05.27 China
12. Yoto Oh , Yoshiaki Wakabayashi , Yoshiro Kurosa , Koji Fujita , Atsushi Okawa . Pathogenic mechanism and treatment precaution for atypical femoral fractures: subtype classification through CT-based finite element analysis. 3rd AOTAP Scientific Congress & TK Experts’ Symposium 2016.05.27 China
13. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Masanobu Hirao, Takeshi Muneta, Atsushi Okawa. Limited significance of screening computed tomography after cementless total hip arthroplasty with highly cross-linked polyethylene.. 17th EFORT 2016.06.01 Geneva, Switzerland
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16. Clinical Outcomes of Lumbar Surgery for Hemodialysis Patients. 2016.09.02
17. Hidetoshi Kaburagi, Koji Fujita, Takashi Miyamoto, Yoshiaki Wakabayashi, Ryuichi Kato, Atsushi Okawa. Distal radius fracture patients show reduced ability of dynamic body balancing. The American Society for Bone and Mineral Research 2016 Annual Meeting 2016.09.16 Atlanta, USA

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32. T Hirai, T Yoshii, S Egawa, K Shinomiya, A Okawa.. Long-Term Results Of A Prospective Comparative Study Of Anterior Decompression With Fusion (Adf) And Posterior Decompression With Laminoplasty For The Treatment Of Cervical Spondylotic Myelopathy . 2016 CSRS 2016.11.30 Toronto,Canada

33. T Yoshii, T Hirai, K Sakai, A Okawa, K Shinomiya.. A Prospective Comparative Study in Skin Antiseptic Solutions for Posterior Spine Surgeries: Chlorhexidine-Gluconate Ethanol Vs. Povidone-Iodine . 2016 CSRS 2016.11.30 Toronto,Canada

## Diagnostic Radiology and Nuclear Medicine

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### (1) Outline

While diagnostic radiology and nuclear medicine demand high-level capabilities and therefore extensive training to acquire those capabilities, keeping a watch on developments in medical knowledge and maintaining those skills is also an issue for these disciplines. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Contributing to the community is a basic responsibility of diagnostic radiology so it remains the university's mission to unflinchingly fulfill its responsibility to provide high-level, advanced medical care, working toward resolution of community problems through education, research and medical activities, as well as to develop the diagnostic radiology professionals who will bear the responsibility for providing community medical care, and to develop professionals who have a global outlook and can flourish in this age of globalization. More than ever, advancing the fundamental medical concepts of “patient-oriented medical care” and “thorough medical safety management” are core principles in the field of diagnostic radiology and nuclear medicine, so continuing to maintain capabilities from this perspective is essential in daily practice.

Under the new radiologist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiologist examination (sixth year after graduation). After passing that examination, it is then possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

Diagnostic radiology and nuclear medicine was divided off the specialist field responsible for diagnostic ra-

diology in July 2013. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide it without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 15 external affiliated hospitals approved by JRS as training hospitals. When commencing specialist training, students are allocated to their specialist fields. After the two years of specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. In addition, many also obtain certification as a senior (first class) radiation protection supervisor.

In recent times, diagnostic radiology has been experiencing an increasing load in terms of image processing, the number of image readings, and server storage, owing to improvements in instrument performance. As hybrid imaging such as PET/CT, SPECT/CT, PET/MRI become more prevalent, the diversification of diagnostic methods is accelerating. This trend is expected to continue, so there is a need for work on adequate personnel responses, including infrastructure improvement. And because the combined use of functional images to monitor metabolism and blood flow from morphologic images alone will be fundamental, it is essential that the university goes on enhancing education for radiologists so that they acquire the capabilities to extract and analyze clinically useful information from the complex data gathered.

Remote diagnostic imaging is a good example of this. In regard to its responsibility to contribute to the community, there have been changes in the way diagnostic radiology today has been active in society. The community gives special privileges to the diagnosing doctor, including the exclusive or primary responsibility to provide specified medical services. The university must unwaveringly fulfill its mission as such by providing advanced medical care through medical practice, as well as developing the doctors who will provide healthcare to communities. Although it could not be claimed that the environment surrounding diagnostic radiology in community healthcare has fully matured, as specialists, it is necessary to contribute to the development of local communities and to exercise the privileges granted as specialists: we should carry out our responsibilities while firmly holding to this approach.

## (2) Research

Diagnostic specialists must keep up with the latest research in their fields, applying medical research findings to clinical practice, and making use of continuing education, continuing professional development programs, medical journals, society activities and the internet to maintain their skills. Along with the importance of maintaining awareness of how to interpret and apply research findings to the patient, it is also necessary to go on formulating broad education programs from a specialist perspective, in order to stay well informed about the fundamentals of research methods and to practice appropriate medicine. By managing the faculty effectively, it will go on clarifying radiological perspectives designed to effect inter-disciplinary research activities, taking a whole-university outlook that crosses over the limits of individual departments or graduate schools. The faculty ensures the education and research activities at graduate schools are reflected in the departments while also energetically tackling strategies to secure external funding and strengthen industry collaborations, with the aim of further improving research results. The faculty continues to actively advance international cooperative networks with the Radiological Society of North America (RSNA), the European Congress of Radiology (ECR), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), etc. from the standpoint of diagnostic radiology and nuclear medicine, and continues to advance research based on a thorough awareness of the impacts emerging in the field and the potentialities developing in related practical application fields.

Diagnostic radiology provides diagnoses by extracting information about the morphology of organs and tissues, three-dimensional structures. It is important in terms of learning to systematically organize that information for comparison of imaging study analyses with the reference pathological tissue. Within that, using CT or MRI for tissue characterization that reflects the macro-pathology is important for identifying diseases.

Diagnostic radiology is a discipline in which it is possible to zero in on understanding of a pathological condition by collecting and analyzing blood flow and metabolic data over time. The faculty is continuing research into a minimally invasive method of extracting in vivo blood flow data to enable the use of in vivo dynamic analysis as a biomarker with formulation of dynamic scan protocols that obtain images over time with bolus contrast injection before high-resolution, multi-slice CT or high magnetic field MRI. Texture analysis is applied to both of anatomic and functional imaging modalities. We investigate from first order (kurtosis) to high order (NGLCM, NGTDM, GLSZM). The faculty is also formulating scan protocols that obtain images over time with 3D PET/CT, as a minimally invasive technique of extracting in vivo metabolic data. Known tracers

include 18F-FDG (glucose metabolism), 11C-choline (lipid metabolism), 11C-acetate (lipid metabolism), 18F-FAZA (hypoxia), 18F-FACBC (amino acid metabolism), 62/64Cu-ATSM (redox), 18F-FLT (DNA synthesis), 18F-NaF (bone metabolism), 68Ga-DOTATATE (somatostatin receptor), and 68Ga-DOTA-PEG-RGD/68Ga-DOTA-RGD (angiogenesis). The usefulness of multiple tracers in the discipline of oncology has been observed in numerous carcinomas. As for 68Ga-DOTATATE, theranostics is applied to introduce 177Lu-DOTATATE PRRT. Given the need for examination with standardized imaging and assessment techniques, by conducting a multi-center joint study using PET/CT, the faculty is working to realize and to formulate methodologies for standardization to facilitate participation in global clinical trials in Japan.

### (3) Education

In order to meet the expectations of both the patient and diagnostic radiologist, it is important to know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care, and to continue to independently demonstrate them. Diagnostic radiology demands high-level capabilities, so extensive training is required to acquire those capabilities, while keeping a watch on developments in medical knowledge and maintaining those capabilities is also an issue for the discipline. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global viewpoint, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research capabilities, from the radiological perspective. An essential aspect of postgraduate school education is the ongoing maintenance of capabilities from that perspective.

Under the new radiology specialist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiology specialist examination (sixth year after graduation). After passing that examination, it is possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

In July 2013, radiation oncology was divided into diagnostic radiology and nuclear medicine responsible for diagnostic radiology and radiotherapeutic oncology, in turn responsible for radiotherapy. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide the training without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 11 external affiliated hospitals (five in Tokyo and six in the Kanto region) approved by the Society as training hospitals. When students commence specialist training, they will be allocated to their specialist fields. After the two years of specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all students then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. From the standpoint of managing sealed and unsealed sources in nuclear medicine, many students also obtain certification as a senior (first class) radiation protection supervisor before engaging in clinical and research work.

### (4) Lectures & Courses

The department delivers education based on the university's fundamental policy aimed at realization of its mission: to contribute to the development of society, with a specific mission to bear the responsibility for the basic functions of education, research and medical care. As a department at the core of medical care, it develops professionals who can engage in practice across different fields, taking the approach that the standards of behavior demonstrated by diagnostic radiologists in clinical practice have far more impact than the formal curriculum in ethics.



The department develops professionals who can continue to work to resolve the issues faced by the university hospital, professionals who know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care to meet the expectations of both the patient and student, can independently demonstrate them, and can flourish while maintaining a global outlook. Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global perspective, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research capabilities, from the radiological perspective.

## ( 5 ) Clinical Services & Other Works

### Diagnostic Radiology

- CT: A total of three CT scanners are involved in diagnostic radiology: two in the radiology department (64-slice MDCT) and one in the ER center (16-slice MDCT). Not only has the number of examinations using MDCT increased, but it has been possible to obtain improved diagnostic performance by reading MPR (multi-planar reconstruction) images and 1-mm thick images.
- MRI: A total of four MRI scanners are involved in diagnostic radiology: two 1.5-tesla scanners and two 3-tesla scanners. This has allowed for an increase in examinations.
- Ultrasound: The main examinations carried out by diagnostic radiologists are breast and abdominal examinations.
- Angiography and Interventional Radiology (IVR): In the vascular area: TAE for hepatic carcinoma, PTA and stent placement for occlusive arterial disease, intraarterial injection for pelvic tumor, and emergency hemostasis for ER center patients. In the non-vascular area: mainly CT-guided chest biopsy, breast mass biopsy and lymph node biopsy.
- Breast: The department is responsible for breast diagnostic radiology and collaborates with the breast surgery department in team medical care. The department endeavors to diagnose breast cancer at an early stage, provide accurate pre-surgery diagnoses, and formulate treatment plans by providing high-quality diagnostic radiology services combining mammography reading, ultrasound examination, as well as MRI and FDG-PET/CT, in addition to providing image-guided biopsy and surgical marking.
- Conferences: The department holds inter-disciplinary conferences with all departments on a daily basis. The department holds its internal conference every Friday and participates in externally conducted conferences, as appropriate. The department also takes a lead role in organizing conferences aimed at external attendees (Shoheizaka Radiology: twice a year), and the three-university joint conferences (three times a year).

### Nuclear Medicine

- Since the department began operating its second PET/CT scanner in November 2006, it has been conducting 15 to 16 PET examinations per day, mainly for malignant tumor, as well as eight to 10 general radioisotope examinations per day, mainly brain and myocardial SPECT. PET/CT for radiation planning and C-11 acetate PET/CT for hematologic malignancies were introduced in 2016.

## ( 6 ) Clinical Performances

Being a core diagnosis and treatment department, diagnostic radiology and nuclear medicine is a department that engages in inter-disciplinary clinical practice forming strong partnerships to meet the needs of its internal client departments and works to resolve issues faced by the university hospital, bearing its responsibility to unswervingly fulfill its mission from a global perspective. Diagnostic radiology and nuclear medicine is equipped with the capabilities to process large volumes of imaging information, it develops problem presentation, technical skill acquisition, and collaboration with all departments, and possesses the characteristics to go on conscientiously tackling new modalities, probes and contrasts as well as clinical trials.



## (7) Publications

## [Original Articles]

1. Shibata H, Kato S, Sekine I, Abe K, Araki N, Iguchi H, Izumi T, Inaba Y, Osaka I, Kato S, Kawai A, Kinuya S, Kodaira M, Kobayashi E, Kobayashi T, Sato J, Shinohara N, Takahashi S, Takamatsu Y, Takayama K, Takayama K, Tateishi U, Nagakura H, Hosaka M, Morioka H, Moriya T, Yuasa T, Yurikusa T, Yomiya K, Yoshida M. Diagnosis and treatment of bone metastasis: comprehensive guideline of the Japanese Society of Medical Oncology, Japanese Orthopedic Association, Japanese Urological Association, and Japanese Society for Radiation Oncology. *ESMO Open*. 2016; 1(2); e000037
2. Yoshio Kitazume, Shin-ichi Taura, Shuichiro Nakaminato, Osamu Noguchi, Yuki Yoshi Masaki, Ichiro Kasahara, Mitsuhiro Kishino, Ukihide Tateishi. Diffusion-Weighted Magnetic Resonance Imaging to Differentiate Malignant from Benign Gallbladder Disorders *European Journal of Radiology*. 2016;
3. Matsuhisa Akiyuki, Kishino Mitsuhiro, Nakadate Masashi, Kudo Toshifumi, Inoue Yoshinori, Tateishi Ukihide. Embolosclectherapy by the Transvenous Approach for Lower Extremity Arteriovenous Malformation in Cowden Syndrome: A Case Report. *Ann Vasc Dis*. 2016; 9(1); 66-69
4. Uehara Takeaki, Takeno Mitsuhiro, Hama Maasa, Yoshimi Ryusuke, Suda Akiko, Ihata Atsushi, Ueda Atsuhisa, Tateishi Ukihide, Ishigatsubo Yoshiaki. Deep-inspiration breath-hold (18)F-FDG-PET/CT is useful for assessment of connective tissue disease associated interstitial pneumonia. *Mod Rheumatol*. 2016.01; 26(1); 121-127
5. Yamada I, Hikishima K, Miyasaka N, Kato K, Kojima K, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H. Gastric carcinoma: evaluation with diffusion-tensor MR imaging and tractography ex vivo. *Magn Reson Imaging*. 2016.02; 34(2); 144-151
6. Yoshiaki Katada, Shunichi Kondo, Eitoshi Tsuboi, Kyu Rokkaku, Yoshihito Irie, Hitoshi Yokoyama. Endovascular Total Arch Repair Using In Situ Fenestration for Arch Aneurysm and Chronic Type A Dissection. *Ann. Thorac. Surg.*. 2016.02; 101(2); 625-630
7. Nakaigawa Noboru, Kondo Keiichi, Tateishi Ukihide, Minamimoto Ryogo, Kaneta Tomohiro, Namura Kazuhiro, Ueno Daiki, Kobayashi Kazuki, Kishida Takeshi, Ikeda Ichiro, Hasumi Hisashi, Makiyama Kazuhide, Kubota Yoshinobu, Inoue Tomio, Yao Masahiro. FDG PET/CT as a prognostic biomarker in the era of molecular-targeting therapies: max SUVmax predicts survival of patients with advanced renal cell carcinoma. *BMC Cancer*. 2016.02; 16; 67
8. Torii Ikuo, Tateishi Ukihide, Terauchi Takashi, Inoue Tomio. Prognostic implications of diffusion-weighted magnetic resonance imaging in patients with superior sulcus tumors receiving induction chemoradiation therapy. *Jpn J Clin Oncol*. 2016.03; 46(3); 264-269
9. Oyama Jun, Mori Kouichi, Imamura Masatoshi, Mizushima Yukiko, Tateishi Ukihide. Size of the intracranial optic nerve and optic tract in neonates at term-equivalent age at magnetic resonance imaging. *Pediatr Radiol*. 2016.04; 46(4); 527-533
10. Kazuo Ohtsuka, Kento Takenaka, Yoshio Kitazume, Toshimitsu Fujii, Katsuyoshi Matsuoka, Maiko Kimura, Takashi Nagaishi, Mamoru Watanabe. Magnetic resonance enterography for the evaluation of the deep small intestine in Crohn's disease. *Intest Res*. 2016.04; 14(2); 120-126
11. Haruka Maneyama, Naoyuki Miyasaka, Kimio Wakana, Megumi Nakamura, Yoshio Kitazume, Toshiro Kubota. Vanishing intravenous leiomyomatosis after hysterectomy: Assessment of the need to perform complete resection. *J. Obstet. Gynaecol. Res.*. 2016.04;
12. Iwasa Y, Kitazume Y, Tateishi U, Saida Y, Ban D, Tanabe M, Takemoto A.. Hepatocellular Carcinoma Histological Grade Prediction: A Quantitative Comparison of Diffusion-Weighted, T2-Weighted, and Hepatobiliary-Phase Magnetic Resonance Imaging. *J Comput Assist Tomogr*. . 2016.05; 40(3); 463-470
13. Mitsuhiro Tozaki, Yoshifumi Kuroki, Mari Kikuchi, Yasuyuki Kojima, Kazunori Kubota, Hiroshi Nakahara, Yoshinori Ito, Hirofumi Mukai. The Japanese Breast Cancer Society clinical practice guidelines for screening and imaging diagnosis of breast cancer, 2015 edition *Breast Cancer*. 2016.06;

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15. Hibi Toshifumi, Hirohata Shunsei, Kikuchi Hiroto, Tateishi Ukihide, Sato Noriko, Ozaki Kunihiro, Kondo Kazuoki, Ishigatsubo Yoshiaki. Infliximab therapy for intestinal, neurological, and vascular involvement in Behcet disease: Efficacy, safety, and pharmacokinetics in a multicenter, prospective, open-label, single-arm phase 3 study. *Medicine (Baltimore)*. 2016.06; 95(24); e3863
16. Nakadate Masashi, Miyamoto Norikazu, Starkey Jay, Toriihara Akira, Tateishi Ukihide. Anterograde Degeneration of the Nigrostriatal Pathway Visualized by 123I-FP-CIT SPECT in a Patient With Artery of Percheron Infarction. *Clin Nucl Med*. 2016.06; 41(6); 483-484
17. Yamada I, Hikishima K, Miyasaka N, Kato K, Ito E, Kojima K, Kawano T, Kobayashi D, Eishi Y, Okano H. q-Space MR imaging of gastric carcinoma ex vivo: correlation with histopathologic findings. *Magn Reson Med*. 2016.08; 76(2); 602-612
18. Tomoyuki Fujioka, Kazunori Kubota, Akira Toriihara, Youichi Machida, Kaori Okazawa, Tsuyoshi Nakagawa, Yukihisa Saida, Ukihide Tateishi. Tumor characteristics of ductal carcinoma in situ of breast visualized on [ F-18] fluorodeoxyglucose-positron emission tomography/computed tomography: Results from a retrospective study. *World J Radiol*. 2016.08; 8(8); 743-749
19. Nozaki T, Tasaki A, Horiuchi S, Ochi J, Starkey J, Hara T, Saida Y, Yoshioka H. Predicting Retear after Repair of Full-Thickness Rotator Cuff Tear: Two-Point Dixon MR Imaging Quantification of Fatty Muscle Degeneration-Initial Experience with 1-year Follow-up. *Radiology*. 2016.08; 280(2); 500-509
20. Nozaki T, Morita Y, Hasegawa D, Makidono A, Yoshimoto Y, Starkey J, Kusakawa I, Manabe A, Saida Y. Cervical ultrasound and computed tomography of Kawasaki disease: Comparison with lymphadenitis. *Pediatr Int*. 2016.11; 58(11); 1146-1152
21. Kamo Minobu, Nozaki Taiki, Yoshida Kyoko, Tateishi Ukihide, Akita Keiichi. Kinking of the upper ureter in CT urography: anatomic and clinical significance. *Surg Radiol Anat*. 2016.12; 38(10); 1115-1121
22. Masashi Nakadate, Norikazu Miyamoto, Jay Starkey, Akira Toriihara, Ukihide Tateishi. Anterograde degeneration of the nigrostriatal pathway visualized by 123I-FP-CIT SPECT in patient with artery of Percheron infarction. *Clin Nucl Med*. 41; 483-484
23. Yojiro Umezaki, Anna Miura, Motoko Watanabe, Miho Takenoshita, Akihito Uezato, Akira Toriihara, Toru Nishikawa, Akira Toyofuku. Oral ceneesthopathy Biopsychosoc Med. 10; 20

#### [Books etc]

1. Fukui Tsugiya, Nara Nobuo, Yukihisa Saida et al. . Medical Diagnosis 3rd ed.. 2016.02 (ISBN : 978-4-260-02064-0)

#### [Conference Activities & Talks]

1. T. Fujioka, E. Yamaga, K. Kubota, M. Kishino, Y. Kitazume, Y. Saida, U. Tateishi. Gastrointestinal tumor syndrome; What radiologist should know!! European Congress of Radiology 2016.03
2. Kazunori Kubota, Tomoyuki Fujioka, Kaori Okazawa, Makiko Honda, Emi N Yamaga, Akira Toriihara, Yukihisa Saida, Ukihide Tateishi. Intratumoral heterogeneity of Breast Cancer in Diagnostic Imaging. ECR 2016 2016.03.02
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4. Yoshio Kitazume, Tomoyuki Fujioka, Kento Takenaka, Toshimitsu Fujii, Kazuo Ohtsuka, Yukihisa Saida, Ukihide Tateishi. Can magnetic resonance enterocolonography reflect the presence of partial mucosal healing in patients with Crohn's disease?. European Congress of Radiology 2016.03.02 Vienna

5. Tomoyuki Fujioka, Emi Yamaga, Kazunori Kubota Akira Toriihara, Yukihiisa Saida, Ukihide Tateishi. Diagnostic imaging of olfactory disorder: review according to the 'pathway of smell'. The 4th Congress of the Japan Oncoplastic Breast Surgery Society 2016.04 Yokohama
6. Akira Toriihara, Masashi Nakadate, Tomoyuki Fujioka, Jun Oyama, Atsunobu Tsunoda, Takuro Sumi, Ukihide Tateishi. Utility of pretherapeutic FDG-PET/CT for evaluating cancer of external auditory canal.. JRS 75th Annual Meeting 2016.04.14 Yokohama
7. Yoshio Kitazume , Tomoyuki Fujioka , Kento Takenaka, Kazuo Ohtsuka, Yukihiisa Saida, Ukihide Tateishi. Magnetic Resonance Enterocolonography Reflects the Presence of Partial Mucosal Healing in Patients with Crohn's Disease. The 75th Annual Meeting of the Japan Radiological Society 2016.04.16
8. Kazunori Kubota, Tomoyuki Fujioka, Kaori Okazawa, Akira Toriihara, Makiko Honda, Emi N Yamaga, Yukihiisa Saida, Ukihide Tateishi. Imaging phenotypes of 18F-FDG PET/CT and MRI in Predicting the Clinicopathologic Subtypes of Triple Negative Breast Cancers.. The 75th Annual Meeting of the Japan Radiological Society 2016.04.16
9. Saida Yukihiisa, Yamagiwa Ken, Ito Takashi. Grooves on the hepatic surface: Corset liver or anatomical variants?. GJRA meeting 2016.06
10. Akira Toriihara, Shin Nakamura, Akira Toyofuku, Ukihide Tateishi. Usefulness of molecular imaging for patients with dental diseases.. SNMMI 63rd Annual Meeting 2016.06.12
11. Yukihiisa Saida,Ken Yamagiwa,Namiko Matsui,Tomoyuki Fujioka,Yoshihiro Iwasa,Mitsuhiro Kishino,Takashi Ito. Consideration of the etiology of the accessory hepatic fissures.. The 32nd Annual Meeting of Japanese Society of Abdominal Radiology 2016.06.24
12. Yoshiaki Katada, Yoshihito Irie, Shunichi Kondo, Hitoshi Nakanowatari, Yoshiki Endo, Hitoshi Yokoyama. Transcatheter plug closure of mitral paravalvular leaks by transapical approach.. ISMICS2016 winter workshop 2016.10
13. Yamada I, Yoshino N, Hikishima K, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal Carcinoma: Ex Vivo Evaluation with 3-T High-Spatial-Resolution Quantitative T2 Mapping–Correlation with Histopathologic Findings (Yamada I, et al.). The 102nd Scientific Assembly and Annual Meeting of the Radiological Society of North America 2016.11 Chicago, USA

# Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka

Project Assistant Professor, Ryo Watanabe

## (1) Research

- 1) Elucidation of genetic architecture of human metabolic diseases using genome and meta-genome information
- 2) Identification of biomarkers for personalized medicine
- 3) Pharmacogenomics
- 4) Functional genomics
- 5) Statistical genetics and genome drug discovery

## (2) Lectures & Courses

As we say “Every human is different”, human genetic diversity has essential impacts on clinical fields, e.g. disease risk, clinical efficacy, and drug responses. Our laboratory aims to elucidate the diversity of human being through comprehensive research activities including genome and epi-genome analyses of human diseases, methodological development of statistical genetics, and human resources cultivation to achieve personalized medicine.

## (3) Publications

### [Original Articles]

1. Imamura Minako, Takahashi Atsushi, Yamauchi Toshimasa, Hara Kazuo, Yasuda Kazuki, Grarup Niels, Zhao Wei, Wang Xu, Huerta-Chagoya Alicia, Hu Cheng, Moon Sanghoon, Long Jirong, Kwak Soo Heon, Rasheed Asif, Saxena Richa, Ma Ronald C W, Okada Yukinori, Iwata Minoru, Hosoe Jun, Shojima Nobuhiro, Iwasaki Minaka, Fujita Hayato, Suzuki Ken, Danesh John, Jorgensen Torben, Jorgensen Marit E, Witte Daniel R, Brandslund Ivan, Christensen Cramer, Hansen Torben, Mercader Josep M, Flannick Jason, Moreno-Macias Hortensia, Burt Noel P, Zhang Rong, Kim Young Jin, Zheng Wei, Singh Jai Rup, Tam Claudia H T, Hirose Hiroshi, Maegawa Hiroshi, Ito Chikako, Kaku Kohei, Watada Hirotaka, Tanaka Yasushi, Tobe Kazuyuki, Kawamori Ryuzo, Kubo Michiaki, Cho Yoon Shin, Chan Juliana C N, Sanghera Dharambir, Frossard Philippe, Park Kyong Soo, Shu Xiao-Ou, Kim Bong-Jo, Florez Jose C, Tusie-Luna Teresa, Jia Weiping, Tai E Shyong, Pedersen Oluf, Saleheen Danish, Maeda Shiro, Kadowaki Takashi. Genome-wide association studies in the Japanese population identify seven novel loci for type 2 diabetes. *Nat Commun.* 2016; 7; 10531
2. Okada Yukinori, Muramatsu Tomoki, Suita Naomasa, Kanai Masahiro, Kawakami Eiryo, Iotchkova Valentina, Soranzo Nicole, Inazawa Johji, Tanaka Toshihiro. Significant impact of miRNA-target gene networks on genetics of human complex traits. *Sci Rep.* 2016; 6; 22223
3. Onouchi Yoshihiro, Fukazawa Ryuji, Yamamura Kenichiro, Suzuki Hiroyuki, Kakimoto Nobuyuki, Suenaga Tomohiro, Takeuchi Takashi, Hamada Hiromichi, Honda Takafumi, Yasukawa Kumi, Terai Masaru, Ebata Ryota, Higashi Kouji, Saji Tsutomu, Kemmotsu Yasushi, Takatsuki Shinichi, Ouchi Kazunobu, Kishi Fumio, Yoshikawa Tetsushi, Nagai Toshiro, Hamamoto Kunihiro, Sato Yoshitake, Honda Akihito,

- Kobayashi Hironobu, Sato Junichi, Shibuta Shoichi, Miyawaki Masakazu, Oishi Ko, Yamaga Hironobu, Aoyagi Noriyuki, Yoshiyama Megumi, Miyashita Ritsuko, Murata Yuji, Fujino Akihiro, Ozaki Kouichi, Kawasaki Tomisaku, Abe Jun, Seki Mitsuru, Kobayashi Tohru, Arakawa Hirokazu, Ogawa Shunichi, Hara Toshiro, Hata Akira, Tanaka Toshihiro. Variations in ORAI1 Gene Associated with Kawasaki Disease. *PLoS One*. 2016; 11(1); e0145486
4. Atsuko Konta, Kouichi Ozaki, Yasuhiko Sakata, Atsushi Takahashi, Takashi Morizono, Shinichiro Suna, Yoshihiro Onouchi, Tatsuhiko Tsunoda, Michiaki Kubo, Issei Komuro, Yoshinobu Eishi, Toshihiro Tanaka. A functional SNP in FLT1 increases risk of coronary artery disease in a Japanese population. *J. Hum. Genet.*. 2016.01;
  5. Hirofumi Zempo, Jun-Ichi Suzuki, Masahito Ogawa, Ryo Watanabe, Mitsuaki Isobe. A different role of angiotensin II type 1a receptor in the development and hypertrophy of plantaris muscle in mice. *J. Appl. Genet.*. 2016.02; 57(1); 91-97
  6. Sun Celi, Molineros Julio E, Looger Loren L, Zhou Xu-Jie, Kim Kwangwoo, Okada Yukinori, Ma Jianyang, Qi Yuan-Yuan, Kim-Howard Xana, Motghare Prasenjeet, Bhattarai Krishna, Adler Adam, Bang So-Young, Lee Hye-Soon, Kim Tae-Hwan, Kang Young Mo, Suh Chang-Hee, Chung Won Tae, Park Yong-Beom, Choe Jung-Yoon, Shim Seung Cheol, Kochi Yuta, Suzuki Akari, Kubo Michiaki, Sumida Takayuki, Yamamoto Kazuhiko, Lee Shin-Seok, Kim Young Jin, Han Bok-Ghee, Dozmorov Mikhail, Kaufman Kenneth M, Wren Jonathan D, Harley John B, Shen Nan, Chua Kek Heng, Zhang Hong, Bae Sang-Cheol, Nath Swapan K. High-density genotyping of immune-related loci identifies new SLE risk variants in individuals with Asian ancestry. *Nat Genet*. 2016.03; 48(3); 323-330
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  11. S-W Chang, C W McDonough, Y Gong, T A Johnson, T Tsunoda, E R Gamazon, M A Perera, A Takahashi, T Tanaka, M Kubo, C J Pepine, J A Johnson, R M Cooper-DeHoff. Genome-wide association study identifies pharmacogenomic loci linked with specific antihypertensive drug treatment and new-onset diabetes. *Pharmacogenomics J.*. 2016.09;
  12. Nobue Yagihara, Hiroshi Watanabe, Phil Barnett, Laetitia Duboscq-Bidot, Attack C Thomas, Ping Yang, Seiko Ohno, Kanae Hasegawa, Ryoza Kuwano, Stéphanie Chatel, Richard Redon, Jean-Jacques Schott, Vincent Probst, Tamara T Koopmann, Connie R Bezzina, Arthur A M Wilde, Yukiko Nakano, Takeshi Aiba, Yoshihiro Miyamoto, Shiro Kamakura, Dawood Darbar, Brian S Donahue, Daichi Shigemizu, Toshihiro Tanaka, Tatsuhiko Tsunoda, Masayoshi Suda, Akinori Sato, Tohru Minamino, Naoto Endo, Wataru Shimizu, Minoru Horie, Dan M Roden, Naomasa Makita. Variants in the SCN5A Promoter Associated With Various Arrhythmia Phenotypes. *J Am Heart Assoc*. 2016.09; 5(9);
  13. Masahiro Kanai, Toshihiro Tanaka, Yukinori Okada. Empirical estimation of genome-wide significance thresholds based on the 1000 Genomes Project data set. *J. Hum. Genet.*. 2016.10; 61(10); 861-866
  14. Tumurkhuu T, Fujiwara T, Komazaki Y, Kawaguchi Y, Tanaka T, Inazawa J, Ganburged G, Bazar A, Ogawa T, Moriyama K. Association between maternal education and malocclusion in Mongolian adolescents: a cross-sectional study. *BMJ Open*. 2016.11; 6(11);
  15. Lian Liu, Yusuke Ebana, Jun-Ichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Toshihiro Tanaka, Masatoshi Komura, Mitsuaki Isobe, Tetsushi Furukawa. Genetic Variants Associated With Susceptibility to Atrial Fibrillation in a Japanese Population. *Can J Cardiol*. 2016.11;

16. Hirofumi Zempo, Jun-Ichi Suzuki, Masahito Ogawa, Ryo Watanabe, Katsuhito Fujiu, Ichiro Manabe, Simon J Conway, Yoshiaki Taniyama, Ryuichi Morishita, Yasunobu Hirata, Mitsunori Isobe, Ryozi Nagai. Influence of periostin-positive cell-specific Klf5 deletion on aortic thickening in DOCA-salt hypertensive mice. *Hypertens. Res.* 2016.11; 39(11); 764-768
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19. Chisato Shimizu, Hariklia Eleftherohorinou, Victoria J Wright, Jihoon Kim, Martin P Alphonse, James C Perry, Rolando Cimaz, David Burgner, Nagib Dahdah, Long T Hoang, Chiea Chuen Khor, Andrea Salgado, Adriana H Tremoulet, Sonia Davila, Taco W Kuijpers, Martin L Hibberd, Todd A Johnson, Atsushi Takahashi, Tatsuhiko Tsunoda, Michiaki Kubo, Toshihiro Tanaka, Yoshihiro Onouchi, Rae S M Yeung, Lachlan J M Coin, Michael Levin, Jane C Burns, . Genetic Variation in the SLC8A1 Calcium Signaling Pathway Is Associated With Susceptibility to Kawasaki Disease and Coronary Artery Abnormalities. *Circ Cardiovasc Genet*. 2016.12; 9(6); 559-568

#### [Misc]

1. Toshihiro Tanaka, Akinori Kimura. Cardiovascular genetics. *J. Hum. Genet.* 2016.01; 61(1); 1

#### [Conference Activities & Talks]

1. Onouchi Y, Nakagawa H, Shigemizu D, Ozaki K, Nakamura Y, Asami Y, Seki M, Kobayashi T, Kochi Y, Toda T, Satake W, Hata A, Tsunoda T, Tanaka T, Japan Kawasaki Disease Genome Consortium. Search for genetic variations responsible for giant coronary aneurysms in Kawasaki disease patients by whole exome sequencing. *ICHG2016* 2016.04.04
2. Takeaki Sudo, Yukinori Okada, Hiroaki Kobayashi, Misa Gokyu, Yuichi Izumi, Toshihiro Tanaka. Whole-exome sequencing reveals a novel gene as a cause of Aggressive periodontitis in Japanese consanguineous families. *The 13th International Congress of Human Genetics* 2016.04.04
3. Fares Taie L, Gerber S, Tawara A, Ramirez-Miranda A, Douet JY, Verdin H, Zanteno JC, Kondo H, Passet B, Yamamoto K, Iwai M, Tanaka T, Nakamura Y, Kimura W, Munnich A, Baere ED, Raymond-Letron I, Kaplan J, Calvas P, Roche O, Rozet JM. Submicroscopic deletions at 13q32.1 cause congenital microcoria. *ICHG2016* 2016.04.05
4. Ozaki K, Morizono T, Tsunoda T, Kubo M, Tanaka T. Up-regulation of FLT1 by a novel functional SNP increases risk of coronary artery disease through an inflammatory activation. *ICHG2016* 2016.04.07
5. Kanai M, Tanaka T, Okada Y. Empirical estimation of genome-wide significance thresholds based on the 1000 Genomes Project dataset. *ICHG2016* 2016.04.07
6. Kanai M, Okada Y, Muramatsu T, Suita N, Kawakami E, Iotchkova V, Soranzo N, Inazawa J, Tanaka T. Significant impact of miRNA-target gene networks on genetics of human complex traits. *ICHG2016* 2016.04.07
7. Tanaka T. Exome Analyses of Long QT Syndrome. *Symposium20 Annual Meeting of the Japanese Heart Rhythm Society* 2016 2016.07.16 Sapporo Convention Center

#### [Others]

1. Tanaka T. Chairs, 2016.04  
Complex traits and polygenic disorders2.  
Concurrent Oral Session 20.  
*ICHG2016*



# Applied Regenerative Medicine

Professor: Ichiro SEKIYA  
Assistant Professor: Masafumi HORIE, Koji OTABE,  
Hisako KATANO  
Project Assistant Professor: Nobutake OZEKI, Yusuke NAKAGAWA,  
Mitsuru MIZUNO, Keiichiro KOMORI  
Graduate Student: Kenta KATAGIRI, Yuji KONO, Naoto WATANABE,  
Yoshihisa KUSHIDA, Taihei TODA, Mana NARITOMI  
Technical Staff : Yukie MATSUMOTO, Shizuka FUJII,  
Teruko NAKAMURA  
Assistant Clerk: Mika WATANABE, Kimiko TAKANASHI

## ( 1 ) Outline

Our purpose is to support and advance stem cell research and regenerative medicine for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury.

## ( 2 ) Research

- 1) Development of regenerative medicine with stem cells.
- 2) Realization and industrialization of cell and regenerative therapy.
- 3) Establishment of safety test for regenerative medicine.
- 4) Translational research.

## ( 3 ) Clinical Services & Other Works

We have started a clinical study in that autologous synovial mesenchymal stem cells were transplanted with meniscus repair to regenerate lateral osteoarthritis of the knee in which the lateral meniscus was extruded and the cartilage was defected.

## ( 4 ) Publications

### [Original Articles]

1. Yusuke Nakagawa, Ichiro Sekiya, Shimpei Kondo, Takashi Tabuchi, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Takeshi Muneta. Relationship between MRI T1 rho value and histological findings of intact and radially incised menisci in microminipigs. J Magn Reson Imaging. 2016.02; 43(2); 434-445
2. Yusuke Nakagawa, Takeshi Muneta, Koji Otabe, Nobutake Ozeki, Mitsuru Mizuno, Mio Udo, Ryusuke Saito, Katsuaki Yanagisawa, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Cartilage Derived from Bone Marrow Mesenchymal Stem Cells Expresses Lubricin In Vitro and In Vivo. PLoS ONE. 2016.02; 11(2); e0148777



3. Chisato Sato, Yoshitaka Iso, Takuya Mizukami, Koji Otabe, Masahiro Sasai, Masaaki Kurata, Takeyuki Sanbe, Ichiro Sekiya, Akira Miyazaki, Hiroshi Suzuki. Fibroblast growth factor-23 induces cellular senescence in human mesenchymal stem cells from skeletal muscle. *Biochem. Biophys. Res. Commun.* 2016.02; 470(3); 657-662
4. Shimpei Kondo, Takeshi Muneta, Yusuke Nakagawa, Hideyuki Koga, Toshifumi Watanabe, Kunikazu Tsuji, Shinichi Sotome, Atsushi Okawa, Shinji Kiuchi, Hideo Ono, Mitsuru Mizuno, Ichiro Sekiya. Transplantation of autologous synovial mesenchymal stem cells promotes meniscus regeneration in aged primates. *J. Orthop. Res.* 2016.02;
5. Toshifumi Watanabe, Takeshi Muneta, Kazuyoshi Yagishita, Kenji Hara, Hideyuki Koga, Ichiro Sekiya. Closed Suction Drainage Is Not Necessary for Total Knee Arthroplasty: A Prospective Study on Simultaneous Bilateral Surgeries of a Mean Follow-Up of 5.5 Years. *J Arthroplasty.* 2016.03; 31(3); 641-645
6. Katsuaki Yanagisawa, Takeshi Muneta, Nobutake Ozeki, Yusuke Nakagawa, Mio Udo, Ryusuke Saito, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Weekly injections of Hylan G-F 20 delay cartilage degeneration in partial meniscectomized rat knees. *BMC Musculoskelet Disord.* 2016.04; 17(1); 188
7. Kazumasa Miyatake, Takeshi Muneta, Miyoko Ojima, Jun Yamada, Yu Matsukura, Kahaer Abula, Ichiro Sekiya, Kunikazu Tsuji. Coordinate and synergistic effects of extensive treadmill exercise and ovariectomy on articular cartilage degeneration. *BMC Musculoskelet Disord.* 2016.05; 17(1); 238
8. Mai Katakura, Hideyuki Koga, Kaori Nakamura, Ichiro Sekiya, Takeshi Muneta. Effects of different femoral tunnel positions on tension changes in anterolateral ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2016.05;
9. N Ozeki, T Muneta, H Koga, Y Nakagawa, M Mizuno, K Tsuji, Y Mabuchi, C Akazawa, E Kobayashi, K Matsumoto, K Futamura, T Saito, I Sekiya. Not single but periodic injections of synovial mesenchymal stem cells maintain viable cells in knees and inhibit osteoarthritis progression in rats. *Osteoarthr. Cartil.* 2016.06; 24(6); 1061-1070
10. Hiroki Katagiri, Kaori Nakamura, Toshifumi Watanabe, Hideyuki Koga, Kazuyoshi Yagishita, Ichiro Sekiya, Takeshi Muneta. Increase of patellofemoral height has decreased maximum knee flexion after total knee arthroplasty of posterior cruciate-substituting prosthesis in a clinical series. *J Orthop Sci.* 2016.07; 21(4); 458-462
11. M Udo, T Muneta, K Tsuji, N Ozeki, Y Nakagawa, T Ohara, R Saito, K Yanagisawa, H Koga, I Sekiya. Monoiodoacetic acid induces arthritis and synovitis in rats in a dose- and time-dependent manner: proposed model-specific scoring systems. *Osteoarthr. Cartil.* 2016.07; 24(7); 1284-1291
12. Takeshi Muneta, Hideyuki Koga, Tomomasa Nakamura, Masafumi Horie, Toshifumi Watanabe, Ichiro Sekiya. Behind-remnant arthroscopic observation and scoring of femoral attachment of injured anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc.* 2016.09; 24(9); 2906-2914
13. Koga H, Muneta T, Watanabe T, Mochizuki T, Horie M, Nakamura T, Otabe K, Nakagawa Y, Sekiya I.. Two-Year Outcomes After Arthroscopic Lateral Meniscus Centralization Arthroscopy. 2016.10; 32(10); 2000-2008
14. Watanabe T, Muneta T, Koga H, Horie M, Nakamura T, Otabe K, Nakagawa Y, Katakura M, Sekiya I.. In-vivo kinematics of high-flex posterior-stabilized total knee prosthesis designed for Asian populations. *Int Orthop.* 2016.11; 40(11); 2295-2302
15. Kaori Nakamura, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Takeshi Muneta. Dynamic Evaluation of Pivot-Shift Phenomenon in Double-Bundle Anterior Cruciate Ligament Reconstruction Using Triaxial Accelerometer. *Arthroscopy.* 2016.12; 32(12); 2532-2538
16. Inoue M, Muneta T, Ojima M, Nakamura K, Koga H, Sekiya I, Okazaki M, Tsuji K.. Inflammatory cytokine levels in synovial fluid 3, 4 days postoperatively and its correlation with early-phase functional recovery after anterior cruciate ligament reconstruction: a cohort study. *J Exp Orthop.* 2016.12; 3(1); 30

17. Toshiyuki Ohara, Takeshi Muneta, Yusuke Nakagawa, Yu Matsukura, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. < Original Article> Hypoxia enhances proliferation through increase of colony formation rate with chondrogenic potential in primary synovial mesenchymal stem cells. J. Med. Dent. Sci.. 2016.12; 63(4); 61-70

#### [Conference Activities & Talks]

1. Yusuke Nakagawa, Hideyuki Koga, Takeshi Muneta, Kiuchi S, Ono H, Nagata T, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Hisako Katano, Ichiro Sekiya. Three-dimensional Reconstructed MRI Evaluation of Arthroscopic Centralization Technique for Extruded Lateral Meniscus. ORS 2016 2016.03.05
2. Koji Otabe, Ken Watanabe, Norio Shimizu, Takeshi Muneta, Ichiro Sekiya. High Sensitivity Virus / Mycoplasma Screening Test Reveals High Prevalence of Parvovirus B19 Infection In Synovial Tissues and Bone Marrow. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
3. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Nobutake Ozeki, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya. PDGF-AA/AB In Human Serum Are Potential Indicators Of The Proliferative Capacity Of Human Synovial Mesenchymal Stem Cells. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
4. Mitsuru Mizuno, Hisako Katano, Yo Mabuchi, Yusuke Ogata, Shizuko Ichinose, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Nobutake Ozeki, Kunikazu Tsuji, Chihiro Akazawa, Takeshi Muneta, Ichiro Sekiya. Properties of MSCs Derived From Surface, Stroma, and Perivascular Synovium Of Oa Patients. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
5. Kenta Katagiri, Takeshi Muneta, Koji Otabe, Yu Matsukura, Hisako Katano, Ichiro Sekiya. Fibrous Synovium Releases Higher Number Of MSCs Than Adipose Synovium in a Suspended Synovium Culture Model. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
6. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya. Interleukin-1  $\beta$  Promotes In Vitro Chondrogenesis Of Synovial Mesenchymal Stem Cells. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
7. Nobutake Ozeki, Junpei Matsuda, Takeshi Muneta, Hideyuki Koga, Kunikazu Tsuji, Kenta Katagiri, Mitsuru Mizuno, Tomoyuki Saito, Ichiro Sekiya. Biomechanical Analysis of Centralization With an Anchor for Meniscus Extrusion in a Porcine Model. Orthopaedic Research Society 2016 Annual Meeting 2016.03.07 Orlando, USA
8. Yusuke Nakagawa, Hideyuki Koga, Takeshi Muneta, Shinji Kiuchi, Hideo Ono, Tsuyoshi Nagata, Toshifumi Watanabe, Masafumi Horie, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Hisako Katano, Ichiro Sekiya. Three-Dimensional Reconstructed MRI Evaluation of Arthroscopic Centralization Technique for Extruded Lateral Meniscus. Orthopaedic Research Society 2016 Annual Meeting 2016.03.07 Orlando, USA
9. Ichiro Sekiya. Adult stem cell-based approaches (Intraarticular delivery, model systems vs humans) Overview. ICRS Summit 2016.04.10 Kyoto, JAPAN
10. Ichiro Sekiya. Scientific update: the synovial joint milieu - implications for cartilage repair. ICRS World Congress 2016.09.23 Naples, Italy

#### [Awards & Honors]

1. Ichiro Sekiya, The Japanese Society for Regenerative Medicine Award (Clinical Category), The Japanese Society for Regenerative Medicine, 2016.03
2. Koji Otabe, Excellence in Translational Science Award from Journal of Orthopaedic Research, Orthopaedic Research Society, 2016.03
3. Mitsuru Mizuno, Young Investigator Award, The Japanese Tissue Culture Association, 2016.05
4. Yusuke Nakagawa, Grant for Study Abroad by Mitsukoshi Health and Welfare Foundation, Mitsukoshi Health and Welfare Foundation, 2016.08

## JFCR Cancer Biology

Professor Takuro NAKAMURA  
 Professor Kiyotaka SHIBA  
 Professor Akihiro TOMIDA  
 Professor Toru HIROTA  
 Associate Professor Kengo TAKEUCHI  
 Graduate Students Yuki TOGASHI, Yui  
 SAKAIDA

### (1) Research

Understanding the mechanisms of carcinogenesis and cancer progression. Studying the basics of personalized medicine for innovative cancer therapy.

### (2) Education

We are committed to training talented and motivated graduate students, helping launch careers in basic and translational cancer research.

1. Molecular mechanisms of carcinogenesis and identification of cell-of-origin of cancer (Nakamura)
2. Pathological and genetic analysis of human cancer such as malignant lymphoma and lung cancer (Takeuchi)
3. Application of nanobiotechnology in cancer diagnostics (Shiba)
4. Strategy for innovative drug therapy based on cancer biology (Tomida)
5. Signaling pathways that induce cellular senescence in vivo and to elucidate how these pathways are perturbed in cancer cells
6. Understanding mitotic chromosome dynamics in cancer, to exploit mitotic control to cancer intervention (Hirota)

### (3) Publications

#### [Original Articles]

1. Iwai, K., Minamisawa, T., Suga, K., Yajima, Y., Shiba, K. Isolation of human salivary extracellular vesicles by iodixanol density gradient ultracentrifugation and their characterizations. *J Extracell Vesicles* 5, 30829, 2016.
2. Tsukumo, Y., Tsukahara, S., Furuno, A., Iemura, S., Natsume, T., Tomida, A. TBL2 associates with ATF4 mRNA via its WD40 domain and regulates its translation

- during ER stress. *J Cell Biochem*, 117:500-509, 2016.
3. Koido, M., Sakurai, J., Tsukahara, S., Tani, Y., Tomida, A. PMEPA1, a TGF- $\beta$  and hypoxia-inducible gene that participates in hypoxic gene expression networks in solid tumors. *Biochem Biophys Res Commun*, 479:615-6214, 2016.
4. Hiratsuka T, Takei Y, Ohmori R, Imai Y, Ozeki M, Tamaki K, Nakamura T, Tsuruyama T. ZFP521 contributes to pre-B-cell lymphomagenesis through modulation of the pre-B-cell receptor signaling pathway. *Oncogene*, 35:3227-3238, 2016.
5. Yokoyama T, Nakatake M, Kuwata T, Couzinet A, Goitsuka R, Tsutsumi S, Aburatani H, Valk PJM, Delwel R, Nakamura T. MEIS1-mediated transactivation of synaptotagmin like 1 promotes CXCL12/CXCR4 signaling and leukemogenesis. *J Clin Invest*, 126:1664-1678, 2016.
6. Tsuruyama T, Hiratsuka T, Aini W, Nakamura T. STAT5A modulates chemokine receptor CCR6 expression and enhances pre-B cell growth in a CCL20-dependent manner. *J Cell Biochem*, 117:2630-2642, 2016.
7. Minas TZ, Surdez D, Tahereh J, Tanak M, Howarth M, Kang HJ, Han J, Han ZY, Sax B, Kream BE, Hong SH, Tirode F, Tuckermann J, Toretsky JA, Kenner L, Kovar H, Lee S, Sweet-Cordero A, Nakamura T, Moriggi R, Delattre O, Uren A. Combined experience of six independent laboratories attempting to create an Ewing sarcoma mouse model. *Oncotarget*, DOI:10.18632/oncotarget.9388, 2016.
8. Keeshan K, Vieugue P, Chaudhury S, Rishi L, Gallard C, Liang L, Garcia E, Nakamura T, Omidvar N, Kogan SC. Cooperative leukaemogenesis in acute myeloid leukaemia and acute promyelocytic leukaemia reveal C/EBP $\alpha$  as a common target of TRIB1 and PML/RARA. *Haematologica*, 101:1228-1236, 2016.
9. Takahashi, M., Wakai, T., Hirota, T. Condensin I-mediated mitotic chromosome assembly requires association with chromokinesin KIF4A. *Genes Dev*. 30: 1931-1936, 2016.
10. Nagasaka, K., Hossain, JM., Roberti, JM., \*Ellenberg, J., Hirota, T. Sister chromatid resolution is an intrinsic part of chromosome organization in prophase. *Nat Cell Biol*. 18: 692-699, 2016.
11. Abe, Y., Sako, K., Takagaki, K., Hirayama, Y., Uchida, KSK., Herman, J., DeLuca, JG., Hirota, T. HP1-assisted Aurora B kinase activity prevents chromosome segregation errors. *Dev. Cell*. 36: 487-497, 2016.
12. Abe, Y., Hirota, T. System-level deficiencies in Aurora B control in cancers. *Cell Cycle*. 10:1-2, 2016.
13. Takahashi, M., Tanaka, K., Wakai, T., Hirota, T. Phosphoproteomic analysis of human mitotic chromosomes identified a chromokinesin KIF4A. *Biomed Res*. 37: 161-165, 2016.
14. Harada Y, Koyama T, Takeuchi K, Shoji K, Hoshi K, Oyama Y. NUT midline carcinoma mimicking a germ cell tumor: a case report. *BMC Cancer*. 16:895, 2016.
15. Shigematsu Y, Matsuura M, Nishimura N, Tsuyama N, Takeuchi K, Terui Y,

- Takeshima N, Hatake K. Intravascular Large B-cell Lymphoma of the Bilateral Ovaries and Uterus in an Asymptomatic Patient with a t(11;22)(q23;q11) Constitutional Translocation. *Intern Med.* 55:3169-3174, 2016.
16. Chang ST, Chen SW, Ho CH, Kuo CC, Sakata S, Takeuchi K, Chuang SS. Immunophenotypic and genetic characteristics of diffuse large B-cell lymphoma in Taiwan. *J Formos Med Assoc.* 115:961-967, 2016.
  17. Koyama M, Terauchi T, Koizumi M, Tanaka H, Takeuchi K. Sinonasal oncocytic Schneiderian papilloma accompanied by intravascular lymphoma: A case report on FDG-PET/CT imaging. *Medicine (Baltimore).* 95:e4646, 2016.
  18. Kurita D, Takeuchi K, Kobayashi S, Hojo A, Uchino Y, Sakagami M, Ohtake S, Takahashi H, Miura K, Iriyama N, Sugitani M, Miyoshi H, Hatta Y, Ohshima K, Takei M. A cyclin D1-negative mantle cell lymphoma with an IGL-CCND2 translocation that relapsed with blastoid morphology and aggressive clinical behavior. *Virchows Arch.* 469:471-476, 2016.
  19. Kataoka K, Shiraishi Y, Takeda Y, Sakata S, Matsumoto M, Nagano S, Maeda T, Nagata Y, Kitanaka A, Mizuno S, Tanaka H, Chiba K, Ito S, Watatani Y, Kakiuchi N, Suzuki H, Yoshizato T, Yoshida K, Sanada M, Itonaga H, Imaizumi Y, Totoki Y, Munakata W, Nakamura H, Hama N, Shide K, Kubuki Y, Hidaka T, Kameda T, Masuda K, Minato N, Kashiwase K, Izutsu K, Takaori-Kondo A, Miyazaki Y, Takahashi S, Shibata T, Kawamoto H, Akatsuka Y, Shimoda K, Takeuchi K, Seya T, Miyano S, Ogawa S. Aberrant PD-L1 expression through 3'-UTR disruption in multiple cancers. *Nature.* 534:402-406, 2016.
  20. Katsushima H, Fukuhara N, Ichikawa S, Ota Y, Takeuchi K, Ishizawa K, Sasano H, Harigae H, Ichinohasama R. Non-biased and complete case registration of lymphoid leukemia and lymphoma for five years: a first representative index of Japan from an epidemiologically stable Miyagi Prefecture. *Leuk Lymphoma.* 1-9, 2016.
  21. Harada A, Oguchi M, Terui Y, Takeuchi K, Igarashi M, Kozuka T, Harada K, Uno T, Hatake K. Radiation therapy for localized duodenal low-grade follicular lymphoma. *J Radiat Res.* 57:412-417, 2016.
  22. Inoue M, Toki H, Matsui J, Togashi Y, Dobashi A, Fukumura R, Gondo Y, Minowa O, Tanaka N, Mori S, Takeuchi K, Noda T. Mouse models for ROS1-fusion-positive lung cancers and their application to the analysis of multikinase inhibitor efficiency. *Carcinogenesis.* 37:452-460, 2016.
  23. Horiike A, Takeuchi K, Uenami T, Kawano Y, Tanimoto A, Kaburaki K, Tambo Y, Kudo K, Yanagitani N, Ohyanagi F, Motoi N, Ishikawa Y, Horai T, Nishio M. Sorafenib treatment for patients with RET fusion-positive non-small cell lung

- cancer. *Lung Cancer*. 93:43-46, 2016.
24. Katayama R, Sakashita T, Yanagitani N, Ninomiya H, Horiike A, Friboulet L, Gainor JF, Motoi N, Dobashi A, Sakata S, Tambo Y, Kitazono S, Sato S, Koike S, John Iafrate A, Mino-Kenudson M, Ishikawa Y, Shaw AT, Engelman JA, Takeuchi K, Nishio M, Fujita N. P-glycoprotein Mediates Ceritinib Resistance in Anaplastic Lymphoma Kinase-rearranged Non-small Cell Lung Cancer. *EBioMedicine*. 3:54-66, 2016.
  25. Kusano H, Togashi Y, Akiba J, Moriya F, Baba K, Matsuzaki N, Yuba Y, Shiraishi Y, Kanamaru H, Kuroda N, Sakata S, Takeuchi K, Yano H. Two Cases of Renal Cell Carcinoma Harboring a Novel STRN-ALK Fusion Gene. *Am J Surg Pathol*. 40:761-769, 2016.
  26. Sakamoto K, Nakasone H, Togashi Y, Sakata S, Tsuyama N, Baba S, Dobashi A, Asaka R, Tsai CC, Chuang SS, Izutsu K, Kanda Y, Takeuchi K. ALK-positive large B-cell lymphoma: identification of EML4-ALK and a review of the literature focusing on the ALK immunohistochemical staining pattern. *Int J Hematol*. 103:399-408, 2016.
  27. Dobashi A, Tsuyama N, Asaka R, Togashi Y, Ueda K, Sakata S, Baba S, Sakamoto K, Hatake K, Takeuchi K. Frequent BCOR aberrations in extranodal NK/T-Cell lymphoma, nasal type. *Genes Chromosomes Cancer*. 55:460-471, 2016.
  28. Takeuchi K, Togashi Y, Kamihara Y, Fukuyama T, Yoshioka H, Inoue A, Katsuki H, Kiura K, Nakagawa K, Seto T, Maemondo M, Hida T, Harada M, Ohe Y, Nogami N, Yamamoto N, Nishio M, Tamura T. Prospective and clinical validation of ALK immunohistochemistry: results from the phase I/II study of alectinib for ALK-positive lung cancer (AF-001JP study). *Ann Oncol*. 27:185-192, 2016.

#### [Review Articles]

1. Tanaka, K., Hirota, T. Chromosomal instability: a common feature and a therapeutic target of cancer. Review. *Biochim Biophys Acta*. 1866: 64-75, 2016.

#### [Conference Activities & Talks]

1. Shiba K. Differentiation of extracellular vesicles using aptamer functionalized substrate surface. XXV International Materials Research Congress 2016 (Cancun) August, 2016
2. Nakamura T. Signaling and transcriptional networks in myeloid leukemogenesis. The 5th JCA-AACR Special Joint Conference (Urayasu) July, 2016
3. Nakamura T. Modeling soft part sarcoma to clarify interaction between sarcoma cells and

- microenvironment. The JSA and JSCS Joint Annual Meeting 2016 (Kyoto) December, 2016
4. Hirota, T. HP1-mediated allosteric regulation of Aurora B prevents chromosome segregation errors. International symposium on chromosome orchestration system. (Awaji) March, 2016
  5. Hirota, T. Kinetic control of the M/A transition in failsafe mitosis. SKKU International symposium on biomedical science. (Suwon) October, 2016



# Minimally Invasive Medical Treatment

Professor KOJIMA Kazuyuki

## (1) Outline

1. Investigation and research for the social needs identification of minimally invasive medical treatment in the next generation of the medical and the dental areas.
2. Medical equipment and development of treatment to meet the needs of minimally invasive medical treatment in the next generation of the medical and the dental fields.
3. Research and development of the education curriculum and evaluation methods of minimally invasive treatment in the medical and the dental fields.
4. Development and operation of minimally invasive treatment of industry-academia cooperation in the medical and the dental fields.
5. Development and operation of technology certification strategy of minimally invasive treatment in the medical and the dental areas.

## (2) Publications

### [Original Articles]

1. Inokuchi M, Otsuki S, Ogawa N, Tanioka T, Okuno K, Gokita K, Kawano T, Kojima K. Postoperative Complications of Laparoscopic Total Gastrectomy versus Open Total Gastrectomy for Gastric Cancer in a Meta-Analysis of High-Quality Case-Control Studies. *Gastroenterology Res Pract*.
2. Nishikawaji T, Akiyama Y, Shimada S, Kojima K, Kawano T, Eishi Y, Yusa Y, Tanaka S. Onco-genic roles of the SETDB2 histone methyltransferase in gastric cancer. *Oncotarget*.
3. Higuchi K, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. Cadherin 5 expression correlates with poor survival in human gastric cancer. *J Clin Pathol*.
4. Nakagawa M, Kojima K, Inokuchi M, Kato K, Sugita H, Otsuki S, Sugihara K. Identification of frequency, severity and risk factors of complications after open gastrectomy: Retrospective analysis prospectively collected database using the Clavien-Dindo classification. *J Med Dent Sci*.
5. Yamada I, Hikishima K, Miyasaka N, Kato K, Ito E, Kojima K, Kawano T, Kobayashi D, Eishi Y, Okano H. q-Space MR Imaging of Gastric Carcinoma Ex Vivo: Correlation with Histopathologic Findings. *Magn Reson Med*.
6. Inokuchi M, Otsuki S, Murase H, Kojima K, Kawano T. Feasibility of laparoscopy-assisted gastrectomy for patients with poor physical status: A propensity-score matching study. *Int J Surg*.
7. Akiyama Y, Koda Y, Byeon SJ, Shimada S, Nishikawaji T, Sakamoto A, Chen Y, Kojima K, Kawano T, Eishi Y, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. *Oncotarget*.
8. Kobayashi K, Inokuchi M, Takagi Y, Otsuki S, Fujimori Y, Sato Y, Yanaka Y, Higuchi K, Aburatani T, Tomii C, Uetake H, Kojima K, Kawano T. Prognostic significance of PAK4 expression in gastric cancer. *J Clin Pathol*.

9. Yamada I, Hikishima K, Miyasaka N, Kato K, Kojima K, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H. Gastric carcinoma: evaluation with diffusion-tensor MR imaging and tractography ex vivo. Magnetic Resonance Imaging.

**[Conference Activities & Talks]**

1. Kazuyuki Kojima. Laparoscopic Proximal Gastrectomy with Double Tract Reconstruction under 3D Laparoscopy. The New Golden Standard:3D Laparoscopic Gastric Surgery 2016.08.06 Pusan
2. Kazuyuki Kojima. Learning Pathway to Transition from Open to Lap, speaker. Gastric Inovation Forum 2016.10.14 Seoul
3. Kazuyuki Kojima. Laparoscopic reconstruction using circular stapler, speaker. Yonsei Gastric Cancer Symposium 2016.10.15 Seoul

## Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi  
Junior Associate Professor: Takahiro Arakawa  
Assistant Professor: Koji Toma  
Lecturer (part-time): Kazuyoshi Yano  
Postdoctoral Researcher: Kumiko Miyajima

### ( 1 ) Outline

Our research is based on a broad range of areas such as electrochemistry, mechanical engineering, electrical engineering, material science and biochemistry. The group aims to pursue interdisciplinary research in bio-MEMS, bio-optics, bio-electronics or bioinformatics by combining biotechnology and information technology.

### ( 2 ) Research

1. Detachable “Cavitas sensors” as bioinformation monitoring systems in body cavities  
"Cavitas sensors" such as a soft contact-lens biosensor and a mouth guard biosensor have been developed for novel biomonitoring methods by using advanced polymer microelectromechanical systems (MEMS) techniques.
2. Biochemical gas sensor "Bio-sniffers" and spatiotemporal gas visualization system “Sniff-camera” for volatile organic compounds from human body  
Highly selective gas sensors "Bio-sniffers" and gas visualization systems "Sniff-camera" for acquiring spatiotemporal information of distribution of volatile chemicals have been developed by exploiting metabolizing enzymes in human liver. Potential applications of these gas sensors include halitosis analysis, breath alcohol and aldehyde measurement, medical screening or dental health, etc.
3. Immunosensors for medical treatment and environmental medicine  
Development of optical or surface acoustic wave immunosensors have been pursued for semi-continuous (rapid and repeated) measurement of antigens in body and airborne allergens in living environment.
4. “Organic engine” based on chemo-mechanical energy conversion  
A novel chemo-mechanical energy conversion system (organic engine) that utilizes enzyme reactions and active transport of chemicals have been constructed. Biomedical applications (chemical pumps, drug release systems, etc.) are also investigated.

### ( 3 ) Education

In advanced medicine, technologies enabling to accurately measure biological information are highly demanded. The development of “human-friendly” non-invasive measurement methods could release patients from the pain and the risks of sampling. The students will learn the basic knowledge and skills of biological information measurement through the lectures (e.g., “Biomedical Device Science and Engineering”, “Practice in Global Linkage between University and Industry” and “Nanobiotechnology” ), seminars and practical training. Especially research including biochemical measurement, the development of biosensing devices and their applications to medicine will be carried out based on “sensor and biomedical engineering.

**(4) Lectures & Courses**

The students will learn the basic technology related to advanced medicine and biological information measurement. Through practical training, they will also engage in research activities for biochemical measurement, the development of biosensing devices and their applications to medicine based on “sensor and biomedical engineering”. The objective of this course is to help the students be able to think about and conduct a research by themselves throughout the activities with academic researches.

**(5) Publications****[Original Articles]**

1. Koji Toma, Kumiko Miyajima, Shin-ichi Sawada, Takahiro Arakawa, Hiroyuki Kudo, Kazunari Akiyoshi, Kohji Mitsubayashi. Direct measurement of gaseous formaldehyde from food with a fiber-optic biochemical gas sensor (bio-sniffer) *Sensors and Materials*. 2016; 28(12); 1265-1272
2. Po-Jen Chien, Ming Ye, Takuma Suzuki, Koji Toma, Takahiro Arakawa, Yasuhiko Iwasaki, Kohji Mitsubayashi. Optical isopropanol biosensor using NADH-dependent secondary alcohol dehydrogenase (S-ADH) *Talanta*. 2016; 159; 418-424
3. Takahiro Arakawa, Yusuke Kuroki, Hiroki Nitta, Prem Chouhan, Koji Toma, Shin-ichi Sawada, Shuhei Takeuchi, Toshiaki Sekita, Kazunari Akiyoshi, Shunsuke Minakuchi, Kohji Mitsubayashi. Mouthguard biosensor with telemetry system for monitoring of saliva glucose: A novel cavitas sensor *Biosensors and Bioelectronics*. 2016; 84; 106-111
4. Hirokazu Saito, Yuki Hashimoto, Takeshi Minamide, Takuo Kon, Koji Toma, Takahiro Arakawa, and Kohji Mitsubayashi. Fiber optic bio-sniffer (biochemical gas sensor) for gaseous dimethyl sulfide *Sensors and Materials*. 2016; 28(12); 1295-1301
5. Koji Toma, Yurika Suzuki, Mana Saito, Kumiko Miyajima, Takahiro Arakawa, Hiroji Shimomura, Kohji Mitsubayashi. Fiber-optic chemifluorescent immunosensor for influenza virus monitoring *Journal of Analytical Bio-Science*. 2016; 39(4); 271-276
6. Takahiro Arakawa, Kenta Iitani, Toshiyuki Sato, Koji Toma, Kohji Mitsubayashi. Ethanol vapor imaging system “sniffer camera” for evaluation of alcohol metabolism from breath and palm skin gas *Procedia Engineering*. 2016; 168; 522-528

**[Misc]**

1. Takahiro Arakawa, Kohji Mitsubayashi. Cavitas sensors: Contact lens type sensors & mouthguard sensors *Electroanalysis*. 2016; 28; 1170-1187

**[Conference Activities & Talks]**

1. Toma K, Suzuki Y, Saito M, Miyajima K, Arakawa T, Shimomura H, Mitsubayashi K. A chemi-fluorescence immunosensor with disposable PMMA fiber for detection of influenza viruses. *EUROPT(R)ODE XIII* 2016.03.20 Graz, Austria
2. Toma K, Arakawa T, Mitsubayashi K. Advanced immunosensors for health care and clinical medicine. *EPFL, Tokyo Tech, TMDU Joint Workshop* 2016.04.19 Tokyo, Japan
3. Arakawa T, Iitani K, Sato T, Toma K, Mitsubayashi K. 2D fluorometric sniff-cam with ADH immobilized mesh and UV-LED sheet for gaseous ethanol imaging from a palm skin. *Biosensors 2016* 2016.05.25 Gothenburg, Sweden
4. Arakawa T, Kuroki Y, Nitta H, Toma K, Sawada S, Takeuchi S, Sekita T, Akiyoshi K, Minakuchi S, Mitsubayashi K. A wireless (BLE) mouthguard-biosensor with dental materials for real-time measurement of saliva glucose in oral cavity. *Biosensors 2016* 2016.05.25 Gothenburg, Sweden
5. Toma K, Miki D, Kishikawa C, Yoshimura N, Miyajima K, Arakawa T, Yatsuda H, Mitsubayashi K. A surface acoustic wave (SAW) immunosensor with a regeneratable surface enabling repetitive measurement of dust mite allergens. *Biosensors 2016* 2016.05.25 Gothenburg, Sweden

6. Ye M, Chien PJ, Suzuki T, Toma K, Sawada S, Arakawa T, Akiyoshi K, Mitsubayashi K. Acetone biosniffer (gas-phase biosensor) by detecting NADH consumption on S-ADH reverse reaction for real-time breath monitoring. Biosensors 2016 2016.05.25 Gothenburg, Sweden
7. Mitsubayashi K. Cavity (cavity) sensors and Imaging system of human volatiles as non-invasive approaches. Biotechnology and Biochemical Engineering Society of Taiwan (BEST) 2016.06.24
8. Iitani K, Naisierding M, Sato T, Toma K, Arakawa T, Mitsubayashi K. Sniff-cam (gaseous chemical imaging system) for breath acetaldehyde as a metabolite of ethanol after drinking. APCOT2016 2016.06.26 Kanazawa, Japan
9. Chien PJ, Ye M, Suzuki T, Toma K, Arakawa T, Mitsubayashi K. Gas phase biosensor “bio-sniffer” for acetone measurement and exhaled breath analysis. APCOT2016 2016.06.26 Kanazawa, Japan
10. Iitani K, Naisierding M, Sato T, Toma K, Arakawa T, Mitsubayashi K. Gas-phase imaging system “sniff-camera” using enzyme mesh for breath acetaldehyde after drinking. IMCS2016 2016.07.10 Jeju, Korea
11. Toma K, Miki D, Yoshimura N, Miyajima K, Arakawa T, Yatsuda H, Mitsubayashi K. A regeneratable SAW ( Surface Acoustic Wave) immunosensor for repetitive measurement of dust mite allergen. IMCS2016 2016.07.10 Jeju, Korea
12. Kuroki Y, Nitta H, Toma K, Arakawa T, Mitsubayashi K. A mouthguard glucose sensor for monitoring of saliva sugar with ble telemetry system. 2016 IEEE Sixth International Conference on Communications and Electronics 2016.07.27 Ha Long Bay, Vietnam
13. Arakawa T, Iitani K, Sato T, Naisierding M, Toma K, Mitsubayashi K. Fluorometric imaging system "Sniffer-cam" for human breath and skin gas in evaluation of alcohol metabolism. 2016 International Conference on Optical MEMS and Nanophotonics 2016.07.31 Singapore
14. Arakawa T, Iitani K, Sato T, Toma K, Mitsubayashi K. Ethanol vapor imaging system “sniffer camera” for evaluation of alcohol metabolism from breath and palm skin gas. Eurosensors2016 2016.09.04 Budapest, Hungary
15. Mitsubayashi K. Cavity sensors for bio/chemical monitoring: Soft-contact lens & Mouthguard sensors. 2016 International Conference on Flexible and Printed Electronics 2016.09.06
16. Chien P J, Ye M, Suzuki T, Toma K, Arakawa T, Mitsubayashi K. Bio-Sniffer (Gas Phase Biosensor) for Breath Acetone as a Volatile Product of Lipid Metabolism. PRiME 2016 2016.10.02 Honolulu, USA
17. Iitani K, Naisierding M, Sato T, Toma K, Arakawa T, Mitsubayashi K. Sniff-Cam (Bio-Fluorometric Gas-Imaging System) for Breath Acetaldehyde after Drinking. PRiME 2016 2016.10.02 Honolulu, USA
18. Toma K, Nitta H, Zhang Z, Tomoto K, Shintani Y, Takeuchi S, Arakawa T, Sekita T, Iwasaki Y, Kawarada H, Minakuchi S, Mitsubayashi K. A Mouthguard Biosensor Using UV Curable Biocompatible Polymer for Stable Enzyme Immobilization in Saliva Glucose Monitoring. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan
19. Mitsubayashi K. Cavity sensors and sniff-cam for biomonitoring: Soft contact lens & Mouthguard sensors, optical bio-sniffing of human VOCs. IEEE SENSORS2016 2016.10.30
20. Kishikawa C, Miki D, Miyajima K, Yoshimura N, Yatsuda H, Toma K, Arakawa T, Mitsubayashi K. SAW immunosensor for on-site monitoring of airborne mite allergen Der f 1 in residential environment. International Symposium on Biomedical Engineering 2016.11.10 Tokyo, Japan
21. Arakawa T, Mitsubayashi K. Mouthguard and soft contact lens biosensors for non-invasive cavity-monitoring. International Symposium on Biomedical Engineering, 2016.11.10
22. Chien P J, Ye M, Suzuki T, Tsujii M, Toma K, Arakawa T, Mitsubayashi K. Fluorometric acetone bio-sniffer enabling breath analysis for non-invasive assessment of lipid metabolism. ISLS2016 2016.11.22 Taipei, Taiwan
23. Toma K, Horibe M, Kishikawa C, Yoshimura N, Arakawa T, Yatsuda H, Shimomura H, Mitsubayashi K. Rapid measurement of mite allergens by a surface acoustic wave (SAW) immunosensor for airborne allergen monitoring. Bio4Apps2016 2016.12.14 Gold coast, Australia

## Biomedical Information

Professor Yuji Miyahara (Concurrent)  
 Associate Professor Fumimasa NOMURA  
 Graduate Student Masao ODAKA  
 Yoshihiro SUGIO

### ( 1 ) Research

Studies on Epigenetic Information Stored Living System using Constitutive Reconstruction Strategy

- 1) Constructing “On-chip Organ Model” using Microfabrication-Bio Technology.
- 2) Constructing “Artificial Cell Model” using Liposome Technology.

### ( 2 ) Publications

#### [Original Articles]

1. López-Redondo F, Kurokawa J, Nomura F, Kaneko T, Hamada T, Furukawa T, Yasuda K. A distribution analysis of action potential parameters obtained from patch-clamped human stem cell-derived cardiomyocytes *Journal of Pharmacological Sciences*. 2016.04; 131(2); 141-145
2. Terazono H, Kim H, Nomura F, Yasuda K. Development of a microprocessing-assisted cell-systematic evolution of ligands by exponential enrichment method for human umbilical vein endothelial cells *Japanese Journal of Applied Physics*. 2016.05; 55; 06GN03
3. Nomura F, Hattori A, Terazono H, Kim H, Odaka M, Sugio Y, Yasuda K. Predictive lethal proarrhythmic risk evaluation using a closed-loop-circuit cell network with human induced pluripotent stem cells derived cardiomyocytes *Japanese Journal of Applied Physics*. 2016.05; 55; 06GN07

#### [Conference Activities & Talks]

1. Hayashi T, Tokihiro T, Kurihara H, Nomura F, Yasuda K. Community effect of cardiomyocytes in beating rhythms is ruled by stable cells. 2016.11.25

## Bioelectronics

### Staff

Yuji Miyahara (Professor)  
Akira Matsumoto (Associate Professor)  
Tatsuro Goda (Assistant Professor)  
Miyuki Tabata (JSPS Research Fellow)  
Yukichi Horiguchi (Project Assistant Professor)  
Yoshizumi Toshihiro (Project Assistant Professor)  
Taiki Miyazawa (Project Assistant Professor)  
Hiroko Matsumoto (Associate Research Scientist)  
Yuki Morooka (Associate Research Scientist)  
Chiharu Mizoi (Associate Research Scientist)  
Sayo Kotaki (Associate Research Scientist)  
Kayoko Nakagawa (Office Staff)

### Graduate student

Yuki Imaizumi, Hai Wenfeng, Masahiro Touya, Tomoko Sakamaki  
Chindanai RATANAPORNCHAROEN, Dilinaer AINIWAER, Hiroaki Hatano

### (1) Outline

Bioelectronics group is engaged in developing methodologies to determine and analyze functions of biomolecules and their relationships to diseases based on solid-state biosensor technology. Our interests include design & understanding of physicochemical properties of the interface between biomolecules and the device materials, signal-transduction mechanism as well as the pursuit of improved sensitivity and selectivity. These technologies involve many different disciplines of science and engineering, through which we propose new solutions to future medicine.

### (2) Research

#### 1. Bioelectronics for Next-generation DNA Sequencing

Our research is focused on the development of nano-interfaces between biomolecules and semiconducting materials for label-free and highly sensitive electrical monitoring of nucleotide base sequences and their amplification processes. The goal of the project is to provide a smaller and cheaper alternative next-generation DNA sequencer to the traditional techniques that involve optical sensing using fluorescence and bioluminescence.

#### 2. Devices for Early Cancer Diagnosis

For applications to early-stage diagnostics of cancers, we aim to establish the device technology enabling detection of small amount of cancer markers out of blood samples with remarkable quickness and sensitivity. The focus is on the design of nano-interfaces that involves chemical modification of biomolecular targets as well as solid/ liquid interfaces in order to achieve efficient biomolecular recognitions on the electrode surfaces. We also pursue optimized materials and the surface property of the electrode in order to obtain remarkably target-specific signals out of complicated electrical signals obtained from raw biological samples.

#### 3. Discovering Intra/Extracellular Molecular Dynamics on Inflammatory Response

Molecular dynamics at inflammation and bacterial infection is investigated using biomimetic surfaces. The term “biomimetics” in this context represents mimicking the interplay between biomolecules and local changes of



microenvironment that has evolved as a mechanism for inauguration of immune responses. Our new nano-bio-technology will reveal unidentified active molecular dynamics in pathophysiology.

#### 4. “Artificial Pancreas” to Treat Diabetes

Development of self-regulated insulin delivery systems to treat diabetes is a long-standing challenge of biomedical engineering. We propose a synthetic gel based solution, which could offer a remarkably simple, “electronics-free” and thus significantly low-cost alternative to the ongoing efforts of artificial pancreas.

### (3) Education

1. Engagement: we are engaged in teaching a part of Biomedical Engineering course and mentoring master & doctor students.

2. Course objective: Serum components play crucial roles in metabolic cycles and their concentration homeostasis reflects dynamic equilibrium of life. On occasion of abnormal metabolic pathway, it is manifested as a fluctuation of each specific serum component. Our lecture provides an overview of advanced materials and engineering aimed at determination of body fluids including serum components and mechanisms for their concentration homeostasis.

3. Deepen knowledge of theory, mechanisms, methodologies, application, and limitation of detection technology for biomolecules in various clinical samples. Learn integrative technology of advanced materials/devices and biology/medicine, present problems and future perspective in bioelectronics. Familiarize each student with other related techniques, lab skills including planning of experiments, presenting research results and preparing reports.

### (4) Publications

#### [Original Articles]

1. Akira Matsumoto, Mai Yuasa, Hiroko Matsumoto, Mai Sanjo, Miyuki Tabata, Tatsuro Goda, Toru Hoshi, Takao Aoyagi, Yuji Miyahara. Boronate Functionalized Polymer Gel Based Insulin Delivery System with Improved Stability in Performance: A Comparative Structure-Function Study 2016.02; 45(4); 460-462
2. Tatsuro Goda, Eriko Yamada, Yurika Katayama, Miyuki Tabata, Akira Matsumoto, Yuji Miyahara. Potentiometric responses of ion-selective microelectrode with bovine serum albumin adsorption Biosensors and Bioelectronics. 2016.03; 77; 208-214
3. Ayaka Seichi, Nanami Kozuka, Yuko Kashima, Miyuki Tabata, Tatsuro Goda, Akira Matsumoto, Naoko Iwasawa, Daniel Citterio, Yuji Miyahara, Koji Suzuki. Real-time Monitoring and Detection of Primer Generation-Rolling Circle Amplification of DNA using an Ethidium Ion-Selective Electrode Anal. Sci.. 2016.03; 32(5); 505-510
4. Daniel Schaffhauser, Michael Fine, Miyuki Tabata, Tatsuro Goda, Yuji Miyahara. Measurement of Rapid Amiloride-Dependent pH Changes at the Cell Surface Using a Proton-Sensitive Field-Effect Transistor Biosensors. 2016.03; 6(2); 11
5. Yuki Imaizumi, Tatsuro Goda, Yutaro Toya, Akira Matsumoto, Yuichi Miyahara. Oleyl Group-functionalized Insulating Gate Transistors for Measuring Extracellular pH of Floating Cells Sci. Technol. Adv. Mater.. 2016.07; 17(1); 337-345
6. Tatsuro Goda, Yuji Miyahara. Engineered Zwitterionic Phosphorylcholine Monolayers for Elucidating Multivalent Binding Kinetics of C-reactive Protein Acta Biomater.. 2016.08; 40; 46-53
7. Zhenyu Gao, Yukichi Horiguchi, Kei Nakai, Akira Matsumura, Minoru Suzuki, Koji Ono, Yukio Nagasaki. Use of boron cluster-containing redox nanoparticles with ROS scavenging ability in boron neutron capture therapy to achieve high therapeutic efficiency and low adverse effects Biomaterials. 2016.10; 104; 201-212
8. Miyuki Tabata, Chindanai Ratanaporncharoen, Aoi Asano, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami, Yuji Miyahara. Miniaturized Ir/IrOx pH Sensor for Quantitative Diagnosis of Dental Caries Procedia Eng.. 2016.11; 168; 598-601

9. Miyuki Tabata, Yurika Katayama, Fahmida Mannan, Ayaka Seichi, Koji Suzuki, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Label-free and Electrochemical Detection of Nucleic Acids Based on Isothermal Amplification in Combination with Solid-state pH Sensor *Procedia Eng.* 2016.11; 168; 419-422

#### [Books etc]

1. Yukichi Horiguchi, Yukio Nagasaki. *Encyclopedia of Biocolloid and Biointerface Science*. John Wiley & Sons, Inc., 2016.06 (ISBN : 978-1-1185-4276-7)

#### [Misc]

1. Miyuki Tabata, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Field-Effect Transistors for Detection of Biomolecular Recognition Intelligent Nanosystems for Energy, Information and Biological Technologies. 2016.09; 13-25
2. Tatsuro Goda. Sensing Cellular Microenvironments Using Ion-sensitive Field-effect Transistors 2016.10; 34(3); 204-209
3. Tatsuro Goda. Sensing Nanomaterials-induced Cytotoxicity and Nanomedicine Chemical Industry. 2016.11; 67(11); 834-844

#### [Conference Activities & Talks]

1. Goda T, Miyahara Y. Conducting Polymers Bearing Phosphorylcholine Group for Metal-free, Antibody-free, and Low-impedance Biosensing of C-reactive Protein. 7th Japan-Taiwan Nanomedicine Symposium 2016.01.21 Kyoto, Japan
2. Matsumoto A, Miyahara Y. “Borono-lectin” based Platforms for Bio-sensing and Drug Delivery Applications. The 33rd International Conference on Photopolymer Science and Technology 2016.01.24 Chiba, Japan
3. Matsumoto A. Phenylboronate based Strategies for Drug Delivery Systems and Nanobiosensing. 8th International Symposium on Advanced Plasma Science and its Applications for Nitrides and Nanomaterials/9th International Conference on Plasma-Nano Technology & Science (ISPlasma2016 / IC-PLANTS2016) 2016.03.06 Higashiyama Campus, Nagoya University, Aichi, Japan
4. Ratanaporncharoen C, Tabata M, Kitasako Y, Ikeda M, Tagami J, Goda T, Matsumoto A, Miyahara Y. Fabrication of Micro Ir/IrOx pH Sensor for Dental Applications. PITTCON 2016 2016.03.06 Atlanta, Georgia, USA
5. Matsumoto A. Synthetic Gel based Approaches towards “Electronics-free” Artificial Pancreas. EPFL, Tokyo Tech, TMDU Joint Workshop 2016.04.19 TMDU, Japan
6. Horiguchi Y, Goda T, Matsumoto A, Takeuchi H, Yamaoka S, Miyahara Y. Rapid and Label-free Influenza Virus Detection with Densely Immobilized Sialic Acids on Gold Electrode. ImPACT Mitata PM International Symposium on InSECT 2016 2016.04.26 Nagoya, Japan
7. Yoshizumi T, Goda T, Matsumoto A, Miyahara Y. Development Progress of a FET Type Gas Sensor Consisting of Gas-Sensitive Polymer and Porous Gate. ImPACT International Symposium on InSECT 2016 2016.04.26 Nagoya, Japan
8. Goda T, Miyahara Y. Organic bioelectronics create ionic microenvironments of inflammation and infection on phospholipid polymer to elucidate molecular dynamics of C-reactive protein. 10th World Biomaterials Congress (WBC 2016) 2016.05.17 Montreal, QC, Canada
9. Goda T, Miyahara Y. Cells-Attached pH-Sensing Transistor System Detects Proton-Permeable Nanopores on Plasma Membranes by Exogenous Chemical Compounds. Biosensors 2016 2016.05.25 Gothenburg, Sweden
10. Ratanaporncharoen C, Tabata M, Kitasako Y, Ikeda M, Tagami J, Goda T, Matsumoto A, Miyahara Y. Fabrication of Ir/IrOx Micro pH Sensor for Quantitative Dental Caries Evaluation. Asia-Pacific Conference of Transducers and Micro-Nano Technology 2016 (APCOT 2016) 2016.06.26 Kanazawa, Japan

11. Goda T. Evaluation of plasma membrane leakage using protons. 2nd International Symposium on Nanoarchtectonics for Mechanobiology 2016.07.27 Tsukuba, Ibaraki, Japan
12. Matsumoto A. Takayoshi Suganami, Electronics-free and Symthetic Materials Based Approach toward Artificial Pancreas. Seminar at City of Hope 2016.08.23 Pasadena, USA
13. Goda T, Toya M, Hai W, Matsumoto A, Miyahara Y. Functional poly(3,4-ethylenedioxythiophenes) for bioanalytics and diagnostics. Biointerfaces International 2016 2016.08.23 University of Zurich, Zurich, Switzerland
14. Tabata M, Ratanaporncharoen C, Asano A, Kitasako Y, Ikeda M, Goda T, Matsumoto A, Tagami J, Miyahara Y. Miniaturized Ir/IrOx pH sensor for quantitative diagnosis of dental caries. Eurosensors2016 2016.09.04 Budapest, Hungary
15. Tabata M, Katayama Y, Mannan F, Seichi A, Suzuki K, Goda T, Matsumoto A, Miyahara Y. Label-free and electrochemical detection of nucleic acids based on isothermal amplification in combination with solid-state pH sensor. Eurosensors2016 2016.09.04 Budapest, Hungary
16. Tabata M, Katayama Y, Mannan F, Seichi A, Suzuki K, Goda T, Matsumoto A, Miyahara Y. Label-free and electrochemical detection of nucleic acids based on isothermal amplification in combination with solid-state pH sensor. Eurosensors2016 2016.09.04 Budapest, Hungary
17. Goda T, Toya M, Matsumoto A, Miyahara Y. Zwitterionic phosphorylcholine<sup>+</sup>-tethered polythiophenes for electrochemical detection of acute-phase biomarker. International Conference on Flexible and Printed Electronics (ICFPE) 2016 2016.09.06 Yonezawa, Yamagata, Japan
18. Hai W, Horiguchi Y, Goda T, Matsumoto A, Takeuchi H, Yamaoka S, Miyahara Y. Label-free and specific Human influenza virus detection using sialyllactose-immobilized gold electrode. International Conference on Flexible and Printed Electronics (ICFPE) 2016 2016.09.06 Yonezawa, Yamagata, Japan
19. Sakamaki T, Matsumoto A, Kondo S, Sakai T, Sato S, Kikuchi A, Tei Y, Goda T, Miyahara Y. Demonstration of environment-sensitive tetra-gel by using stimuli-sensitive macromer. The International Symposium on Visualization in Joining & Welding Science through Advanced Measurements and Simulation in conjunction with Symposium on the Research Activities of Joint Usage/Research Center on Joining and Welding & The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Hotel Hankyu Expo Park, Osaka, Japan
20. Ratanaporncharoen C, Tabata M, Ishihara N, Masu K, Sriyudthsak M, Goda T, Matsumoto A, Miyahara Y. Miniaturized Ir/IrOx wireless pH sensor for bio-sensing system. The 34th Sensor Symposium on Sensors, Micromachines and Applied Systems 2016 2016.10.24 Hirado Bunka Center, Nagasaki, Japan
21. Horiguchi Y, Goda T, Matsumoto A, Miyahara Y,. Label-free detection of influenza subtypes based on multisite binding to sialic acid receptors immobilized gold electrode. 9th International Microprocesses and Nanotechnology Conference (MNC 2016) 2016.11.08 Kyoto, Japan
22. Tabata M, Tenaglia E, Goda T, Matsumoto A, Guiducci C, Miyahara Y. pH-based nucleic acid amplification detection on a silicon nanowire chip. International Symposium on Biomedical Engineering, 2016 2016.11.10 Tokyo, Japan
23. Hai W, Goda T, Matsumoto A, Takeuchi H, Yamaoka S, Miyahara Y. Label-free and specific human influenza virus detection using sialyllactose-grafted conducting polymers. International Symposium on Biomedical Engineering 2016.11.10 Tokyo, Japan
24. Sakamaki T, Matsumoto A, Kondo S, Sakai T, Sato S, Kikuchi A, Tei Y, Goda T, Miyahara Y. Preparation of environment-sensitive tetra-gel by using stimuli-sensitive macromer. International Symposium on Biomedical Engineering 2016.11.10 Tokyo, Japan
25. Toya M, Goda T, Matsumoto A, Miyahara Y. Poly(3,4-ethylenedioxythiophene) bearing zwitterionic group for biosensing application. International Symposium on Biomedical Engineering 2016.11.10 Tokyo, Japan
26. Ratanaporncharoen C, Tabata M, Kitasako Y, Ikeda M, Goda T, Matsumoto A, Tagami J, Miyahara Y. Fabrication and characterization of Ir/IrOx pH sensor for quantitative dental caries analysis. International Symposium on Biomedical Engineering 2016.11.10 Tokyo, Japan

27. Miyahara Y. Detection of biomolecular recognition using bio-transistors. International Symposium on Biomedical Engineering 2016.11.11 Tokyo, Japan
28. Goda T. Application of Zwitterionic Materials: From Infection Biomarker Sensing to Cell Therapy. the 18th Takayanagi Kenjiro Memorial Symposium 2016.11.15 Shizuoka University Hamamatsu Campus, Hamamatsu, Shizuoka, Japan.
29. Matsumoto A, Suganami T, Matsumoto H, Tanaka M, Ochi K, Moro-oka Y, Ogawa Y, Ishii T, Kataoka K, Miyahara Y. Electronics-free and synthetic polymeric materials based approach toward artificial pancreas. 3rd International Conference on Biomaterials Science in Tokyo 2016.11.28 Tokyo, Japan
30. Goda T, Imaizumi Y, Hatano H, Matsumoto A, Miyahara Y. Sensing cell barrier functions by proton dynamics. 3rd International Conference on Biomaterials Science in Tokyo 2016.11.28 Tokyo, Japan
31. Horiguchi Y, Goda T, Matsumoto A, Miyahara Y. Label-free and specific virus detection using densely immobilized sialic acid receptors. 3rd International Conference on Biomaterials Science in Tokyo 2016.11.28 Tokyo, Japan
32. Miyazawa T, Nakagawa K, Harigae T, Itaya M, Miyazawa T. Effects of encapsulation in poly-(lactic-co-glycolic acid) on metabolism of curcumin via oral administration. 3rd International Conference on Biomaterials Science in Tokyo 2016.11.28 Tokyo, Japan
33. Sakamaki T, Matsumoto A, Kondo S, Sakai T, Sato S, Kikuchi A, Tei Y, Goda T, Miyahara Y. Preparation of environment-sensitive tetra-gel by using stimuli-sensitive macromer. 3rd International Conference on Biomaterials Science in Tokyo 2016.11.28 Tokyo, Japan
34. Miyahara Y. Semiconductor devices for biomedical applications. The 3 rd Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2016.12.15 Bangkok, Thai

# Material-Based Medical Engineering

Prof. Akio KISHIDA  
Assoc. Prof. Tsuyoshi KIMURA  
Assist. Prof. Yoshihide HASHIMOTO  
Research Associate Naoko NAKAMURA

Division of Acellular Tissue and Regenerative Medical Material  
Assoc. Prof. Seiichi FUNAMOTO  
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Assist. Prof. Yongwei ZHANG

Secretary Naomi HIWATARI

Doctor Course Student  
Masaki WATANABE

## (1) Outline

In our laboratory, we deal with many research topics from the fundamental study of biomaterials in terms of material engineering to the application study of the medical devices.

The key words of our policy are "contribution to medical care" and "exploration of basic scientific principles".

## (2) Research

In order to develop technologies that contribute to the medical and dental care, there is a need for a system to build up the design concepts at the molecular level and to realize it. Based on polymer chemistry, organic chemistry, and physical chemistry, we proceed a research aimed at specific clinical applications using cell engineering, genetic engineering techniques. Target area are new medical material development, regenerative medicine, gene therapy, and the treatment engineering.

### (1) Regenerative medicine using decellularized biological tissue

In order to remove the xenogeneic cells, the living tissue is decellularized using a new processing method, high-hydrostatic pressure (HHP) method has been developed. Using this process, complete removal of infectious bacteria, viruses, and cells was accomplished.

(2) Molecular aggregates formed by the high-hydrostatic pressure process. Hydrogen bond assembles molecular assembly under high pressure. Using the HHP processing of more than 6,000 atmospheres, we prepare the nucleic acid assembly and apply them as gene delivery system.

### (3) Extracellular matrix remodeling

We are conducting research on tissue remodeling using artificially reconstructed extracellular matrix structure. Specifically, we are researching the application of as artificial skin and artificial cornea of precision design artificial extracellular matrix structure.

(4) Immune control system: technology of specific cell capture and release

In cancer immunotherapy, by removing regulatory T cells (Treg) that negatively regulates immune reactions, to be able to enhance the anti-tumor immune responses have been revealed. We are developing technologies to capture and recover Treg using interfacial science.

**(3) Education**

In the Graduate School of Medical and Dental Sciences, we provide the lectures entitled “biological functional materials science”, “applied biomaterials”, and “medical, dental and pharmaceutical industrial engineering”.

**(4) Publications**

**[Original Articles]**

1. Y. Hashimoto, S. Mukai, S. Sawada, Y. Sasaki, K. Akiyoshi. Advanced artificial extracellular matrices using amphiphilic nanogel-crosslinked thin films to anchor adhesion proteins and cytokines *ACS Biomater Sci Eng.* 2016.02; 2(3); 375-384
2. Y. Suwa, K. Nam, K. Ozeki, T. Kimura, A. Kishida, T. Masuzawa. Thermal denaturation behavior of collagen fibrils in wet and dry environment *J Biomed Mater Res Part B: Appl Biomater.* 2016.04; 104(3); 538-545
3. Y. Hashimoto, S. Hattori, S. Sasaki, T. Honda, T. Kimura, S. Funamoto, H. Kobayashi, A. Kishida. Ultrastructural analysis of the decellularized cornea after interlamellar keratoplasty and microkeratome-assisted anterior lamellar keratoplasty in a rabbit model *Sci Rep.* 2016.06; 6; 27734
4. H. Suzuki, Y. Ito, M. Shinohara, S. Yamashita, S. Ichinose, A. Kishida, T. Oyaizu, T. Kayama, R. Nakamichi, N. Koda, K. Yagishita, MK. Lotz, A. Okawa, H. Asahara. Gene targeting of the transcription factor mohawk in rats causes heterotopic ossification of achilles tendon via failed tenogenesis *Proc Natl Acad Sci USA.* 2016.07; 113(28); 7840-7845
5. K. Akazawa, K. Iwasaki, M. Nagata, N. Yokoyama, H. Ayame, K. Yamaki, Y. Tanaka, I. Honda, C. Morioka, T. Kimura, M. Komaki, A. Kishida, Y. Izumi, I. Morita. Double-layered cell transfer technology for bone regeneration *Sci Rep.* 2016.09; 6; 33286
6. T. Kimura, N. Nakamura, N. Sasaki, Y. Hashimoto, S. Sakaguchi, S. Kimura, A. Kishida. Capture and release of target cells using a surface that immobilizes an antibody via desthiobiotin–avidin interaction *Sens Mater.* 2016.12; 28(12); 1255-1263

**[Misc]**

1. Y. Sawa, K. Matsuda, E. Tatsumi, G. Matsumiya, T. Tsukita, T. Abe, K. Fukunaga, A. Kishida, K. Kokubo, T. Masuzawa, A. Myoui, M. Nishimura, T. Nishimura, T. Nishinaka, E. Okamoto, S. Tokunaga, T. Tomo, Y. Yagi, T. Yamaoka. Journal of Artificial Organs 2015:the year in review *Journal of Artificial Organs.* 2016.03; 19(1); 1-7
2. N. Nakamura, T. Kimura, A. Kishida. Overview of the development, applications, and future perspectives of decellularized tissues and organs *ACS Biomater Sci Eng.* 2016.11; 1-9

**[Conference Activities & Talks]**

1. K. S. Furukawa, E. G. Santoso, K. Yoshida, Y. Hirota, O. Yoshino, A. Kishida, T. Hiraoka, Y. Osuga, S. Saito, T. Ushida. Uterine tissue engineering using a decellularized scaffold by hydrostatic pressure. 10th World Biomaterials Congress 2016.05.17 Montreal, Canada
2. T. Kimura, H. Morita, P. Wu, N. Nakamura, T. Fujisato, A. Kishida. Electrospun fibers covering of small-diameter decellularized vascular graft for compliance matching. 10th World Biomaterials Congress 2016.05.17 Montreal, Canada

3. A. Kishida, Y. Zhang, K. Nam, T. Kimura. Preparation of gradient-type decellularized tissue/polymer complex for soft tissue-polymer interlinking device. CIMTEC2016 2016.06.05 Perugia, Italy
4. A. Kishida. Biological tissues as new biomaterials. Ireland-Japan Biomaterials and Tissue Engineering Meeting 2016.06.22 Galway,Ireland
5. A. Kishida. Reconstruction of periodontal tissue using decellularized biological tissue. 2nd Bone and Biomaterials Workshop 2016.08.07 Inari, Finland
6. T. Kimura, P. Wu, N. Nakamura, Y. Hashimoto, A. Yamashita, S. Funamoto, T. Fujisato, A. Kishida. Development of small-diameter decellularized vascular graft combined with electrospun fibers. 2016 Annual Conference of the Asia-Pacific Society for Artificial Organs 2016.08.27 Tianjin,China
7. N. Nakamura, T. Kimura, Y. Hashimoto, T. Fujisato, T. Tsuji, A. Kishida. Preparation of decellularized periodontal ligament for periodontal reconstruction. 2016 Annual Conference of the Asia-Pacific Society for Artificial Organs 2016.08.27 Tianjin,China
8. T. Kimura, P. Wu, H. Morita, N. Nakamura, Y. Hashimoto, A. Yamashita, S. Funamoto, T. Fujisato, A. Kishida. Mechanical and biological properties of small-diameter decellularized vascular graft covered by electrospun fibers. 9th International Conference on Fiber and Polymer Biotechnology 2016.09.07 Osaka,Japan
9. A. Yamashita, Y. Hashimoto, Y. Zhang, S. Funamoto, A. Kishida. Animal model for evaluation of anti-adhesive materials after open heart surgery. 9th International Conference on Fiber and Polymer Biotechnology 2016.09.07 Osaka,Japan
10. T. Kimura, Y. Hashimoto, N. Nakamura, Y. Igari, T. Kubota, M. Kondo, S. Higashino, A. Kishida. Development of decellaraized tissues for controlling stem cell functions. The International Symposium on Visualization in Joining & Welding Science through Advanced Measurements and Simulation 2016.10.17 Osaka,Japan
11. T. Kimura, N. Nakamura, Y. Hashimoto, S. Sakaguchi, S. Kimura, A. Kishida. Capture and release of lymphocyte on an antibody-immobilized surface. ICBS2016 2016.11.28 Tokyo,Japan
12. N. Nakamura, T. Kimura, Y. Hashimoto, T. Fujisato, T. Tsuji, A. Kishida . Periodontal tissue reconstruction using decellularized PDL matrix and 3D-printed tooth. 2016 TERMIS-Americas Conference & Exhibition 2016.12.11 San Diego,USA
13. T. Kimura, N. Nakamura, Y. Hashimoto, S. Sakaguchi, S. Kimura, A. Kishida . Label-free capture and collection of target cells using a surface immobilizing antibody. 2016 TERMIS-Americas Conference & Exhibition 2016.12.11 San Diego,USA



## Organic and Medicinal Chemistry

Professor Hiroyuki KAGECHIKA  
Assistant Professor Syuichi MORI  
Assistant Professor Mari YUASA  
Eng Official Emiko KAWACHI  
Secretary Mayumi SHIKAMA

Graduate Student  
Dilihumaer AINIWAER  
Yusuke Okazaki  
Nozomi Tsuemoto  
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Hidekazu Yokoo  
Hiroto Iinuma  
Kazuhiro Imaida  
Ryohei Iwashita  
Tsuyoshi Oikawa  
Yuki Noji  
Mititake Hirano  
Takahiro Miura  
Daiki Kato  
Chihiro Komatsu  
Rie Tsukamoto

### (1) Outline

#### 1) Medicinal Chemistry of Retinoids

Retinoids regulates various significant biological phenomena, such as cell differentiation, proliferation, morphogenesis, metabolism and homeostasis. We have developed novel synthetic retinoid, Am80 (tamibarotene) as drug for acute promyelocytic leukemia. Novel synthetic retinoids have been developed for clinical use in the field of autoimmune diseases, neurodegenerative diseases, metabolic syndromes.

#### 2) Medicinal Chemistry of Nuclear Receptors

Small hydrophobic molecules such as steroid hormones and activated vitamins A/D control various biological phenomena, including growth, development, metabolism, and homeostasis, by binding to and activating specific nuclear receptors. Nuclear receptors have become one of the most significant molecular targets for drug discovery in the fields of cancer, metabolic syndrome, autoimmune diseases, and so on. In this project, novel ligands of various nuclear receptors have been developed.

#### 3) Development of Novel Functional Fluorescent Molecules for Elucidation of Intracellular Signal Transduction Pathways

Functional fluorescent molecules useful in many fields of scientific research, including analytical chemistry or cell biology have been developed.

#### 4) Aromatic Architecture Based on the Steric Properties of N-Methylated Amides

The amide bond structure of amide derivatives often plays a key role in functions such as molecular recognition events or biological activities. In contrast to the extended trans structures of most secondary amides, the corresponding N-methylated compounds exist in cis form in the crystals and predominantly in cis form in various solvents. The cis conformational preference is useful as a building block to construct aromatic molecules with

unique crystal or solution structures.

## (2) Lectures & Courses

Organic and Medicinal Chemistry covers several aspects of organic chemistry, medicinal chemistry and chemical biology. Through this course, students are expected to understand the fundamental knowledge, recent topics, and experimental techniques related to these fields.

## (3) Publications

### [Original Articles]

1. Tsukada, H.; Kawabe, H.; Ohtaka, A.; Saito, Y.; Okamoto, Y.; Tori, M.; Kagechika, H.; Hirota, H.; Gong, X.; Kuroda, C.; Ohsaki, A.. Two new diterpenoids from *Salvia przewarskii* Natural Product Communications. 2016.01; 11(2); 159-161
2. Persaud, S. D.; Park, S. W.; Ishigami-Yuasa, M.; Koyano-Nakagawa, N.; Kagechika, H.; Wei, L.-N.. All trans-retinoic acid analogs promote cancer cell apoptosis through non-genomic Crabp1 mediating ERK1/2 phosphorylation Science Reports. 2016.03; 6; 22396
3. Shawna D Persaud, Sung Wook Park, Mari Ishigami-Yuasa, Naoko Koyano-Nakagawa, Hiroyuki Kagechika, Li-Na Wei. All trans-retinoic acid analogs promote cancer cell apoptosis through non-genomic Crabp1 mediating ERK1/2 phosphorylation. Sci Rep. 2016.03; 6; 22396
4. Takemoto, Y.; Ito, A.; Niwa, H.; Okamura, M.; Fujiwara, T.; Hirano, T.; Handa, N.; Umehara, T.; Sonoda, T.; Ogawa, K.; Tariq, M.; Nishino, N.; Dan, S.; Kagechika, H.; Yamori, T.; Yokoyama, S.; Yoshida, M.. Identification of Cyproheptadine as an Inhibitor of SET Domain Containing Lysine Methyltransferase 7/9 (Set7/9) That Regulates Estrogen-Dependent Transcription Journal of Medicinal Chemistry. 2016.04; 59(8); 3650-3660
5. Yasushi Takemoto, Akihiro Ito, Hideaki Niwa, Mutsumi Okamura, Takashi Fujiwara, Tomoya Hirano, Noriko Handa, Takashi Umehara, Takeshi Sonoda, Kenji Ogawa, Mohammad Tariq, Norikazu Nishino, Shingo Dan, Hiroyuki Kagechika, Takao Yamori, Shigeyuki Yokoyama, Minoru Yoshida. Identification of Cyproheptadine as an Inhibitor of SET Domain Containing Lysine Methyltransferase 7/9 (Set7/9) That Regulates Estrogen-Dependent Transcription. J. Med. Chem.. 2016.04; 59(8); 3650-3660
6. Shunta Nagashima, Junichi Maruyama, Shodai Kawano, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiroshi Nishina, Yutaka Hata. Validation of chemical compound library screening for transcriptional co-activator with PDZ-binding motif inhibitors using GFP-fused transcriptional co-activator with PDZ-binding motif. Cancer Sci.. 2016.06; 107(6); 791-802
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8. Nagashima, S.; Maruyama, J.; Kawano, S.; Iwasa, H.; Nakagawa, K.; Ishigami-Yuasa, M.; Kagechika, H.; Nishina, H.; Hata, Y.. Validation of the chemical compound library screening for TAZ inhibitors by use of green fluorescence protein-fused TAZ Cancer Science. 2016.06; 107(6); 791-802
9. Fujiwara, T.; Ohira, K.; Urushibara, K.; Ito, A.; Yoshida, M.; Kanai, M.; Tanatani, A.; Kagechika, H.; Hirano, T.. Steric structure-activity relationship of cyproheptadine derivatives as inhibitors of histone methyltransferase Set7/9 Bioorganic & Medicinal Chemistry. 2016.07; 24; 4318-4323
10. Yokoo, H.; Ohsaki, A.; Kagechika, H.; Hirano T.. Structural development of canthin-5,6-dione moiety as a fluorescent dye and its application to novel fluorescent sensors Tetrahedron . 2016.08; 72; 5872-5879
11. Tomoya Hirano, Yuki Noji, Takuya Shiraishi, Mari Ishigami-Yuasa, Hiroyuki Kagechika. Development of an ‘OFF-ON-OFF’ fluorescent pH sensor suitable for the study of intracellular pH Tetrahedron. 2016.08; 72; 4925-4930

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13. Yamada, A.; Kazui, Y.; Yoshioka, H.; Tanatani, A.; Mori, S.; Kagechika, H.; Fujii, S. . Development of N-(4-Phenoxyphenyl)benzenesulfonamide Derivatives as Novel Nonsteroidal Progesterone Receptor Antagonists *ACS Medicinal Chemistry Letters*. 2016.09; 7(12); 1028-1033
14. Takashi Fujiwara, Kasumi Ohira, Ko Urushibara, Akihiro Ito, Minoru Yoshida, Misae Kanai, Aya Tanatani, Hiroyuki Kagechika, Tomoya Hirano. Steric structure-activity relationship of cyproheptadine derivatives as inhibitors of histone methyltransferase Set7/9. *Bioorg. Med. Chem.*. 2016.09; 24(18); 4318-4323
15. Hidetomo Yokoo, Ayumi Ohsaki, Hiroyuki Kagechika, Tomoya Hirano. Structural development of canthin-5,6-dione moiety as a fluorescent dye and its application to novel fluorescent sensors *Tetrahedron*. 2016.09; 72; 5872-5879
16. Okamoto-Uchida, Y.; Yu, R.; Miyamura, N.; Arima, N.; Ishigami-Yuasa, M.; Kagechika, H.; Yoshida, S.; Hosoya, T.; Nawa, M.; Kasama, T.; Asaoka, Y.; Alois, R. W.; Elling, U.; Penninger, J. M.; Nishina, S.; Azuma, N.; Nishina, H.. The mevalonate pathway regulates primitive streak formation via protein farnesylation *Science Reports*. 2016.10; 6; 37697
17. Okamoto-Uchida Y, Yu R, Miyamura N, Arima N, Ishigami-Yuasa M, Kagechika H, Yoshida S, Hosoya T, Nawa M, Kasama T, Asaoka Y, Alois RW, Elling U, Penninger JM, Nishina S, Azuma N, Nishina H. The mevalonate pathway regulates primitive streak formation via protein farnesylation *Sci Rep*. 2016.11; 6; 37697
18. Marie Kinoshita, Mai Negishi, Haruka Sakai, Tomoya Hirano, Shuichi Mori, Shinya Fujii, Hiroyuki Kagechika, Aya Tanatani. Development of 6-arylcoumarins as nonsteroidal progesterone antagonists. Structure-activity relationships and fluorescence properties. *Bioorg. Med. Chem.*. 2016.11; 24(21); 5602-5610

#### [Books etc]

1. Research Coaching. Yodosha, 2016.12 (ISBN : 978-4-7581-0159-2)

#### [Conference Activities & Talks]

1. Shuichi Mori, Yusuke Okazaki, Takashi Fujiwara, Asuka Takaguchi, Tomoya Hirano, Hiroyuki Kagechika. Development of novel assay methods for detection of N-monomethylated lysine using SNAr reaction. International Symposium for International Symposium for RIKEN Epigenetics Program 2016 2016.02 Saitama
2. Tomoya Hirano, Michitake Hirano, Takashi Fujiwara, Kasumi Ohira, Akihiro Ito, Minoru Yoshida, Hiroyuki Kagechika. Structure-activity relationships of cyproheptadine derivatives as inhibitors of histone methyltransferase, Set7/9. International Symposium for International Symposium for RIKEN Epigenetics Program 2016 2016.02 Saitama
3. Hirano, T., Hirano, M., Fujiwara, T., Ohira, K., Ito, A., Yoshida, M., Kagechika, H. . Structure-activity relationships of cyroheptadine as inhibitors of histone methyltransferase, Set7/9. International symposium for RIKEN epigenetics program 2016.02 Tokyo
4. Mori, S., Okazaki, Y., Fujiwara, T., Takaguchi, A., Hirano, T., Kagechika, H.. Development of novel assay methods for detection of N-monomethylated lysine using SNAr reaction. International symposium for RIKEN epigenetics program, 2016.02 Tokyo
5. Tomoya Hirano, Takuya Shiraishi, Yuki Noji, Daiki Kato, Hiroyuki Kagechika. Development and biological application of fluorescent sensors for microenvironmental change. The 96th CSJ Annual Meeting 2016.03.25 Kyoto
6. Takuya Shiraishi, Tomoya Hirano, Toshiki Saito, Hiroyuki Kagechika. Development of fluorescent sensors for zinc ion activated by enzymatic reaction. The 96th CSJ Annual Meeting 2016.03.26 Kyoto

7. Ishigami-Yuasa M, Ekimoto H, Kagechika H.. Synergistic inhibition of several human cancer cell proliferations by a synthetic retinoid tamibarotene (Am80) in combination with the epigenetic modulators.. The 3RD International conference on Retinoids 2016.06.19 Florida, USA
8. Kagechika, H.. Development of novel retinoids with unique hydrophobic pharmacophore. FASEB meeting on retinoid 2016.06.20 Florida, USA
9. Hirano, T., Shiraishi, T., Noji, Y., Kato, D., Kagechika, H.. Development of fluorescent sensors for microenvironmental change based on fluorescent compounds library. 252nd ACS National Meeting 2016.08 Philadelphia, USA
10. Yokoo, H., Hirano, T., Ohsaki, A., Kagechika, H.. Development of Novel Fluorescent Sensors Based on Fluorescent Natural Compounds. 252nd ACS National Meeting 2016.08 Philadelphia, USA
11. Tanatani, A., Tojo, Y., Urushibara, K., Yamamoto, S., Mori, H., Masu, H., Kudo, M., Hirano, T., Kagechika, H.. N-Alkylated Pyrroleamide Oligomers with Folded Cis-Amide Conformation. Symposium on Foldamers 2016 2016.09.26 Bordeaux-Pessac, France
12. Mori, S., Oshida, Y., Watanabe, Y., Yuasa, M., Kagechika, H.. Development of novel store-operated calcium entry inhibitors. Int. Chem. Biol. Symp 2016.10 Madison, USA
13. Okazaki, Y., Fujiwara, T., Takaguchi, A., Hirano, T., Mori, S., Kagechika, H.. Development of a facile method to detect the activity of histone methyltransferase based on SNAr reaction. Int. Chem. Biol. Symp 2016.10 Madison, USA
14. Rawangkan, A., Oya, Y., Iida, K., Kagechika, H., Shudo, K., Fujiki, H., Suganuma, M. . Innovative strategy of cancer treatment with the combination of Am80, a potent synthetic retinoid, and green tea catechin via down-regulation of histone deacetylase 4, -5, and -6. Int. Symp. Biomed. Engineer. 2016.11.10 Tokyo
15. Hirano, T., Noji, Y., Kato, D., Shiraishi, T., Kagechika, H.. Development of fluorescent sensors for microenvironmental change. Int. Symp. Biomed. Engineer. 2016.11.10 Tokyo
16. Mori, S., Takagaki, R., Fujii, S., Matsumura, M., Tanatani, A., Kagechika, H.. Development of m-carborane-based progesterone receptor ligands and their optical resolution by lipase reaction. Int. Symp. Biomed. Engineer. 2016.11.10 Tokyo
17. Ishigami-Yuasa, M., Ekimoto, H., Kagechika, H.. Synergistic inhibition of several human cancer cell proliferations by a synthetic retinoid tamibarotene (Am80) in combination with the epigenetic modulators. Int. Symp. Biomed. Engineer. 2016.11.10 Tokyo
18. Kagechika, H.. Development of Functional Molecules with Unique Scaffolds. The 3rd Joint Symp. IBB/TMDU & Chulalongkorn Univ. Biomed. Mater. Engineer. 2016.12.15 Bangkok
19. Ishigami-Yuasa, M., Ekimoto, H., Kagechika, H.. Synergistic inhibition of several human cancer cell proliferations by a synthetic retinoid tamibarotene (Am80) in combination with the epigenetic modulators. FASEB meeting on retinoid Florida, USA
20. Tsuemoto, N., Mori, S., Kawachi, E., Kagechika, H.. Design and synthesis of novel RAR ligands containing pentafluorosulfanyl group. FASEB meeting on retinoid Florida, USA

#### [Patents]

1. Lck binding protein, Patent Number : United States Patent 5891673
2. IKK3 kinase, Patent Number : United States Patent 6576439
3. A protein kinase (IKK4) involved in the phosphorylation of IKB, Patent Number : WO/2001/044444

#### [Works]

1. Expression Vectors <http://dna.brc.riken.jp/search/dep3357.html>, Other, RIKEN

#### [Awards & Honors]

1. The Vitamin Society of Japan Award, Vitamin Society of Japan, 2016.06

## Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Suguru YOSHIDA
Assistant Professor	Yoshitake NISHIYAMA
Technical Assistant	Yoshihiro MISAWA, Yuki HAZAMA, Tomoko KURIBARA
Graduate Students	Takamoto MORITA, Kazuya KANEMOTO, Keisuke UCHIDA, Tomohiro MEGURO, Kei AKIYAMA, Kazuhiro OYA, Akira NAGAI, Hana NAKAJIMA, Yu NAKAMURA, Naoaki MAKIO, Kotaro MUTSUURA, Shonan CHIN, Youngchan KIM, Tsubasa MATSUZAWA, Yuya TAMURA
Collaborators	Shuhei KAMADA, Yoshihira MIYATA Keita SHIMIZU, Norikazu TERASHIMA

### ( 1 ) Outline

Development of new organic synthetic methods, new chemical methodologies, and new chemical tools, those are useful for biological and drug discovery researches.

### ( 2 ) Research

- 1) Development of novel generation methods for benzyne species and their synthetic applications.
- 2) Development of new bioconjugation methods using strained alkynes.
- 3) Target identification of drugs or drug candidates by photoaffinity labeling based on diazido probe method..
- 4) Development of new molecular ligation methods based on new azido chemistry.
- 5) Design and synthesis of efficient substrates for bioluminescence reactions and fluorescent probes for bioimaging and diagnosis of diseases.
- 6) Design and synthesis of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

### ( 3 ) Publications

#### [Original Articles]

1. Isao Kii, Yuto Sumida, Toshiyasu Goto, Rie Sonamoto, Yukiko Okuno, Suguru Yoshida, Tomoe Kato-Sumida, Yuka Koike, Minako Abe, Yosuke Nonaka, Teikichi Ikura, Nobutoshi Ito, Hiroshi Shibuya, Takamitsu Hosoya, Masatoshi Hagiwara. Selective inhibition of the kinase DYRK1A by targeting its folding process. *Nat Commun.* 2016; 7; 11391
2. Tomabechi Y, Hosoya T, Ehara H, Sekine S, Shirouzu M, Inouye S. Crystal structure of nanoKAZ: The mutated 19 kDa component of *Oplophorus* luciferase catalyzing the bioluminescent reaction with coelenterazine. *Biochem Biophys Res Commun.* 2016.01; 470(1); 88-93

3. Uetake Y, Niwa T, Hosoya T. Rhodium-Catalyzed *ipso*-Borylation of Alkylthioarenes via C-S Bond Cleavage Org Lett. 2016.06; 18(11); 2758-2761
4. Yoshida S, Morita T, Hosoya T. Synthesis of Diverse Benzotriazoles from Aryne Precursors Bearing an Azido Group via Inter- and Intramolecular Cycloadditions Chem Lett. 2016.07; 45(7); 726-728
5. Yoshida S, Shimomori K, Kim Y, Hosoya T. Single C-F Bond Cleavage of Trifluoromethylarenes with an *ortho*-Silyl Group Angew Chem Int Ed Engl. 2016.08; 55(35); 10406-10409
6. Controlled Generation of 3-Triflyloxyarynes Synthesis. 2016.08; 48(23); 4099-4109
7. Tanaka T, Okuyama-Dobashi K, Murakami S, Chen W, Okamoto T, Ueda K, Hosoya T, Matsuura Y, Ryo A, Tanaka Y, Hagiwara M, Moriishi K. Inhibitory effect of CDK9 inhibitor FIT-039 on hepatitis B virus propagation Antiviral Res. 2016.09; 133; 156-164
8. Yoshida S, Yano T, Nishiyama Y, Misawa Y, Kondo M, Matsushita T, Igawa K, Tomooka K, Hosoya T. Thiazolobenzyne: a versatile intermediate for multisubstituted benzothiazoles Chem Commun. 2016.09; 52(75); 11199-11202
9. Doi H, Sato K, Shindou H, Sumi K, Koyama H, Hosoya T, Watanabe Y, Ishii S, Tsukada H, Nakanishi K, Suzuki M. Blood-brain barrier permeability of ginkgolide: Comparison of the behavior of PET probes 7  $\alpha$ -[ $^{18}\text{F}$ ] fluoro- and 10-*O-p*-[ $^{11}\text{C}$ ] methylbenzyl ginkgolide B in monkey and rat brains Bioorg Med Chem. 2016.11; 24(21); 5148-5157
10. Sumida Y, Sumida T, Hashizume D, Hosoya T. Preparation of Aryne-Nickel Complexes from *ortho*-Borylaryl Triflates Org Lett. 2016.11; 18(21); 5600-5603
11. Okamoto-Uchida Y, Yu R, Miyamura N, Arima N, Ishigami-Yuasa M, Kagechika H, Yoshida S, Hosoya T, Nawa M, Kasama T, Asaoka Y, Alois RW, Elling U, Penninger JM, Nishina S, Azuma N, Nishina H. The mevalonate pathway regulates primitive streak formation via protein farnesylation Sci Rep. 2016.11; 6; 37697
12. Ochiai H, Niwa T, Hosoya T. Stereoinversion of Stereocongested Carbocyclic Alcohols via Triflylation and Subsequent Treatment with Aqueous *N,N*-Dimethylformamide Org Lett. 2016.12; 18(23); 5982-5985
13. Yoshida S, Nakamura Y, Uchida K, Hazama Y, Hosoya T. Aryne Relay Chemistry en Route to Aminoarenes: Synthesis of 3-Aminoaryne Precursors via Regioselective Silylamination of 3-(Triflyloxy)arynes. Org Lett. 2016.12; 18(23); 6212-6215

#### [Conference Activities & Talks]

1. Uchida K, Yoshida S, Igawa K, Tomooka K, Hosoya T. An efficient generation method and remarkable reactivities of 3-triflyloxybenzyne. The 12th International Symposium on Organic Reactions (ISOR-12) 2016.04.22 Kyoto, Japan
2. Nakamura Y, Uchida K, Hazama Y, Yoshida S, Hosoya T. Facile Synthesis of 3-Aminoaryne Precursors via Aminosilylation of 3-Triflyloxyarynes. The 12th International Symposium on Organic Reactions (ISOR-12) 2016.04.23 Kyoto, Japan
3. Yoshida S, Uchida K, Nakamura Y, Nonaka T, Morita T, Nagai A, Igawa K, Tomooka K, Hosoya T. Trimethylsilylmethyl Grignard Reagent: a Mild Activator Triggering Efficient Generation of Arynes from Various *ortho*-Iodoaryl Triflates. 11th International Symposium on Carbanion Chemistry (ISCC-11) 2016.07.20 Rouen, France
4. Hosoya T. Azido-type selective reactions for target identification and probe synthesis. 3rd Symposium of SPU Innovative Project for Pharmaceutical Analyses of Covalent Modification in Biomolecules "Chemistry-Natural Product Chemistry, Structural Chemistry, Synthetic Chemistry and Chemical Biology" 2016.09.01 Tokyo, Japan

# Biomechanics

Kenji Kawashima  
Takahiro Kanno

## ( 1 ) Outline

Our Lab. mainly working on the development of medical devises and systems based on control engineering, robotics and fluid dynamics.

Key word is system integration such as hardware and software, electrical and pneumatics, human and machine.

## ( 2 ) Research

- 1) Forceps manipulator for minimally invasive surgery
- 2) Power assist devices using pneumatic actuators
- 3) Medical devices using soft actuators
- 4) Surgical robot system
- 5) Tele-operation of robots using biological information

## ( 3 ) Education

Learn about mechanical design and control engineering for medical devices based on biomechanics. Master a basic skill to develop the devices from the researchers and engineers working on the medical devices and systems. Learn the basic control method of a surgical robot using a personal computer.

## ( 4 ) Lectures & Courses

The object is to provide the ability to design and develop medical devices based on biomechanics, which studies the structure and function of biological systems, with mechanical dynamics, robotics and control engineering.

## ( 5 ) Publications

### [Original Articles]

1. Hongbing Li, Kenji Kawashima. Bilateral teleoperation with delayed force feedback using time domain passivity controller Robotics and Computer-Integrated Manufacturing. 2016.02; 37; 188-196



2. Mohammadreza Kamali, Seyed Ali Jazayeri, Farid Najafi, Kenji Kawashima, Toshiharu Kagawa. Integrated Nozzle-Flapper Valve with Piezoelectric Actuator and Isothermal Chamber; A Feedback Linearization Multi-Control Device *Journal of Mechanical Science and Technology*. 2016.05; 20(5); 2293-2301
3. Mohammadreza Kamali, Seyed Ali Jazayeri, Farid Najafi, Kenji Kawashima, Toshiharu Kagawa. Study on Performance and Control of Piezo-Actuated Nozzle-Flapper Valve with Isothermal Chamber *Journal of Mechanical Engineering*. 2016.05; 62(5); 318-328
4. Haruka Sakurai, Takahiro Kanno, Kenji Kawashima . Thin-diameter Chopsticks Robot for Laparoscopic Surgery *IEEE International Conference on Robotics and Automation*. 2016.05; 4122-4127
5. Kengo Watanabe, Takahiro Kanno, Kazuhisa Ito, Kenji Kawashima. Human-Integrated Automation of suturing task with One-Master Two-Slave System for Laparoscopic Surgery *IEEE International Conference on Advanced Intelligent Mechatronics*. 2016.07; 1180-1185
6. Kyouhei Takikawa, Ryoken Miyazaki, Takahiro Kanno, Gen Endo, Kenji Kawashima. Pneumatically driven multi-DOF surgical forceps manipulator with a bending joint using continuums *Journal of Robotics and Mechatronics*. 2016.08; 28(4); 559-567
7. Sho Yoshida, Takahiro Kanno, Kenji Kawashima,. A Novel RCM Mechanism Using Pneumatically Driven Flexible Joint for Laparoscopic Forceps Holder *IEEE International Symposium on Robot and Human Interactive Communication (RO-MAN 2016)*. 2016.08;
8. Ryoken Miyazaki, Takahiro Kanno, Kenji Kawashima,. Pneumatically-Driven Hand-held Forceps with Wrist Joint Operated by Built-in Master Controller *IEEE ICMA 2016*. 2016.09; 442-447
9. Masahiko Minamoto, Kenji Kawashima, Takahiro Kann. Effect of Force Feedback on a Bulldozer-Type Robot *IEEE ICMA 2016*. 2016.09; 2203-2208
10. Hongbing Li, Kenji Kawashima. Achieving Stable Tracking in Wave-Variable-Based Teleoperation. (ACCEPT) *IEEE/ASME Transactions on Mechatronics (TMECH)*.

# Molecular Cell Biology

Professor Hiroshi Shibuya  
Associate Professor Toshiyasu Goto  
Assistant Professor Atsushi Sato

## ( 1 ) Lectures & Courses

Various signaling molecules inducing the cell-growth and differentiation regulate morphogenesis and organogenesis of the vertebrate. The failure of these signal molecules has also been caused with induction of the diseases. Therefore, the elucidation of signal transduction network regulating generation and differentiation is important upon clarifying the mechanism of morphogenesis, organogenesis and diseases. Our research aim is to clarify the signal transduction network regulating the mechanisms of morphogenesis and organogenesis in developmental process. We serve these research and following education to provide graduate students who will become senior scientists in life sciences.

## ( 2 ) Publications

### [Original Articles]

1. Isao Kii, Yuto Sumida, Toshiyasu Goto, Rie Sonamoto, Yukiko Okuno, Suguru Yoshida, Tomoe Kato-Sumida, Yuka Koike, Minako Abe, Yosuke Nonaka, Teikichi Ikura, Nobutoshi Ito, Hiroshi Shibuya, Takamitsu Hosoya, Masatoshi Hagiwara. Selective inhibition of the kinase DYRK1A by targeting its folding process. *Nat Commun.* 2016; 7; 11391
2. Takashi Fukuzono, Strahil Iv Pastuhov, Okinobu Fukushima, Chun Li, Ayuna Hattori, Shun-Ichiro Iemura, Tohru Natsume, Hiroshi Shibuya, Hiroshi Hanafusa, Kunihiro Matsumoto, Naoki Hisamoto. Chaperone complex BAG2-HSC70 regulates localization of *Caenorhabditis elegans* leucine-rich repeat kinase LRK-1 to the Golgi. *Genes Cells.* 2016.04; 21(4); 311-324
3. Toshiyasu Goto, Junhei Matsuzawa, Shun-Ichiro Iemura, Tohru Natsume, Hiroshi Shibuya. WDR26 is a new partner of Axin1 in the canonical Wnt signaling pathway. *FEBS Lett.* 2016.05; 590(9); 1291-1303
4. Ogawa Y., Nonaka Y., Goto T., Ohnishi E., Hiramatsu T., Kii I., Yoshida M., Ikura T., Onogi H., Shibuya H., Hosoya T., Ito N., Hagiwara M.. Development of a novel selective inhibitor of the Downsyndrome-related kinase Dyrk1A. (INPRES) *Nat. Commun.*

# Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D.  
 Associate Professor Jun Hirayama, Ph.D.  
 Assistant Professor Norio Miyamura, Ph.D.  
 Technical Assistants Yumi Akagawa  
 Secretary Kazuko Tanaka

## (1) Outline

Our goal is to define the molecular basis for the mechanism of organ formation and regeneration using knockout mice and mutant fishes. To accomplish this goal, we have focused on defining signaling molecules and pathways that regulate liver formation and stress responses. Moreover, we are trying to establish a cell therapy for intractable diseases such as liver failures using self-bone marrow cells. Our study will provide new insights into understanding the precise molecular mechanisms that underlie organ failures found in human disease and will lead to the development of new rational therapy for the diseases.

## (2) Research

- 1) Studies on the stress-activated protein kinase (SAPK/JNK) signaling pathway
- 2) Studies on the Hippo signaling pathway
- 3) Studies on the cell differentiation of mouse ES cells
- 4) Studies on liver formation using a small fish, Medaka, *Oryzias latipes*
- 5) Studies on liver regeneration using mice
- 6) Studies on circadian clock using zebrafish and mice

## (3) Publications

### [Original Articles]

1. Miki Nishio, Keishi Sugimachi, Hiroki Goto, Jia Wang, Takumi Morikawa, Yosuke Miyachi, Yusuke Takano, Hiroki Hikasa, Tohru Itoh, Satoshi O Suzuki, Hiroki Kurihara, Shinichi Aishima, Andrew Leask, Takehiko Sasaki, Toru Nakano, Hiroshi Nishina, Yuji Nishikawa, Yoshitaka Sekido, Kazuwa Nakao, Kazuo Shin-Ya, Koshi Mimori, Akira Suzuki. Dysregulated YAP1/TAZ and TGF- $\beta$  signaling mediate hepatocarcinogenesis in Mob1a/1b-deficient mice. *Proc. Natl. Acad. Sci. U.S.A.*. 2016.01; 113(1); E71-E80
2. Yusuke Nasu, Yoichi Asaoka, Misako Namae, Hiroshi Nishina, Hideaki Yoshimura, Takeaki Ozawa. Genetically Encoded Fluorescent Probe for Imaging Apoptosis in Vivo with Spontaneous GFP Complementation. *Anal. Chem.*. 2016.01; 88(1); 838-844
3. Koichi Fujisawa, Shuji Terai, Taro Takami, Naoki Yamamoto, Takahiro Yamasaki, Toshihiko Matsumoto, Kazuhito Yamaguchi, Yuji Owada, Hiroshi Nishina, Takafumi Noma, Isao Sakaida. Modulation of anti-cancer drug sensitivity through the regulation of mitochondrial activity by adenylate kinase 4. *J. Exp. Clin. Cancer Res.*. 2016.03; 35; 48
4. Yoichi Asaoka, Yoko Nagai, Misako Namae, Makoto Furutani-Seiki, Hiroshi Nishina. SLC7 family transporters control the establishment of left-right asymmetry during organogenesis in medaka by activating mTOR signaling. *Biochem. Biophys. Res. Commun.*. 2016.05; 474(1); 146-153

5. Takanori Chiba, Erika Ishihara, Norio Miyamura, Rika Narumi, Mihoko Kajita, Yasuyuki Fujita, Akira Suzuki, Yoshihiro Ogawa, Hiroshi Nishina. MDCK cells expressing constitutively active Yes-associated protein (YAP) undergo apical extrusion depending on neighboring cell status. *Sci Rep.* 2016.06; 6; 28383
6. Shunta Nagashima, Junichi Maruyama, Shodai Kawano, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiroshi Nishina, Yutaka Hata. Validation of chemical compound library screening for transcriptional co-activator with PDZ-binding motif inhibitors using GFP-fused transcriptional co-activator with PDZ-binding motif. *Cancer Sci.* 2016.06; 107(6); 791-802
7. Okamoto-Uchida Y, Yu R, Miyamura N, Arima N, Ishigami-Yuasa M, Kagechika H, Yoshida S, Hosoya T, Nawa M, Kasama T, Asaoka Y, Alois RW, Elling U, Penninger JM, Nishina S, Azuma N, Nishina H. The mevalonate pathway regulates primitive streak formation via protein farnesylation *Sci Rep.* 2016.11; 6; 37697

# Immunology

Professor: Takeshi TSUBATA, M.D., Ph.D.  
 Associate Professor: Takahiro ADACHI, Ph.D.  
 Assistant Professors: Naoko MATSUBARA Ph.D.  
 Specially Appointed Assistant Professor: Chizuru AKATSU Ph.D.  
 Specially Appointed Junior Associate Professor: Ji-Yang WANG Ph.D.  
 Project Researcher: Miao Tang Ph.D., Toshitaro Takata, Ph.D., Mohanmmad Aslam, Ph.D.  
 Technicians: Yukie KURUSU, Shigeko NAKANO  
 Secretary: Chikako SAWADA  
 Graduate Students: Nazim Medzhidov, Yang-Yang Feng  
 Graduate Students: Amin ALBORZIAN DESHEIKH,  
 Graduate Students: Sundararaman RENGARAJAN,  
 Graduate Students: Yang Hongrui, Li Xuexin

## ( 1 ) Research

The nature of immune responses depends on whether they respond to protein or non-protein antigens because T lymphocytes recognize only protein antigens. Normal immune system removes pathogens and cancer cells but does not respond to non-microbial foreign substances or self-antigens. Immune responses to non-microbial foreign substances and self-antigens cause allergy and autoimmune diseases, respectively. How the immune system distinguishes pathogens from non-microbial antigens and self-antigens is already clarified for protein antigens. However, little is know about such distinction for non-protein antigens. Immune responses to non-protein antigens play crucial roles in host defense against pathogens such as tuberculosis bacilli and meningococci, and autoimmune diseases such as lupus and immuno-neurological disorders. Thus, immune responses to non-protein antigens constitute a remaining frontier in immunology research. Followings are our research subjects.

## ( 2 ) Education

Lecture course on immunology at the master course aims at giving the students the basic ideas how immune system recognize and respond to the antigens, and how immune system efficiently remove pathogens without responding to self-antigens and environmental antigens. In the lecture course in bioscience at the doctor course, lectures on immune responses are given so that the students are introduced with the current topics in the field of humoral immune responses. Research projects in both master and doctor courses aims at training the students to acquire basic research techniques on immunology, molecular biology and biochemistry, and abilities to conduct cutting-edge research in the field of immunology by themselves under supervision.

## ( 3 ) Publications

### [Original Articles]

1. Li, Y., Takahashi, Y., Fujii, S., Suzuki, A., Tsubata, T., Hase, K. and Wang, J-Y.. EAF2 mediates germinal center B cell apoptosis to suppress excessive immune responses and prevent autoimmunity Nature Communications. 2016; 7(10836);

2. Tsubata, T.. CD22 and CD72 are inhibitory receptors dominantly expressed in B lymphocytes and regulate systemic autoimmune diseases. *Z. Rheumatol.* 2016; 75; 86-89
3. Akatsu, C., Shinagawa, K., Numoto, N., Liu, Z., Konuscan, A.U., Aslam, M., Phoon, S., Adachi, T., Furukawa, K., Ito, N. and Tsubata. T.. CD72 negatively regulates B lymphocyte responses to the lupus-related endogenous Toll-like receptor 7 ligand Sm/RNP. *J. Exp. Med.* 2016; 213; 2691-2706
4. Adachi T, Kakuta S, Aihara Y, Kamiya T, Watanabe Y, Osakabe N, Hazato N, Miyawaki A, Yoshikawa S, Usami T, Karasuyama H, Kimoto-Nira H, Hirayama K, Tsuji NM.. Visualization of Probiotic-Mediated Ca<sup>2+</sup> Signaling in Intestinal Epithelial Cells In Vivo. *Front Immunol.* 2016; 7(601);

#### [Books etc]

1. Li, Y., Takahashi, Y., Fujii, S., Suzuki, A., Tsubata, T., Hase, K. and Wang, J-Y.. EAF2 mediates germinal center B cell apoptosis to suppress excessive immune responses and prevent autoimmunity. *Nature Communications*, 2016

#### [Conference Activities & Talks]

1. Kai Jin, Toshihiro Imada, Yusuke Izuta, Shigeru Nakamura, Takahiro Adachi, Kazuo Tsubota. IN VIVO VISUALIZATION OF Ca<sup>2+</sup> DYNAMICS OF MYOEPITHELIAL CELLS IN LACRIMAL GLAND. 8th International Conference on the Tea Film & Ocular Surface Basic Science and Clinical Relevance 2016.09.08 FRANCE
2. Chizuru Akatsu, Kenro Shinagawa, Nobutaka Numoto, Zhihong Liu, Mohommad Aslam, Nobutoshi Ito, Takeshi Tsubata. B cells reactive to Sm/RNP, a lupus-related self-antigen. 12th International Conference on Protein Phosphatase (ICPP12) 2016.10.28 OSAKA
3. Takeshi Tsubata. B lymphocytes and autoimmunity. Fudan University School of Basic Medical Sciences, China 2016.11.07 SHANGHAI, CHINA
4. Takeshi Tsubata. Development of a novel glycomimetic with unique immunological activity. . 15th Surugadai International Symposium "Current Status and Future of Drug Discovery" 2016.11.29 TOKYO
5. TSUJI Noriko M, KAMIYA Tomonori, WATANABE yohei, KAKUTA Shigeru, ADACHI Takahiro. Effects of fermented food on immune response and gut microbiota of human faecal flora-associated (HFA) mice. The 45th Annual Meeting of The Japanese Society for Immunology (JSI) 2016.12.05 OKINAWA
6. Medzhidov Nazim, Takata toshitaro, Suzuki Mitsuhiro, Ichinose Shizuko, Tsubata Takeshi. Distinct ubiquitination level and sorting of B cell receptor. The 45th Annual Meeting of The Japanese Society for Immunology (JSI) 2016.12.06 OKINAWA
7. ADACHI Takahiro, KARASUYAMA Hajime, YOSHIKAWA Soichiro. Visualization of immune responses by intravital imaging of Ca<sup>2+</sup> signals. The 45th Annual Meeting of The Japanese Society for Immunology (JSI) 2016.12.07 OKINAWA

# Epigenetics

Professor Fumitoshi Ishino  
 Associate Professor Takashi Kohda  
 Assistant Professor Hirosuke Shiura  
 Assistant Professor Yuki Kawasaki  
 Project Lecturere Jiyoung Lee  
 Adjunct Lecturere Shin Kobayashi

## ( 1 ) Outline

Epigenetics and Genetics are basics of biology that enables us to elucidate several ‘genomic functions’ in inheritance, development and evolution of the organisms including our human beings. Genomic imprinting is a mammalian-specific epigenetic mechanism that gives rise to functional differences between paternally- and maternally-derived genomes in development, behavior and growth. Somatic cloned animals give us unique chances to examine ‘genetically identical but epigenetically diverged animals’. Mammalian-specific LTR retrotransposon-derived genes are essential for mammalian development, such as placenta and brain functions. These studies show us how Epigenetics and Genetics are important in mammalian biology. We focus on these mammalian-specific genomic functions to elucidate how these genomic functions work and have been evolved as new genomic functions during evolution. Our final goal is to contribute to the human biology as well as medicine in the 21st century by novel understanding of genomic functions.

## ( 2 ) Research

- 1) Genomic imprinting in human and mammalian development.
- 2) Placenta function and its evolution in mammals.
- 3) Somatic cloning: its epigenetic effects and application to regenerative medicine.
- 4) Assisted reproductive technology: its epigenetic effects and safer application.
- 5) Role of retrotransposon-derived genes in mammalian specific genomic functions.

## ( 3 ) Education

Graduate School of Medical and Dental Science  
 Life Science and Technology Track  
 Bioscience I  
 Medical and Dental Science and Technology Track  
 Molecular and Cellular Biology  
 Developmental and Regenerative Bioscience  
 Molecular Cell Biology  
 Introduction to Human Molecular Genetics

Faculty of Medicine  
 Molecular Genetics



**( 4 ) Lectures & Courses**

Obtain basic and applicative knowledges and techniques by challenging cutting-edge themes.

**( 5 ) Clinical Services & Other Works**

Research Center for Science Systems, Senior Researcher

Japan Society for Biological Sciences, Board member

Japan Society for Epigenetics, Secretary

**( 6 ) Publications**

**[Original Articles]**

1. Masahito Irie, Akihiko Koga, Tomoko Kaneko-Ishino, Fumitoshi Ishino. An LTR Retrotransposon-Derived Gene Displays Lineage-Specific Structural and Putative Species-Specific Functional Variations in Eutherians. *Front Chem.* 2016.06; 4; 26
2. Kobayashi S\*, Hosoi Y, Shiura H, Yamagata K, Takahashi S, Fujihara Y, Kohda T, Okabe M and Ishino F.. Live imaging of X chromosome reactivation dynamics in early mouse development can discriminate naïve from primed pluripotent stem cells. *Development.* 2016.08; 143(16); 2958-2964
3. Yuki Kawasaki, Yukiko Kuroda, Isao Suetake, Shoji Tajima, Fumitoshi Ishino, Takashi Kohda. A Novel method for the simultaneous identification of methylcytosine and hydroxymethylcytosine at a single base resolution. *Nucleic Acids Res.* 2016.10; 45(4); e24

**[Conference Activities & Talks]**

1. Masahito Irie, Tomoko Kaneko-Ishino, Fumitoshi Ishino. Cognitive function regulated by an LTR retrotransposon-derived gene, Sirh11/Zcchc16. . 1st Korea-Japan International Symposium for Transposable Elements 2016.06.10 Busan, Korea
2. Fumitoshi Ishino. Mammalian-specific genomic functions: Newly acquired traits generated by genomic imprinting and LTR retrotransposon-derived genes in mammals. . Annual Meeting of Korean Society for Life Science 2016.08.22 K-Hotel, Gyeongju, Korea
3. Fumitoshi Ishino, Tomoko Kaneko-Ishino. . Mammalian evolution by gene acquisition from Retrotransposons.. The 20th Evolutionary Biology Meeting at Marseilles 2016.09.21 CRDP, Marseilles, France
4. Tomoko Kaneko-Ishino, Masahito Irie, Akihiko Koga, Fumitoshi Ishino.. An LTR retrotransposon derived SIRH11/ZCCHC16 gene involved in cognitive function displays lineage-specific structural and putative species-specific functional variations in eutherians. . The 20th Evolutionary Biology Meeting at Marseilles 2016.09.22 CRDP, Marseilles, France
5. Futmitoshi Ishino, Tomoko Kaneko-Ishino. Fumitoshi Ishino. Regulation of placental function by mammalian-specific genes from retrotransposons.. The 2nd IMCR Symposium on Endocrine and Metabolism:International Frontiers in Homeostatic Regulation Research 2016.11.21 Tojo Hall, Gunma University, Gunma
6. Fumitoshi Ishino, Tomoko Kaneko-Ishino. . Mammalian evolution by gene acquisition from retrotransposons. . Symposium : Unidentified functions of the genome, The 39th Annual Meeting of MBSJ 2016.12.01 Pacifico Yokohama, Yokohama

# Medical Science Mathematics

Professor: Tatsuhiko Tsunoda, Junior Associate Professor: Daichi Shigemizu, Assistant Professor: Fuyuki Miya

## (1) Outline

Medical application of rapidly progressing omic profiling technologies and, in particular, the promotion of personalized/precision/preventive medicine have been keenly desired. Our department overcomes such medical science issues by using a combination of mathematics and computational sciences: (1) Integrative analysis of clinical and omic data for exploring etiologies of intractable diseases, (2) Molecular classification of and systems approach to understanding disease based on omic profiling, and (3) Prediction for personalized/precision/preventive medicine - we apply mathematical methods, e.g, machine learning techniques, to optimum therapy prediction for each patient when she/he visits to a hospital/medical institute, and we can also apply these methods to disease prevention based on an individual's health check records.

## (2) Publications

### [Original Articles]

1. Cristian Pattaro, ..., Madhumathi Rao, Maksim Struchalin, Marcus E Kleber, Margherita Cavalieri, Margot Haun, Marilyn C Cornelis, Marina Ciullo, Mario Pirastu, Mariza de Andrade, Mark A McEvoy, Mark Woodward, Martin Adam, Massimiliano Cocca, Matthias Nauck, Medea Imboden, Melanie Waldenberger, Menno Pruijm, Marie Metzger, Michael Stumvoll, Michele K Evans, Michele M Sale, Mika Kähönen, Mladen Boban, Murielle Bochud, , , , , , , ICBP Consortium; AGEN Consortium; CARDIOGRAM; CHARGE-Heart Failure Group; ECHOGEn Consortium, , , , , , , Tonu Esko, Toshiko Tanaka, Ulf Gyllenstein, Uwe Völker, Valur Emilsson, Veronique Vitart, Ville Aalto, Vilmundur Gudnason, Vincent Chouraki, Wei-Min Chen, Wilmar Igl, Winfried März, Wolfgang Koenig, Wolfgang Lieb, Ruth J F Loos, Yongmei Liu, Harold Snieder, Peter P Pramstaller, Afshin Parsa, Jeffrey R O'Connell, Katalin Susztak, Pavel Hamet, Johanne Tremblay, Ian H de Boer, Carsten A Böger, Wolfram Goessling, Daniel I Chasman, Anna Köttgen, W H Linda Kao, Caroline S Fox. Genetic associations at 53 loci highlight cell types and biological pathways relevant for kidney function. *Nat Commun.* 2016.01; 7; 10023
2. Maki Morishita, Tomoki Muramatsu, Yumiko Suto, Momoki Hirai, Teruaki Konishi, Shin Hayashi, Daichi Shigemizu, Tatsuhiko Tsunoda, Keiji Moriyama, Johji Inazawa. Chromothripsis-like chromosomal rearrangements induced by ionizing radiation using proton microbeam irradiation system. *Oncotarget.* 2016.03; 7(9); 10182-10192
3. James Lyons, Kuldeep K Paliwal, Abdollah Dehzangi, Rhys Heffernan, Tatsuhiko Tsunoda, Alok Sharma. Protein fold recognition using HMM-HMM alignment and dynamic programming. *J. Theor. Biol.* 2016.03; 393; 67-74
4. Atsuko Konta, Kouichi Ozaki, Yasuhiko Sakata, Atsushi Takahashi, Takashi Morizono, Shinichiro Suna, Yoshihiro Onouchi, Tatsuhiko Tsunoda, Michiaki Kubo, Issei Komuro, Yoshinobu Eishi, Toshihiro Tanaka. A functional SNP in FLT1 increases risk of coronary artery disease in a Japanese population. *J. Hum. Genet.* 2016.05; 61(5); 435-441

5. Akihiro Fujimoto, Yukinori Okada, Keith A Boroevich, Tatsuhiko Tsunoda, Hiroaki Taniguchi, Hidewaki Nakagawa. Systematic analysis of mutation distribution in three dimensional protein structures identifies cancer driver genes. *Sci Rep.* 2016.05; 6; 26483
6. Akihiro Fujimoto, Mayuko Furuta, Yasushi Totoki, Tatsuhiko Tsunoda, Mamoru Kato, Yuichi Shiraishi, Hiroko Tanaka, Hiroaki Taniguchi, Yoshiiku Kawakami, Masaki Ueno, Kunihito Gotoh, Shun-Ichi Aritsumi, Christopher P Wardell, Shinya Hayami, Toru Nakamura, Hiroshi Aikata, Koji Arihiro, Keith A Boroevich, Tetsuo Abe, Kaoru Nakano, Kazuhiro Maejima, Aya Sasaki-Oku, Ayako Ohsawa, Tetsuo Shibuya, Hiromi Nakamura, Natsuko Hama, Fumie Hosoda, Yasuhito Arai, Shoko Ohashi, Tomoko Urushidate, Genta Nagae, Shogo Yamamoto, Hiroki Ueda, Kenji Tatsuno, Hidenori Ojima, Nobuyoshi Hiraoka, Takuji Okusaka, Michiaki Kubo, Shigeru Marubashi, Terumasa Yamada, Satoshi Hirano, Masakazu Yamamoto, Hideki Ohdan, Kazuaki Shimada, Osamu Ishikawa, Hiroki Yamaue, Kazuki Chayama, Satoru Miyano, Hiroyuki Aburatani, Tatsuhiko Shibata, Hidewaki Nakagawa. Whole-genome mutational landscape and characterization of noncoding and structural mutations in liver cancer. *Nat. Genet.* 2016.05; 48(5); 500-509
7. Ikumi Hori, Fuyuki Miya, Kei Ohashi, Yutaka Negishi, Ayako Hattori, Naoki Ando, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh. Novel splicing mutation in the ASXL3 gene causing Bainbridge-Ropers syndrome. *Am. J. Med. Genet. A.* 2016.07; 170(7); 1863-1867
8. Hori I\*, Miya F\*, Ohashi K, Negishi Y, Hattori A, Ando N, Okamoto N, Kato M, Tsunoda T, Yamasaki M, Kanemura Y, Kosaki K, Saitoh S.. Novel Splicing Mutation in the ASXL3 gene causing Bainbridge-Ropers Syndrome. *Am. J. Med. Genet.* 2016.07; (A 170); 1863-1867
9. Alok Sharma, Daichi Shigemizu, Keith A Boroevich, Yosvany López, Yoichiro Kamatani, Michiaki Kubo, Tatsuhiko Tsunoda. Stepwise iterative maximum likelihood clustering approach. *BMC Bioinformatics.* 2016.08; 17(1); 319
10. Fumihito Nozaki, Takashi Kusunoki, Nobuhiko Okamoto, Yuto Yamamoto, Fuyuki Miya, Tatsuhiko Tsunoda, Kenjiro Kosaki, Tomohiro Kumada, Minoru Shibata, Tatsuya Fujii. ALDH18A1-related cutis laxa syndrome with cyclic vomiting. *Brain Dev.* 2016.08; 38(7); 678-684
11. Nozaki F, Kusunoki T, Okamoto N, Yamamoto Y, Miya F, Tsunoda T, Kosaki K, Kumada T, Shibata M, Fujii T. . ALDH18A1-related cutis laxa syndrome with cyclic vomiting. *Brain Dev.* 2016.08; (38); 678-684
12. S-W Chang, C W McDonough, Y Gong, T A Johnson, T Tsunoda, E R Gamazon, M A Perera, A Takahashi, T Tanaka, M Kubo, C J Pepine, J A Johnson, R M Cooper-DeHoff. Genome-wide association study identifies pharmacogenomic loci linked with specific antihypertensive drug treatment and new-onset diabetes. *Pharmacogenomics J.* 2016.09;
13. Nobue Yagihara, Hiroshi Watanabe, Phil Barnett, Laetitia Duboscq-Bidot, Atack C Thomas, Ping Yang, Seiko Ohno, Kanae Hasegawa, Ryoza Kuwano, Stéphanie Chatel, Richard Redon, Jean-Jacques Schott, Vincent Probst, Tamara T Koopmann, Connie R Bezzina, Arthur A M Wilde, Yukiko Nakano, Takeshi Aiba, Yoshihiro Miyamoto, Shiro Kamakura, Dawood Darbar, Brian S Donahue, Daichi Shigemizu, Toshihiro Tanaka, Tatsuhiko Tsunoda, Masayoshi Suda, Akinori Sato, Tohru Minamino, Naoto Endo, Wataru Shimizu, Minoru Horie, Dan M Roden, Naomasa Makita. Variants in the SCN5A Promoter Associated With Various Arrhythmia Phenotypes. *J Am Heart Assoc.* 2016.09; 5(9);
14. Mari Ichikawa, Takeshi Aiba, Seiko Ohno, Daichi Shigemizu, Junichi Ozawa, Keiko Sonoda, Megumi Fukuyama, Hideki Itoh, Yoshihiro Miyamoto, Tatsuhiko Tsunoda, Takeru Makiyama, Toshihiro Tanaka, Wataru Shimizu, Minoru Horie. Phenotypic Variability of ANK2 Mutations in Patients With Inherited Primary Arrhythmia Syndromes. *Circ. J.* 2016.11; 80(12); 2435-2442
15. Chisato Shimizu, Hariklia Eleftherohorinou, Victoria J Wright, Jihoon Kim, Martin P Alphonse, James C Perry, Rolando Cimaz, David Burgner, Nagib Dahdah, Long T Hoang, Chiea Chuen Khor, Andrea Salgado, Adriana H Tremoulet, Sonia Davila, Taco W Kuijpers, Martin L Hibberd, Todd A Johnson, Atsushi Takahashi, Tatsuhiko Tsunoda, Michiaki Kubo, Toshihiro Tanaka, Yoshihiro Onouchi, Rae S M Yeung, Lachlan J M Coin, Michael Levin, Jane C Burns, . Genetic Variation in the SLC8A1 Calcium Signaling Pathway Is Associated With Susceptibility to Kawasaki Disease and Coronary Artery Abnormalities. *Circ Cardiovasc Genet.* 2016.12; 9(6); 559-568

16. Ronesh Sharma, Shiu Kumar, Tatsuhiko Tsunoda, Ashwini Patil, Alok Sharma. Predicting MoRFs in protein sequences using HMM profiles. *BMC Bioinformatics*. 2016.12; 17(Suppl 19); 504
17. Harsh Saini, Sunil Pranit Lal, Vimal Vikash Naidu, Vincel Wince Pickering, Gurmeet Singh, Tatsuhiko Tsunoda, Alok Sharma. Gene masking - a technique to improve accuracy for cancer classification with high dimensionality in microarray data. *BMC Med Genomics*. 2016.12; 9(Suppl 3); 74
18. Makiko Tsutsumi, Setsuri Yokoi, Fuyuki Miya, Masafumi Miyata, Mitsuhiro Kato, Nobuhiko Okamoto, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh, Hiroki Kurahashi. Novel compound heterozygous variants in PLK4 identified in a patient with autosomal recessive microcephaly and chorioretinopathy. *Eur. J. Hum. Genet.*. 2016.12; 24(12); 1702-1706
19. Tsutsumi M, Yokoi S, Miya F, Miyata M, Kato M, Okamoto N, Tsunoda T, Yamasaki M, Kanemura Y, Kosaki K, Saitoh S, Kurahashi H.. Novel compound heterozygous variants in PLK4 identified in a patient with autosomal recessive microcephaly and chorioretinopathy. *Eur. J. Hum. Genet.*. 2016.12; (24); 1702-1706

### [Misc]

1. Daichi Shigemizu, Yukihide Momozawa, Michiaki Kubo, Tatsuhiko Tsunoda. How to select exome enrichment kit *Experimental Medicine*. 2016.04; 34; 955-960

### [Conference Activities & Talks]

1. Tatsuhiko Tsunoda. Toward new cancer therapy with genomic/omic analysis. 2016.01.20 Chiba
2. Tatsuhiko Tsunoda. Big data analysis paves the way to personalized medicine. 2016.02.04 Tokyo
3. Tatsuhiko Tsunoda. Disease Multi-Omits Analysis on the Basis of Medical Big Data. CREST Symposium "Elucidation of Life System with Trans-omics" 2016.03.03 Tokyo, Japan
4. Tatsuhiko Tsunoda. Multi-omic big data analysis drives precision medicine. CREST International Symposium on Big Data Application 2016.03.04 Tokyo, Japan
5. Daichi Shigemizu, Yukihide Momozawa, Testuo Abe, Takashi Morizono, Keith A. Boroevich, Sadaaki Takata, Kyota Ashikawa, Michiaki Kubo, Tatsuhiko Tsunoda. Performance comparison of four commercial human whole-exome capture platforms. The 13th International Congress of Human Genetics 2016.04.03 Kyoto, Japan
6. Fuyuki Miya, Mitsuhiro Kato, Tadashi Shiohama, Nobuhiko Okamoto, Shinji Saitoh, Mami Yamasaki, Daichi Shigemizu, Tetsuo Abe, Takashi Morizono, Keith A. Boroevich, Kenjiro Kosaki, Yonehiro Kanemura, Tatsuhiko Tsunoda. A combination of targeted enrichment methodologies for whole-exome sequencing reveals novel pathogenic mutations. The 13th International Congress of Human Genetics 2016.04.03 Kyoto, Japan
7. Nobuhiko Okamoto, Fuyuki Miya, Kenichi Nishioka, Hidenobu Soejima, Tatsuhiko Tsunoda, Mitsuhiro Kato, Shinji Saitoh, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki. Novel MCA/ID syndrome with ASH1L mutation. The 13th International Congress of Human Genetics 2016.04.03
8. Ikumi Hori, Fuyuki Miya, Kei Ohashi, Yutaka Negishi, Ayako Hattori, Naoki Ando, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh. Novel Splicing Mutation in the ASXL3 gene causing Bainbridge-Ropers Syndrome. The 13th International Congress of Human Genetics 2016.04.03
9. Yonehiro Kanemura, Fuyuki Miya, Tomoko Shofuda, Ema Yoshioka, Daisuke Kanematsu, Kyoko Itoh, Shinji Fushiki, Takeshi Okinaga, Haruhiko Sago, Rika Kosaki, Kyoko Minagawa, Nobuhiko Okamoto, Tatsuhiko Tsunoda, Mitsuhiro Kato, Shinji Saitoh, Kenjiro Kosaki, Mami Yamasaki. Novel compound heterozygous mutations in ISPD gene from two cases of Japanese Walker- Warburg syndrome identified by whole-exome sequencing. The 13th International Congress of Human Genetics 2016.04.03 Kyoto, Japan
10. Nobuhiko Okamoto, Fuyuki Miya, Tatsuhiko Tsunoda, Mitsuhiro Kato, Shinji Saitoh, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki. Homozygous ADCY5 mutation causes movement disorder with severe intellectual disability. The 13th International Congress of Human Genetics 2016.04.03

11. Yutaka Negishi, Fuyuki Miya, Ayako Hattori, Naoki Ando, Ikumi Hori, Takao Togawa, Kohei Aoyama, Kei Ohashi, Shinobu Fukumura, Seiji Mizuno, Ayako Umemura, Yoko Kishimoto, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh. Combination of genetic and biochemical analyses for the diagnosis of PI3K-AKT-mTOR pathway associated megalencephaly syndromes. The 13th International Congress of Human Genetics 2016.04.03 Kyoto, Japan
12. Fuyuki Miya, Mitsuhiro Kato, Tadashi Shiohama, Nobuhiko Okamoto, Shinji Saitoh, Mami Yamasaki, Daichi Shigemizu, Tetsuo Abe, Takashi Morizono, Keith A Boroevich, Kenjiro Kosaki, Yonehiro Kanemura, Tatsuhiko Tsunoda. A combination of targeted enrichment methodologies for whole-exome sequencing reveals novel pathogenic mutations. ICHG (The 13th International Congress of Human Genetics) 2016.04.03
13. Nobuhiko Okamoto, Fuyuki Miya, Kenichi Nishioka, Hidenobu Soejima, Tatsuhiko Tsunoda, Mitsuhiro Kato, Shinji Saitoh, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki. Novel MCA/ID syndrome with ASXL1 mutation. ICHG (The 13th International Congress of Human Genetics) 2016.04.03
14. Ikumi Hori, Fuyuki Miya, Kei Ohashi, Yutaka Negishi, Ayako Hattori, Naoki Ando, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh. Novel Splicing Mutation in the ASXL3 gene causing Bainbridge-Ropers Syndrome. ICHG (The 13th International Congress of Human Genetics) 2016.04.03
15. Yonehiro Kanemura, Fuyuki Miya, Tomoko Shofuda, Ema Yoshioka, Daisuke Kanematsu, Kyoko Itoh, Shinji Fushiki, Takeshi Okinaga, Haruhiko Sago, Rika Kosaki, Kyoko Minagawa, Nobuhiko Okamoto, Tatsuhiko Tsunoda, Mitsuhiro Kato, Shinji Saitoh, Kenjiro Kosaki, Mami Yamasaki. Novel compound heterozygous mutations in ISPD gene from two cases of Japanese Walker- Warburg syndrome identified by whole-exome sequencing. ICHG (The 13th International Congress of Human Genetics) 2016.04.03
16. Nobuhiko Okamoto, Fuyuki Miya, Tatsuhiko Tsunoda, Mitsuhiro Kato, Shinji Saitoh, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki. Homozygous ADCY5 mutation causes movement disorder with severe intellectual disability. ICHG (The 13th International Congress of Human Genetics) 2016.04.03
17. Yutaka Negishi, Fuyuki Miya, Ayako Hattori, Naoki Ando, Ikumi Hori, Takao Togawa, Kohei Aoyama, Kei Ohashi, Shinobu Fukumura, Seiji Mizuno, Ayako Umemura, Yoko Kishimoto, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh. Combination of genetic and biochemical analyses for the diagnosis of PI3K-AKT-mTOR pathway associated megalencephaly syndromes. ICHG (The 13th International Congress of Human Genetics) 2016.04.03
18. Tatsuhiko Tsunoda. Multi-Omic Analysis on the Basis of Medical Big Data. Kuroda Laboratory Seminar 2016.05.11 Tokyo, Japan
19. Atsuko Harada, Fuyuki Miya, Hidetsuna Utsunomiya, Takumi Yamanaka, Yamato Yoshikawa, Michiko Miki, Shofuda Tomoko, Mitsuhiro Kato, Shinji Saitoh, Nobuhiko Okamoto, Kenjiro Kosaki, Tatsuhiko Tsunoda, Yonehiro Kanemura, Mami Yamasaki. Genetic and biochemical analyses for the diagnosis of mTOR pathway associated megalencephaly syndromes. The 58th Annual Meeting of the Japanese Society of Child Neurology 2016.06.02
20. Clinical heterogeneity of genetically confirmed nine patients with Vici syndrome. The 58th Annual Meeting of the Japanese Society of Child Neurology 2016.06.02
21. Genetic analysis in Dandy-Walker malformation. The 58th Annual Meeting of the Japanese Society of Child Neurology 2016.06.02
22. Saeko Sasaki, Fumihito Nozaki, Nobuhiko Okamoto, Kenjiro Kosaki, Fuyuki Miya, Tatsuhiko Tsunoda, Tomohiro Kumada, Minoru Shibata, Ikuko Hiejima, Anri Hayashi, Mioko Mori, Kenji Inoue, Tetsuya Fujii. ALDH18A1 Associated Dermatollis: First Case in Japan. The 58th Annual Meeting of the Japanese Society of Child Neurology 2016.06.02
23. Daichi Shigemizu. Current Exome Analysis for Identifying Disease Causing Genes. The 2nd Bioinformatics Agora 2016.07.15 Tokyo, Japan
24. Kumar, S., Sharma, R., Sharma, A., Tsunoda, T.. Decimation Filter with Common Spatial Pattern and Fishers Discriminant Analysis for Motor Imagery Classification. IEEE World Congress on Computational Intelligence, IJCNN 2016.07.24 Vancouver, Canada



25. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. CREST Big Data Field Joint Symposium 2016.08.05 Tokyo, Japan
26. Yosvany López, Alok Sharma, Tatsuhiko Tsunoda. Survey of Highly Mutated Transcription Factor Binding Sites in Human Cancers. 15th International Conference on Bioinformatics (InCoB 2016) 2016.09.21 Singapore
27. Tatsuhiko Tsunoda. Precision Medicine on the Basis of Medical Big Data Analysis. Symposium of the Japan Gene Therapy Association Symposium "Foundations of Genetic Statistics and Clinical Application" 2016.10.07 Tokyo, Japan
28. Daichi Shigemizu, Fuyuki Miya, Akihiro Fujimoto, Keith A. Boroevich, Shujiro Okuda, Tatsuhiko Tsunoda. Development of a long indel detection method using the realignment of the misaligned reads. The American Society of Human Genetics 2016.10.18 Vancouver, Canada
29. Makiko Tsutsumi, Setsuri Yokoi, Fuyuki Miya, Masafumi Miyata, Mitsuhiro Kato, Nobuhiko Okamoto, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh, Hiroki Kurahashi. Missense mutations in the PLK4 gene identified in a patient with autosomal recessive microcephaly and chorioretinopathy. The American Society of Human Genetics 2016.10.18
30. Makiko Tsutsumi, Setsuri Yokoi, Fuyuki Miya, Masafumi Miyata, Mitsuhiro Kato, Nobuhiko Okamoto, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh, Hiroki Kurahashi. Missense mutations in the PLK4 gene identified in a patient with autosomal recessive microcephaly and chorioretinopathy. The 66th Annual Meeting of the American Society of Human Genetics 2016.10.18
31. Tatsuhiko Tsunoda. Trans-omic analysis strategy for precision medicine. The 26th Hot Spring Harbor International Symposium - Trans-omics: New Approaches in Biology and Medicine 2016 2016.11.02 Fukuoka, Japan
32. Daichi Shigemizu. Trend of exome analysis for identifying disease causing gene mutation. Science Research Foundation Research A Symposium (I) Large-scale data analysis and modeling to understand complex life phenomena 2016.11.07 Kurume
33. Artem Lysenko, Piotr J. Kamola, Keith A. Boroevich, Tatsuhiko Tsunoda. Strategies for discovering disease-associated modules in integrated biological networks. 9th Annual RECOMB/ISCB Conference on Regulatory & Systems Genomics 2016.11.07
34. Artem Lysenko, Piotr J. Kamola, Keith A. Boroevich, Tatsuhiko Tsunoda. Comparative evaluation of approaches for module identification in biological networks. 9th Annual RECOMB/ISCB Conference on Regulatory & Systems Genomics 2016.11.07
35. Chikahiko Numakura, Kazuyuki Nakamura, Fuyuki Miya, Jun Mizota, Tetsuo Mitsui, Mitsuhiro Kato. Two siblings of skeletal ciliopathy with restrictive ventilatory impairment harbouring mutations in C21orf2 gene. The 50th Annual Meeting of the Japanese Society for Pediatric Endocrinology and the 9th Biennial Scientific Meeting of the Asia Pacific Pediatric Endocrinology Society 2016.11.16 Tokyo, Japan
36. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. CREST Big Data Fields Joint Meeting 2016.11.29 Tokyo, Japan
37. Kumar, S., Sharma, A., Mamun, K., Tsunoda, T.. A deep learning approach for motor imagery EEG signal classification. IEEE Asia-Pacific World Congress on Computer Science 2016.12.04
38. Makiko Tsutsumi, Setsuri Yokoi, Fuyuki Miya, Masafumi Miyata, Mitsuhiro Kato, Nobuhiko Okamoto, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh, Hiroki Kurahashi. The effect of novel missense mutation of PLK4 gene identified in microcephaly patients on central body duplication. The 39th Annual Meeting of the Japan Society of Pediatric Genetics 2016.12.09 Tokyo, Japan
39. Shinji Saitoh, Izumi Hori, Fuyuki Miya, Daisuke Ieda, Yutaka Negishi, Nobuhiko Okamoto, Ayako Hattori, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Hiroki Kurahashi. Two cases of Bainbridge-Ropers syndrome in which ASXL3 gene mutation was identified. The 39th Annual Meeting of Japan Society of Pediatric Genetics 2016.12.09 Tokyo, Japan

**[Patents]**

1. METHOD FOR SELECTING IPS CELL CLONE, AND METHOD FOR SELECTING GENE USED IN METHOD FOR SELECTING SAME, Announcement Number : WO 2012/115270

**[Works]**

1. HML: Tool to perform Hierarchical Maximum Likelihood (HML) Clustering, Software, 2016.03
2. SIML: Matlab package of SIML clustering approach, Software, 2016.08

**[Awards & Honors]**

1. Dream Challenges Certificate of Best Performance - Disease Module Identification DREAM Challenge Sub-Challenge 2, DREAM Challenge, 2016.11



# Structural Biology

Professor Nobutoshi ITO  
Associate Professor Teikichi IKURA  
Assistant Professor Nobutaka NUMOTO

## ( 1 ) Outline

The advance of genome science and proteomic analysis has produced a large amount of information about the primary structure of proteins and their spatial and temporal distributions. On the other hand, most of the proteins only function when they take certain three dimensional structures. As obviously seen in so-called prion diseases, proteins which are chemically correct but structurally incorrect not only fail to function properly but also can harm cells. Our laboratory aims to understand the function of biological macromolecules at atomic level through structure analysis and other methods of physical chemistry, in the hope that accumulation of such knowledge will eventually lead to development of drugs. We are also involved in providing database of such structural data to scientists through the activities of Protein Data Bank Japan.

## ( 2 ) Research

Collaborating with groups within and outside of the university, we are engaged in various research projects including;

- 1) Physicochemical analysis on the mechanism of the signal transduction for activation of T cells
- 2) Structural analyses of B-cell coreceptors
- 3) Molecular basis of suppression of HIV-1
- 4) Structural basis of giant hemoglobins
- 5) Analysis of interactions between tau protein and Pin1
- 6) Structure based drug design for protein kinases
- 7) Structural analyses of potential drug targets such as nuclear receptors
- 8) Improvement in Protein Data Bank

## ( 3 ) Lectures & Courses

The students learn theoretical basis of structure determination, mainly X-ray crystallography, of proteins and other biological macromolecules. Recent advance in structural biology is also discussed in seminar. Students learn lab techniques related to large-scale production, purification and crystallization of protein samples. They also learn computational methods to determine and refine crystal structures.

## ( 4 ) Publications

### [Original Articles]

1. Isao Kii, Yuto Sumida, Toshiyasu Goto, Rie Sonamoto, Yukiko Okuno, Suguru Yoshida, Tomoe Kato-Sumida, Yuka Koike, Minako Abe, Yosuke Nonaka, Teikichi Ikura, Nobutoshi Ito, Hiroshi Shibuya,

- Takamitsu Hosoya, Masatoshi Hagiwara. Selective inhibition of the kinase DYRK1A by targeting its folding process. *Nat Commun.* 2016; 7; 11391
2. Manjiri R Kulkarni, Nobutaka Numoto, Nobutoshi Ito, Yutaka Kuroda. Modeling and experimental assessment of a buried Leu-Ile mutation in dengue envelope domain III. *Biochem. Biophys. Res. Commun.* 2016.02; 471(1); 163-168
  3. Akira Nakamura, Jun Ohtsuka, Tatsuki Kashiwagi, Nobutaka Numoto, Noriyuki Hirota, Takahiro Ode, Hidehiko Okada, Koji Nagata, Motosuke Kiyohara, Ei-Ichiro Suzuki, Akiko Kita, Hitoshi Wada, Masaru Tanokura. In-situ and real-time growth observation of high-quality protein crystals under quasi-microgravity on earth. *Sci Rep.* 2016.02; 6; 22127
  4. Tomomi Imamura, Kyota Fujita, Kazuhiko Tagawa, Teikichi Ikura, Xigui Chen, Hidenori Homma, Takuya Tamura, Ying Mao, Juliana Bosso Taniguchi, Kazumi Motoki, Makoto Nakabayashi, Nobutoshi Ito, Kazunori Yamada, Kentaro Tomii, Hideyuki Okano, Julia Kaye, Steven Finkbeiner, Hitoshi Okazawa. Identification of hepta-histidine as a candidate drug for Huntington's disease by in silico-in vitro- in vivo-integrated screens of chemical libraries. *Sci Rep.* 2016.09; 6; 33861
  5. Chizuru Akatsu, Kenro Shinagawa, Nobutaka Numoto, Zhihong Liu, Ayse Konuskan Ucar, Mohammad Aslam, Shirley Phoon, Takahiro Adachi, Koji Furukawa, Nobutoshi Ito, Takeshi Tsubata. CD72 negatively regulates B lymphocyte responses to the lupus-related endogenous toll-like receptor 7 ligand Sm/RNP. *J. Exp. Med.* 2016.11; 213(12); 2691-2706

#### [Misc]

1. Teikichi Ikura, Nobutoshi Ito. Crystal Structure of the Vitamin D Receptor Ligand-Binding Domain with Lithocholic Acids. *Vitam. Horm.* 2016; 100; 117-136

#### [Conference Activities & Talks]

1. Nobutaka Numoto, Taro Nakagawa, Nobutoshi Ito, Yoshihiro Fukumori, Kunio Miki. Analysis of the oxygen-dissociation intermediate states of the giant hemoglobin. The 16th Annual Meeting of the Protein Science Society of Japan 2016.06 Fukuoka
2. Teikichi Ikura, Nobutoshi Ito. Analysis of catalytic mechanism of a protease derived from Pin1. The 16th Annual Meeting of the Protein Science Society of Japan 2016.06.08 Fukuoka
3. Nobutaka Numoto, Taro Nakagawa, Nobutoshi Ito, Yoshihiro Fukumori, Kunio Miki. Oxygen-dissociation intermediate of the giant hemoglobin from *Oligobranchia mashikoi*. Annual Meeting 2016 and General Assembly of the Crystallographic Society of Japan 2016.11 Ibaraki
4. Nobutaka Numoto, Taro Nakagawa, Nobutoshi Ito, Yoshihiro Fukumori, Kunio Miki. Crystallographic and spectroscopic analysis of the oxygen-dissociation intermediate of the giant hemoglobin. The 54th Annual Meeting of the Biophysical Society of Japan 2016.11 Ibaraki
5. Satomi Inaba, Nobutaka Numoto, Shuhei Ogawa, Hisayuki Morii, Teikichi Ikura, Ryo Abe, Nobutoshi Ito, Masayuki Oda. Structural and thermodynamic analysis of interactions between CD28 and SH2 domains. The 54th Annual Meeting of the Biophysical Society of Japan 2016.11.25 Tsukuba
6. Teikichi Ikura, Nobutoshi Ito. Activity of a protease derived from Pin1 for tau protein. The 54th Annual Meeting of the Biophysical Society of Japan 2016.11.26 Tsukuba

# Neuroscience

Professor Kohichi Tanaka  
 Associate Professor Tomomi Aida  
 Assistant Professor Saeko Ishida  
 Assistant Professor Yuichi Hiraoka (2015/5/1 )

Graduate Student (doctor course)  
 Zhao Zhuoyang  
 Kaori Sugiyama  
 Takehisa Handa

Graduate Student (master course)  
 Mina Kusunose  
 Moeko Tanaka  
 Haruka Takigawa  
 Hiroshi Ogawa

Technical Staff  
 Harumi Ishikubo

Secretary  
 Satomi Ohno

## ( 1 ) Outline

The final goal of our research is to understand molecular, cellular, and neuronal ensemble mechanisms underlying higher order brain functions including learning and memory. For that purpose, we combine molecular genetics, physiological and behavioral methods. The laboratory also studies the mechanism that underlies neuronal cell death and regeneration.

## ( 2 ) Research

### 1. Functions of glutamate transporters in the brain

Glutamate is a major excitatory neurotransmitter and plays an important role in neuronal plasticity and neurotoxicity in the central nervous system. Glutamate transport proteins provide the mechanism by which synaptically released glutamate is inactivated and kept below toxic levels in the extracellular space. By now, five subtypes of high-affinity glutamate transporters have been identified in the mammalian brain. Our lab studies the physiological and pathological roles of glutamate transporter subtypes using subtype-specific knockout mice. Clinical phenotypes of spinocerebellar ataxia type-5 (SCA5) and spectrin-associated autosomal recessive cerebellar ataxia type-1 (SPARCA1) are mirrored in mice lacking  $\beta$ -III spectrin ( $\beta$ -III<sup>-/-</sup>). One function of  $\beta$ -III spectrin is the stabilization of the Purkinje cell-specific glutamate transporter EAAT4 at the plasma membrane. In  $\beta$ -III<sup>-/-</sup> mice EAAT4 levels are reduced from an early age. In contrast levels of the glutamate transporter GLAST, expressed in Bergmann glia, only fall progressively from 3 months onwards. Here we elucidated the roles of these two glutamate transporters in cerebellar pathogenesis mediated through loss of  $\beta$ -III spectrin function by studying EAAT4 and GLAST knockout mice as well as crosses of both with  $\beta$ -III<sup>-/-</sup> mice. Our

data demonstrate that EAAT4 loss, but not abnormal AMPA receptor composition, in young  $\beta$ -III<sup>-/-</sup> mice underlies early Purkinje cell hyper-excitability and that subsequent loss of GLAST, superimposed on the earlier deficiency of EAAT4, is responsible for Purkinje cell loss and progression of motor deficits. Yet the loss of GLAST appears to be independent of EAAT4 loss, highlighting that other aspects of Purkinje cell dysfunction underpin the pathogenic loss of GLAST. Finally, our results demonstrate that Purkinje cells in the posterior cerebellum of  $\beta$ -III<sup>-/-</sup> mice are most susceptible to the combined loss of EAAT4 and GLAST, with degeneration of proximal dendrites, the site of climbing fibre innervation, most pronounced. This highlights the necessity for efficient glutamate clearance from these regions and identifies dysregulation of glutamatergic neurotransmission particularly within the posterior cerebellum as a key mechanism in SCA5 and SPARCA1 pathogenesis.

We investigated the cytoprotective effect of geranylgeranylacetone (GGA) on RGCs degeneration using a normal tension glaucoma (NTG) mouse model, which lacks GLAST. Three-week-old GLAST<sup>+/-</sup> mice were given oral administration of GGA at 100, 300, or 600 mg/kg/day or vehicle alone, and littermate control mice were given vehicle alone for 14 days, respectively. The number of RGCs of GLAST<sup>+/-</sup> mice significantly decreased, as compared to that of control mice. RGC loss was significantly suppressed by administration of GGA at 600 mg/kg/day, compared with vehicle alone. Following GGA administration, HSP70 was significantly upregulated together with reduction in the activities of caspase-9 and -3. Our studies highlight HSP70 induction in the retina is available to suppress RGC degeneration, and thus GGA may be applicable for NTG as a promising therapy.

## 2. Development of genome editing technologies

Although CRISPR/Cas enables one-step gene cassette knock-in, assembling targeting vectors containing long homology arms is a laborious process for high-throughput knock-in. We recently developed the CRISPR/Cas-based precise integration into the target chromosome (PITCh) system for a gene cassette knock-in without long homology arms mediated by microhomology-mediated end-joining.

Here, we identified exonuclease 1 (Exo1) as an enhancer for PITCh in human cells. By combining the Exo1 and PITCh-directed donor vectors, we achieved convenient one-step knock-in of gene cassettes and floxed allele both in human cells and mouse zygotes. Our results provide a technical platform for high-throughput knock-in.

## (3) Education

### Goals/Outline:

Students should generate genetically modified animals to comprehensively understand the cognitive mechanisms at the level of molecule to behavior. Then, students should analyze cognitive deficits of mutant animals and those molecular mechanisms.

### Available programs:

Participation in the ongoing research project; as needed

Training for cell biology: five times a year 13:00 – 16:00

### Experiment:

1. Gene cloning and generation of targeting vector.
2. Generation of genetically modified mice
3. Behavioral analysis of the mice
4. Morphological analysis of central nervous systems.

## (4) Lectures & Courses

The aim of this practice is to learn molecular biological, anatomical, electrophysiological and psychological approaches to elucidate the mechanism of cognition. Moreover, based on previous case reports of cognitive deficits, students should plan and discuss what kinds of the researches are possible and meaningful to elucidate the pathology of these diseases, leading to unveil the mechanism of cognition.

**( 5 ) Publications****[Original Articles]**

1. Emma M Perkins, Daumante Suminaite, Yvonne L Clarkson, Sin Kwan Lee, Alastair R Lyndon, Jeffrey D Rothstein, David J A Wyllie, Kohichi Tanaka, Mandy Jackson. Posterior cerebellar Purkinje cells in an SCA5/SPARCA1 mouse model are especially vulnerable to the synergistic effect of loss of  $\beta$ -III spectrin and GLAST. *Hum. Mol. Genet.*. 2016.10; 25(20); 4448-4461
2. Zhenyu Dong, Yasuhiro Shinmei, Yoko Dong, Saori Inafuku, Junichi Fukuhara, Ryo Ando, Nobuyoshi Kitaichi, Atsuhiro Kanda, Kohichi Tanaka, Kousuke Noda, Takayuki Harada, Shinki Chin, Susumu Ishida. Effect of geranylgeranylacetone on the protection of retinal ganglion cells in a mouse model of normal tension glaucoma. *Heliyon*. 2016.10; 2(10); e00191
3. Tomomi Aida, Shota Nakade, Tetsushi Sakuma, Yayoi Izu, Ayu Oishi, Keiji Mochida, Harumi Ishikubo, Takako Usami, Hidenori Aizawa, Takashi Yamamoto, Kohichi Tanaka. Gene cassette knock-in in mammalian cells and zygotes by enhanced MMEJ. *BMC Genomics*. 2016.11; 17(1); 979

# Epigenetic Epidemiology

Professor: Masaaki MURAMATSU

Associate Professor : Noriko SATO

Assistant Professor : Chihiro Imai

Adjunct Instructor : Katsuko SUDO, Jun-ichi TAGUCHI

Graduate Student: Kaung Si Thu,

Khin Thet Thet Zaw, Yuko Maeda, Fujitani,

Tay Zar Kyaw, Tadaaki Katsuta, Shilpa Pavethynath

Maidina Abudushataer, Ake Ko Ko Minn

Norihiko Satake, Kenji Suzuki, Hirokazu Sakamoto

Yui Tsubota

Research Resident: Zong Yuan

## ( 1 ) Outline

Many common chronic diseases are multifactorial in that they are caused by multiple genetic and environmental factors. By applying the technology and information of human genome to epidemiological studies, we aim to clarify the role of genetic polymorphisms, epigenetic changes, as well as their interaction with environmental factors, which may contribute to the development of these diseases.

## ( 2 ) Research

Our research subjects are as follows.

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Responder vs non-responder of prodrugs and polymorphisms of drug metabolizing enzymes.
4. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
5. The role of epigenetic regulation and fetal programming in common diseases.
6. Likelihood ratio based integrated personal risk assessment of type 2 diabetes.

## ( 3 ) Education

Masaaki Muramatsu: Holistic Study of Disease Prevention I

Masaaki Muramatsu: Environmental/Social Health

Masaaki Muramatsu: Negotiation and Debate in English

Noriko Sato, Masaaki Muramatsu: Bioscience I

Noriko Sato: Molecular and Cellular Biology

Noriko Sato: Introduction to Human Molecular Genetics

**( 4 ) Lectures & Courses**

We focus on common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis which are caused by multiple genetic and environmental factors, and aim to decipher these factors as well as their interactions by applying the technology and information of human genome to epidemiology. Our goal is not only to identify disease genes and polymorphisms but also to elucidate gene-environment interactions that contribute to the onset and progression of the diseases. Epigenetic changes in common diseases are also in our scope. A new project has been started to study methods for educating genome-based health literacy by employing information generated from personal genome sequences

**( 5 ) Publications****[Original Articles]**

1. Kumpei Tanisawa, Yasumichi Arai, Nobuyoshi Hirose, Hiroshi Shimokata, Yoshiji Yamada, Hisashi Kawai, Motonaga Kojima, Shuichi Obuchi, Hirohiko Hirano, Hideyo Yoshida, Hiroyuki Suzuki, Yoshinori Fujiwara, Kazushige Ihara, Maki Sugaya, Tomio Arai, Seijiro Mori, Motoji Sawabe, Noriko Sato, Masaaki Muramatsu, Mitsuru Higuchi, Yao-Wen Liu, Qing-Peng Kong, Masashi Tanaka. Exome-wide Association Study Identifies CLEC3B Missense Variant p.S106G as Being Associated With Extreme Longevity in East Asian Populations. *J. Gerontol. A Biol. Sci. Med. Sci.* 2016.05;
2. Kaung Si Thu, Noriko Sato, Shinobu Ikeda, Makiko Naka-Mieno, Tomio Arai, Seijiro Mori, Motoji Sawabe, Masaaki Muramatsu, Masashi Tanaka. Association of polymorphisms of the transporter associated with antigen processing (TAP2) gene with pulmonary tuberculosis in an elderly Japanese population. *APMIS*. 2016.08; 124(8); 675-680
3. Khin Thet Thet Zaw, Noriko Sato, Shinobu Ikeda, Kaung Si Thu, Makiko Naka Mieno, Tomio Arai, Seijiro Mori, Tetsushi Furukawa, Tetsuo Sasano, Motoji Sawabe, Masashi Tanaka, Masaaki Muramatsu. Association of ZFH3 gene variation with atrial fibrillation, cerebral infarction, and lung thromboembolism: An autopsy study. *J Cardiol*. 2016.12;
4. Yuko Maeda, Noriko Sato, Makiko Naka-Mieno, Seijiro Mori, Tomio Arai, Masashi Tanaka, Masaaki Muramatsu, Motoji Sawabe. Association of non-synonymous variants in WIPF3 and LIPA genes with abdominal aortic aneurysm: an autopsy study. *J Geriatr Cardiol*. 2016.12; 13(12); 960-967

**[Conference Activities & Talks]**

1. Noriko Sato, et al.. Cohort profile: Birth Cohort- Gene and Environment Interaction Study of TMDU (BC-GENIST). The 5th Annual Meeting of the Japan Society for Developmental Origins of Health and Disease 2016.07.23 Tokyo
2. Noriko Sato. To understand the mechanisms by which metabolic disease develop due to antenatal nutritional environment . The 63rd meeting for the Japanese society of nutrition and dietetics 2016.09.08



## RIKEN Molecular and Chemical Somatology

Visiting Professor	Soichi Kojima
Visiting Professor	Mikiko Sodeoka
Visiting Professor	Nobumoto Watanabe
Visiting Professor	Yoshiki Yamaguchi
Visiting Professor	Takashi Saito
Visiting Professor	Motomasa Tanaka
Visiting Lecturer	Takeshi Nakano
Visiting Lecturer	Kosuke Dodo
Visiting Lecturer	Yutaka Furutani
Visiting Lecturer	Qin Xian-Yang
Visiting Lecturer	Akiko Tane
Visiting Lecturer	Ambara R. Pradipta
Visiting Lecturer	Masamichi Nagae
Visiting Lecturer	Nobuhiko Miyasaka
Visiting Lecturer	Tetsuya Koide
Graduate Students	
D3	Sayoko Yamasaki
	Hari Prasad Dulal
	Ryo Fukazawa
D2	Kruthi Sharamjeet Suvarna
D1	Mengqian Li
M2	Sho Fukushima

### (1) Research

Molecular and Chemical Somatology is an interdisciplinary field to understand basis of Bioorganic Chemistry, Chemical Biology, Structural Biology, Molecular Immunology, and Molecular Neuroscience as well as their applications to Medicine and Biology by dealing with variety of molecules that regulate cellular functions including low molecular weight organic compounds, proteins, sugars, and hormones. Students will hear and discuss about outlines and/or latest topics on discovery, structure, synthesis, biology, and management of these key molecules/factors, and deepen their understanding of this new study field.

## (2) Education

### 1) Synthetic Organic Chemistry

- Design and synthesis of bioactive molecules based on synthetic organic chemistry and chemical biology research.

### 2) Chemical Biology

- Discovery, target identification and analyses of mechanism of action of bioactive compounds that regulate biological function.

### 3) Molecular Cellular Pathology

- Clarification of pathogenesis of diseases at molecular and cellular levels utilizing bioprobes.

### 4) Structural Biology

- Analyses of structure and functions of bioactive glycoproteins and related proteins

### 5) Molecular Immunology

- Regulatory mechanisms for the lymphocyte activation and immune responses.

### 6) Molecular Neuropathology

- Molecular basis of psychiatric diseases and neurodegenerative disorders

## (3) Publications

### [Original Articles]

1. Ando, J., Asanuma, M., Dodo, K., Yamakoshi, H., Kawata, S.; Fujita, K., Sodeoka, M. Alkyne-Tag SERS Screening and Identification of Small-Molecule-Binding Sites in Protein. *J. Am. Chem. Soc.* 138: 13901-13910, 2016.
2. Subedi, A., Futamura, Y., Nishi, A., Ryo, A., Watanabe, N., and Osada, H. Highthroughput screening identifies artesunate as selective inhibitor of cancer stemness. Involvement of mitochondrial metabolism. *Biochem Biophys Res Commun.* 477, 737-742 (2016)
3. Dulal HP, Nagae M, Ikeda A, Morita-Matsumoto K, Adachi Y, Ohno N, Yamaguchi Y, Enhancement of solubility and yield of a  $\beta$ -glucan receptor Dectin-1 C-type lectin-like domain in *Escherichia coli* with a solubility-enhancement tag. *Protein Expr. Purif.*, 123, 97-104 (2016)
4. Takeuchi, A., Badr, M.E.S.G., Miyauchi, K., Ishihara C., Onishi R., Guo Z., Sasaki, T., Ike H., Takumi, A., Tsuji N.M., Murakami, Y., Katakai, T. Kubo M. and Saito, T.: CRTAM determines the CD4+ cytotoxic T lymphocyte lineage. *J. Exp.Med.* 213:123-138, 2016.

5. Hashimoto-Tane A., Sakuma M., Ike H., Yokosuka T., Kimura Y., Ohara O. and Saito T.: Micro adhesion-ring surrounding TCR microclusters are essential for T cell activation. *J. Exp.Med.* 213:1609-1625, 2016.
6. Shrestha, R., Shrestha, R., Qin, X-Y., Kou, T.-F., Oshima, Y., Iwatani, S., Teraoka, R., Fujii, K., Hara, M., Li, M., Takahashi-Nakaguchi, A., Chibana, H., Lu, J., Cai, M., Kajiwarra, S., and Kojima, S. Fungus-derived hydroxyl radicals kill hepatic cells by enhancing nuclear transglutaminase. *Sci Rep.* in press., 2017

#### [Review Articles]

1. Hirai, G., Asanuma, M., Tsuchiya, A., Sodeoka, M. Development of dual-specificity protein phosphatases inhibitors based on focused library approach: Modification of a core structure and unique inhibition mechanism. *J. Synth. Org. Chem., Japan.* 74: 532-540, 2016.
2. Watanabe, N., Osada, H. Small molecules that target phosphorylation dependent protein-protein interaction. *Bioorg Med. Chem.* 24, 3264-3254 (2016)
3. Hashimoto-Tane, A and Saito, T.: Dynamic regulation of TCR-microcluster and microsynapse for T cell activation. *Front. Immunol* 7:255, 2016, doi: 10.3389/fimmu.2016.00255
4. Tatsukawa, H., Furutani, Y., Hitomi, K., and Kojima, S. Transglutaminase 2, has opposing roles in the regulation of cellular functions as well as cell growth and death. (Review) *Cell Death & Disease.* 7:e2244, 2016

#### [Books]

1. Furutani, Y. and Kojima, S. Control of TG functions depending on their localization. In *Transglutaminase – multiple functional modifiers and targets for new drug discovery* (Hitomi, K., Kojima, S., and Fesus, L. eds) Springer Tokyo, 43-62, 2016

#### [Conference Activities & Talks]

1. Sodeoka, M. “Enantioselective Reactions of  $\alpha$ -Ketoesters.” 27th International Conference on Organometallic Chemistry, Melbourne, Australia, 2016.
2. Saito T. Hashimoto-Tane A. “Microsynapse composed of micro-adhesion ring surrounding TCR microcluster is essential for T cell activation” EMBO conference (Siena, Italy) September, 2016
3. Saito T. “Dynamic Regulation of T cell Activation at Immune Synapse” POSTEC Symposium (Pohang, Korea) July, 2016

4. Kojima, S. “Molecular mechanism by which acyclic retinoid induces nuclear localization of transglutaminase 2 resulting in selective cell death in liver cancer stem cells” 3rd International Federation of American Societies for Experimental Biology (FASEB) Conference on Retinoids, West Palm Beach, FL, USA, June, 2016.

## Metallic Biomaterials

Takao HANAWA Prof  
Yusuke TSUTSUMI Assoc Prof  
Maki ASHIDA Assist Prof  
Peng CHEN Assist Prof  
Hisashi DOI Assist Prof  
Tomoko SETOYUCHI Secretary

### (1) Outline

#### 1. Bio-functionalization of metals with surface modification

Bio-functionalization of metals is investigated with surface treatment techniques, such as molecule immobilization and anodic oxidation. These surface treatments make it possible to inhibit protein adsorption, platelet adhesion, and biofilm formation, and to enhance wear resistance and hard-tissue compatibility.

#### 2. Development of novel alloys and porous composites for biomedical applications

Novel alloy systems for biomedical applications are designed from the viewpoints of mechanical properties and biocompatibility. Co-Cr-Mo alloys having high strength and ductility for dental applications are developed. The porous alloys having low Young's modulus are obtained with selective laser melting technique.

#### 3. Development of Zr-based alloys for minimizing MRI artifacts

Zr-based alloys with low magnetic susceptibility, high strength and corrosion resistance are investigated for minimizing MRI artifact by controlling their microstructure and constituent phase for aneurysm clips, artificial joints, and dental implants, etc.

#### 4. Effort to minimize metal allergy

Countermeasure techniques for metal ion release from metallic biomaterials which causes metal allergy are investigated. Novel reagents of patch testing for the detection of sensitization to metal ions are developed.

### (2) Lectures & Courses

Metallic biomaterials play an important role as medical devices. Our laboratory mainly deals with effects of crystal structure, process, and thermal treatment on mechanical properties (e.g. strength or toughness). We also focus on structure and property of nanometer-scaled surface phenomena: Formation of living tissue on metals, especially, reactions between biomolecules or cells and metals, changes in surface oxide layers in living tissues, and electrochemical property of metallic biomaterials. The aim of the education is perfect understanding of metallic biomaterials, enabling students to select a proper material for medical treatments or researches.

### (3) Publications

#### [Original Articles]

1. Park JW, Kang DG, Hanawa T. New bone formation induced by surface strontium-modified ceramic bone graft substitute Oral Dis.. 2016.01; 22(1); 53-61
2. Kajima Y, Takaichi A, Yasue T, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Evaluation of the shear bond strength of dental porcelain and the low magnetic susceptibility Zr-14Nb alloy J. Mech. Behav. Biomed. Mater.. 2016.01; 53; 131-141

3. Tsukamoto M, Kawa T, Shinonaga T, Chen P, Nagai A, Hanawa T. Cell spreading on titanium periodic nanostructures with periods of 200, 300 and 600 nm produced by femtosecond laser irradiation Appl. Phys. A.. 2016.02; 122(2); 120
4. Tsutsumi Y, Niinomi M, Nakai M, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T. Electrochemical surface treatment of a  $\beta$ -titanium alloy to realize an antibacterial property and bioactivity Metals. 2016.03; 6(4); 76
5. Chen P, Nagai A, Tsutsumi Y, Ashida M, Doi H, Hanawa T . Differences in the calcification of preosteoblast cultured on sputter-deposited titanium, zirconium, and gold J Biomed Mater Res A. 2016.03; 104(3); 639-651
6. Fukuhara Y, Kyuzo M, Tsutsumi Y, Nagai A, Chen P, Hanawa, T. Phospholipid polymer electrodeposited on titanium inhibits platelet adhesion J Biomed Mater Res B Appl Biomater. 2016.04; 104(3); 554-560
7. Lee TJ, Ueno T, Nomura N, Wakabayashi N, Hanawa T. Titanium-zirconium binary alloy as dental implant material: analysis of the influence of compositional change on mechanical properties and in vitro biologic response Int. J. Oral Maxillofac.. 2016.05; 31(3); 547-554
8. Kajima Y, Takaichi A, Nakamoto T, Kimura T, Yogo Y, Ashida M, Doi H, Nomura N, Takahashi H, Hanawa T, Wakabayashi N. Fatigue strength of Co-Cr-Mo alloy clasps prepared by selective laser melting J. Mech. Behav. Biomed. Mater.. 2016.06; 59; 446-458
9. Sato M, Chen P, Tsutsumi Y, Shiota M, Hanawa T, Kasugai S . Effect of strontium ions on calcification of preosteoblasts cultured on porous calcium- and phosphate-containing titanium oxide layers formed by micro-arc oxidation Dental Materials Journal. 2016.07; 35(4); 627-634
10. Chen P, Ashida M, Doi H, Tsutsumi Y, Horita Z, Hanawa T . Cytocompatibility of Ti-6Al-7Nb through high-pressure torsion processing Mater Trans. 2016.11; 57(12); 2020-2025
11. Kondo R, Nomura N, Doi H, Matsumoto H, Tsutsumi Y, Hanawa T. Effect of heat treatment and the fabrication process on mechanical properties of Zr-14Nb alloy Mater. Trans. . 2016.12; 57(12); 2060-2064
12. Tsutsumi Y, Ashida M, Nakahara K, Serizawa A, Doi H, Grandini CR, Rocha LA, Hanawa T. Micro arc oxidation of Ti-15Zr-7.5Mo alloy Mater. Trans.. 2016.12; 57(12); 2015-2019
13. Tsutsumi Y, Doi H, Nomura N, Ashida M, Chen P, Kawasaki A, Hanawa T. Surface composition and corrosion resistance of Co-Cr alloys containing high chromium Mater. Trans.. 2016.12; 57(12); 2033-2040

#### [Misc]

1. Hanawa T. Electrodeposition of calcium phosphates, oxides, and molecules to achieve Biocompatibility of metals Ref. Module Chem. Mol. Sci. Chem. Eng. . 2016.06;

#### [Conference Activities & Talks]

1. Hanawa T. Future of metallic biomaterials. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
2. Hanawa T, Nomura N, Nakano T. Advanced researches of additive manufacturing for medicine in Japan. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
3. Yoshihara C, Ueno T, Chen P, Tsutsumi Y, Hanawa T, Wakabayashi N. Inverse behavior between osteoblasts and fibroblasts on carbon-coated titanium surfaces. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
4. Akimoto T, Ueno T, Tsutsumi Y, Doi H, Hanawa T, Wakabayashi N. The Corrosion Resistance of Ti-Zr Binary Alloy with Compositional Change. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
5. Nomura N, Suyalatu, Tsutsumi Y, Hanawa T, Nakamoto T, Kimura T, Kikuchi K, Kawasaki A. Effect of powder fabrication process on microstructure and mechanical properties of selective laser melted metals for biomedical applications. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada

6. Chen P, Tsutsumi Y, Ashida M, Doi H, Hanawa T . Different mechanisms of bone formation of pre-osteoblast on metals in vitro. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
7. Tsutsumi Y, Shimabukuro M, Chen P, Ashida M, Doi H, Hanawa T. Anti-bacterial surface coating on metallic biomaterials by simple electrochemical surface treatment. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
8. Chen P, Aso T, Sasaki R, Tsutsumi T, Ashida M, Doi H, Hanawa T. Role of hierarchical topography of titanium surface on mesenchymal stem cells adhesion and differentiation behaviours in vitro. 10th World Biomaterials Congress (WBC2016) 2016.05.17 Montreal,Canada
9. Hanawa T, Nomura N, Ashida M, Tsutsumi Y, Doi H, Chen P. Development of Zr-Mo alloy with low magnetic susceptibility for spinal instruments to decrease MRI artifact. THERMEC'2016 2016.05.29 Graz,Austria
10. Hanawa T. Mesenchymal stem cell differentiation on nano pattern fabricated by femtosecond laser. International Conference on Small Science(ICSS2016) 2016.06.25 Prague, Czech Republic
11. Hanawa T. Morphological Modification versus Chemical Modification in Metallic Implants. 9th Pacific Rim International Conference on Advanced Materials and Processing (PRICM 9) 2016.08.01 Kyoto,Japan
12. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Evaluation of the allergenic properties of titanium by metal ion release test in a simulated body environment. 9th Pacific Rim International Conference on Advanced Materials and Processing (PRICM 9) 2016.08.01 Kyoto,Japan
13. Hanawa T. Variety of differentiation of hMSC on nano-pattern fabricated by femto-second laser. 2nd Bone and Biomaterials Workshop 2016.08.07 Inari, Finland
14. Tsutsumi Y. Electrochemical surface modification techniques for metallic biomaterials. 2nd Bone and Biomaterials Workshop 2016.08.07 Inari, Finland
15. Hanawa T. Research and development of metallic biomaterials meeting clinical demand. 9th Latin American Congress on Artificial Organs and Biomaterials (COLAOB 2016) 2016.08.24 Iguas falls, Brazil
16. Correa DRN, Rocha LA, Doi H, Tsutsumi Y, Hanawa T. Micro-arc oxidation of Ti-15Zr-based alloys for osseointegrative implants. XVSBPMat 2016.09.25 Campinas, Brazil
17. Tsukada J, Tsutsumi Y, Ashida M, Chen P, Doi H, Sugawara U, Muto I, Hara N, Hanawa T. Pitting corrosion behavior of zirconium in a simulated body fluid containing chloride ions. Pacific Rim Meeting on Electrochemical and Solid-State Science (PRiME2016) 2016.10.02 Hawaii, USA
18. Shimabukuro M, Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Electrochemical surface treatment for controlling the release of silver ion as antibacterial agent on titanium. Pacific Rim Meeting on Electrochemical and Solid-State Science (PRiME2016) 2016.10.02 Hawaii, USA
19. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Corrosion behaviors and metal ion releases of metallic biomaterials in simulated body fluid. Pacific Rim Meeting on Electrochemical and Solid-State Science (PRiME2016) 2016.10.02 Hawaii, USA
20. Liu H, Isik M, Niinomi M, Chen P, Hanawa T, Fujii H. Microstructure and mechanical properties of a biomedical Co-Cr-Mo alloy processed by high pressure torsion. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan
21. Uo M, Wada T, Maekawa M, Kanno Z, Ono T, Hanawa T. Development of super engineering plasticV (PEEK) made orthodontic wires. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan
22. Miyake M, Tsukamoto M, Sato Y, Oga T, Nagai A, Chen P, Hanawa T. Dependence of Ti plate surface morphology varied by femtosecond laser irradiation on cell spreading . The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan



23. Chen P, Kawa T, Miyake M, Ooga T, Tsukamoto M, Ashida M, Tsutsumi Y, Doi H, Hanawa T. Calcification of preosteoblast on nano topography fabricated by femtosecond laser. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan
24. Tsutsumi Y. Surface modification of biomedical metallic materials. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan
25. Tsutsumi Y, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T. Simple electrochemical surface treatment to achieve antibacterial property on titanium. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-1) 2016.10.17 Osaka, Japan
26. Morita M, Ashida M, Tsutsumi Y, Nomura N, Chen P, Doi H, Hanawa T. Development of MRI compatible Zr-1Mo alloy. Biomaterials International 2016 2016.10.30 Kenting,Taiwan
27. Hanawa T. Biofunctionalization of metals meeting clinical demand. Biomaterials International 2016 2016.10.30 Kenting,Taiwan
28. Honma K, Shimojo M, Doi H, Ashida M, Chen P, Tsutsumi Y, Hanawa T. A designing and properties of multidimensional system Zr alloys. Biomaterials International 2016 2016.10.30 Kenting,Taiwan
29. Kajima Y, Takaichi A, Kittikundecha N, Nakamoto T, Doi H, Takahashi H, Nomura N, Hanawa T, Wakabayashi N. Effects of heat treatment on the microstructure and mechanical property of selective laser melted Co-Cr-Mo alloys. International Dental Materials Congress 2016 (IDMC2016) 2016.11.04 Bali, Indonesia
30. Hanawa T. Surface treatment and modification of metals to add biofunctions. International Dental Materials Congress 2016 (IDMC2016) 2016.11.04 Bali, Indonesia
31. Tsutsumi Y, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T. The surface treatment to realize both antibacterial property and bioactivity. International Dental Materials Congress 2016 (IDMC2016) 2016.11.04 Bali, Indonesia
32. Takaichi A, Kajima Y, Kittikundecha N, Nakamoto T, Nomura N, Tkahashi H, Hanawa T, Wakabayashi N. Effects of support structure on the fatigue strength of selective laser melted Co-Cr-Mo clsp. International Dental Materials Congress 2016 (IDMC2016) 2016.11.04 Bali, Indonesia
33. Oishi M, Tsutsumi Y, Chen P, Doi H, Hanawa T. Change in surface of yttria-stabilized zirconia in water and Hanks'solution characterized using XPS. International Dental Materials Congress 2016 (IDMC2016) 2016.11.04 Bali, Indonesia
34. Tsutsumi Y, Hanawa T. Evaluation of accelerated corrosion reaction of titanium under thin electrolyte layer simulating oral cavity environment. The 3rd Joint Symposium between IBB/TMDU and Chulalongkorn University on "Biomedical Materials and Engineering" 2016.12.15 Chulalongkorn University, Bangkok, Thailand
35. Biofunctinaolization of metallic biomaterials by plasma electrolytic oxidation technique. 26th Annual Meeting of MRS-J (The Materials Research Society of Japan) 2016.12.19 Yokohama

# Inorganic Biomaterials

Professor Kimihiro Yamashita  
Associate Prof. Miho Nakamura  
Assistant Prof. Naohiro Horiuchi  
Research Associate Takako Takuma

## (1) Outline

### (1) Development of Electrovector ceramics

Some ceramics, such as a hydroxyapatite, are able to be ionically polarized by thermoelectrical treatments. Consequently, the polarized ceramics have large and time-durable induced electrostatic charges on their surfaces. The effects of the induced charges profoundly dominate the proximate few millimeter regions. We named the effects “Electrovector effects” and develop “Electrovector ceramics” defined as ceramics emitting the Electrovector Effects.

### (2) Control of electrical space on Electrovector ceramic

To translate the Electrovector ceramics into practical applications for medical devices, electrical space on Electrovector ceramics should be suitably controlled under the poling process. We are evaluating the poling mechanisms of some bioceramics, based on the various disciplines. In particular, we are putting emphasis on the relationship between the origin of electrical space and the crystal structure on the surface of the polarized bio-ceramics. The crystal defect, crystal distortion and fine change of ion composition of Electrovector ceramics polarized under various conditions are systematically investigated.

### (3) Manipulation of biological responses by Electrovector ceramics

The electrostatic energies of the Electrovector effects aforementioned dominate the limited proximate areas and can control reactions locally. Therefore, the Electrovector ceramics can manipulate biological responses in a target space by both of the surface character and the electrostatic energies of the Electrovector ceramics at ion and tissue levels. We have demonstrated that the Electrovector ceramics enhanced protein adsorption, proliferation, adhesion, and differentiation of cultured cells on the ceramics as well as osteoconductivities in vivo by molecular biological and immunological detections.

### (4) Development of applicable devices by ceramic technologies

We apply the Electrovector ceramics aforementioned to implant systems, such as artificial bones, bone joints, tooth roots, and are developing implantable devices with autograft-like osteoconductivities. We are undergoing improvements of sol-gel method for hydroxyapatite thin film coating and materials for vascular regeneration. We are extending our researches based on ceramic technologies farther, such as a control of oral environment, an improvement of oral esthetics, more effective and precise diagnosis systems for clinical laboratory medicine.

## (2) Publications

### [Original Articles]

1. Kosuke Nozaki, Risa Yamada, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. Antibacterial activity of silver nanoparticles coating on zirconia against oral bacteria Visual-JW 2016. 2016; 41

2. Norio Wada, Naohiro Horiuchi, Kohei Ohta, Shintaro Urasaki, Kohei Yamauchi, and Kimihiro Yamashita. Controlled in Vivo Nacre Formation in Flat Pearls with Hydroxyapatite Bioceramic Nuclei Crystal Growth & Design. 2016.01; 16(1); 167-173
3. Norio Wada, Naohiro Horiuchi, Kastuyuki Mukougawa, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Toshinori Okura, and Kimihiro Yamashita. Electrostatic induction power generator using hydroxyapatite ceramic electrets Materials Research Bulletin. 2016.02; 74; 50-56
4. Naohiro Horiuchi, Norio Wada, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, and Kimihiro Yamashita. Dielectric relaxation in monoclinic hydroxyapatite: Observation of hydroxide ion dipoles Journal of Applied Physics. 2016.02; 119(8); 084903-6

#### [Books etc]

1. K. Yamashita. Electrically Active Materials for Medical Devices. Imperial College Press, 2016.10

#### [Misc]

1. Kimihiro Yamashita, Naohiro Horiuchi. Cutting-edge Bio-interface Engineering for Design and Production of Innovative Bioceramics International Journal of Metallurgical & Materials Engineering. 2016; 2(2); 128
2. T. Okura, N. Yoshida, K. Yamashita. Na<sup>+</sup> Superionic Conducting Silicophosphate Glass-Ceramics-Review Solid State Ionics, 285. 2016.02; 28; 143-154
3. Kazuhiro Kohata, Soichiro Itoh, Naohiro Horiuchi, Taro Yoshioka, and Kimihiro Yamashita. The role of the collaborative functions of the composite structure of organic and inorganic constituents and their influence on the electrical properties of human bone Bio-Medical Materials and Engineering. 2016.08; 27(2-3); 305-314

#### [Conference Activities & Talks]

1. Iwata N, Nozaki K, Miura H, Yamashita K, Nagai A. Surface modification of Ti implant with controlled micro/nano-structured topography. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
2. Risa Yamada, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita and Akiko Nagai. Antimicrobial activity of silver nanoparticle-coated yttria-stabilized zirconia. AADR/CADR Annual Meeting & Exhibition 2016.03.17 Los Angeles, CA, USA
3. Fujita K, Nozaki K, Yamashita K, Miura H, and Nagai A. Differentiation of periodontal ligament cell on hydroxyl- and carbonated-apatites. AADR/CADR Annual Meeting & Exhibition 2016.03.19 Los Angeles, CA, USA
4. Nozaki K, Fujita K, Miura H, Yamashita K, Nagai A. Bone remodeling-optimization of carbonated apatite for guided bone regeneration. AADR/CADR Annual Meeting & Exhibition 2016.03.19 Los Angeles, CA, USA
5. Akiko Nagai, Takaaki Masutani, Kosuke Nozaki, Kimihiro Yamashita. Electric stimulation induced by polarized hydroxyapatite regulates osteoblast proliferation through ERK activation. 10th World Biomaterials Congress 2016.05.18
6. Kosuke Nozaki, Kazuhisa Fujita, Naohiro Horiuchi, Miho Nakamura, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. In vivo evaluation of the role of carbonate ion in hydroxyapatite for bone remodeling. 10th World Biomaterials Congress 2016.05.20
7. Fabrication and evaluation of yttria-stabilized zirconia with antimicrobial properties. 2016.07.09
8. Osteoblast behavior on controlled micro/nano structured titanium surface. 2016.07.09
9. Alkaline Phosphatase Activity of Periodontal Ligament Cell on Collagen-coated Hydroxyl-Apatites. 2016.07.09
10. In vivo evaluation of calcium phosphate with optimized osteoconductivity and solubility by carbonate ion. 2016.07.10

11. Fabrication of antibacterial yttria-stabilized zirconia using silver nanoparticle . 2016.09.09
12. Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Phase transition in calcium hydroxyapatite observed by thermally stimulated current method. The 9th International Symposium on Inorganic Phosphate Materials (ISIPM-9) 2016.09.26 Tokyo Metropolitan University, Tokyo, Japan
13. Kosuke Nozaki, Risa Yamada, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. Antibacterial activity of silver nanoparticles coating on zirconia against oral bacteria. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development 2016.10.17
14. Naohiro Horiuchi, Norio Wada, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, and Kimihiro Yamashita. Surface charges on hydroxyapatite electrets studied by Kelvin probe method. The 28th Annual Meeting of the International Society for Ceramics in Medicine (Bioceramics 28) 2016.10.20 Charlotte, North Carolina, USA

#### **[Patents]**

1. METHOD FOR CONTROLLING ORGANISMS AND MATERIAL THEREFORE, METHOD FOR SELECTIVE ADSORPTION OF PROTEINS AND MATERIAL THEREFORE, CEMENT MATERIAL AND BIOMATERIAL, Patent Number : US6777214B1
2. Material for controlling organisms and for selective adsorption of protein, cement and biomaterial, Patent Number : EU 00104225.8-2107

# Organic Materials

Professor:Nobuhiko YUI  
 Assistant Professor:Atsushi TAMURA  
 Assistant Professor:Yoshinori ARISAKA  
 Secretary:Nanae NISHI

## ( 1 ) Research

### 1. Design of Dynamic Biomaterials Surfaces

Biomaterials surfaces with dynamic properties are designed by utilizing a molecularly movable architecture of polyrotaxanes, and examined their effects on a variety of interactions with living body.

### 2. Modulation of Cellular Functions by Dynamic Ligand-Polymers

Biologically active ligands are introduced into cyclic molecules in polyrotaxanes, and examined the effects of their movability on multivalent interactions with receptor proteins and the subsequent events including intracellular metabolisms.

### 3. Modulation of Cellular Functions by Complexation of Intracellular Functional Supermolecules with Biomolecules

Cytocleavable polyrotaxanes to form complexes with biomolecules such as nucleic acid and protein are designed and their cellular functions are evaluated.

### 4. Cytocleavable Polyrotaxanes as Molecular Therapeutics for Congenital Metabolic disorders

Cyclodextrins released from cytocleavable polyrotaxanes specifically at lysosomes are effective to reduce excess cholesterol accumulation in lysosomes as well as ameliorate impaired autophagy in lysosomal disorders.

## ( 2 ) Publications

### [Original Articles]

1. Yoshinori Arisaka, Jun Kobayashi, Kazuo Ohashi, Kohei Tatsumi, Kyungsook Kim, Yoshikatsu Akiyama, Masayuki Yamato, Teruo Okano. A heparin-modified thermoresponsive surface with heparin-binding epidermal growth factor-like growth factor for maintaining hepatic functions in vitro and harvesting hepatocyte sheets Regenerative Therapy. 2016; 3; 97-106
2. Yoshinori Arisaka, Yuka Nishijima, Shin-ichi Yusa, Naoya Takeda. Photo-induced in situ crosslinking of polymer brushes with dimethyl maleimide moieties for dynamically stimulating stem cell differentiation Journal of Biomaterials Science: Polymer Edition. 2016; 27(13); 1331-1340
3. Ai Ozaki, Yoshinori Arisaka, Naoya Takeda. Self-driven perfusion culture system using a paper-based double-layered scaffold Biofabrication. 2016; 8(3); 035010
4. Atsushi Tamura, Asato Tonegawa, Yoshinori Arisaka, Nobuhiko Yui. Versatile synthesis of end-reactive polyrotaxanes applicable to fabrication of supramolecular biomaterials Beilstein Journal of Organic Chemistry. 2016; 12; 2883-2892

5. A. Tamura, K. Nishida, N. Yui. Lysosomal pH-inducible supramolecular dissociation of polyrotaxanes possessing acid-labile N-triphenylmethyl end groups and their therapeutic potential for Niemann-Pick type C disease. *Science and Technology of Advanced Materials* . 2016.07; 17(1); 361-371
6. K. Nishida, A. Tamura, N. Yui. Tailoring the temperature-induced phase transition and coacervate formation of methylated  $\beta$ -cyclodextrins-threaded polyrotaxanes in aqueous solution. *Macromolecules*. 2016.08; 49(16); 6021-6030
7. M. Terauchi, T. Inada, A. Tonegawa, A. Tamura, S. Yamaguchi, K. Harada, N. Yui. Supramolecular inclusion complexation of simvastatin with methylated  $\beta$ -cyclodextrins for promoting osteogenic differentiation. *International Journal of Biological Macromolecules*. 2016.11; 93; 1492-1498

#### [Conference Activities & Talks]

1. Yoshinori Arisaka, Atsushi Tamura, Nobuhiko Yui. Supermolecule-coated metal surfaces for fabricating dynamic biointerfaces. The 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development 2016.10.17 Osaka, Japan
2. Atsushi Tamura. Development of acid-labile polyrotaxanes for the treatment of Niemann-Pick type C disease. The 8th International Workshop on Advanced Materials Science and Nanotechnology (IWAMSN 2016) 2016.11.09 Ha Long City, Vietnam
3. Yoshinori Arisaka, Atsushi Tamura, Nobuhiko Yui. Polyrotaxane-based 2D and 3D materials design for biomedical applications. International Symposium on Biomedical Engineering 2016.11.10 Tokyo, Japan
4. Yoshinori Arisaka, Atsushi Tamura, Nobuhiko Yui. Supramolecular surfaces with hydrated molecular mobility for constructing dynamic biointerfaces. 3rd International Conference on Biomaterials Science(ICBS2016) 2016.11.28 Tokyo, Japan

# Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D.  
 Associate Professor Wataru NOMURA, Ph.D.  
 Assistant Professor Takaaki MIZUGUCHI, Ph.D.  
 Assistant Professor Nami OHASHI, Ph.D.  
 Technical Assistant Miho TANABE, Ami MASUDA  
 Assistant Tomoe KAMEI  
 Adjunct Lecturer Takaki KOIDE

Graduate students

D3 Shohei TAKETOMI, Takuya KOBAYAKAWA, Hikaru TAKANO, Takayoshi HIGASHI  
 D2 Kiju KONNO, Kei TOYAMA, Kenichi HIRAMATSU, Yuzuna HONDA, Maxwell SAKYIAMAH  
 D1 Daisuke MATSUMOTO, Daisuke MIYAKI  
 M2 Yusuke ISHIDA, Moemi KANEKO, Naoyuki KURATA, Ayumi SAITOU, Toshihiko TSUKINOKI  
 M1 Kento EBIHARA, Tsukasa HASHIMOTO

External Collaborators  
 Yuko YAMADA, Keisuke HARADA

## (1) Outline

Research in the lab is mainly focused to two topics; 1) development of artificial enzymes for regulation of gene functions and (2) exploration and analyses of cellular functions by methods based on peptide chemistry. Students will learn how to design research, experimental techniques, and analysis methods of research data. Research themes are related to multiple research fields such as molecular biology, chemistry, chemical biology, and synthetic biology.

## (2) Research

1. Development of conformational-constrained templates for drug discovery.  
 Drug-discovery templates for conformational restriction, which enable pharmacophores of bioactive compounds (ex. peptides) to be suitably disposed in three-dimensional space, are being developed. Drug discovery for the chemotherapy of cancer, AIDS, Alzheimer's disease, rheumatoid arthritis, SARS, etc. is being performed based on targeting several receptors, enzymes, etc.
2. Development of bio-probes, bio-sensing, medicinal chemistry towards chemical biology.  
 Bio-probes that specifically recognize each receptor or enzyme are being developed for research on chemical biology involving imaging and sensing.
3. Structural analysis of the interactions between receptors/enzymes and their ligands.  
 Using X-ray crystal structural analysis, the mechanism of signal transduction operated by binding of ligands to receptors/enzymes is being analyzed.
4. Development of applications of zinc finger protein for gene therapy and nano technology.  
 Utilizing DNA sequence-specific recognition of zinc finger protein, technologies for DNA recombination, modifications, and DNA labeling are being developed.



### ( 3 ) Education

#### Practice

##### Goals/Outline:

Presenter reports about the recent topics related to molecular biomedicine from Journals. The report must come with the backgrounds and motivations of research fields. Research designs, experimental methods, data analyses, and perspectives for future development will be discussed about the topics. Students are also encouraged to attend to lectures for the graduate course and discuss about the topics with lecturers.

##### Available programs:

Lectures for the graduate course: as occasion

Journal Club: Every Thursday from 15:00 to 16:30

#### Lab

##### Goals/Outline:

Research in the lab is mainly focused to two topics; 1) development of artificial enzymes for regulation of gene functions and (2) exploration and analyses of cellular functions by methods based on peptide chemistry. Students will learn how to design research, experimental techniques, and analysis methods of research data. Research themes are related to multiple research fields such as molecular biology, chemistry, chemical biology, and synthetic biology.

##### Available program:

Lab meeting (progress report): every week, about 1 hour per person (will be announced)

### ( 4 ) Lectures & Courses

#### Format:

Small group

#### Venue:

Practice: Seminar room (603) at Institute of Biomaterials and Bioengineering

Lab: Laboratory of Medicinal Chemistry (602) at Institute of Biomaterials and Bioengineering

#### Grading:

Practice: Attendance and report

Lab: Progress of research and report

### ( 5 ) Publications

#### [Original Articles]

1. Mizuguchi T, Harada S, Miura T, Ohashi N, Narumi T, Mori H, Irahara Y, Yamada Y, Nomura W, Matsushita S, Yoshimura K, Tamamura H. A Minimally Cytotoxic CD4 Mimic as an HIV Entry Inhibitor. *Bioorg. Med. Chem. Lett.* 2016; 2(26); 397-400
2. Ohashi N, Harada S, Mizuguchi T, Irahara Y, Yamada Y, Kotani M, Nomura W, Matsushita S, Yoshimura K, Tamamura H. Small Molecular CD4 Mimics Containing Mono-cyclohexyl Moieties as HIV Entry Inhibitors. *ChemMedChem* a joint special issue with *ChemBioChem: Protein-Protein Interactions*. 2016; 11(8); 940-946
3. Toyama K, Mizuguchi T, Nomura W, Tamamura H. Functional Evaluation of Fluorescein-Labeled Derivatives of a Peptide Inhibitor of the EGF Receptor Dimerization *Bioorg. Med. Chem.* 2016; 24(16); 3406-3412
4. Hiramatsu K, Honjo T, Rauniyar V, and Toste F.D. Enantioselective Synthesis of Fluoro — Dihydroquinazolones and — Benzooxazinones by Fluorination-Initiated Asymmetric Cyclization Reactions. *ACS Catal.* 2016; 6(1); 151-154

5. Zhou L, Holt M. T, Ohashi N, Zhao A, Müller M. M, Wang B, and Muir T. W. Evidence that ubiquitylated H2B corrals hDot1L on the nucleosomal surface to induce H3K79 methylation. *Nat Commun.* 2016;
6. Abduelmula A, Huang R, Pu Q, Tamamura H, Puopolo G. M & Saberi B. B. SDF-1 Controls the Muscle and Blood Vessel Formation of the Somite. *Int. J. Dev. Biol.* 2016; 60(1-2-3)(29-38);
7. Kobayakawa T, Tamamura H. Efficient Synthesis of Xaa-Gly Type (Z)-Chloroalkene Dipeptide Isosteres via Organocuprate Mediated Reduction. *Tetrahedron.* 2016; 72(32); 4968-4971
8. Mizuguchi T, Ohashi N, Matsumoto D, Hashimoto C, Nomura W, Yamamoto N, Murakami T, Tamamura H. Development of Anti-HIV Peptides Based on a Viral Capsid Protein. *Biopolymers: Peptide Science.* 2016; in press;
9. Hiramatsu K, Tamamura H. A Mild Method for the Direct Fluorination of Pyrroles by Using a Lipophilic Anionic Phase-Transfer Catalyst. *Eur. J. Org. Chem.* 2016; 21; 3491-3494
10. Tanaka T, Aoki T, Nomura W, Tamamura H. Bivalent 14-mer Peptide Ligands of CXCR4 with Polyproline Linkers with Anti-Chemotactic Activity against Jurkat Cells *J. Pept. Sci.* 2016; in press;
11. Nakamura T, Campbell J.R, Moore A.R, Otsu S, Aikawa H, Tamamura H, Mitsuya H. Development and Validation of a Cell-based Assay System to Assess Human Immunodeficiency Virus Type 1 Integrase Multimerization *J. Virol. Methods.* 2016; 236; 196-206
12. Takano H, Narumi T, Nomura W, Tamamura H. Microwave-Assisted Synthesis of Azacoumarin Fluorophores and the Fluorescence Characterization *J. Org. Chem.* 2016; in press;

#### [Misc]

1. Nomura W, Mizuguchi T & Tamamura H. Multimerized HIV-gp41-derived Peptides as Fusion Inhibitors and Vaccines *Biopolymers: Peptide Science.* 2016; 106(4); 622-628

#### [Conference Activities & Talks]

1. Takano H, Narumi T, Nomura W, Furuta T, Tamamura H. Development of water-soluble and highly photosensitive 8-azacoumarin-4-ylmethyl-type photolabile-protecting groups for dynamic analysis of bioactive molecules. 251st American Chemical Society National Meeting 2016.03.16 San Diego, USA
2. Nomura W, Ohashi N, Tamamura H. In-cell fluorogenic tag-probe system for protein localization and dynamics imaging. 251st American Chemical Society National Meeting 2016.03.17 San Diego, USA
3. Nomura W, Ohashi N, Tamamura H. Tag-probe Systems for Protein Dynamics Imaging. The 16th Akabori Conference: Japanese-German Symposium on Peptide Science 2016.05.24 Kobe, Japan
4. Nomura W, Sugii T, Tamamura H. Chemically-inducible gene regulation system utilizing sequence-specificity of TALE and dCas9. FASEB SRC: Genome Engineering: Cutting-Edge Research and Applications 2016.06.08 Lisbon, Portugal
5. Tamamura H. Mid-Size Drugs: HIV Fusion Inhibitors Based on the C34 Dimer/Trimer Derived from gp41. The 20th Korean Peptide Protein Society Symposium 2016.06.24 Yangyang, Korea
6. Toyama K, Mizuguchi T, Nomura W, and Tamamura H. Development of New Fluorescein-Labeled Peptides with Inhibitory Effect on the EGF Receptor Activation. The 20th Korean Peptide Protein Society Symposium 2016.06.24 Yangyang, Korea
7. Nomura W, Ohashi N, Tamamura H. Protein Dynamics Imaging Using Tag-probe Systems. The 14th Chinese International Peptide Symposium & the 5th Asia-Pacific International Peptide Symposium 2016.07.06 Nanjing, China
8. Miyaki D, Mizuguchi T, Nomura T, Takahashi D, Tamamura H. Synthesis of Anti-Integrase Stapled Peptides with a Soluble Linker. The 14th Chinese International Peptide Symposium & the 5th Asia-Pacific International Peptide Symposium 2016.07.06 Nanjing, China
9. Kobayakawa T, Tamamura H. Development of synthetic methodology of chloroalkene-type dipeptide isosteres for peptidomimetics. 252nd American Chemical Society National Meeting 2016.08.23 Philadelphia, USA

10. Tamamura H. Mid-Size Drugs: Dimer& Trimer Mimics of HIV-gp41 Peptides as Fusion Inhibitors. 34th European Peptide Symposium 2016 & 8th International Peptide Symposium 2016.09.05 Leipzig, Germany
11. Takano H, Nomura W, Tamamura H. Development of a Hydrophilic Caged PKC Ligand with an 8-Azacoumarin Photolabile Protecting Group for the Precise Photocontrol of PKC Activation. 34th European Peptide Symposium 2016 & 8th International Peptide Symposium 2016.09.08 Leipzig, Germany
12. Toyama K, Mizuguchi T, Nomura W, Tamamura H. Functional Evaluation of Fluorescein-Labeled Peptides Based on the EGF Receptor Dimerization Arm Sequences. 34th European Peptide Symposium 2016 & 8th International Peptide Symposium 2016.09.08 Leipzig, Germany
13. Tamamura H. Mid-sized drugs based on peptide mimetics. 15th Surugadai International Symposium 2016.11.29 Tokyo, Japan
14. Kobayakawa T, Matsuzaki Y, Nomura W, Hozumi K, Nomizu M and Tamamura H. Development of Chloroalkene Dipeptide Isosteres as Peptidomimetics and Their Application. 2016.12.08 Singapore, Singapore
15. Tamamura H. Mid-size Drugs: Peptide-lead Anti-HIV Agents. The 2nd Peptides and Proteins Symposium Singapore 2016.12.09 Singapore, Singapore
16. Nomura W, Tamamura H. Design of synthetic peptides mimicking dynamic supramolecular mechanisms in HIV fusion as antigens and inhibitors against trimer-form of gp41. Antibody Engineering & Therapeutics 2016.12.12 San Diego, California
17. Tamamura H. Medicinal Chemistry/Peptide & Protein Chemistry/Chemical Biology- Peptidomimetic-based Mid-Size Drugs -. The 3rd Joint Symposium between Chulalongkorn University and IBB/TMDU on Biomedical Materials and Engineering, Chulalongkorn University 2016.12.15 Bangkok, Thailand

## NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA
Visiting Professor	Kenkichi MASUTOMI
Visiting Professor	Ryuji HAMAMOTO
Visiting Associate Professor	Masahiro YASUNAGA
Visiting Associate Professor	Genichiro ISHII
Visiting Associate Professor	Tsutomu OHTA
Visiting Associate Professor	Masato ENARI
Visiting Lecturer	Tohru KIYONO
Visiting Lecturer	Kazunori AOKI
Visiting Lecturer	Koji OKAMOTO
Visiting Lecturer	Issay KITABAYASHI
Graduate Students	D3 Kasumi OTSUBO
	D2 Yuki YAMAMOTO
	M2 Masaki NAGASATO, Minori YUMOTO, Sayaka SUGITA, Manami MIURA
	M1 Marina HENMI Hidenobu SUZUKI Taichi IIJIMA

### (1) Research

1. Carcinogenesis and molecular mechanism
2. Functions of cancer-associated genes and their alterations
3. Genomic, epigenomic and proteomic analysis of cancer and personalized medicine
4. Tumor microenvironment
5. Cancer stem cells/non-coding RNA/signaling pathway
6. Molecular target/drug delivery/diagnosis and therapy

### (2) Education

To learn knowledge and skill for cancer research, students attend lectures and seminars, and attend and/or practice research meeting, journal club, scientific meeting, etc. These practices will enable students to develop an ability to conduct their studies as an

independent cancer researcher in the future. To obtain good skills to carry out experiments that are required for cancer research, students belong to one of our research groups, and conduct their own studies under the guidance of the instructor and/or staff. Students perform various experiments involved in genetics, gene technology, biochemistry, cellular biology, molecular biology, physiology, experimental animal, pathology, genomic/epigenomic/proteomic analysis, imaging, next generation sequencing, etc.

### (3) Publications

#### [Original Articles]

1. Kamino H, Nakamura Y, Tsuneki M, Sano H, Miyamoto Y, Kitamura N, Futamura M, Taniguchi H, Kanai Y, Shida D, Kanemitsu Y, Moriya Y, Yoshida K, Arakawa H. Micap-regulated mitochondrial quality control is frequently inactivated in human colorectal cancer. *Oncogenesis*. 5: e181, 2016.
2. Maida Y, Yasukawa M, Masutomi K. De novo RNA synthesis by RNA-dependent RNA polymerase activity of TERT. *Mol Cell Biol*. 36: 1248-1259, 2016.
3. Piao L, Nakakido M, Suzuki T, Dohmae N, Nakamura Y, Hamamoto R. Automethylation of SUV39H2, an oncogenic histone lysine methyltransferase, regulates its binding affinity to substrate proteins. *Oncotarget*. 7: 22846-22856, 2016.
4. Saloura V, Vougiouklakis T, Zewde M, Kiyotani K, Park JH, Gao G, Karrison T, Lingen M, Nakamura Y, Hamamoto R. WHSC1L1 drives cell cycle progression through transcriptional regulation of CDC6 and CDK2 in squamous cell carcinoma of the head and neck. *Oncotarget*. 7: 42527-42538, 2016.
5. Fujiwara Y, Furuta M, Manabe S, Koga Y, Yasunaga M, Matsumura Y. Imaging mass spectrometry for the precise design of antibody-drug conjugates. *Sci Rep*. 6: 24954, 2016.
6. Obonai T, Fuchigami H, Furuya F, Kozuka N, Yasunaga M, Matsumura Y. Tumour imaging by the detection of fibrin clots in tumour stroma using an anti-fibrin Fab fragment. *Sci Rep*. 6: 23613, 2016.
7. Neri S, Hashimoto H, Kii H, Watanabe H, Masutomi K, Kuwata T, Date H, Tsuboi M, Goto K, Ochiai A, Ishii G. Cancer cell invasion driven by extracellular matrix remodeling is dependent on the properties of cancer-associated fibroblasts. *J Cancer Res Clin Oncol*. 142: 437-446, 2016.
8. Saruwatari K, Ikemura S, Sekihara K, Kuwata T, Fujii S, Umemura S, Kirita K, Matsumoto S, Yoh K, Niho S, Ohmatsu H, Ochiai A, Kohrogi H, Tsuboi M, Goto K, Ishii G. Aggressive tumor

microenvironment of solid predominant lung adenocarcinoma subtype harboring with epidermal growth factor receptor mutations. *Lung Cancer*. 91: 7-14, 2016.

9. Suda Y, Neri S, Hashimoto H, Higuchi Y, Ishibashi M, Sugano M, Masutomi K, Tsuboi M, Ochiai A, Ishii G. Clonal heterogeneity in osteogenic potential of lung cancer-associated fibroblasts: promotional effect of osteogenic progenitor cells on cancer cell migration. *J Cancer Res Clin Oncol*. 142: 1487-1498, 2016.
10. Uesato S, Matsuura Y, Matsue S, Sumiyoshi T, Hirata Y, Takemoto S, Kawaratani Y, Yamai Y, Ishida K, Sasaki T, Enari M. Discovery of new low-molecular-weight p53-Mdmx disruptors and their anti-cancer activities. *Bioorg Med Chem*. 24: 1919-1926, 2016.
11. Shima Y, Yumoto M, Katsumoto T, Kitabayashi I. MLL is essential for NUP98-HOXA9-induced leukemia. *Leukemia*, in press. doi: 10.1038/leu.2017.62. [Epub ahead of print]

#### [Review Articles]

1. Hamamoto R, Nakamura Y. Dysregulation of protein methyltransferases in human cancer: an emerging target class for anticancer therapy. *Cancer Sci*. 107: 377-384, 2016.
2. Ishii G, Ochiai A, Neri S. Phenotypic and functional heterogeneity of cancer-associated fibroblast within the tumormicroenvironment. *Adv Drug Deliv Rev*. 99: 186-1896, 2016.

#### [Conference Activities & Talks]

1. Yoichiro Yoshioka, Yusuke Nakamura, Ryuji Hamamoto. Critical role of SMYD3-mediated methylation in the oncogenic activity of AKT1. AACR/JCA 10<sup>th</sup> Joint Conference (Maui, USA), February, 2016.
2. Xiaolan Deng, Yusuke Nakamura, Ryuji Hamamoto. PRMT1 enhances formation of chromosomal passenger complex (CPC) through arginine methylation of INCENP in human cancer cells. AACR/JCA 10<sup>th</sup> Joint Conference (Maui, USA), February, 2016.
3. Theodore Vougiouklakis, Vassiliki Saloura, Yusuke Nakamura, Ryuji Hamamoto. SUV420H1 enhances the phosphorylation and transcription of ERK1 in cancer cells. AACR 107<sup>th</sup> annual meeting (New Orleans, USA), April, 2016.
4. Xiaolan Deng, Yusuke Nakamura, Ryuji Hamamoto. SMYD2-mediated lysine methylation regulates nuclear transport of beta-catenin in human cancer cells. AACR

107<sup>th</sup> annual meeting (New Orleans, USA), April, 2016.

5. Masahiro Yasunaga, Yasuhiro Matsumura. The role of the taurine transporter SLC6A6 in promoting prosurvival activity and multidrug resistance of colorectal cancer.

American Association for Cancer Research Annual Meeting (New Orleans, USA), April, 2016.

6. Masahiro Yasunaga, Shino Manabe, Atushi Tsuji, Masaru Furuta, Koretsugu Ogata, Yuki Fujiwara, Yoshikazu Koga, Yasuhiro Matsumura. Development of CAST therapy by utilizing molecular imaging. World Molecular Imaging Congress (New York, USA), September, 2016.

7. Masahiro Yasunaga, Shino Manabe, Atushi Tsuji, Masaru Furuta, Koretsugu Ogata, Yuki Fujiwara, Yoshikazu Koga, Yasuhiro Matsumura. Development of ADC utilizing molecular imaging. 27th Antibody Engineering & Therapeutics (San Diego, USA), December, 2016.

8. Shima Y, Yumoto M, Katsumoto T, Kitabayashi I. MLL Is Essential for NUP98-HOXA9-Induced Leukemia. The 10th AACR-JCA Joint Conference (Maui, USA), February, 2016.



# Cellular and Molecular Medicine

associate professor Yumiko Oishi MD., Ph.D

assistant professor Shinichiro Hayashi Ph.D

assistant professor Sumio Hayakawa Ph.D

## (1) Outline

Cardiovascular disease, as a consequent of the obesity related metabolic syndrome, remains a significant cause of morbidity and mortality in industrialized societies. A major effort of our laboratory has been to investigate the molecular mechanism of an initiation and progression of metabolic syndrome from the viewpoint of transcriptional regulation. Since macrophages contribute to all phases of the pathogenesis of atherosclerosis, we have extensively studied the macrophage diversity that respond to various stress within tissue environment. Additionally, it is recognized that sarcopenia (skeletal muscle loss with) is important for the pathogenesis of metabolic syndrome. The long term goals of our current study are to elucidate: 1) the mechanism of the link between cellular metabolism and immune response of macrophage 2) the mechanism of chronic inflammation that leads to metabolic syndrome, and 3) the mechanism responsible for pathogenesis of sarcopenia and skeletal muscle degeneration.

## (2) Research

### 1. Mechanisms of Coordinated regulation of inflammatory response and lipid homeostasis in macrophage

Chronic low-grade inflammation has been recognized as a key contributing factor in the onset and progression of metabolic syndrome and atherosclerosis. As a multifunctional effector cell, macrophage play pivotal roles in both the enhancement and resolution of this inflammatory process. By utilizing molecular biology technique, lipidomics and bioinformatics, we found that the lipid homeostasis is coordinately regulated with inflammatory response in macrophage. TLR4 activation rapidly, and transiently inhibits Liver X receptor (LXR) signaling, and subsequently activates Sterol regulatory element-binding protein (SREBP). In the late phase of inflammation, LXR and SREBP work together to increase anti-inflammatory fatty acid synthesis, necessary for a resolution of inflammation. Thus, transcriptional/signaling network involving LXR and SREBP play a pivotal role in the regulation of lipid homeostasis and cellular function. By elucidating the crosstalk between cellular function and metabolism, we would be able to accumulate beneficial knowledge to develop novel therapeutic strategy targeting macrophages for the prevention and treatment of metabolic syndrome.

### 2. Mechanism of skeletal muscle degeneration

Skeletal muscle consume 40% of total energy, playing a key role for the pathogenesis of metabolic syndrome. Sarcopenia is the degenerative loss of skeletal muscle mass, quality and strength associated with aging. Although the causes and mechanisms of sarcopenia still remains unclear, one of the hypotheses is reduction of the number of satellite cells, stem cells in adult muscle, and failure of satellite cell activation. We identified KLF5 as a novel factor that play a pivotal role in skeletal muscle degeneration. KLF5 is a Zinc-finger transcription factor involved in the self-renewal and proliferation of embryonic stem cell and cancer stem cell. KLF5 is transiently induced in the myoblast during differentiation and it plays critical role for muscle degeneration and repair. Although Klf5 is not expressed in the quiescent satellite cells, its expression is dramatically increased in the satellite cells with age. Now we are testing the hypothesis whether the dysregulation of Klf5 causes a malfunction of satellite cells.

### ( 3 ) Education

Lecture: Doctoral Program, Life Science and Technology Track #6110, Bioscience I

Lecture: Master's Program, Medical and Dental Science and Technology Track, Molecular biology

Lecture: School of Dentistry, Second grade, Basic molecular mechanisms of life

### ( 4 ) Publications

#### [Original Articles]

1. Rumi Hachiya, Takuya Shiihashi, Ibuki Shirakawa, Yorihiro Iwasaki, Yoshihiro Matsumura, Yumiko Oishi, Yukiteru Nakayama, Yoshihiro Miyamoto, Ichiro Manabe, Kozue Ochi, Miyako Tanaka, Nobuhito Goda, Juro Sakai, Takayoshi Suganami, Yoshihiro Ogawa. The H3K9 methyltransferase Setdb1 regulates TLR4-mediated inflammatory responses in macrophages. *Sci Rep.* 2016.06; 6; 28845
2. Taisho Yamada, Hiromasa Horimoto, Takeshi Kameyama, Sumio Hayakawa, Hiroaki Yamato, Masayoshi Dazai, Ayato Takada, Hiroshi Kida, Debbie Bott, Angela C Zhou, David Hutin, Tania H Watts, Masahiro Asaka, Jason Matthews, Akinori Takaoka. Constitutive aryl hydrocarbon receptor signaling constrains type I interferon-mediated antiviral innate defense. *Nat. Immunol.* 2016.06; 17(6); 687-694
3. Shinichiro Hayashi, Ichiro Manabe, Yumi Suzuki, Frédéric Relaix, Yumiko Oishi. Klf5 regulates muscle differentiation by directly targeting muscle-specific genes in cooperation with MyoD in mice. *Elife.* 2016.10; 5;

#### [Books etc]

1. Takuji Suzuki, Noriyuki Miyoshi, Sumio Hayakawa, Shinjiro Imai, Mamoru Isemura, and Yoriyuki Nakamura. Beverage Impacts on Health and Nutrition. Springer International Publishing, 2016

#### [Misc]

1. Sumio Hayakawa, Kieko Saito, Noriyuki Miyoshi, Tomokazu Ohishi, Yumiko Oishi, Mamoru Miyoshi, Yoriyuki Nakamura. Anti-Cancer Effects of Green Tea by Either Anti- or Pro- Oxidative Mechanisms. *Asian Pac. J. Cancer Prev.* 2016; 17(4); 1649-1654
2. Yumiko Oishi, Ichiro Manabe. Chronic inflammation and atherosclerosis 2016.01; 45(1); 12-17
3. Yumiko Oishi, Ichiro Manabe. Integrated regulation of the cellular metabolism and function of immune cells in adipose tissue. *Clin. Exp. Pharmacol. Physiol.* 2016.03; 43(3); 294-303
4. Yumiko Oishi, Ichiro Manabe. Immune system in the organ crosstalk and metabolism *Journal of Clinical and Experimental Medicine.* 2016.05; 257(6); 597-600
5. Yumiko Oishi, Ichiro Manabe. Transcriptional, epigenetic, and transcriptome analysis of macrophage *Journal of Clinical and Experimental Medicine.* 2016.06; 257(6); 733-737
6. Yumiko Oishi, Ichiro Manabe. Macrophages in age-related chronic inflammatory diseases *Aging and Mechanisms of Disease.* 2016.07; 2; 16018
7. Yumiko Oishi, Ichiro Manabe. Zinc-finger transcription factors 2016.08; 175-180
8. Yumiko Oishi, Ichiro Manabe. parabiosis in aging science *Anti-Aging medicine.* 2016.10; 12(5); 650-656
9. Yumiko Oishi, Ichiro Manabe. Macrophage lineages in atherosclerosis *Journal of Clinical and Experimental Medicine.* 2016.10; 259(5); 475-479
10. Yumiko Oishi, Ichiro Manabe. B cells in adipose tissue inflammation *The Medical Frontline.* 2016.11; 71(917); 2217-2221

**[Conference Activities & Talks]**

1. Yumiko Oishi. Coordinated regulation of immune response, circadian rhythm and cellular metabolism in macrophage as a novel therapeutic target. The 80th Annual Scientific meeting of the Japanese Circulation Society 2016.03.20
2. Sumio Hayakawa, Yumiko Oishi . The crosstalk between chronic inflammation and lipid metabolism. The 24th International Symposium on Molecular Cell Biology of Macrophage 2016.06.04 Tokyo, Japan
3. Yumiko Oishi. Coordinated regulation of inflammatory response and lipid metabolism in macrophage. The 48th annual scientific meeting of the Japan Atherosclerosis society 2016.07.15 Tokyo
4. Shinichiro Hayashi, Ichiro Manabe, Yumi Suzuki, Yumiko Oishi. Klf5 regulates skeletal muscle differentiation by directly targeting muscle-specific genes. FASEB SRC -KLF AND SP TRANSCRIPTION FACTORS IN DISEASE AND REGENERATIVE MEDICINE- 2016.08.07 Snowmass, CO
5. S. Hayakawa, Y. Oishi . Inflammatory response regulates the transcription factor SREBP activation. . The 57th International Conference on the Bioscience of Lipids (ICBL) 2016.09.04 Chamonix-Mont-Blanc, France

## Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA  
Junior Associate Professor Keiko KONDO  
Assistant Professor Masayo YASUDA  
Graduate Student Mizuki DOINO, Tona WATANABE  
Resident Hidehiro SHIOYAMA

### ( 1 ) Outline

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care. Regarding research, the effects of the functional waters to organism and clinical application of them were investigated.

### ( 2 ) Research

- 1) Clinical and basic studies on Ozone nano-bubble water (NBW3) :antimicrobial activity and effects to eukaryotic cells (induction of anti-oxidant capacities and wound healing activities etc.)
- 2) Study on virulence factors of periodontopathic bacteria
- 3) Development of education system for dental (oral) hygienists to prevent oral diseases
- 4) Development of assessment program in technical education for dental (oral) hygienists

### ( 3 ) Education

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care.

### ( 4 ) Lectures & Courses

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care.

### ( 5 ) Clinical Services & Other Works

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

**( 6 ) Clinical Performances**

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

**( 7 ) Publications****[Original Articles]**

1. H. Otuska, S. Arakawa, A. Kinoshita, K. Shinada, et al.. Development of an interprofessional education program where dental hygiene students instruct medical and dental students. *Journal of Dental Education*. 2016; 80; 1062-1070
2. Doino, Mizuki; Arakawa, Shinichi; Yokoyama, Miki; Sasaki, Yoshiyuki; Kondo, Keiko; Yasuda, Masayo.. Evaluation of the relationship between salivary concentration of anti-heat shock protein immunoglobulin and clinical manifestations of Beh?et's disease. *Scandinavian Journal of Rheumatology*. 2016;

**[Misc]**

1. Shinichi Arakawa. Ozone antiseptic shows potential for treating severe gum infections *Asia Research News* 2015.

**[Conference Activities & Talks]**

1. Atsushi Oishi, Hitoyata Shimokawa, Wit Yee Wint, Shinichi Arakawa, Michiyo Miyashin. Effects of Nanobubble water on human cells derived from impacted supernumerary teeth. 10th Biennial Conference of the Pediatric Dentistry Association of Asia in conjunction with 54th Annual Conference of the Japanese Society of Pediatric Dentistry 2016.05.26 Tokyo
2. Jun Tsuruta, Kanako Noritake, Kouji Mizutani, Naoko Seki, Keiko Kondou, Shinichi Arakawa, Kouji ARAKI. A new course Working in a team . SEAADE Annual Scientific Meeting 2016.09.08 Ho Chi Minh city, Vietnam
3. Jun Tsuruta,Kanako Noritake, Koji Mizutani, Naoko Seki,Keiko Kondo, Shinichi Arakawa,Kouji Araki. Implementing a new IPW course in the dental student clinic. Peking University School of Stomatology·Tri-university 2016.10.27 Peking University School of Stomatology
4. Seki N, Moross J, Otsuka H, Sunaga M, Naito M, Takatsuna Y, Kondo K, Shinada K, Morio I, Kinoshita A. Learning outcome provided by ESL clinical simulation teaching materials for dental hygiene education. 81st Annual Meeting of the Stomatological Society 2016.11.26 Tokyo
5. Watanabe T. ,Yasuda M,. Kondo K., Arakawa S.,. Evaluation for the method of intervension for oaral health improvement for people with disabilities at the day care center.. The Stomatological Society,Japan 2016.11.26 Tokyo Medical and Dental University

# Oral Care for Systemic Health Support

Professor KABASAWA Yuhji

## (1) Outline

### (1) Education

We teach the knowledge and skills necessary for oral health activities through classes in charge. Specifically, we will teach about the relationship between oral health and general health such as perioperative oral function management and periodontal disease and diabetes. In addition to teaching health assessment of the oral and maxillofacial area, we will acquire basic knowledge and skills through vital signs measurement practice, emergency life-saving activity practice, which is one of general health evaluation indicators.

Furthermore, we lecture on the pathology, diagnosis and treatment related to mandibular oral cavity disease, and teach necessary knowledge on oral health education, prevention of oral diseases of people with basic diseases in the medical field.

### (2) Research

We will conduct research to support maintenance and promotion of health by oral health. Especially contribute to people's health and well-being through research on perioperative oral cavity function management, research on oral care of people with underlying diseases, research on regeneration of jawbone with FGF-2, etc.

### (3) Clinical

In order to maintain and promote general health through oral health, we cooperate with each outpatient at the dentistry hospital and do dental prophylactic treatment of the patient and oral health education at oral care outpatient. In addition to oral care for inpatients at dental and medical hospital while working in cooperation with nurses, nutritionists, pharmacists and others, they practice oral care according to the condition of patients as a member of team medicine.

## (2) Research

1. Oral health care of patients with oral cancer, cleft lip and palate and other oral diseases
2. Oral health related QOL of patients with oral cancer, cleft lip and palate, dry mouth
3. Basic research of tooth brush, peeling sponge and tooth paste
4. Morphological, functional research, and oral health of patients with cleft lip and palate
5. Research for safety in supplements in oral functions
6. Basic research for bone regeneration using FGF-2.

## (3) Lectures & Courses

From the standpoint of oral health and general health, educate dental hygienists who can contribute to people's health and welfare by teaching the knowledge and skills necessary for oral health care centering on oral medicine education.

## (4) Clinical Services & Other Works

Oral care department, in cooperation with each outpatient in the dental school attached hospital, in order to maintain and improve the general health through oral health, do patients' dental preventive measures and oral

health education in oral care outpatient. In addition, we do oral care for hospitalized patients in the dentistry department and medical hospital affiliated hospitals, we receive consultation about patient oral care from ward nurses, and instruct oral care methods according to patient condition.

In oral surgery unit, we are engaged in diagnosis, treatment, oral health guidance etc of various oral disease patients.

#### **( 5 ) Clinical Performances**

Based on knowledge of oral medicine through oral care department, we are conducting perioperative oral function management with more specialized expertise.



## Preventive Oral Health Care Sciences

Professor Kayoko SHINADA  
Assistant Professor Hiromi OTSUKA  
Part-time lecturer Atsushi OHYAMA  
Chiyoko HAKUTA  
Graduate Students Master Course  
Tomomi ABE,  
Makoto KAWANO,  
Chie YOSHIZU,

### ( 1 ) Outline

In order to cultivate students' abilities to prevent and detect oral diseases at an early stage, which are important to maintain and improve the nation's health, we help students acquire deep academic knowledge and high standard skills in preventive oral health care such as skills to check over the condition of oral cavities. Additionally, we help students develop skills to provide oral health counseling and oral health promotion, and nurture human resources who can actively contribute the development of oral health promotion.

### ( 2 ) Research

- 1) Preventive Oral Health Care Sciences
  - ① Incident factors and preventive methods on dental caries
  - ② Incident factors and preventive methods on periodontal disease
  - ③ Incident factors and preventive methods on oral malodor
  - ④ Incident factors and preventive methods on other oral diseases
- 2) Development of education system for the patients to prevent oral diseases and for dental hygiene students.
- 3) Development of new assessment programs in technical education for dental hygienist students.

### ( 3 ) Clinical Services & Other Works

In our Oral Health Care Clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases, for the patients to maintain their oral health for the entire lifetime.

### ( 4 ) Publications

#### [Original Articles]

1. Hiromi O, Keiko K, Yuki O, Masayo Y, Natsuki K, Masayo S, Keiko E, Shinichi A, Atsuhiko K, Kayoko S. An inter- and intraprofessional education program in which dental hygiene students instruct medical and dental students Journal of Dental Education. 2016.09; 80(9); 1062-1070

**[Conference Activities & Talks]**

1. Naito M, Shinada K, Kunitsuka K, Yamamoto R, Onishi T, Nishi M, Seki N, Morio I, Taniyama K. Intervention survey on oral health at newspaper printing factories. 89th Annual Meeting of the Japan Society for Occupational Health 2016.05.27 Fukushima city
2. Moross J, Seki N, Sunaga M, Otsuka H, Naito M, Shinada K, Morio I, Kinoshita A. Development of ESL clinical simulation teaching materials for dental hygienist education. Annual Meeting of the 35th Japanese Dental Education Association 2016.07.02 Osaka, Japan
3. Kanako Toda, Tomomi Abe, Makoto Kawano, Chie Yoshizu, Hiromi Ohtsuka, Isao Minami, Yoshihiro Ogawa, Koji Araki, Kayoko Shinada. The effect of oral health education to body and oral health with diabetic patients. The 11th Annual Meeting of Japan Dental Hygienists' Association 2016.09.18 Hiroshima
4. Kanako Toda, Keiko Matsuo, Mayuka Taga, Hitomi Arimatsu, Takuo Ishii, Masayoshi Hukushima, Yuichi Ohshima, Yoshinori Toriyama. Research discussion on "Interprofessional work". The 11th Annual Meeting of Japan Dental Hygienists' Association 2016.09.19 Hiroshima
5. Yoko Ishii, Kanako Toda, Yuka Shizuma, Hiroko Mega, Kayoko Shinada. Follow-up survey of oral environment and oral health situation in infants. The 75th Annual Meeting of Japanese Society of Public Health 2016.10.26 Osaka
6. Seki N, Moross J, Otsuka H, Sunaga M, Naito M, Takatsuna Y, Kondo K, Shinada K, Morio I, Kinoshita A. Learning outcome provided by ESL clinical simulation teaching materials for dental hygiene education. 81st Annual Meeting of the Stomatological Society 2016.11.26 Tokyo
7. Tomomi Abe, Makoto Kawano, Hiromi Otsuka, Kayoko Shinada. Effects of oral care and function improvement program on nursing care elderly. The 81th Stomatological Society Meeting 2016.11.26 Tokyo
8. Kawano Makoto, Abe Tomomi, Yoshizu Chie, Toda Kanako, Otsuka Hiromi, Shinada Kayoko. Survey on educational present condition and dental hygiene process. The 81th Stomatological Society Meeting 2016.11.26

## Oral Health Sciences for Community Welfare

Professor Junichi FURUYA  
Junior Associate Professor Keiko ENDO  
Graduate Student Michiyo OBANA  
Graduate Student Chiaki MATSUBARA  
Graduate Research Student Junji TOKUNAGA

### ( 1 ) Outline

The role of Department of Oral Health Sciences for Community Welfare is to develop education, practice, research for people who can play an important role in medical care and welfare of super-aging society. The department is particularly focusing on improving oral health such as mastication, swallowing, and oral hygiene through dysphagia rehabilitation, diet modification support, multi-disciplinary team approach so that the department contributes to prevent and improve aspiration pneumonia, malnutrition, and quality of life.

All educational and research activities are based on clinical practice and experiences so that knowledge and skills of oral function will be acquired. Concretely, oral functional rehabilitation and oral hygiene care are performed as oral health management for hospitalized and institutionalized patients, and out patient in clinic. In addition, we supply multi-disciplinary team approach as a member of NST (Nutrition Support Team), PCT (Palliative Care Team), Visiting Dysphagia Rehabilitation Team in medical hospital of TMDU.

### ( 2 ) Research

1. Oral hygiene, dysphagia rehabilitation, and diet modification support in medical care with multi-disciplinary team approach.
2. Welfare, well-being and life support for people with dysphagia.
3. Oral function, nutrition, and enjoyment of eating in older people.
4. Professional oral hygiene care by dental hygienists
5. Collaboration of medical care, health, nursing-care, and welfare.

### ( 3 ) Education

Gerodontology  
Welfare for older people  
Nursing-care for older people  
Prosthodontics  
Home visiting dentistry  
Community dental care  
Social work  
etc

#### ( 4 ) Publications

##### [Original Articles]

1. S Onodera, J Furuya, H Yamamoto, Y Tamada, H Kondo. Effects of wearing and removing dentures on oropharyngeal motility during swallowing. J Oral Rehabil. 2016.11; 43(11); 847-854

##### [Conference Activities & Talks]

1. S Onodera, J Furuya, Y Tamada, H Yamamoto, T Sato, A Hara, A Itsukaichi, S Aki, H Kondo. Impacts of wearing dentures on oro-pharyngeal movement during pharyngeal swallowing . Twenty-fourth Annual Meeting of the Dysphagia Research Society 2016.02.26 Tuscon, Arizona, the USA
2. Junichi Furuya. Functional Occlusal Scheme for complete dentures. Peking University Hospital of Stomatology First Clinical Division 2016.11.05 Beijing
3. CMatsubara, K Endo, M Obana, J Furuya. Relationships among experience of health education, oral Function, and oral health-related quality of life in community-dwelling older individuals. The 81st meeting of Stomatological Society 2016.11.25 Tokyo

## Oral Health Care Education

Associate Professor Keiko Endo  
Junior Associate Professor Yuki Ohara

### ( 1 ) Research

- 1) Education for dental hygienist students
- 2) Oral health promotion program
- 3) Development of dental hygiene process

### ( 2 ) Education

Oral health care education is special field of study which deals with establishment of theoretic and skill for health promotion to contribute to the development of the health. Educational objects of Oral health care education in the graduate course is to foster human resources who will be able to implement health promotion program in collaboration with other career or residents in many fields.

### ( 3 ) Clinical Services & Other Works

In oral health care clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases for the patients to maintain their oral and general health in the entire lifetime.

### ( 4 ) Publications

#### [Original Articles]

1. Yuki Ohara, Hirohiko Hirano, Hideyo Yoshida, Shuichi Obuchi, Kazushige Ihara, Yoshinori Fujiwara, Shiro Mataka. Prevalence and factors associated with xerostomia and hyposalivation among community-dwelling older people in Japan. *Gerodontology*. 2016.03; 33(1); 20-27
2. Daisuke Takagi, Hirohiko Hirano, Yutaka Watanabe, Ayako Edahiro, Yuki Ohara, Hideyo Yoshida, Hunkyung Kim, Kohji Murakami, Shouji Hironaka. Relationship between skeletal muscle mass and swallowing function in patients with Alzheimer's disease. *Geriatr Gerontol Int*. 2016.05;
3. Chiyoko Hakuta, Ayako Okada, Kaoru Sogabe, Erika Kakuta, Keiko Endo, Susumu Imai, Masaaki Okamoto, Yoshiaki Nomura, Nobuhiro Hanada. Opportunistic Bacteria in Tonsil and Dental Plaque are Indicator for Oral Care Opportunistic Bacteria in Tonsil and Dental Plaque are Indicator for Oral Care. 2016.05; 2(1); 30-34
4. Shiho Morishita, Yutaka Watanabe, Yuki Ohara, Ayako Edahiro, Emiko Sato, Takeo Suga, Hirohiko Hirano. Factors associated with older adults' need for oral hygiene management by dental professionals. *Geriatr Gerontol Int*. 2016.08; 16(8); 956-962
5. Yuki Ohara, Naomi Yoshida, Hisashi Kawai, Shuichi Obuchi, Hideyo Yoshida, Shiro Mataka, Hirohiko Hirano, Yutaka Watanabe. Development of an oral health-related self-efficacy scale for use with older adults. *Geriatr Gerontol Int*. 2016.08;

6. Yutaka Watanabe, Hirohiko Hirano, Hidenori Arai, Shiho Morishita, Yuki Ohara, Ayako Edahiro, Masaharu Murakami, Hiroyuki Shimada, Takeshi Kikutani, Takao Suzuki. Relationship Between Frailty and Oral Function in Community-Dwelling Elderly Adults. *J Am Geriatr Soc.* 2016.09;
7. Hiromi Otsuka, Keiko Kondo, Yuki Ohara, Masayo Yasuda, Natsuki Kishimoto, Masayo Sunaga, Keiko Endo, Shinichi Arakawa, Atsuhiro Kinoshita, Kayoko Shinada. An Inter- and Intraprofessional Education Program in Which Dental Hygiene Students Instruct Medical and Dental Students. *J Dent Educ.* 2016.09; 80(9); 1062-1070

#### **[Misc]**

1. Hunkyung Kim, Hirohiko Hirano, Ayako Edahiro, Yuki Ohara, Yutaka Watanabe, Narumi Kojima, Miji Kim, Erika Hosoi, Yuko Yoshida, Hideyo Yoshida, Shoji Shinkai. Sarcopenia: Prevalence and associated factors based on different suggested definitions in community-dwelling older adults. *Geriatr Gerontol Int.* 2016.03; 16 Suppl 1; 110-122
2. Problems and the attempt to improve patients safety education at dental hygiene education in our university 2016.05; 7(1); 39-44

#### **[Conference Activities & Talks]**

1. Yuki Ohara, Hirohiko Hirano, Yutaka Watanabe, Ayako Edahiro, Shiho Morishita, Maki Shirobe, Keiko Endo. Risk factors associated with aspiration in older persons requiring long-term care: An investigation with a 2-year follow-up. The 12th International Conference of Asian Academy of Preventive Dentistry 2016.05.27 Tokyo
2. Shino Suma, Yutaka Watanabe, Hidenori Arai, Kenji Matsushita, Takashi Sakurai, Hirohiko Hirano, Ayako Edahiro, Yuki Ohara. Differential factors affect the appetite in AD and MCI patients. The 12th International Conference of Asian Academy of Preventive Dentistry 2016.05.27
3. Yuki Ohara. Implication of oral function for frailty and disability. 2nd Asian Conference for frailty and sarcopenia Asian Aging Forum 2016.11.04 Nagoya

## Basic Sciences of Oral Health Care

Junior Associate Professor Yujiro Sakamoto

### ( 1 ) Outline

Graduate School of Medical and Dental Sciences has been reorganized in April 2012, and the section of Basic Sciences of Oral Health Care was established in Medical and Dental Science and Technology master's program course.

### ( 2 ) Research

- 1) Basic medical and dental studies for oral health care
- 2) Basic study on clinical application of oral health care
- 3) Gross anatomical study of head and neck region

### ( 3 ) Education

Purpose of Education

Basic sciences of oral health care is a branch of morphological sciences, developmental biology, pathology and the neurosciences to understand the structure and function of human body and its pathological conditions. Students are taught in more detail about the normal tooth anatomy and occlusal function as well as the anatomy of the head and neck with specific attention to the skull, muscles, nerves, and arteries associated with the mouth and teeth. In addition, students are also taught the oral pathology and dental pharmacology and pharmaceuticals.

Subjects and contents.

- Structure and function of human body I and II: anatomy, histology, physiology, embryology, oral anatomy, oral histology, oral physiology.
- Mechanism of disease and promotion of recovery process: pathology, oral pathology, microbiology, immunology, pharmacology.
- Dental Pharmacology and Pharmaceuticals.
- Graduation thesis:

### ( 4 ) Publications

#### [Books etc]

1. Sakamoto Y. 26, Pharyngeal muscles; 28, Prevertebral and craniocervical junction muscles. In: Bergman's Comprehensive Encyclopedia of Human Anatomic Variation. Wiley-Blackwell, 2016 (ISBN : 978-1-118-43035-4)
2. Sakamoto Y. 26, Pharyngeal muscles; 28, Prevertebral and craniocervical junction muscles. In: Bergman's Comprehensive Encyclopedia of Human Anatomic Variation (E-book). Wiley-Blackwell, 2016 (ISBN : 978-1-118-43030-9)



**[Conference Activities & Talks]**

1. Sakamoto Y. Gross anatomical observations on the configuration of the extrinsic muscles of the tongue.  
The 33rd annual meeting American Association of Clinical Anatomists. 2016.06 Oakland, USA.

## Basic Oral Health Engineering

Professor Kazuhiro Aoki  
Associate Professor    Meiko Oki  
Assistant Professor    Shingo Kamijoh

### ( 1 ) Outline

Basic Oral Health Engineering is a department assigned to basic science field of oral health in three master course departments which were reorganized from the departments of Oral Health Engineering Course in 2015. The department is originated in Basic Oral Health Sciences.

The department of Basic Oral Health Engineering aims to create a scientific foundation for the clinical applications based on interdisciplinary research between engineering and biology and/or interface studies between basic and clinical sciences. We believe that these research activities, which are focused on the region of the oral cavity, can contribute to attaining healthy and happy living conditions. We have the responsibility to train our students to be medical personnel who are eager to contribute to people's happiness through a broad range of educational courses from basic level courses to professional level courses, which integrate areas of study such as the structure and function of the human body, stomatognathic region, pharmacology and the research process.

### ( 2 ) Research

Research Subjects

- 1) The development of surface coating materials for the prevention of plaque growth
- 2) Research related to the connection between oral bacteria and systemic health
- 3) The development of non-invasive methods of bone mass augmentation
- 4) The fabrication of facial prostheses using a three-dimensional rapid manufacturing method
- 5) Clinical studies of treatments for patients with maxillofacial defects
- 6) The development of materials for facial prostheses
- 7) The relationship between "medical care to support life" and the dental technician
- 8) The education of dental technicians using computer simulation training

### ( 3 ) Lectures & Courses

Basic Oral Health Engineering is a department of oral health engineering which deals with the basic oral health sciences to perform evidence-based oral health care and prosthetic treatments to support people to promote oral health and improve quality of life. Main objective of Basic Oral Health Engineering in the undergraduate course is to provide students opportunity to study the structure and function of the human body, fabrication of dental and maxillofacial prostheses, dental CAD/CAM technology and research process.

### ( 4 ) Clinical Performances

Clinical activities

- Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects
- Making dental and maxillofacial prostheses

**( 5 ) Publications****[Original Articles]**

1. Imura Hiroko, Shimada Masahiko, Yamazaki Yoko, Sugimoto Kumiko. Characteristic changes of saliva and taste in burning mouth syndrome patients Journal of Oral Pathology and Medicine. 2016.03; 45(3); 231-236
2. Shizuka Tanaka, Naoko Uehara, Natsumi Tsuchihashi, Kumiko Sugimoto. Emotional relationships between child patients and their mothers during dental treatments Journal of Dental Sciences. 2016.03; 11; 287-292
3. Meiko Oki, Tetsuya Suzuki, Hidekazu Takahashi. A modified indirect method for fabricating silicone soft-lined complete dentures Journal of Prosthetic Dentistry. 2016.07;
4. Oki M, Kanazaki A, Taniguchi H. Osteoradionecrosis following carbon ion radiotherapy: Case history report of a soft palate defect. International Journal of Prosthodontics. 2016.09; 29(5); 448-450
5. Taki Sekiya, Hiroko Imura, Sachiko Ito, Michiyo Miyashin, Kumiko Sugimoto. Development of real-time stress monitoring system in pediatric dentistry: Assessment from autonomic nerve and brain activities The Japanese Journal of Pediatric Dentistry. 2016.12; 54(4); 443-449

**[Conference Activities & Talks]**

1. Hiroji Shimomura, Kiyoko Kanamori, Yasuko Kawakami, Kumiko Sugimoto, Ayako Kubota. Survey of oral health status and behavior of medical university students. Collaborative Project Workshop 2015 of Bunkyo Gakuin University Research Institute 2016.05.07 Tokyo
2. Yoko Kono, Ayako Kubota, Mika Matsushima, Masato Taira, Kumiko Sugimoto. Effect of intraoral stimulation with capsaicin on salivary secretion and neural activity. 17th International Symposium on Olfaction and Taste 2016.06.05 Yokohama
3. Yu-mi TSUCHIDA, Yuji KABASAWA, Namiaki TAKAHARA, Shingo, KAMIJO, Tetsuya SUZUKI. Accuracy of a 3D Model for Surgical Support in Orthognathics. Advanced Digital Technology (ADT) North America & Japan Regional Leadership Groups Conference 2016.06.17 San Diego California USA
4. Kayo Kimura, Kazuo Shimazaki, Kumiko Sugimoto, Takashi Ono. Influence of habitual mouth-breathing on taste sensation. 94th General Session and Exhibition of The IADR 2016.06.22 Seoul
5. Ayako Kubota, Yoko Kono, Hiroko Imura, Hiroji Shimomura, Kiyoko Kanamori, Yasuko Kawakami, Shiro Mataka, Kumiko Sugimoto. Oral health status and behavior of Japanese university students. . International Symposium on Dental Hygiene 2016 2016.06.23 Basel
6. Kumiko Sugimoto, Naomi Yoshida, Yoko Yamazaki, Hiroko Imura, Yoko Kono, Ayako Kubota, Sato Yamanaka, Hiroyuki Sakamaki, Asako Kimura. Objective assessment of oral and holistic health in dental hygienists at menopausal stage. International Symposium on Dental Hygiene 2016 2016.06.23 Basel
7. Naomi Yoshida, Kumiko Sugimoto, Sato Yamanaka, Hiroyuki Sakamaki, Yoko Yamazaki, Asako Kimura, Hiroko Imura, Yoko Kono, Ayako Kubota. Oral and holistic health evaluation and dental health status in dental hygienists at menopausal stage. International Symposium on Dental Hygiene 2016 2016.06.23 Basel
8. Ayako Kubota, Yasunari Miyazaki, Yoshimi Sakurai, Shiro Mataka, Kumiko Sugimoto. Cross-sectional study on oral health of university students. Japan Dental Hygienists' Association The 11th Academic Meeting 2016.09.17 Hiroshima
9. Ai Hasegawa, Hiromi Otsuka, Kumiko Sugimoto. Investigation of influences of habitual mouth-bleathing on halitosis and lip function. The 11th Academic Meeting of Japan Dental Hygienists' Association 2016.09.17 Hiroshima

10. Ayako Kubota, Yasunari Miyazaki, Yoshimi Sakurai, Shiro Mataka, Kumiko Sugimoto. Cross-sectional survey of oral healthcare for university students in Kanto-Koshinetsu District Association . The 54th Annual Meeting of Japan University Health Association 2016.10.05 Osaka
11. Tamaki Hada, Hidekazu Takahashi, Shingo Kamijo, Masaomi Ikeda, Toshio Kitamura, Shizuo Higuchi, Tetsuya Suzuki. EFFECT OF CAD/CAM FABRICATED FRAMEWORK ON COMPLETE DENTURE DEFORMATION. ACADEMY OF DENTAL MATERIALS (ADM) Annual Meeting 2016.10.12 Chicago, IL, USA
12. Yui Kasai, Kumiko Sugimoto, Shingo Kamijo, Meiko Oki. Investigation on the role of dental technicians among the dentists practicing home-visit dental care. The 81th Annual Meeting of the Stomatological Society 2016.11.26 Tokyo
13. Kumiko Sugimoto. Mechanisms undelying the function of eating. The 7th Annual Meeting of Japan Society of Dental Hygiene Education 2016.12.10 Tokyo

## Oral Biomaterials Development Engineering

Professor	Hidekazu TAKAHASHI
Junior Associate Professor	Tohru YASUE
Assistant Professor	Naohiko IWASAKI

Graduate student (Master course) Yuko NAKAJIMA  
Special research student Sasipin LAUVAHUTANON (April to May, Chulalongkorn Univ)  
Research student Chen Hsuan (July, Taipei Medical Univ.)  
Research student Lin, Jhih-Ni (July, Taipei Medical Univ.)

### (1) Outline

Basic knowledge of dental materials and devices for oral health engineering are provided for student. Basic exercise for dental materials and prosthetic training are also provided. Development and evaluation of new dental materials are performed.

### (2) Research

1. Evaluation of various factors on mechanical properties of teeth substance.
2. Evaluation of fatigue properties of dentin and dental materials using miniature testing pieces
3. Measurement of characteristics of dental ceramic materials and establishment of new testing methods for dental ceramics
4. Measurement of precise deformation using non-contact methods
5. Development of new composite resin with similar machinability of dentin
6. Study on dental root fracture mechanism
7. Application of various types of fiberglass for dentistry
8. Evaluation of composite resin mechanical properties and improvement their bonding efficiency to various materials.
9. Evaluation of impact force absorption of mouthguard and face protect materials

### (3) Education

Dental material science is not only one of basic medical and dental science but also one of clinical dental science. In our department, we will educate students to obtain practical knowledge of the dental materials and devices used in dentistry and to improve skill how to deal with these materials and devices. Our goals of education are to achieve high quality of dental practice with well-understanding dental material and devices.

The aim for education is to obtain the basic knowledge of dental material science and technology. The lecture is simultaneously provided with the laboratory instructions within the limit of the possible.

#### **( 4 ) Lectures & Courses**

Dental material science is not only one of basic medical and dental science but also one of clinical dental science. In our department, we will educate students to obtain practical knowledge of the dental materials and devices used in dentistry and to improve skill how to deal with these materials and devices. Our goals of education are to achieve high quality of dental practice with well-understanding dental material and devices.

The aim for education is to obtain the basic knowledge of dental material science and technology. The lecture is simultaneously provided with the laboratory instructions within the limit of the possible. Presentation not only domestic but also international meeting is strongly encouraged.

#### **( 5 ) Clinical Services & Other Works**

Participation in various congresses are strongly recommended. Assistance for standard publication is also cooperated. Especially, Prof. Takahashi, head of Oral Biomaterials Engineering acts as the chairperson of ISO TC106 Dentistry/SC9 Dental CAD/CAM systems for publishing ISO standards.

#### **( 6 ) Publications**

##### **[Misc]**

1. Hidekazu TAKAHASHI. Outlook of CAD/CAM resin blocks approved by social insurance system Journal of Japan Academy of Digital Dentistry. 2016.07; 6(1); 3-6

##### **[Conference Activities & Talks]**

1. Hidekazu TAKAHASHI. General information for CAD/CAM composite resin blocks.. Project seminar of Japanese Academy of Digital Dentistry 2016.02.21 Tokyo
2. Takahashi H, Iwasaki N, Suzuki T. Flexural properties of recent composite resin blocks for CAD/CAM. 2nd meeting of International Academy of Digital Dental Medicine 2016.09.03 Busan
3. Nakajima Y, Iwasaki N, Takahashi H, Yoshida M, Honda E, Kurabayashi T. MRI Artifacts and Radiopacity of CAD/CAM Composite Resin Blocks. The 2016 Academy of Dental Materials Annual Meeting 2016.10.13 Chicago
4. Takahashi H, Iwasaki N, Sumi Y. Effect of Cavity Design on Gap Formation Observed by OCT. The 2016 Academy of Dental Materials Annual Meeting 2016.10.14 Chicago
5. Takahashi H, Iwasaki N, Yasue T, Sumi Y. Observation of dental restoration gap formation using optical coherence tomography. 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher 2016.10.17 Suita, Osaka, Japan

##### **[Awards & Honors]**

1. Best Poster Award (3rd prize), International Academy for Digital Dental Medicine, 2016.09

# Oral Prosthetic Engineering

Professor Tetsuya SUZUKI  
Junior Associate Professor Masaomi IKEDA  
Research Associate Kouichi FUKAWA

## ( 1 ) Outline

Oral Health Information Technology educates deepen understanding of the production of the dental prosthesis using the latest computer science and cultivate basics power to new technology development. This course cultivates the ability to offer high quality medical technology taking advantage of expertise or knowledge. And the purpose of this section is to educate professional dental technologists who has ability to apply newly developed materials and technologies and who is able to contribute in not only clinical situation but also research institution or educational organization at international levels. Presently, the latest technologies such as dental implant and dental CAD/CAM etc became popular by the development of materials and the progress in technologies among dental treatment. Therefore, it is necessary to understand and lean knowledge about newly developed materials and technologies for properly control the dental laboratory works. Furthermore, It is necessary that the communication skill for report information about the materials and technologies to dentists and dental hygienists. Based on these evidences, it is an education in which specialists are raised to not be bound by classification as technologist and have ambition.

## ( 2 ) Research

- 1) The advanced technology which utilized a CAD/CAM system.
- 2) The education of dental technician which utilized computer simulation training.
- 3) Relation of "medical care to support life" and the dental technician.
- 4) Evaluation of newly developed materials.

## ( 3 ) Education

Introduction of Oral Health Engineering, Introduction of Clinical Dental Technology, Formative Arts Practice, Basic Technology of Manufacturing, Teeth Morphological Curving, Advanced Teeth Morphological Curving, Conservative Dentistry, Science of Occlusion, Advanced Science of Occlusion, Communication Theory, Health Promotion, Basic Fixed Prosthodontics, Advanced Fixed Prosthodontics, Complete Denture Prosthodontics, Removable Partial Prosthodontics, Oral Rehabilitation Engineering, Laws for Dental Technologists, CAD/CAM System Technology, CAD/CAM System Technology Practice, Advanced Technology for Oral Health, Ceramic Processing Technology Practice, Management and Regulation for Dental Technologists, Pediatric Dental Technology, Orthodontic Dental Technology, Maxillofacial Prosthetics Technology, Digital Image Processing Practice, Oral Appliances, Comprehensive Oral Rehabilitation Engineering Practice, Graduation Research, Graduation Product



#### (4) Publications

##### [Original Articles]

1. Fang-Yu Fan , Chung-Chieh Chang , Jhih-Ni Lin , Yi-Yun Cai , Chien-Yie Tsay , Tetsuya Suzuki , Hidekazu Takahashi , Yung-Ning Pan , Chung-Kwei Lin. Characterization of bioactive glass coated carbon nanotubes prepared by sol-gel process International Journal of Applied Glass Science. 2016;
2. Tezuka H, Shimada Y, Matin K, Ikeda M, Sadr A, Sumi Y, Tagami J.. Assessment of cervical demineralization induced by Streptococcus mutans using swept-source optical coherence tomography. J Med Imaging. 2016.01; 3(1);
3. Shinagawa J, Inoue G, Nikaido T, Ikeda M, Sadr A, Tagami J.. Dentin bonding performance and interface observation of an MMA-based restorative material. Dent Mater J.. 2016.07; 35(4); 578-584
4. Meiko Oki, Tetsuya Suzuki, Hidekazu Takahashi. A modified indirect method for fabricating silicone soft-lined complete dentures Journal of Prosthetic Dentistry. 2016.07;
5. Horie K, Shimada Y, Matin K, Ikeda M, Sadr A, Sumi Y, Tagami J.. Monitoring of cariogenic demineralization at the enamel-composite interface using swept-source optical coherence tomography. Dent Mater.. 2016.09; 32(9); 1103-1112
6. Suguru Kimoto, Yasuhiko Kawai, Atsuko Gunji, Hisatomo Kondo, Taro Nomura, Tomohiko Murakami, Akito Tsuboi, Guang Hong, Shunsuke Minakuchi, Yusuke Sato, Gaku Ohwada, Tetsuya Suzuki, Katsuhiko Kimoto, Noriyuki Hoshi, Makiko Saita, Yoshikazu Yoneyama, Yohei Sato, Masakazu Morokuma, Joji Okazaki, Takeshi Maeda, Kenichiro Nakai, Tetsuo Ichikawa, Kan Nagao, Keiko Fujimoto, Hiroshi Murata, Tadafumi Kurogi, Kazuhiro Yoshida, Masahiro Nishimura, Yasuhiro Nishi, Mamoru Murakami, Toshio Hosoi, Taizo Hamada. Study protocol for a multi-center, randomized controlled trial to develop Japanese denture adhesive guidelines for patients with complete dentures: the Denture Adhesive Guideline trial: study protocol for a randomized controlled trial Trials. 2016.10; 17;

##### [Conference Activities & Talks]

1. Yuki Naruse, Tomohiro Tkakagaki, Naoko Matsui, Takaaki Sato, Toru Nikaido, Masaomi Ikeda, Junji Tagami. Effects of alumina-blasting for a CAD/CAM resin block on adhesion. 45th Annual meeting of American Association for Dental Research 2016.03.17 Los Angels
2. Arakida T, Kanazawa M, Yamamoto S, Iwaki M, Minakuchi S, Suzuki T. The effect if external light of digital impression. The effect of external light of digital impression 2016.05.29
3. Microtensile bond strength to dentin of a newly developed one-step self-etch system containing hydrophilic amide monomer. 2016.06.09
4. Yu-mi TSUCHIDA, Yuji KABASAWA, Namiaki TAKAHARA, Shingo, KAMIJO, Tetsuya SUZUKI. Accuracy of a 3D Model for Surgical Support in Orthognathics. Advanced Digital Technology (ADT) North America & Japan Regional Leadership Groups Conference 2016.06.17 San Diego California USA
5. Multicenter Randomized Clinical Study of Denture Adhesive to Establish the Guideline: Study by the Subgroup Analysis for a Denture Adhesive on the Effect of the Masticatory Performance. 2016.07.09
6. Arakida T, Kanazawa M, Yamamoto S, Iwaki M, Minakuchi S, Suzuki T, Oki M, Kamijo S, Ando K, Morisawa K. The effect of external light of digital impression time and accuracy. 2016.07.09

## Department of Nanomedicine

Lecturer Kengo Iwasaki

Associate Professor Motohiro Komaki

Project researchers Kenichi Morinaga (~2017.3.31 Naoki Yokoyama)

### ( 1 ) Outline

Department of Nanomedicine has been established as endow courses in 2005 by a suggestion of Ikuo Morita (Executive director and Executive vice president of Research and International Cooperation) and financing of Dai Nippon Printing Co., Ltd (DNP). We work on a team from Medical, Dental and Science to conduct basic researches of “off-the-shelf” regenerative therapies using stem cells or their derivatives.

### ( 2 ) Research

Mesenchymal stem cells residing within tissues are a promising source of cells for regenerative therapy due to their multi-differentiation and high proliferative potency. We study to develop safer and more effective therapeutic application of stem cells. We study novel periodontal regenerative therapy by using cell-transfer and -patterning technique. Also we study cell-free system (stem cell-conditioned medium and extracellular vesicles) for various disease.

### ( 3 ) Lectures & Courses

In the lecture for periodontology (D4, D5), we learn biological principle necessary for periodontal regeneration and the basics of periodontal surgical procedure. In graduate school lecture, we understand a mechanism of wound healing and a principle of therapeutic potential of stem cells through the latest findings such as wound healing-stimulating activity by the humoral factor secreted by stem cells. Also, we introduce novel intercellular communication vehicle as such extra cellular vesicles (exosomes), transfer and patterning technique and give an outline about application of stem cells to tissue engineering.

### ( 4 ) Clinical Services & Other Works

In dental hospital (Periodontics), Drs. Komaki and Iwasaki as periodontal specialists and preceptors offer dental treatments of the highest standard in accord with the needs of patients and clinical training of students.

### ( 5 ) Publications

#### [Original Articles]

1. Tooi M, Komaki M, Morioka C, Honda I, Iwasaki K, Yokoyama N, Ayame H, Izumi Y, Morita I. Placenta Mesenchymal Stem Cell Derived Exosomes Confer Plasticity on Fibroblasts. J. Cell. Biochem.. 2016.07; 117(7); 1658-1670
2. Noda M, Aoki A, Mizutani K, Lin T, Komaki M, Shibata S, Izumi Y. High-frequency pulsed low-level diode laser therapy accelerates wound healing of tooth extraction socket: An in vivo study. Lasers in Surgery and Medicine. 2016.07; 48(10); 955-964

3. Keiko Akazawa, Kengo Iwasaki, Mizuki Nagata, Naoki Yokoyama, Hirohito Ayame, Kazumasa Yamaki, Yuichi Tanaka, Izumi Honda, Chikako Morioka, Tsuyoshi Kimura, Motohiro Komaki, Akio Kishida, Yuichi Izumi, Ikuo Morita. Double-layered cell transfer technology for bone regeneration. Scientific Reports. 2016.09; 6; 33286

**[Conference Activities & Talks]**

1. Komaki M, Aoki A, Iwasaki K, Izumi Y. Coverage of class III gingival recession localized at anterior mandibular teeth using connective tissue graft case report. 59th Spring Meeting for Japanese Society of Periodontology 2016.05.19 Kagoshima
2. Komaki M, Aoki A, Iwasaki K, Izumi Y. Coverage of class III gingival recession localized at anterior mandibular teeth using connective tissue graft. The 59th Spring Meeting of The Japanese Society of Periodontology 2016.05.21
3. Tooi M, Komaki M, Iwasaki K, Yokoyama N, Nagata M, Izumi Y, Morita I. Placenta mesenchymal stem cell derived exosomes alter differentiation competence in fibroblasts. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.09 Utsunomiya
4. Komaki M, Tooi M, Iwasaki K, Morita I. MSC exosomes alter competency of fibroblasts to differentiation stimuli. The 34th Annual Meeting of the Japanese Society for Bone and Mineral Research 2016.07.20 Osaka
5. Komaki M, Tooi M, Iwasaki K, Morita I. Mesenchymal stem cell derived exosomes alter differentiation competence in fibroblasts. The 34th Annual Meeting of the Japanese Society for Bone and Mineral Research 2016.07.22 Osaka
6. Masahiro Noda, Akira Aoki, Koji Mizutani, Taichen Lin, Motohiro Komaki, Shunichi Shibata, Yuichi Izumi. Effect of low level laser irradiation on early stage of wound healing of tooth extraction socket. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10 Fukuoka
7. Kengo Iwasaki, Mizuki Nagata, Keiko Akazawa, Naoki Yokoyama, Motohiro Komaki, Ikuo Morita. The effect of spheroid culture on the expression of stem cell-related genes in periodontal ligament stem cells. The 145th Meeting of The Japanese Society of Conservative Dentistry 2016.10.28 Matsumoto

## Department of Liver Disease Control

Professor                                      Yasuhiro ASAHINA  
 Senior Associate Professor              Sei KAKINUMA

Graduate Student  
 (collaboration with Department of Gastroenterology and Hepatology in TMDU)  
 Fumio GOTO(-03/2016), Shun KANEKO, Hiroko NAGATA, Yu ASANO,  
 Emi INOUE, Tomoyuki TSUNODA, Masato MIYOSHI,  
 Ayako SATO (04/2016-)

### (1) Outline

Patients died from chronic liver diseases, including liver cancer, are about 40,000 persons per a year in Japan. Liver transplantation remains the only effective treatment available to patients with end-stage liver diseases. Because of a serious shortage of donors for allogeneic liver transplantation, an alternative therapy is needed. Prevention of hepatocarcinogenesis and hepatic fibrosis is also necessary for patients with chronic hepatitis, and the development of effective treatment for progressive liver diseases has been quite essential. We believe that the central role of clinical departments in the graduate school of TMDU is to establish basis for the innovative medical treatment in the next generation. To achieve our mission, both basic research lead by clinical concepts and development of novel therapeutics established upon basic research are required.

Our section is a donation-funded department collaborating with the Department of Gastroenterology and Hepatology in TMDU. Most of basic research projects, education for students, and clinical contributions including multicenter studies are collaboration with the Department of Gastroenterology and Hepatology in TMDU. The goal of our education is to promote students to become a well-developed hepatologist, and also a leading expert in the field of Hepatology and Gastroenterology.

### (2) Research

Our principle is to achieve a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice.

We focus on the basic studies of molecular mechanism regulating development, pathophysiology, progression, and therapeutic resistance of hepatocellular carcinoma (HCC). We also focus on the development of novel disease models using human induced pluripotent stem cells, the research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis, the study for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells, analysis of mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and factors for therapeutic resistance against antiviral agents.

Research projects

- Research for mechanism regulating development, pathophysiology, progression, and therapeutic resistance of HCC, based on molecular biology and genome informatics
- Development of novel disease models using human induced pluripotent stem cells to elucidate the pathophysiology of liver diseases
- Research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis

- Research for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells
- Analyses of molecular mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and clinical factors for therapeutic resistance against antiviral agents.

### ( 3 ) Education

Primary goal for education in our section is to train highly educated and experienced clinician-researchers in the field of hepatology. Our goal for education of graduate students is to produce clinical researchers thinking from a wide perspective and to bring up leaders of the next generation in hepatology.

### ( 4 ) Lectures & Courses

Our lectures and courses are collaboration with the Department of Gastroenterology and Hepatology in School of Medicine, TMDU. We also educate clinical residents in Medical Hospital of TMDU and graduate students of the Department of Gastroenterology and Hepatology, in TMDU in collaboration with such department.

### ( 5 ) Clinical Services & Other Works

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. In the clinical section, we pursue development and application of highly advanced technologies, including novel procedures, for sophisticated diagnosis and treatment of diseases of liver, biliary duct, and pancreas. We also operate a lot of multicenter study collaborating with the Department of Gastroenterology and Hepatology in TMDU. We participate in four research projects for treatment and eradication of hepatitis virus funded by Japan Agency for Medical Research and Development (AMED). We published a lot of studies in peer-reviewed international journals and presented the recent works in a lot of international and domestic conferences as described below.

### ( 6 ) Clinical Performances

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. We have recently established the outpatient department specialized for chronic hepatitis, cirrhosis, and HCC. We have operated a lot of multicenter study about efficacy of treatment against viral hepatitis, named as “Ochyanomizu Liver Conference”. More than 2000 patients with viral hepatitis were enrolled in such studies, and they have clarified the clinical factors predicting accurately the therapeutic prognosis and risk for development of HCC. We are developing the screening programs for the early detection of HCC in patients with chronic hepatitis after eradication of viruses utilizing non-invasive elastography, novel serum markers, and dynamic contrast-enhanced ultrasonography. For the treatment of HCC, three-dimensional location and structure of tumors and vessels are evaluated by multilateral approaches using dynamic contrast-enhanced ultrasonography, Gd-EOB-DTPA enhanced MRI, and real-time virtual ultrasonography (RVS). We have reported the utility and safety of such therapeutic approaches. We are providing patients the appropriate therapeutic option based on collective multimodal therapeutic strategy in collaboration with departments of surgery and radiology.

### ( 7 ) Publications

#### [Original Articles]

1. Jun Itakura, Masayuki Kurosaki, Chitomi Hasebe, Yukio Osaki, Kouji Joko, Hitoshi Yagisawa, Shinya Sakita, Hiroaki Okushin, Takashi Satou, Hiroyuki Hisai, Takehiko Abe, Keiji Tsuji, Takashi Tamada, Haruhiko Kobashi, Akeri Mitsuda, Yasushi Ide, Chikara Ogawa, Syotaro Tsuruta, Kouichi Takaguchi, Miyako Murakawa, Yasuhiro Asahina, Nobuyuki Enomoto, Namiki Izumi. Complex Pattern of Resistance-Associated Substitutions of Hepatitis C Virus after Daclatasvir/Asunaprevir Treatment Failure. PLoS ONE. 2016; 11(10); e0165339

2. Yasuhiro Asahina, Mamoru Watanabe. Need for appropriate programs for prevention of hepatitis B infection: Lessons from the latest nationwide survey in Japan. *J. Gastroenterol. Hepatol.* 2016.01; 31(1); 12-13
3. Satoshi Otani, Sei Kakinuma, Akihide Kamiya, Fumio Goto, Shun Kaneko, Masato Miyoshi, Tomoyuki Tsunoda, Yu Asano, Fukiko Kawai-Kitahata, Sayuri Nitta, Toru Nakata, Ryuichi Okamoto, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Yasuhiro Asahina, Tomoyuki Yamaguchi, Naohiko Koshikawa, Motoharu Seiki, Hiromitsu Nakauchi, Mamoru Watanabe. Matrix metalloproteinase-14 mediates formation of bile ducts and hepatic maturation of fetal hepatic progenitor cells. *Biochem. Biophys. Res. Commun.* 2016.01; 469(4); 1062-1068
4. Yasuhiro Asahina, Namiki Izumi, Kumada Hiromitsu, Masayuki Kurosaki, Kazuhiko Koike, Fumitaka Suzuki, Hajime Takikawa, Atsushi Tanaka, Eiji Tanaka, Yasuhiro Tanaka, Hirohito Tsubouchi, Norio Hayashi, Naoki Hiramatsu, Hiroshi Yotsuyanagi. JSH Guidelines for the Management of Hepatitis C Virus Infection: A 2016 update for genotype 1 and 2. *Hepatol. Res.* 2016.02; 46(2); 129-165
5. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shinji Tanaka, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Satoshi Otani, Miki Taniguchi, Fumio Goto, Hiroko Nagata, Shun Kaneko, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Mina Nakagawa, Minoru Tanabe, Shinichi Takano, Mitsuharu Fukasawa, Minoru Sakamoto, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma with clinicopathological features. *J. Gastroenterol.* 2016.03; 51(5); 473-486
6. Miki Taniguchi, Megumi Tasaka-Fujita, Mina Nakagawa, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Fumio Goto, Hiroko Nagata, Shun Kaneko, Sayuri Nitta, Miyako Murakawa, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Kenichi Mori, Shintaro Yagi, Sei Kakinuma, Yasuhiro Asahina, Mamoru Watanabe. Evaluation of Interferon Resistance in Newly Established Genotype 1b Hepatitis C Virus Cell Culture System. *J Clin Transl Hepatol.* 2016.03; 4(1); 5-11
7. Seishin Azuma, Yasuhiro Asahina, Yuki Nishimura-Sakurai, Sei Kakinuma, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Ootani, Fukiko Kawai-Kitahata, Miki Taniguchi, Miyako Murakawa, Takako Watanabe, Megumi Tasaka-Fujita, Yasuhiro Itsui, Mina Nakagawa, Mamoru Watanabe. Efficacy of additional radiofrequency ablation after transcatheter arterial chemoembolization for intermediate hepatocellular carcinoma. *Hepatol Res.* 2016.04; 46(4); 312-319
8. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Hironori Nishitsuji, Saneyuki Ujino, Kunitada Shimotohno, Masashi Iwamoto, Koichi Watashi, Takaji Wakita, Mamoru Watanabe. Human induced pluripotent stem cell-derived hepatic cell lines as a new model for host interaction with hepatitis B virus. *Sci Rep.* 2016.07; 6; 29358
9. Hiroko Nagata, Mina Nakagawa, Yuki Nishimura-Sakurai, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Fumio Goto, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Naoko Tojo, Shuji Tohda, Yasuhiro Asahina, Mamoru Watanabe, . Serial measurement of Wisteria floribunda agglutinin positive Mac-2-binding protein is useful for predicting liver fibrosis and the development of hepatocellular carcinoma in chronic hepatitis C patients treated with IFN-based and IFN-free therapy.[Epub ahead of print] *Hepatol Int.* 2016.07;
10. Fumio Goto, Sei Kakinuma, Masato Miyoshi, Tomoyuki Tsunoda, Shun Kaneko, Ayako Sato, Yu Asano, Satoshi Otani, Seishin Azuma, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Yasuhiro Asahina, Mamoru Watanabe. Bone morphogenetic protein-4 modulates proliferation and terminal differentiation of fetal hepatic stem/progenitor cells. *Hepatol. Res.* 2016.09;
11. Masato Miyoshi, Sei Kakinuma, Yoko Tanabe, Koji Ishii, Tian-Cheng Li, Takaji Wakita, Yukio Tsuura, Hideki Watanabe, Yasuhiro Asahina, Mamoru Watanabe, Takaaki Ikeda. Chronic Hepatitis E Infection in a Persistently Immunosuppressed Patient Unable to Be Eliminated after Ribavirin Therapy. *Intern. Med.* 2016.10; 55(19); 2811-2817

12. Sayuri Nitta, Yasuhiro Asahina, Mami Matsuda, Norie Yamada, Ryuichi Sugiyama, Takahiro Masaki, Ryosuke Suzuki, Nobuyuki Kato, Mamoru Watanabe, Takaji Wakita, Takanobu Kato. Effects of Resistance-Associated NS5A Mutations in Hepatitis C Virus on Viral Production and Susceptibility to Antiviral Reagents. *Sci Rep.* 2016.10; 6; 34652
13. Hitomi Takada, Kaoru Tsuchiya, Yutaka Yasui, Natsuko Nakakuki, Nobuharu Tamaki, Shoko Suzuki, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Masayuki Kurosaki, Yasuhiro Asahina, Nobuyuki Enomoto, Namiki Izumi. Irregular vascular pattern by contrast-enhanced ultrasonography and high serum Lens culinaris agglutinin-reactive fraction of alpha-fetoprotein level predict poor outcome after successful radiofrequency ablation in patients with early-stage hepatocellular carcinoma. *Cancer Med.* 2016.11; 5(11); 3111-3120
14. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Mina Nakagawa, Sayuri Nitta, Satoshi Otani, Hiroko Nagata, Shun Kaneko, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhito Tanaka, Sayuki Iijima, Kaoru Tsuchiya, Namiki Izumi, Shuji Tohda, Mamoru Watanabe. Hepatic IFNL4 expression is associated with non-response to interferon-based therapy through the regulation of basal interferon-stimulated gene expression in chronic hepatitis C patients. [Epub ahead of print] *J. Med. Virol.* 2016.12;

### [Conference Activities & Talks]

1. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H, Goto F, Otani S, Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A Model for Interaction between HBV and Host Cells Derived from Human Induced Pluripotent Stem Cells. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
2. Asahina Y. 【HCV 2】 Chair . The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
3. Asahina Y. 【HCV 5】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
4. Kakinuma S. 【Basic science】 Chair. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
5. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Otani S, Goto F, Nagata H, Kaneko S, Asano Y, Miyoshi M, Tsunoda T, Azuma S, Itsui Y, Nakagawa M, Tanabe M, Maekawa S, Enomoto N, Watanabe M. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
6. Nagata H, Sakurai Y, Nakagawa M, Kakinuma S, Azuma S, Murakawa M, Nitta S, Itsui Y, Asahina Y, Watanabe M. Serial changes in M2BPGi levels as predictors of fibrosis and HCC in chronic hepatitis C. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
7. Nitta S, Asahina Y, Wakita T, Kato T.. In vitro characterization and drug sensitivity analysis for HCV NS5A resistance-associated variants.. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
8. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H , Goto F, Otani S, Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A new model for studying interaction between hepatitis B virus and host cells derived from human induced pluripotent stem cells. EASL The International Liver Congress 2016 2016.04.14 Barcelona (Spain)
9. Asahina Y. Hepatocarcinogenesis after hepatitis C viral eradication.. The 10th APASL Single Topic Conference 2016.06.08 Kaoshiung (Taiwan)
10. Asahina Y. Recent progress in anti-HCV therapy and challenges toward HCC eradication.. Academic Forum of Liver Disease in Northeast China and the Annual Convention for the Study of Liver Diseases in Jilin Province in 2016. 2016.10.29 Changchun (China)



11. Asahina Y. 【International Session (Symposium) 1】 Genomics of hepatocellular carcinoma: Hepatitis virus infection and hepatocarcinogenesis. Chair . JDDW2016 2016.11.03 Kobe Convention Center (Kobe JAPAN)
12. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihito Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Ayako Sato, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Mamoru Watanabe. Genetically modified human induced pluripotent stem cell-derived hepatic progenitor-like cell lines as a model for interaction between hepatitis B virus and host cells. AASLD The Liver meeting 2016 2016.11.11 Boston (USA)
13. Wai-Kay Seto , Yasuhiro Asahina , Cheng-Yuan Peng , Carol Stanciu , Djamal Abdurakhmanov , John F. Flaherty , Kyungpil Kim , Anuj Gaggar , Mani Subramanian, Fehmi Tabak, Tuan T. Nguyen, Henry Lik-Yuen Chan. Reduced Changes In Bone Mineral Density In CHB Patients Receiving Tenofovir Alafenamide (TAF) Compared With Tenofovir disoproxil fumarate. AASLD The Liver meeting 2016 2016.11.11 Boston (USA)

## Department of Advanced Therapeutics for GI Diseases

Professor	Tetsuya NAKAMURA
Junior Associate Professor	Katsuyoshi MATSUOKA
Assistant Professor	Tomohiro MIZUTANI (-03/2016)
	Michio ONIZAWA (08/2016-)
Graduate Student	
	Yuka MATSUMOTO, Shintaro AKIYAMA

### ( 1 ) Outline

The goal of our department is to develop novel therapeutic strategies for inflammatory bowel diseases (IBD) in humans. With multiple layers of support of corporations who wish to contribute to our mission, we have been focusing on IBD research from the clinical and basic science perspectives, providing an exceptional education program for graduate students at TMDU.

### ( 2 ) Research

Our research activities focus on the key areas listed below. We have a particular emphasis on translational (bench to clinic) research on IBD.

- Research on the intestinal epithelium to develop regenerative medicine approaches for IBD
- The study of mucosal immunology to develop novel approaches for the diagnosis and treatment of IBD

### ( 3 ) Education

We share our expertise and teaching program in graduate course education with the Department of Gastroenterology and Hepatology at TMDU. We are also involved in many programs designed for undergraduates.

### ( 4 ) Lectures & Courses

Our goal is to create future leaders who are able to reach the highest level of quality in IBD research through the training of fellows and graduate/undergraduate students.

### ( 5 ) Clinical Services & Other Works

We focus on developing highly advanced technologies, including novel procedures, for diagnosis and treatment of IBD in collaboration with the Department of Gastroenterology and Hepatology at TMDU. In addition, we have been playing a major role in nation-wide survey and multi-center studies on IBD, which is funded by the Japanese Ministry of Health, Labor and Welfare.

**(6) Clinical Performances**

- Development of new treatment protocol for IBD patients with stem cell therapy or immunomodulators.
- Development of minimally-invasive diagnostic modalities for inflammatory bowel diseases (i.e. MRE).
- Diagnosis and treatment of small intestinal lesions of inflammatory bowel diseases by double-balloon enteroscopy.

**(7) Publications****[Original Articles]**

1. Kengo Nozaki, Wakana Mochizuki, Yuka Matsumoto, Taichi Matsumoto, Masayoshi Fukuda, Tomohiro Mizutani, Mamoru Watanabe, Tetsuya Nakamura. Co-culture with intestinal epithelial organoids allows efficient expansion and motility analysis of intraepithelial lymphocytes. *J. Gastroenterol.* 2016.03; 51(3); 206-213
2. Shunsuke Komoto, Satoshi Motoya, Yuji Nishiwaki, Toshiyuki Matsui, Reiko Kunisaki, Katsuyoshi Matsuoka, Naoki Yoshimura, Takashi Kagaya, Makoto Naganuma, Nobuyuki Hida, Mamoru Watanabe, Toshifumi Hibi, Yasuo Suzuki, Soichiro Miura, Ryota Hokari, . Pregnancy outcome in women with inflammatory bowel disease treated with anti-tumor necrosis factor and/or thiopurine therapy: a multicenter study from Japan. *Intest Res.* 2016.04; 14(2); 139-145
3. Kazuo Ohtsuka, Kento Takenaka, Yoshio Kitazume, Toshimitsu Fujii, Katsuyoshi Matsuoka, Maiko Kimura, Takashi Nagaishi, Mamoru Watanabe. Magnetic resonance enterography for the evaluation of the deep small intestine in Crohn's disease. *Intest Res.* 2016.04; 14(2); 120-126
4. Ryohei Hayashi, Kiichiro Tsuchiya, Keita Fukushima, Nobukatsu Horita, Shuji Hibiya, Keisuke Kitagaki, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Eriko Okada, Akihiro Araki, Kazuo Ohtsuka, Shinji Fukuda, Hiroshi Ohno, Ryuichi Okamoto, Tetsuya Nakamura, Shinji Tanaka, Kazuaki Chayama, Mamoru Watanabe. Reduced Human  $\alpha$ -defensin 6 in Noninflamed Jejunal Tissue of Patients with Crohn's Disease. *Inflamm. Bowel Dis.* 2016.05; 22(5); 1119-1128
5. Taichi Matsumoto, Wakana Mochizuki, Yoichi Nibe, Shintaro Akiyama, Yuka Matsumoto, Kengo Nozaki, Masayoshi Fukuda, Ayumi Hayashi, Tomohiro Mizutani, Shigeru Oshima, Mamoru Watanabe, Tetsuya Nakamura. Retinol Promotes In Vitro Growth of Proximal Colon Organoids through a Retinoic Acid-Independent Mechanism. *PLoS ONE.* 2016.08; 11(8); e0162049
6. Shuji Hibiya, Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Nobukatsu Horita, Sho Watanabe, Tomoaki Shirasaki, Ryu Nishimura, Natsuko Kimura, Tatsunori Nishimura, Noriko Gotoh, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Long-term inflammation transforms intestinal epithelial cells of colonic organoids. *J Crohns Colitis.* 2016.10;
7. Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Toru Nakata, Tatsuro Murano, Go Ito, Hiromichi Shimizu, Tomohiro Mizutani, Shigeru Oshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Akihiro Araki, Kazuo Ohtsuka, Ryuichi Okamoto, Mamoru Watanabe. PGE2 is a direct and robust mediator of anion/fluid secretion by human intestinal epithelial cells. *Sci Rep.* 2016.11; 6; 36795
8. Masanori Kobayashi, Shigeru Oshima, Chiaki Maeyashiki, Yoichi Nibe, Kana Otsubo, Yu Matsuzawa, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. The ubiquitin hybrid gene UBA52 regulates ubiquitination of ribosome and sustains embryonic development. *Sci Rep.* 2016.11; 6; 36780
9. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Katsuyoshi Matsuoka, Toshimitsu Fujii, Masakazu Nagahori, Maiko Kimura, Tomoyuki Fujioka, Akihiro Araki, Mamoru Watanabe. Magnetic resonance evaluation for small bowel strictures in Crohn's disease: comparison with balloon enteroscopy. [Epub ahead of print] *J. Gastroenterol.* 2016.11;

**[Conference Activities & Talks]**

1. K. Matsuoka, E. Saito, T. Fujii, K. Takenaka, F. Iwamoto, M. Kimura, M. Nagahori, K. Ohtsuka, M. Watanabe. Efficacy and safety of sequential rescue therapy with infliximab and tacrolimus in patients

- with corticosteroid-refractory Ulcerative Colitis. 11th Congress of ECCO - European Crohn's and Colitis Organisation 2016.03.19 Amsterdam (Nederland)
2. Takenaka K, Ohtsuka K, Kitazume Y, Nagahori M, Matsuoka K, Fujii T, Kimura M, Fujioka T, Watanabe M. Enteroscopic and MR findings of small intestine in Crohn's disease. The 7th APTC 2016.04.20 Tokyo (JAPAN)
  3. Tetsuya Nakamura. 【Session 2: Gut homeostasis and IBD】 Intestinal stem cell transplantation and regenerative medicine. The 102nd JSGE-The 5th International Forum 2016.04.21 Tokyo (JAPAN)
  4. Shuji Hibiya, Kiichiro Tsuchiya, Tomoaki Shirasaki, Keita Fukushima, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Construction of in vitro model for inflammatory bowel disease using primary colonic organoid. DDW2016 2016.05.21 San Diego (USA)
  5. Kohei Suzuki, Satoru Fujii, Ami Kawamoto, Fumiaki Ishibashi, Toru Nakata, Go Ito, Hiromichi Shimizu, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Otsuka, Ryuichi Okamoto, Mamoru Watanabe. Single-cell level analysis reveals heterogeneous expression of stem-cell specific genes in human small intestinal organoids. DDW2016 2016.05.21 San Diego (USA)
  6. Taichi Matsumoto, Wakana Mochizuki, Yoichi Nibe, Shintaro Akiyama, Yuka Matsumoto, Kengo Nozaki, Tomohiro Mizutani, Shigeru Ochima, Mamoru Watanabe, Tetsuya Nakamura. Rethinol stimulates proliferation of epithelial stem cells of the proximal colon through a retinoic acid-independent mechanism. DDW2016 2016.05.21 San Diego (USA)
  7. Toru Nakata, Go Ito, Hiromichi Shimizu, Satoru Fujii, Kohei Suzuki, Fumiaki Ishibashi, Ami Kawamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Katsuto Hozumi, Ryuichi Okamoto, Mamoru Watanabe. Jagged1 is indispensable for the maintenance of tumor stem cell niche in APC-Deficient intestinal adenomas. DDW2016 2016.05.22 San Diego (USA)
  8. Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Toru Nakata, Go Ito, Hiromichi Shimizu, Tomohiro Mizutani, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Ohtsuka, Ryuichi Okamoto, Mamoru Watanabe. In Vitro organoid model reveals PGF2 as a Robust Mediator of chloride & water secretion by human intestinal epithelial cells. DDW2016 2016.05.23 San Diego (USA)
  9. Kazuo Ohtsuka, Kento Takenaka, Toshimitsu Fujii, Katsuyoshi Matsuoka, Masakazu Nagahori, Kengo Nozaki, Masayoshi Fukuda, Mamoru Watanabe. Mucosal Healing is important for better outcomes of endoscopic balloon dilatation for small intestinal stricture of Crohn's disease. DDW2016 2016.05.23 San Diego (USA)
  10. Tetsuya Nakamura. 【Innovative Approaches to Curing Intestinal Failure: The Future of Cell and Tissue Therapy】 Therapeutic Transplantation of Human Intestinal Stem Cells. DDW2016 2016.05.23 San Diego (USA)
  11. Katsuyoshi Matsuoka, Makoto Naganuma, Toshiyuki Matsui, Makoto Arai, Satoshi Tanida, Kazuya Kitamura, Noriyuki Horiki, Mikihiro Fujiya, Masaki Iimuro, Keiichi Mitsuyama, Masayuki Saruta, Takayuki Matsumoto, Hiroko Nebiki, Motohiro Esaki, Fukunori Kinjo, Kiyoshi Oketani, Seiichiro Hojo, Hideto Akama, Toshio Imai, Hirohito Tsubouchi, Toshifumi Hibi, Takanori Kanai. Safety, Tolerability and Efficacy of E6011, Anti-Human Fractalkine Monoclonal Antibody, in the First-in-Patient Study for Crohn's Disease. DDW2016 2016.05.23 San Diego (USA)
  12. Shinta Mizuno, Kosaku Nanki, Katsuyoshi Matsuoka, Keiko Ono, Makoto Mutaguchi, Mari Arai, Shinya Sugimoto, Hiroki Kiyohara, Kozue Takeshita, Makoto Naganuma, Takanori Kanai. Efficacy and safety of fecal microbiota transplantation on ulcerative colitis. AOCC2016 2016.07.07 Kyoto International Conference Center, Kyoto (JAPAN)
  13. Meng-Tzu Weng, Katsuyoshi Matsuoka, Mamoru Watanabe, JY Lee, Sang Hyoun Park, Suk-Kyun Yang, Shu-Chen Wei. Thromboembolic events associated with inflammatory bowel disease in Asia: incidence and possible risk factors analysis. AOCC2016 2016.07.07 Kyoto International Conference Center, Kyoto (JAPAN)
  14. Tetsuya Nakamura. Stem-Cell Based Therapies for Intestinal Diseases. AOCC 2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)

15. Katsuyoshi Matsuoka, Naoki Yoshimura, Mamoru Watanabe, Satoshi Motoya, Keiichi Tominaga, Ryuichi Iwakiri, Kenji Watanabe, Toshifumi Hibi, For the AJM300 Study Group. AJM300, an oral  $\alpha$  4 integrin antagonist, as induction therapy for active ulcerative colitis: a randomized trial. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
16. Tomoaki Shirasaki, Kiichiro Tsuchiya, Shuji Hibiya, Ryu Nishimura, Keita Fukushima, Sho Watanabe, Ryuichi Okamoto, Tetsuya Nakamura and Mamoru Watanabe. Stimulation with the ligands of Toll like receptors in primary human organoids. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
17. Maiko Kimura, Katsuyoshi Matsuoka, Eiko Saito, Toshimitsu Fujii, Kento Takenaka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Salvage therapy for corticosteroid-refractory ulcerative colitis patients. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
18. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Masakazu Nagahori, Katsuyoshi Matsuoka, Toshimitsu Fujii, Maiko Kimura, Tomoyuki Fujioka, Mamoru Watanabe. Enteroscopic and MR findings of small bowel in Crohn' s disease. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
19. Minami Hama, Ayumi Hayashi, Tomohiro Mizutani, Satoru Fujii, Tatsuro Murano, Kiichiro Tsuchiya, Tetsuya Nakamura, Ken Watanabe, Norio Shimizu, Ryuichi Okamoto, Mamoru Watanabe. Prevalence of viral DNA in the mucosal tissue and cultured organoids of inflammatory bowel disease patients.. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
20. Shuji Hibiya, Kiichiro Tsuchiya, Tomoaki Shirasaki, Keita Fukushima, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Mouse colonic organoid acquires wnt-independent survival property after long-term inflammation. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
21. Toshimitsu Fujii, Kento Takenaka, Maiko Kimura, Katsuyoshi Matsuoka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. The evaluation for small bowel strictures on MR enterocolonography in patients with Crohn' s disease. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
22. Kiichiro Tsuchiya, Shuji Hibiya, Keita Fukushima, Tomoaki Shirasaki, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Atoh1 protein stabilization in colon tumor acquires the phenotype of signet ring cell carcinoma with cancer stem cell enrichment. AOCC2016 2016.07.08 Kyoto International Conference Center, Kyoto (JAPAN)
23. Kazuo Ohtsuka, Kento Takenaka, Toshimitsu Fujii, Katsuyoshi Matsuoka, Masakazu Nagahori, Maiko Kimura, Masayoshi Fukuda, Nobuhiro Katsukura, Mamoru Watanabe. Mucosal healing improves prognosis of endoscopic balloon dilatation for small intestinal strictures of Crohn' s disease. AOCC2016 2016.07.09 Kyoto International Conference Center, Kyoto (JAPAN)
24. Tetsuya Nakamura. Therapeutic transplantation of intestinal stem cells. International Conference on Bio-fabrication and Bio-monitoring (ICBB 2016) 2016.10.14 National Taiwan University, Taipei (China)
25. Toshimitsu Fujii, Kento Takenaka, Maiko Kimura, Katsuyoshi Matsuoka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. MR enterocolonography evaluation for small bowel strictures in patients with Crohn' s disease: comparison with balloon enteroscopy. UEGW2016 2016.10.18 Vienna (Austria)
26. Hibiya S, Tsuchiya K, Watanabe S, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Construction of in vitro model of ulcerative colitis using mouse primary colonic organoid. UEGW2016 2016.10.18 Vienna (Austria)
27. Tsuchiya K, Hibiya S, Fukushima K, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Atoh1 protein stabilization in colon tumor acquires the morphological change to signet ring cell carcinoma with cancer stem cell enrichment. APDW2016 2016.11.03 Kobe convention center, KOBE (JAPAN)
28. Fujii T, Takenaka K, Kitazume Y, Kimura M, Matsuoka K, Nagahori M, Ohtsuka K, Watanabe M. MR enterocolonography can detect small bowel strictures and predict surgery in patients with Crohn' s disease: Comparison with balloon enteroscopy. APDW2016 2016.11.03 Kobe convention center, KOBE (JAPAN)
29. Tetsuya Nakamura. Stem cell-based therapies for intestinal diseases. International Conference on Recent Advances in Inflammation 2016 2016.11.11 National Cheng Kung University, Tainan (Taiwan)

## Department of Sleep Modulatory Medicine

Professor: Naohiko Inase  
Associate Professor: Meiyo Tamaoka  
Assistant Professor: Mizue Hobo  
Assistant Professor: Toshihide Fujie  
Technician: Megumi Sato

### ( 1 ) Research

- 1.Effects of NMDA-type glutamate receptor co-agonist on gamma oscillations and sleep in schizophrenia.
- 2.Open-label trial of hyperbaric oxygen therapy on sleep quality
- 3.Development of the evaluation system for the efficacy of oral appliances on obstructive sleep apnea syndrome.
- 4.Development of portable home polysomnograph system.
- 5.The association between OSA and short term blood-pressure variability.
- 6.The association between OSA and interstitial pneumonia.
7. 24 hours SpO2 monitoring for patients with chronic respiratory failure

### ( 2 ) Education

Education of sleep medicine for students, residents and technicians

### ( 3 ) Clinical Services & Other Works

Clinical Center for Pleasant Sleep provides a variety of medical service for sleep disorder especially for sleep apnea syndrome.

· Out-patient Clinic

Monday: AM Dr. Terada (Pulmonary Medicine)

PM Dr. Fujie (Pulmonary Medicine)

Tuesday: AM Dr. Hirai (Psychiatry)

Wednesday: AM Dr. Miyazaki (Health Service Center)

Thursday: AM Dr. Tamaoka (Sleep Modulatory Medicine)

PM Dr. Tamaoka (Sleep Modulatory Medicine)

Friday: AM Dr. Uezato (Psychiatry)

AM Dr. Tateishi (Pulmonary Medicine)

PM Dr. Tateishi(Pulmonary Medicine)

· Outpatient visits: 5,282 (New:311) for FY 2016

· Examination: polysomnography: 134 patiensts for FY 2016

**( 4 ) Publications****[Original Articles]**

1. Chiba S, Tsuchiya K, Nukui Y, Sema M, Tamaoka M, Sumi Y, Miyazaki Y, Inase N.. Interstitial Changes in Asthma-COPD Overlap Syndrome (ACOS) The Clinical Respiratory Journal. 2016.02;
2. Hobo M, Uezato A, Nishiyama M, Suzuki M, Kurata J, Makita K, Yamamoto N, Nishikawa T. A case of malignant catatonia with idiopathic pulmonary arterial hypertension treated by electroconvulsive therapy BMC Psychiatry. 2016.05; 16; 130

**[Conference Activities & Talks]**

1. Meiyo Tamaoka, et al.. CPAP treatment for SAS in multiple system atrophy. The 56th Annual Meeting of Japanese Respiratory Society 2016.04.08 Kyoto
2. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Chisato Ida, Yuko Mitsuma, Shota Hayashi, Akihito Uesato, Toshihide Fujie, Meiyo Tamaoka, Yasunari Miyazaki, Masahiko Shimada, Noriyuki Wakabayashi . Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy and compliance in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial.. Japanese Society of Sleep Research the 41th Annual Meeting 2016.07.07 Tokyo
3. Meiyo Tamaoka. Current status of CPAP therapy for OSAS in late stage elderly at our hospital. The 41st annual meeting of Japanese Society of Sleep Research 2016.07.07 Tokyo
4. Akihito Uezato, Meiyo Tamaoka. Evaluation of Sleep Apnea Syndrome using a portable electroencephalograph.. The 8th Congress of Integrated Sleep Medicine Society Japan 2016.08.06



## Department of Women's Health

Professor Masakazu Terauchi MD PhD; Assistant Professor Asuka Hirose MD PhD (concurrent)

### (1) Outline

Japanese women boast world's #1 longevity, although the final stage of their lives is not necessarily of good health-related quality. To stay physically and psychologically sound in later life, women need to optimize their health starting from their midlife, especially through good diet and exercise. Tokyo Medical and Dental University (TMDU) Department of Obstetrics and Gynecology have promoted midlife women's health with our renowned Systemic Health and Nutrition Education Program (SHNEP) since 1995, which inspired Kikkoman Corporation to generously support to establish a new department in TMDU focusing on "Health Maintenance of Women through Food and Nutrition" in 2012. Dr. Masakazu Terauchi, Associate Professor and Chair of TMDU Department of Women's Health, is intensively studying with his colleagues about the changes in women's bodies and minds induced by aging, and the effects of bioactive food ingredients on them.

### (2) Research

Department of Women's Health has dealt with a variety of topics listed below since its inception in 2012, mainly focusing our research on the effects of bioactive food ingredients on women's physical and psychological health.

- Effects of grape seed extract on middle-aged women's health-related quality of life
- Effects of hormone therapy and keishibukuryogan on blood pressure in perimenopausal and postmenopausal women
- Effects of nonbenzodiazepine, melatonin receptor agonist, and Kampo medication on sleep disturbances in perimenopausal and postmenopausal women
- Effects of selective serotonin reuptake inhibitors on subjective and objective sleep parameters in middle-aged women with depression
- Effects of oral contraceptive pills on sleep disturbances in young women with primary dysmenorrhea
- Effects of tomato juice on cardiovascular risk markers in middle-aged women
- Effects of soy isoflavone aglicone on middle-aged women's health-related quality of life
- Menopausal hormone therapy: route of administration and platelet-derived microparticles
- Effects of soy lecithin on middle-aged women's tiredness
- Effects of soy milk on middle-aged women's sleep

### (3) Education

Cooperating with the Department of Obstetrics and Gynecology, we have shared responsibility in the education of Obstetrics and Gynecology, as well as in the training of medical students on clinical clerkship.

### (4) Clinical Services & Other Works

Cooperating with the Department of Obstetrics and Gynecology, we have provided a comprehensive diagnosis, treatment, and disease management solution for women suffering from:

- menopausal symptoms

- premature ovarian insufficiency
- postmenopausal osteoporosis
- dyslipidemia
- hypertension
- pelvic organ prolapse
- lower urinary tract syndrome
- depression
- anxiety disorder
- insomnia
- dysmenorrhea
- premenstrual syndrome etc.

## ( 5 ) Publications

### [Original Articles]

1. Asuka Hirose, Masakazu Terauchi, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Depressive symptoms are associated with oxidative stress in middle-aged women: a cross-sectional study. *Biopsychosoc Med.* 2016; 10; 12
2. Asuka Hirose, Masakazu Terauchi, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Low-dose isoflavone aglycone alleviates psychological symptoms of menopause in Japanese women: a randomized, double-blind, placebo-controlled study. *Arch. Gynecol. Obstet.* 2016.03; 293(3); 609-615
3. A Hirose, M Terauchi, M Akiyoshi, Y Owa, K Kato, T Kubota. Subjective insomnia is associated with low sleep efficiency and fatigue in middle-aged women. *Climacteric.* 2016.08; 19(4); 369-374

### [Misc]

1. Masakazu Terauchi. Menopausal symptoms and the Kampo medicine: Tokishakuyakusan, Kamishoyosan, and Keishibukuryogan Recent Progress in Kampo Medicine in Obstetrics and Gynecology. 2016.04; 33; 23-30

### [Conference Activities & Talks]

1. Masakazu Terauchi. Palpitation in middle-aged women is associated with anxiety. 68th Annual Congress of Japan Society of Obstetrics and Gynecology 2016.04.22
2. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Toshiro Kubota. Palpitation in Middle-aged Women Is Associated with Anxiety. 18th International Society of Psychosomatic Obstetrics and Gynecology Congress 2016.05.12 Malaga, Spain
3. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Makoto Iizuka, Naoyuki Miyasaka, Toshiro Kubota. Palpitation in middle-aged women is associated with anxiety. 15th World Congress on the Menopause 2016.09.30 Prague, Czech Republic

## Department of Advanced Surgical Technology Research and Development

Associate Professor Katsuhiro OHUCHI, Ph.D  
Associate Professor Tomohiro MIZUNO, MD, Ph.D  
Part-time Lecturer Naoyuki YOKOYAMA, Ph.D  
Part-time Lecturer Tarou KIMURA, Ph.D  
Part-time Lecturer Daisuke SAKOTA, Ph.D  
Part-time Lecturer Nobuo WATANABE, Ph.D

### (1) Outline

Surgical technology has been improving follows to the development of advanced instruments and therapeutic strategies. On the one hand, innovation in surgery inevitably requires individual operator's skill and tailoring of the intervention to the patient. The aim of our laboratory is research and development of developmental pathway for modern surgical technology through the large animal experiment. Following to the framework for the stages in surgical innovation, such as ideas, development, exploration, assessment and pre-clinical study, we will serve as a mediator between basic science and clinical practice. And more, implementation of human resources development in the field of advanced surgery is also another intention of our laboratory.

### (2) Publications

#### [Original Articles]

1. Fujiwara T, Sakota D, Ouchi K, Endo S, Tahara T, Murashige T, Kosaka R, Oi K, Mizuno T, Maruyama O, Arai H.. Optical dynamic analysis of thrombus inside a centrifugal blood pump during extracorporeal mechanical circulatory support in a porcine model *Artif Organs*. 2016; In Press;
2. Daisuke Sakota, Tomotaka Murashige, Ryo Kosaka, Tatsuki Fujiwara, Katsuhiro Ouchi, Masahiro Nishida, Osamu Maruyama. Noninvasive optical imaging of thrombus formation in mechanical circulatory support devices *Journal of Biorheology*. 2016; 30; 6-12
3. Daisuke Sakota, Tatsuki Fujiwara, Katsuhiro Ouchi, Katsuyuki Kuwana, Hiroyuki Yamazaki, Osamu Maruyama. Development of an Optical Detector of Thrombus Formation on the Pivot Bearing of a Rotary Blood Pump. *Artificial Organs*. 2016.09; 40(9); 834-841

#### [Conference Activities & Talks]

1. K Ohuchi, T Mizuno, K Oi, M Yashima, T Hachimaru, E Nagaoka, T Fujiwara, H Kuroki, D Tasaki, M Takeshita, R Kinoshita, S Endo, M Kanai, S Suzuki, T Kimura, H Arai. Attempt for the Development of Cardiac Surgery Training Program Combined with Live Animal Surgery. The 63rd Annual Meeting of Japanese Association for Animal Science 2016.05.18
2. Ohuchi K, Mizuno T, Oi K, Yashima M, Hachimaru T, Nagaoka E, Fujiwara T, Kuroki H, Tasaki D, Takeshita M, Kinoshita R, Endo S, Kanai M, Kimura T, Arai H. Development of Heart Surgery Training Program Combined with Live Animal Surgery. 24th Congress of the International Society for Rotary Blood Pumps 2016.09.21
3. Fujiwara T, Arai H, Mizuno T, Oi K, Yashima M, Hachimaru T, Nagaoka E, Kuroki H, Tasaki D, Takeshita M, Kinoshita R, Ohuchi K. Which is a better acute-phase circulatory support for cardiogenic

shock patients in INTERMACS Profile-1: A pulsatile VAD or a centrifugal pump?. 24th Congress of the International Society for Rotary Blood Pumps 2016.09.21

4. Sakota D, Fujiwara T, Ouchi K, Kuwana K, Yamazaki H, Arai H, Maruyama O. Development of an optical thrombus detector on the pivot bearing of a rotary blood pump. 24th Congress of the International Society for Rotary Blood Pumps 2016.09.22

## Department of Arteriosclerosis and Vascular Biology

Associate Professor Shohei Shinozaki  
Assistant Professor Yasuko Abe

### ( 1 ) Outline

The overall focus of our laboratory is to clarify the mechanism of the arteriosclerosis clear as well as aiming at development of the novel remedy of the arteriosclerosis. We also try to understand the role of nitrogen oxide in the molecular pathogenesis in human diseases. Inflammation is implicated in a variety of human diseases, whereas it is a necessary and adaptive response to environmental or intrinsic stress. We found that S-nitrosylation (the covalent attachment of nitric oxide to thiols) plays the important role in insulin resistance and aging related diseases. We're analyzing these mechanisms using the technique of the biochemistry, the molecular biology, proteomic approach and genetic alteration mouse, such as S-nitrosoglutathione reductase (GSNOR) deficiency or transgene.

### ( 2 ) Research

- Basic research on arteriosclerosis
- Search and identification for novel S-nitrosylated protein
- Molecular mechanism of metabolic syndromes through S-nitrosylation

### ( 3 ) Education

In accordance with aging and westernization of diet, atherosclerotic disease has been increasing in Japan. Recently, the chronic inflammation has been focused as the mechanism of arteriosclerosis. It has been demonstrated that inflammation is deeply involved in the initial stage of atherosclerosis. However, treatments with anti-inflammatory drugs, such as NSAIDs, for atherosclerosis generally have not been successes. Thus we consider that there are some unknown mechanisms between development of arteriosclerosis and inflammation.

### ( 4 ) Lectures & Courses

Our course's education policy is to obtain basic research skills for elucidating pathogenesis of atherosclerosis.

### ( 5 ) Publications

#### [Original Articles]

1. Sasaki Mari, Shinozaki Shohei, Shimokado Kentaro. Sulforaphane promotes murine hair growth by accelerating the degradation of dihydrotestosterone. *Biochem Biophys Res Commun.* 2016.03; 472(1); 250-254
2. Chiba Tsuyoshi, Noji Keiko, Shinozaki Shohei, Suzuki Sachina, Umegaki Keizo, Shimokado Kentaro. Diet-induced non-alcoholic fatty liver disease affects expression of major cytochrome P450 genes in a mouse model. *J Pharm Pharmacol.* 2016.12; 68(12); 1567-1576

**[Conference Activities & Talks]**

1. Shohei Shinozaki . S-nitrosylation of SIRT1 as a hub of and inflammatory spira. The 16th Annual Scientific Meeting of the Nitric Oxide Society of Japan 2016.05.20 Sendai
2. Shohei Shinozaki. Type 2 diabetes and chronic inflammation.. The 58th Annual meeting of Japan Geriatrics Society 2016.06.09 Kanazawa

**[Others]**

1. Grant-in-Aid for Young Scientists (B) JSPS KAKENHI (16K19048)  
S-nitrosylation, a novel posttranslational protein modification, mediated glycolipid metabolism disorder and chronic inflammation. 2016-2017
2. Takeda Science Foundation for Medical Research  
The missing link between the metabolic syndrome pathogenesis and chronic inflammation. 2016-2018
3. Grant-in-Aid for Exploratory Research JSPS KAKENHI (16K15120)  
Elucidation of a role of de-nitrosylation in septic myocardial injury and development for therapeutic drugs.  
PI: Toshihiro Tanioka. Role on Project: Co- Investigator 2016-2017

## Department of Translational Oncology

< Department of Translational Oncology >

Associate Professor: Megumi ISHIGURO

Junior Associate Professor (concurrent): Toshiaki ISHIKAWA

### (1) Outline

Department of Translational Oncology aims to establish the “personalized therapy” in chemotherapy for gastrointestinal cancers through identification of the predictive factors for chemo-responsiveness and prognosis.

### (2) Research

Main themes of our research activities is identification of the predictive factors for chemo-responsiveness and prognosis by using our well-organized clinical database, fresh frozen and paraffin-embedded samples, and molecular biological technique, i.e. gene expression micro array analysis, and DNA copy number analysis.

### (3) Publications

#### [Original Articles]

1. Masuda T, Ishikawa T, Mogushi K, Okazaki S, Ishiguro M, Iida S, Mizushima H, Tanaka H, Uetake H, Sugihara K.. Overexpression of the S100A2 protein as a prognostic marker for patients with stage II and III colorectal cancer. *Int J Oncol.* 2016; 48(3); 975-982
2. Ishikawa T, Uetake H, Murotani K, Kobunai T, Ishiguro M, Matsi S, Sugihara K.. Genome-wide DNA Copy-number Analysis in ACTS-CC Trial of Adjuvant Chemotherapy for Stage III Colonic Cancer. *Anticancer Research.* 2016; 36; 853-860
3. Baba H, Ishikawa T, Mogushi K, Ishiguro M, Uetake H, Tanaka H, Sugihara K.. Identification of SATB1 as a specific biomarker for lymph node metastasis in colorectal cancer. *Anticancer Research.* 2016; 36; 4069-4076

#### [Conference Activities & Talks]

1. Kajiwarara Y, Ishiguro M, Teramukai S, Matsuda C, Fujii S, Kinugasa Y, Nakamoto Y, Kotake M, Sakamoto Y, Kurachi K, Maeda A, Komori K, Tomita N, Simada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Sugihara K.. A randomized phase III trial of 1-year adjuvant chemotherapy with oral tegafur-uracil (UFT) vs. surgery alone in stage II colon cancer.. American Society of Clinical Oncology (ASCO) 2016 Annual Meeting 2016.06.04 Chicago (USA)
2. Miura T, Sunami E, Kusumoto T, Ota M, Yoshida K, Tomita N, Maeda A, Mochizuki I, Okabe M, Kunieda K, Yamauchi J, Itabashi M, Kotake K, Takahashi K, Baba H, Boku N, Aiba K, Ishiguro M, Morita S, Sugihara K.. Planned safety analysis of the ACTS-CC 02 trial: A randomized phase III trial of S-1/oxaliplatin (SOX) versus UFT/LV as adjuvant chemotherapy for high-risk stage III colon cancer.. American Society of Clinical Oncology (ASCO) 2016 Annual Meeting 2016.06.04 Chicago (USA)



3. Ishiguro M.. Colorectal cancer database in Japan.. 68th Congress of the Korean Surgical Society.  
2016.11.05 Seoul (Korea)

## Clinical Laboratory

General Manager  
-Professor : Shuji Tohda

Associate Manager  
-Junior Associate Professor : Tadashi Kanouchi

Assistant Professor : Naomi Murakami  
Assistant Professor : Ryoko Azuma  
Assistant Professor : Miyako Murakawa  
Medical Staff : Shintaro Iida

### ( 1 ) Research

Our research subjects are

- 1) New genetic tests for hematological disorders,
- 2) Development of tests for molecular pathology and drug sensitivity of hematological malignancies,
- 3) Morphological abnormalities of the cells in myelodysplastic syndrome and myeloproliferative disorders,
- 4) Genotypic analysis of bacteria for monitoring those transmission in the hospital,
- 5) Development of electrophysiological diagnostic tests for peripheral neuropathies,
- 6) Clinical and electrophysiological study for amyotrophic lateral sclerosis,
- 7) Quality control of nerve conduction study,
- 8) Development of medical information system for clinical laboratory tests.

### ( 2 ) Education

The staffs lectured on clinical laboratory medicine and gave technical training on clinical laboratory tests and physiological function tests to not only the medical students and medical technologist students in the faculty of medicine of the university but also those in the other vocational school for medical technologists. We gave lessons to our university students in the master's course of graduate school of medical and dental sciences, too. In our clinical laboratory in 2016, ten junior residents of the medical hospital of university had a general training for clinical laboratory medicine, including bacteriological examinations and ultrasonography. Hands-on seminars of Gram staining, urinary sediment, cardiac and abdominal ultrasonography have been repeatedly held for residents of the hospital.

### ( 3 ) Clinical Services & Other Works

Clinical laboratory bears an important responsibility for advanced and high quality medical care. Our clinical laboratory is based on the principle of providing the speedy and high quality tests. The highest level of advanced tests, such as qualitative and quantitative analysis of various viral DNA by the PCR method, are also introduced here. We start taking a blood sample at 8:05 and it results in shortening the waiting time of patients and in speedy report of the test results. In the night time and holidays, the clinical laboratory provides blood products for transfusion in cooperation with the blood transfusion service of the hospital. The updated

information on antibiotic sensitivity of the pathogens in each ward is also provided online regularly. Together with the division of infection control and prevention, we monitor the nosocomial transmission of bacteria such as MRSA by genotypic analysis of those. Our clinical laboratory and blood transfusion service have received accreditation of ISO15189 (Medical laboratories - Particular requirements for quality and competence) in June 2014, and renewed it with the latest version in December 2016. It means that the clinical laboratory is an international standard on quality and that our hospital is allowed to conduct the international clinical trials.

#### (4) Publications

##### [Original Articles]

1. Mari Kamiya, Peter Y Shane, Makoto Soejima, Shuji Tohda, Nobuyuki Miyasaka, Hitoshi Kohsaka. IgG4-Related Sialoadenitis with a Skin Lesion and Multiple Mononeuropathies Suggesting Coexistent Cryoglobulinemic Vasculitis. *Intern. Med.* 2016; 55(10); 1355-1361
2. Uchida Emi, Watanabe Ken, Oshikawa Gaku, Sakasita Chizuko, Kurosu Tetsuya, Fukuda Tetsuya, Arai Ayako, Murakami Naoki, Miura Osamu, Yamamoto Masahide. Refractory primary myeloid sarcoma of the breast with MLL-AF9 rearrangement. *The Japanese Journal of Clinical Hematology*. 2016.01; 57(1);
3. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shinji Tanaka, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Satoshi Otani, Miki Taniguchi, Fumio Goto, Hiroko Nagata, Shun Kaneko, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Mina Nakagawa, Minoru Tanabe, Shinichi Takano, Mitsuharu Fukasawa, Minoru Sakamoto, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma with clinicopathological features. *J. Gastroenterol.* 2016.03; 51(5); 473-486
4. Yokota T, Kanouchi T, Ohkubo T. ALS: Quantitative analysis of disease progression from a new point of view 2015 Annual report of the research committee of CNS degenerative diseases, The ministry of health, labour and welfare of Japan. 2016.03; 58-61
5. Miki Taniguchi, Megumi Tasaka-Fujita, Mina Nakagawa, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Fumio Goto, Hiroko Nagata, Shun Kaneko, Sayuri Nitta, Miyako Murakawa, Yuki Nishimura-Sakurai, Seishin Azuma, Yasuhiro Itsui, Kenichi Mori, Shintaro Yagi, Sei Kakinuma, Yasuhiro Asahina, Mamoru Watanabe. Evaluation of Interferon Resistance in Newly Established Genotype 1b Hepatitis C Virus Cell Culture System. *J Clin Transl Hepatol.* 2016.03; 4(1); 5-11
6. Seishin Azuma, Yasuhiro Asahina, Yuki Nishimura-Sakurai, Sei Kakinuma, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Ootani, Fukiko Kawai-Kitahata, Miki Taniguchi, Miyako Murakawa, Takako Watanabe, Megumi Tasaka-Fujita, Yasuhiro Itsui, Mina Nakagawa, Mamoru Watanabe. Efficacy of additional radiofrequency ablation after transcatheter arterial chemoembolization for intermediate hepatocellular carcinoma. *Hepatol Res.* 2016.04; 46(4); 312-319
7. Megumi Akiyama, Kota Yoshifuji, Tetsuya Fukuda, Shuji Tohda, Tohru Miki, Osamu Miura, Masahide Yamamoto. Fulminant visceral disseminated varicella-zoster virus infection without skin involvement in a patient with autoimmune hemolytic anemia on prednisolone therapy. *Rinsho Ketsueki.* 2016.04; 57(4); 467-471
8. Noriko Kawaguchi-Ihara, Mai Itoh, Ikuo Murohashi, Shuji Tohda. Establishment of a quenching probe method for detection of NPM1 mutations in acute myeloid leukemia cells. *Oncol Lett.* 2016.04; 11(4); 2429-2432
9. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Hironori Nishitsuji, Saneyuki Ujino, Kunitada Shimotohno, Masashi Iwamoto, Koichi Watashi, Takaji Wakita, Mamoru Watanabe. Human induced pluripotent stem cell-derived hepatic cell lines as a new model for host interaction with hepatitis B virus. *Sci Rep.* 2016.07; 6; 29358
10. Hiroko Nagata, Mina Nakagawa, Yuki Nishimura-Sakurai, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Fumio Goto, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Naoko Tojo, Shuji Tohda, Yasuhiro Asahina, Mamoru

- Watanabe, . Serial measurement of Wisteria floribunda agglutinin positive Mac-2-binding protein is useful for predicting liver fibrosis and the development of hepatocellular carcinoma in chronic hepatitis C patients treated with IFN-based and IFN-free therapy.[ Epub ahead of print] *Hepatol Int.* 2016.07;
11. Fumio Goto, Sei Kakinuma, Masato Miyoshi, Tomoyuki Tsunoda, Shun Kaneko, Ayako Sato, Yu Asano, Satoshi Otani, Seishin Azuma, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Yasuhiro Asahina, Mamoru Watanabe. Bone morphogenetic protein-4 modulates proliferation and terminal differentiation of fetal hepatic stem/progenitor cells. *Hepatol. Res.* 2016.09;
  12. Shinji Ogiwara, Ryoichi Saito, Etsuko Sawabe, Michio Hagihara, Shuji Tohda. First Japanese case of infectious endocarditis due to *Enterococcus faecalis* small-colony variants. *J. Infect. Chemother.* 2016.10; 22(10); 716-719
  13. Gene Igawa, Mika Casey, Etsuko Sawabe, Yoko Nukui, Shu Okugawa, Kyoji Moriya, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Comparison of agar dilution and broth microdilution methods for *Clostridium difficile* antimicrobial susceptibility testing. *J Glob Antimicrob Resist.* 2016.12; 43-45
  14. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Mina Nakagawa, Sayuri Nitta, Satoshi Otani, Hiroko Nagata, Shun Kaneko, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhito Tanaka, Sayuki Iijima, Kaoru Tsuchiya, Namiki Izumi, Shuji Tohda, Mamoru Watanabe. Hepatic IFNL4 expression is associated with non-response to interferon-based therapy through the regulation of basal interferon-stimulated gene expression in chronic hepatitis C patients. [ Epub ahead of print] *J. Med. Virol.* 2016.12;

#### [Conference Activities & Talks]

1. Amano E, Suzuki M, Ozaki K, Ishibashi S, Akaza M, Kanouchi T, Tohda S, Yokota T. A case of sensory dominant CIDP with conduction delay predominantly in the most distal segment (Japanese). 10th Tokyo Metropolitan Neuromuscular Electrodiagnosis Forum 2016.01.30 Tokyo
2. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H, Goto F, Otani S, Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A Model for Interaction between HBV and Host Cells Derived from Human Induced Pluripotent Stem Cells. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
3. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Otani S, Goto F, Nagata H, Kaneko S, Asano Y, Miyoshi M, Tsunoda T, Azuma S, Itsui Y, Nakagawa M, Tanabe M, Maekawa S, Enomoto N, Watanabe M. Comprehensive analyses of mutations and hepatitis B virus integration in hepatocellular carcinoma. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
4. Nagata H, Sakurai Y, Nakagawa M, Kakinuma S, Azuma S, Murakawa M, Nitta S, Itsui Y, Asahina Y, Watanabe M. Serial changes in M2BPGi levels as predictors of fibrosis and HCC in chronic hepatitis C. The 25th Asian Pacific Association for the Study of the Liver 2016.02.22 International Convention Center Pamir, Tokyo (JAPAN)
5. Shohei Nogami, Mai Itoh, Shuji Tohda. Clinical usefulness of allele-specific/quenching probe method for detection of the MYD88 L265P mutation. The 14th Asian Society for Clinical Pathology and Laboratory Medicine Congress 2016.03.26 Taipei
6. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Nitta S, Tsunoda T, Miyoshi M, Asano Y, Nagata H, Goto F, Otani S, Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A new model for studying interaction between hepatitis B virus and host cells derived from human induced pluripotent stem cells. EASL The International Liver Congress 2016 2016.04.14 Barcelona (Spain)
7. Kanouchi T, Sekiguchi T, Yokota T. A pilot study on disease progression of ALS by quantitative analysis from a new viewpoint. 57th annual meeting of the Japanese Society of Neurology 2016.05.18 Kobe
8. Ohta N, Kanouchi T, Akaza M, Aoyagi E, Narumi J, Yanagi N, Sumi Y, Yokota T, Hagihara M, Tohda S. A study of quality control of nerve conduction study. 57th annual meeting of the Japanese Society of Neurology 2016.05.20 Kobe

9. Shintaku H, Kanouchi T, Yokota T. Pathophysiology of myoclonus in corticobasal syndrome. 57th annual meeting of the Japanese Society of Neurology 2016.05.21 Kobe
10. Ohhara M, Sanjo N, Majima T, Kanouchi T, Yokota T. Long term prognosis of anti-MAG antibody positive neuropathy. 57th Annual meeting of the Japanese Society of Neurology 2016.05.21 Kobe
11. Tadashi Kanouchi. Nerve conduction study in the upper extremity. 13th neuromuscular electrodiagnosis seminar 2016.07.02 Tokyo
12. Kanouchi T, Higashihara K. Ulnar entrapment neuropathy. 13th neuromuscular electrodiagnosis seminar 2016.07.02 Tokyo
13. Tadashi Kanouchi. First step in nerve conduction study. 11th technical training courses of clinical neurophysiology, Tokyo 2016.07.31 Tokyo
14. Kazuaki Yamamoto, Seiya Watanabe, Michio Hagihara, Shuji Tohda. Development of a novel measurement method for L-hydroxyproline using a new enzyme. The 32th World Congress of Biomedical Laboratory Science 2016.09.02
15. Naoya Ichimura, Ayako Itoi, Yuki Ohkubo, Yuki Koda, Michio Hagihara, Shuji Tohda. Development of an internal quality control application for immature granulocytes differential. The 32th World Congress of Biomedical Laboratory Science 2016.09.02 Kobe
16. Naoya Ichimura, Ayako Itoi, Yuki Ohkubo, Yuki Koda, Michio Hagihara, Shuji Tohda. Evaluation of an internal QC application for correctly recognizing immature granulocytes on blood smear. The 32th World Congress of Biomedical Laboratory Science 2016.09.02 Kobe
17. Kanouchi T, Sekiguchi T, Tohda S, Yokota T. Does the impairment of upper motor neurons have an influence upon the speed of degeneration of lower motor neurons in ALS. 46th annual meeting of the Japanese Society of Clinical Neurophysiology 2016.10.28 Kohriyama
18. Iida S, Kanouchi T, Suzuki M, Sanjo N, Nishida Y, Yokota T. Distribution patterns of nerve conduction abnormality in CIDP. 46th annual meeting of the Japanese Society of Clinical Neurophysiology 2016.10.28 Kohriyama
19. Aoyagi E, Kanouchi T, Akaza M, Iida S, Narumi J, Ohta N, Sumi Y, Yokota T, Hagihara M, Tohda S. A study of quality control of nerve conduction study. 46th annual meeting of the Japanese Society of Clinical Neurophysiology 2016.10.29 Kohriyama
20. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Masato Miyoshi, Tomoyuki Tsunoda, Sayuri Nitta, Ayako Sato, Yu Asano, Hiroko Nagata, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Mamoru Watanabe. Genetically modified human induced pluripotent stem cell-derived hepatic progenitor-like cell lines as a model for interaction between hepatitis B virus and host cells. AASLD The Liver meeting 2016 2016.11.11 Boston (USA)
21. Erika Shiratori, Mai Itoh, Mika Ohtaka, Shohei Nogami, Shuji Tohda. Mechanisms of suppressive effects of MYD88 Inhibitors on the Growth of Lymphoma and Leukemia Cells. The 58th American Society of Hematology 2016.12.04 San Diego

## Transfusion Medicine

Director(Lecturer) Michiko KAJIWARA  
Assistant Director(Medical Technologist) Naoki OHTOMO  
Section Chief Medical Technologist Keiko BABA  
Assisitant Section Chief Medical Technologist Yukiko OHISHI  
Clinical Fellow Shihoko SUWA  
Medical Technologist Yukari USUI  
Medical Technologist Kaoru OKUYAMA  
Medical Technologist Shiho KOBAYASHI  
Medical Technologist Chihiro TOYAMA  
Medical Technologist Eriko FURUYA

### ( 1 ) Research

- 1) Practice of safe and appropriate transfusion therapy (including prevention of medical accident related transfusion)
- 2) Basic and clinical research of hematopoietic stem cell transplantation

### ( 2 ) Lectures & Courses

Transfusion therapy is a supplementation of the blood component, but it also has aspects of cell therapy and transplantation. So, it is important to practice safe and appropriate transfusion therapy. Clinical tests of transfusion, such as blood type test, are most basic immunological test technique. The accurate understanding and practice of these tests is also necessary for the safety of medical treatment. From this point of view, we educate the students of school of medicine, school of allied health sciences, graduate school of medical and dental sciences, medical doctors, and co-medicals.

### ( 3 ) Clinical Services & Other Works

4. Clinical Services (The result of 2016)
  - 1) The amount of blood products used  
Red cell component products 11,657 Units (5,892 bags)  
Platelet concentration 25,749 Units (2,239 bags)  
Fresh frozen plasma 9,880 Units (4,233 bags)
  - 2) Autologous blood collection and transfusion  
Autologous blood collection 363 cases (468 times, 909 Units)  
Autologous blood transfusion 317 cases (764 Units)
  - 3) The number of clinical tests of transfusion  
Blood typing 10,760  
Anti red blood cell antibody test 5,298  
Cross match 9,152
  - 4) Hematopoietic stem cell harvest  
Autologous peripheral blood stem cell harvest 6 cases 6 times

Allogenic peripheral blood stem cell harvest 5 cases 7 times  
 Autologous peripheral mononuclear cell harvest 0 case 0 time  
 Allogenic bone marrow harvest 13 cases 13 times  
 (Including Japan Marrow Donor Program donors)  
 5) Hematopoietic stem cell transplantation  
 (The evaluation and preservation of the stem cells were done in our department)  
 Autologous peripheral blood stem cell transplantation 7 cases 8 times  
 Allogenic peripheral blood stem cell transplantation 4 cases 4 times  
 Autologous peripheral mononuclear cell transplantation 0 case 0 time  
 Allogenic bone marrow transplantation 14 cases 14 times  
 Allogenic umbilical cord blood transplantation 4 cases 4 times

#### (4) Publications

##### [Original Articles]

1. Yuki Aoki, Reiji Miyawaki, Kohsuke Imai, Masatoshi Takagi, Michiko Kajiware, Yasuyoshi Ishiwata, Masato Yasuhara, Tomohiro Morio, Shuki Mizutani, Daisuke Tomizawa. Haploidentical Bone Marrow Transplantation With Clofarabine and Busulfan Conditioning for a Child With Multiple Recurrent Acute Lymphoblastic Leukemia. *J. Pediatr. Hematol. Oncol.* 2016.01; 38(1); 39-41
2. Takeshi Sato, Tsubasa Okano, Mari Tanaka-Kubota, Shunsuke Kimura, Satoshi Miyamoto, Shintaro Ono, Motoi Yamashita, Noriko Mitsuki, Masatoshi Takagi, Kohsuke Imai, Michiko Kajiware, Takasuke Ebato, Shohei Ogata, Hirotsugu Oda, Osamu Ohara, Hirokazu Kanegane, Tomohiro Morio. Novel compound heterozygous mutations in a Japanese girl with Janus kinase 3 deficiency. *Pediatr Int.* 2016.09; 58(10); 1076-1080
3. Daisuke Tomizawa, Akifumi Endo, Michiko Kajiware, Hirotoshi Sakaguchi, Kimikazu Matsumoto, Makoto Kaneda, Takashi Taga. Acute lymphoblastic leukemia in patients with Down syndrome with a previous history of acute myeloid leukemia. *Pediatr Blood Cancer.* 2016.12;

##### [Conference Activities & Talks]

1. Shiho KOBAYASHI, Naoki OTOMO, Kaoru OKUYAMA, Shihoko SUWA, Michiko KAJIWARA. Study of the performance and usefulness of "ORTHO VISION Max" in TMDU. The 32nd World Congress of Biomedical Laboratory Science 2016.09.02 Kobe International Conference Center, JAPAN
2. Marie Scully, Paul Knoebl, MD, Karim Kentouche, Lawrence Rice, Jerzy Windyga, Reinhard Schneppenheim, Johanna A Kremer Hovinga, Michiko Kajiware, Caterina Maggiore, Jennifer Doralt, Leah Martell, and Bruce M. Ewenstein. Pharmacodynamic Profile of a Recombinant ADAMTS13 (BAX930) in Hereditary Thrombotic Thrombocytopenic Purpura (Upshaw-Schulman Syndrome (USS)). American Society of Hematology, 58th Annual Meeting 2016.12.03 San Diego, CA, USA



## Hyperbaric Medical Center

Senior Director and Associate Professor; Kazuyoshi YAGISHITA

Junior Associate Professor ; Mitsuhiro ENOMOTO

Senior Resident; Takuya OYAIZU

Adjunct Lecturer; Yasushi KOJIMA, Masaharu SHIBAYAMA

Researcher; Masaki HORIE, Toshihiro KONDOH, Naohiro MITSUMOTO

Staff Assistant; Kiyomi ITOH

### ( 1 ) Outline

Hyperbaric oxygen therapy (HBO), which can dissolve oxygen in serum in population to atomic pressure and transport oxygen to ischemic tissue, is an established therapy for treatment of several conditions, including decompression illness, carbon monoxide poisoning, acute anterior disturbance, and peripheral ischemic disease. The mechanism of HBO can be described as hyperoxygenation in ischemic soft tissues, reduction of edema, stimulation of fibroblast proliferation and differentiation, increased collagen formation and cross-linking, angiogenesis, and improved preservation of energy metabolism.

This curious treatment has clinically many kinds of efficacy, however, the mechanism of the effect has not been fully understood, and many researchers in the world still attempt to reveal the mechanism of the effect of HBO. This HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

### ( 2 ) Research

Research Subjects

- 1) Soft tissue injuries related with sports activities
- 2) HBO for conditioning in sports activities
- 3) Diving medicine
- 4) Hyperbaric oxygen therapy

### ( 3 ) Education

HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

### ( 4 ) Clinical Services & Other Works

In 2015, 6,624 times hyperbaric oxygen therapy (HBO) in 685 patients were performed in the university hospital.

**( 5 ) Clinical Performances**

HBO is applied for several conditions, including decompression illness, carbon monoxide poisoning, infection, wound healing, delayed radiation injury, acute arterial disturbance, and peripheral ischemic disease. Recently, for the purpose of rapid recovery from injury, we perform HBO aggressively for soft tissue injury related with sports activities including compartment syndrome, ankle sprain, knee ligament injury, and muscle contusion.

**( 6 ) Publications****[Original Articles]**

1. Saya Watanabe, Junya Aizawa, Manabu Shimoda, Mitsuhiro Enomoto, Tomomasa Nakamura, Atushi Okawa, Kazuyoshi Yagishita. Effect of short-term fatigue, induced by high-intensity exercise, on the profile of the ground reaction force during single-leg anterior drop-jumps. *J Phys Ther Sci.* 2016; 28(12); 3371-3375
2. Toshifumi Watanabe, Takeshi Muneta, Kazuyoshi Yagishita, Kenji Hara, Hideyuki Koga, Ichiro Sekiya. Closed Suction Drainage Is Not Necessary for Total Knee Arthroplasty: A Prospective Study on Simultaneous Bilateral Surgeries of a Mean Follow-Up of 5.5 Years. *J Arthroplasty.* 2016.03; 31(3); 641-645
3. YASUSHI KOJIMA, MITSUHIRO ENOMOTO, TAKUYA OYAIZU, KAZUYOSHI YAGISHITA. What is the optimal management of decompression illness?: Treatment at Medical Hospital of Tokyo Medical and Dental University The Japanese Journal of Hyperbaric and Undersea Medicine. 2016.03; 51(1); 14-18
4. Kairi Hayashi, Toshiyuki Takahashi, Mai Ikegawa, Masaki Horie, Takuya Oyaizu, Mitsuhiro Enomoto, Shunichi Shibata, Kazuyoshi Yagishita, Toshiaki Ueno. The facilitatory effects of hyperbaric oxygen treatment on membrane bone wound healing in a rat calvarial defect model. *Undersea Hyperb Med.* 2016.03; 43(2); 135-142
5. Yoshiike T, Nishida M, Yagishita K, Nariai T, Ishii K, Nishikawa T.. Altered Sleep Spindles in Delayed Encephalopathy after Acute Carbon Monoxide Poisoning. *J Clin Sleep Med.* 2016.06; 12(6); 913-915
6. Suzuki H, Ito Y, Shinohara M, Yamashita S, Ichinose S, Kishida A, Oyaizu T, Kayama T, Nakamichi R, Koda N, Yagishita K, Lotz MK, Okawa A, Asahara H.. Gene targeting of the transcription factor Mohawk in rats causes heterotopic ossification of Achilles tendon via failed tenogenesis. *Proceedings of the National Academy of Sciences of the United States of America.* 2016.07; 113(28); 7840-7845
7. Hiroki Katagiri, Kaori Nakamura, Toshifumi Watanabe, Hideyuki Koga, Kazuyoshi Yagishita, Ichiro Sekiya, Takeshi Muneta. Increase of patellofemoral height has decreased maximum knee flexion after total knee arthroplasty of posterior cruciate-substituting prosthesis in a clinical series. *J Orthop Sci.* 2016.07; 21(4); 458-462
8. Junya Aizawa, Shunsuke Ohji, Hideyuki Koga, Tadashi Masuda, Kazuyoshi Yagishita. Correlations between sagittal plane kinematics and landing impact force during single-leg lateral jump-landings. *J Phys Ther Sci.* 2016.08; 28(8); 2316-2321
9. Yoko Yamamoto, Yoshihiro Noguchi, Mitsuhiro Enomoto, Kazuyoshi Yagishita, Ken Kitamura. Otological complications associated with hyperbaric oxygen therapy. *Eur Arch Otorhinolaryngol.* 2016.09; 273(9); 2487-2493
10. Toshitaka Yoshii, Kenichiro Sakai, Takashi Hirai, Tsuyoshi Yamada, Hiroyuki Inose, Tsuyoshi Kato, Mitsuhiro Enomoto, Shoji Tomizawa, Shigenori Kawabata, Yoshiyasu Arai, Atsushi Okawa. Anterior decompression with fusion versus posterior decompression with fusion for massive cervical ossification of the posterior longitudinal ligament with a  $\geq 50\%$  canal occupying ratio: a multicenter retrospective study. *Spine J.* 2016.11; 16(11); 1351-1357
11. Kazuyoshi Yagishita, Tetsuya Jinno, Daisuke Koga, Tsuyoshi Kato, Mitsuhiro Enomoto, Tsuyoshi Kato, Takeshi Muneta, Atsushi Okawa. Transient osteoporosis of the hip treated with hyperbaric oxygen therapy: a case series. *Undersea Hyperb Med.* 2016.11; 43(7); 847-854

12. Tomomasa Nakamura, Yuriiko Yoshida, Hiroshi Churei, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Shunsuke Ohji, Toshiyuki Takahashi, Mitsuhiro Enomoto, Toshiaki Ueno, Kazuyoshi Yagishita. The Effect of Teeth Clenching on Dynamic Balance at Jump-Landing: A Pilot Study. *J Appl Biomech.* 2016.12; 1-19
13. Toshitaka Yoshii, Takashi Hirai, Kenichiro Sakai, Shinichi Sotome, Mitsuhiro Enomoto, Tsuyoshi Yamada, Hiroyuki Inose, Tsuyoshi Kato, Shigenori Kawabata, Atsushi Okawa. Anterior Cervical Corpectomy and Fusion Using a Synthetic Hydroxyapatite Graft for Ossification of the Posterior Longitudinal Ligament. *Orthopedics.* 2016.12; 1-6

#### [Misc]

1. Mitsuhiro Enomoto, Takashi Hirai, Hidetoshi Kaburagi, Takanori Yokota. Efficient Gene Suppression in Dorsal Root Ganglia and Spinal Cord Using Adeno-Associated Virus Vectors Encoding Short-Hairpin RNA. *Methods Mol. Biol.* 2016; 1364; 277-290
2. Mitsuhiro Enomoto. Therapeutic effects of neurotrophic factors in experimental spinal cord injury models *Journal of Neurorestoratology.* 2016; (4); 15-22

#### [Conference Activities & Talks]

1. Yasushi Kojima, Mitsuhiro Enomoto, Takuya Oyaizu, Akiko Kojima, Kazuyoshi Yagishita, N. Kagaya. Recreational diving related fatalities in Japan (2004-2014). 45th South Pacific Underwater Medicine Society Annual Meeting 2016.05 Natadola coast, FIJI
2. Oyaizu T, Enomoto M, Yagishita K.. Hyperbaric and high-oxygen environments lead to macrophage infiltration, stimulate cell proliferation and accelerate muscle regeneration in contused rat skeletal muscle.. Undersea and Hyperbaric Medical Society Annual Scientific Meeting 2016 2016.06.09 Las Vegas, United States of America
3. Hidetoshi Kaburagi, Takashi Hirai, Takanori Yokota, Atsushi Okawa, Mitsuhiro Enomoto. Role of voltage-gated sodium channels and calcium channel subunit  $\alpha$ -2/delta-1 in the lumbar dorsal root ganglions of persistent peripheral neuropathic pain model mice.. *Neuroscience2016* 2016.11.15 San Diego

## Center for Cell Therapy

Director: Tomohiro Morio (Department of Pediatrics)

Vise Director: Ichiro Sekiya (Center for Stem Cell and Regenerative Medicine)

Quality control manager: Norio Shimizu (Center for Stem Cell and Regenerative Medicine)

Product manager: Michiko Kajiware (Department of Blood Transfusion Medicine)

Technicians: Yuri Kohno, Minhua Sun, Ayako Tsuji

Technicians (From Collaborative Research): Takafumi Kato, Takuya Okazaki

Clerical Assistant: Akiko Hoshikawa, Jun Kusano

### ( 1 ) Research

1. Development of innovative techniques for quality assurance of cell products
2. Development of a novel measure for rapid and sensitive detection of multiple pathogens
3. Development of multi-virus specific T lymphocytes for adoptive immunotherapy
4. Research on a regeneration system of the cartilage bone from the synovial membrane (Department of Orthopedic Surgery)
5. Development of novel peptide-pulsed dendritic therapy for adult T-cell leukemia (Department of Immunotherapeutics / Department of Hematology)

We are planning to start multi-virus specific T cell therapy for opportunistic viral infection post hematopoietic cell transplantation and expanded colon epithelium for various bowel disorders following approval from the certified committee for regenerative medicine and from MHLW.

### ( 2 ) Education

We provide assistance to prepare standard operation procedure (SOP) and offer on-the-job training for cell processing/ manipulating procedures and that for quality assurance at the center. Facility for the education and training was recently installed at the CPC annex.

### ( 3 ) Clinical Services & Other Works

The cell products currently prepared in our center include

#1 Synovium-derived mesenchymal stem cells

#2 Processed peripheral blood stem cells

The center offers our novel detection system for 12 different viruses in rapid and sensitive manner for the doctors at TMDU Medical Hospital. We also measure virus loads of the detected virus using a real time PCR system. We measured 1,190 samples until September, 2016. The multi-virus PCR system has been offered by Department of Clinical Laboratory thereafter.

#### (4) Clinical Performances

Our center in TMDU Medical Hospital was renovated and re-started operation as of March 2015. We have five independent cell processing rooms (class 10,000 clean rooms). All the rooms are equipped with a bio-safety cabinet. The hardware as well as software used in our center fulfills all the guidelines that are required for the preparation of cell products of clinical grade.

#### (5) Publications

##### [Original Articles]

1. Arai A, Sakashita C, Hirose C, Imadome K, Yamamoto M, Jinta M, Fujiwara S, Tomita M, Shimizu N, Morio T, and Miura O.. Hematopoietic stem cell transplantation for adults with EBV-positive T- or NK-cell lymphoproliferative disorders: efficacy and predictive markers Bone Marrow Transplantation. 2016;
2. T Wada, Toma T, M Yasui, M Inoue, K Kawa, K Imai, T Morio, A Yachie. Different Clinical Phenotypes in 2 Siblings With X-Linked Severe Combined Immunodeficiency. J Investig Allergol Clin Immunol. 2016; 26(1); 63-65
3. Tomohiro Kohmoto, Atsumi Tsuji, Kei-Ichi Morita, Takuya Naruto, Kiyoshi Masuda, Kenichi Kashimada, Keisuke Enomoto, Tomohiro Morio, Hiroyuki Harada, Issei Imoto. A novel COL11A1 missense mutation in siblings with non-ocular Stickler syndrome. Hum Genome Var. 2016; 3; 16003
4. Kotaro Kai, Maki Sumida, Yaeko Motoyoshi, Yuichi Ogawa, Katsuyuki Miki, Kazuhiro Iwadoh, Akihito Sannomiya, Toru Murakami, Ichiro Koyama, Kumiko Kitajima, Ichiro Nakajima, Tomohiro Morio, Shohei Fuchinoue. Successful Long-term Graft Survival of a Renal Transplantation Patient with Wiskott-Aldrich Syndrome. Intern. Med.. 2016; 55(13); 1761-1763
5. Yuki Aoki, Reiji Miyawaki, Kohsuke Imai, Masatoshi Takagi, Michiko Kajiwarra, Yasuyoshi Ishiwata, Masato Yasuhara, Tomohiro Morio, Shuki Mizutani, Daisuke Tomizawa. Haploidentical Bone Marrow Transplantation With Clofarabine and Busulfan Conditioning for a Child With Multiple Recurrent Acute Lymphoblastic Leukemia. J. Pediatr. Hematol. Oncol.. 2016.01; 38(1); 39-41
6. Seiichi Hayakawa, Satoshi Okada, Miyuki Tsumura, Sonoko Sakata, Yoshitaka Ueno, Kohsuke Imai, Tomohiro Morio, Osamu Ohara, Kazuaki Chayama, Masao Kobayashi. A Patient with CTLA-4 Haploinsufficiency Presenting Gastric Cancer. J. Clin. Immunol.. 2016.01; 36(1); 28-32
7. Laura Gámez-Díaz, Dietrich August, Polina Stepensky, Shoshana Revel-Vilk, Markus G Seidel, Mitsuki Noriko, Tomohiro Morio, Austen J J Worth, Jacob Blessing, Frank Van de Veerdonk, Tobias Feuchtinger, Maria Kanariou, Annette Schmitt-Graeff, Sophie Jung, Suranjith Seneviratne, Siobhan Burns, Bernd H Belohradsky, Nima Rezaei, Shahrzad Bakhtiar, Carsten Speckmann, Michael Jordan, Bodo Grimbacher. The extended phenotype of LPS-responsive beige-like anchor protein (LRBA) deficiency. J. Allergy Clin. Immunol.. 2016.01; 137(1); 223-230
8. T Muto, Y Takeda, S Tsukamoto, S Sakai, N Mimura, C Ohwada, M Takeuchi, E Sakaida, S Ota, T Iseki, N Shimizu, T Morio, C Nakaseko. Successful treatment of cytomegalovirus enteritis after unrelated allogeneic stem cell transplantation by the infusion of ex vivo-expanded CD4(+) lymphocytes derived from the recipient's peripheral blood donor cells. Transpl Infect Dis. 2016.02; 18(1); 93-97
9. Natsuko Inazawa, Tsukasa Hori, Masaki Yamamoto, Naoki Hatakeyama, Yuko Yoto, Masanori Nojima, Hiroshi Yasui, Nobuhiro Suzuki, Norio Shimizu, Hiroyuki Tsutsumi. HHV-6 encephalitis may complicate the early phase after allogeneic hematopoietic stem cell transplantation: Detection by qualitative multiplex PCR and subsequent quantitative real-time PCR. J. Med. Virol.. 2016.02; 88(2); 319-323
10. Kei Takasawa, Sayaka Takeda, Masato Nishioka, Hiroshi Sakuma, Tomohiro Morio, Masayuki Shimohira. Steroid-responsive Status Epilepticus Caused by Human Parvovirus B19 Encephalitis. Pediatr. Infect. Dis. J.. 2016.02; 35(2); 227-228
11. Yusuke Nakagawa, Ichiro Sekiya, Shimpei Kondo, Takashi Tabuchi, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Takeshi Muneta. Relationship between MRI T1 rho value and histological findings of intact and radially incised menisci in microminipigs. J Magn Reson Imaging. 2016.02; 43(2); 434-445

12. Yumiko Nakano, Takeshi Hayashi, Kentaro Deguchi, Kota Sato, Nozomi Hishikawa, Toru Yamashita, Yasuyuki Ohta, Yoshiki Takao, Tomohiro Morio, Koji Abe. Two young stroke patients associated with regular intravenous immunoglobulin (IVIg) therapy. *J. Neurol. Sci.*. 2016.02; 361; 9-12
13. Kazuhiro Ikegame, Kohsuke Imai, Motoi Yamashita, Akihiro Hoshino, Hirokazu Kanegane, Tomohiro Morio, Katsuji Kaida, Takayuki Inoue, Toshihiro Soma, Hiroya Tamaki, Masaya Okada, Hiroyasu Ogawa. Allogeneic stem cell transplantation for X-linked agammaglobulinemia using reduced intensity conditioning as a model of the reconstitution of humoral immunity. *J Hematol Oncol.* 2016.02; 9(1); 9
14. A Arai, C Sakashita, C Hirose, K-I Imadome, M Yamamoto, M Jinta, S Fujiwara, M Tomita, N Shimizu, T Morio, O Miura. Hematopoietic stem cell transplantation for adults with EBV-positive T- or NK-cell lymphoproliferative disorders: efficacy and predictive markers. *Bone Marrow Transplant.*. 2016.02; 51(6); 879-882
15. Yusuke Nakagawa, Takeshi Muneta, Koji Otabe, Nobutake Ozeki, Mitsuru Mizuno, Mio Udo, Ryusuke Saito, Katsuaki Yanagisawa, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Cartilage Derived from Bone Marrow Mesenchymal Stem Cells Expresses Lubricin In Vitro and In Vivo. *PLoS ONE.* 2016.02; 11(2); e0148777
16. Chisato Sato, Yoshitaka Iso, Takuya Mizukami, Koji Otabe, Masahiro Sasai, Masaaki Kurata, Takeyuki Sanbe, Ichiro Sekiya, Akira Miyazaki, Hiroshi Suzuki. Fibroblast growth factor-23 induces cellular senescence in human mesenchymal stem cells from skeletal muscle. *Biochem. Biophys. Res. Commun.*. 2016.02; 470(3); 657-662
17. Shimpei Kondo, Takeshi Muneta, Yusuke Nakagawa, Hideyuki Koga, Toshifumi Watanabe, Kunikazu Tsuji, Shinichi Sotome, Atsushi Okawa, Shinji Kiuchi, Hideo Ono, Mitsuru Mizuno, Ichiro Sekiya. Transplantation of autologous synovial mesenchymal stem cells promotes meniscus regeneration in aged primates. *J. Orthop. Res.*. 2016.02;
18. Toshifumi Watanabe, Takeshi Muneta, Kazuyoshi Yagishita, Kenji Hara, Hideyuki Koga, Ichiro Sekiya. Closed Suction Drainage Is Not Necessary for Total Knee Arthroplasty: A Prospective Study on Simultaneous Bilateral Surgeries of a Mean Follow-Up of 5.5 Years. *J Arthroplasty.* 2016.03; 31(3); 641-645
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20. Julie Toubiana, Satoshi Okada, Julia Hiller, Matias Oleastro, Macarena Lagos Gomez, Juan Carlos Al-dave Becerra, Marie Ouachée-Chardin, Fanny Fouyssac, Katta Mohan Girisha, Amos Etzioni, Joris Van Montfrans, Yildiz Camcioglu, Leigh Ann Kerns, Bernd Belohradsky, Stéphane Blanche, Aziz Bousfiha, Carlos Rodriguez-Gallego, Isabelle Meyts, Kai Kisand, Janine Reichenbach, Ellen D Renner, Sergio Rosenzweig, Bodo Grimbacher, Frank L van de Veerdonk, Claudia Traidl-Hoffmann, Capucine Picard, Laszlo Marodi, Tomohiro Morio, Masao Kobayashi, Desa Lilic, Joshua D Milner, Steven Holland, Jean-Laurent Casanova, Anne Puel. Heterozygous STAT1 gain-of-function mutations underlie an unexpectedly broad clinical phenotype: an international survey of 274 patients from 167 kindreds. *Blood.* 2016.04; 127(25); 3154-3164
21. Katsuaki Yanagisawa, Takeshi Muneta, Nobutake Ozeki, Yusuke Nakagawa, Mio Udo, Ryusuke Saito, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Weekly injections of Hylan G-F 20 delay cartilage degeneration in partial meniscectomized rat knees. *BMC Musculoskelet Disord.* 2016.04; 17(1); 188
22. Kazumasa Miyatake, Takeshi Muneta, Miyoko Ojima, Jun Yamada, Yu Matsukura, Kahaer Abula, Ichiro Sekiya, Kunikazu Tsuji. Coordinate and synergistic effects of extensive treadmill exercise and ovariectomy on articular cartilage degeneration. *BMC Musculoskelet Disord.* 2016.05; 17(1); 238
23. Mai Katakura, Hideyuki Koga, Kaori Nakamura, Ichiro Sekiya, Takeshi Muneta. Effects of different femoral tunnel positions on tension changes in anterolateral ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2016.05;
24. N Ozeki, T Muneta, H Koga, Y Nakagawa, M Mizuno, K Tsuji, Y Mabuchi, C Akazawa, E Kobayashi, K Matsumoto, K Futamura, T Saito, I Sekiya. Not single but periodic injections of synovial mesenchymal stem cells maintain viable cells in knees and inhibit osteoarthritis progression in rats. *Osteoarthr. Cartil.*. 2016.06; 24(6); 1061-1070



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26. Hiroki Katagiri, Kaori Nakamura, Toshifumi Watanabe, Hideyuki Koga, Kazuyoshi Yagishita, Ichiro Sekiya, Takeshi Muneta. Increase of patellofemoral height has decreased maximum knee flexion after total knee arthroplasty of posterior cruciate-substituting prosthesis in a clinical series. *J Orthop Sci.* 2016.07; 21(4); 458-462
27. Mio Udo, Takeshi Muneta, Kunikazu Tsuji, Nobutake Ozeki, Yusuke Nakagawa, Toshiyuki Ohara, Ryusuke Saito, Katsuaki Yanagisawa, Hideyuki Koga, Ichiro Sekiya. Monoiodoacetic acid induces arthritis and synovitis in rats in a dose- and time-dependent manner: proposed model-specific scoring systems. *Osteoarthritis Cartilage.* 2016.07; 24(7); 1284-1291
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29. Shigeru Takishima, Keisuke Nakajima, Risa Nomura, Atsumi Tsuji-Hosokawa, Nozomi Matsuda, Yohei Matsubara, Makoto Ono, Kentaro Miyai, Kei Takasawa, Tomohiro Morio, Yukihiro Hasegawa, Kenichi Kashimada. Lower body weight and BMI at birth were associated with early adiposity rebound in 21-hydroxylase deficiency patients. *Endocr. J.* 2016.08; 63(11); 983-990
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31. Shumpei Yokota, Yasuhiko Itoh, Tomohiro Morio, Hideki Origasa, Naokata Sumitomo, Minako Tomobe, Kunihiro Tanaka, Seiji Minota. Tocilizumab in systemic juvenile idiopathic arthritis in a real-world clinical setting: results from 1 year of postmarketing surveillance follow-up of 417 patients in Japan. *Ann. Rheum. Dis.* 2016.09; 75(9); 1650-1660
32. Takeshi Muneta, Hideyuki Koga, Tomomasa Nakamura, Masafumi Horie, Toshifumi Watanabe, Ichiro Sekiya. Behind-remnant arthroscopic observation and scoring of femoral attachment of injured anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc.* 2016.09; 24(9); 2906-2914
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36. Watanabe T, Muneta T, Koga H, Horie M, Nakamura T, Otabe K, Nakagawa Y, Katakura M, Sekiya I.. In-vivo kinematics of high-flex posterior-stabilized total knee prosthesis designed for Asian populations. *Int Orthop.* 2016.11; 40(11); 2295-2302



37. Akifumi Endo, Daisuke Tomizawa, Yuki Aoki, Tomohiro Morio, Shuki Mizutani, Masatoshi Takagi. EWSR1/ELF5 induces acute myeloid leukemia by inhibiting p53/p21 pathway. *Cancer Sci.* 2016.12; 107(12); 1745-1754
38. Kaori Nakamura, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Takeshi Muneta. Dynamic Evaluation of Pivot-Shift Phenomenon in Double-Bundle Anterior Cruciate Ligament Reconstruction Using Triaxial Accelerometer. *Arthroscopy*. 2016.12; 32(12); 2532-2538
39. Inoue M, Muneta T, Ojima M, Nakamura K, Koga H, Sekiya I, Okazaki M, Tsuji K.. Inflammatory cytokine levels in synovial fluid 3, 4 days postoperatively and its correlation with early-phase functional recovery after anterior cruciate ligament reconstruction: a cohort study. *J Exp Orthop.* 2016.12; 3(1); 30
40. Toshiyuki Ohara, Takeshi Muneta, Yusuke Nakagawa, Yu Matsukura, Shizuko Ichinose, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. < Original Article> Hypoxia enhances proliferation through increase of colony formation rate with chondrogenic potential in primary synovial mesenchymal stem cells. *J. Med. Dent. Sci.* 2016.12; 63(4); 61-70
41. Daisuke Tomizawa, Akifumi Endo, Michiko Kajiwara, Hirotoshi Sakaguchi, Kimikazu Matsumoto, Makoto Kaneda, Takashi Taga. Acute lymphoblastic leukemia in patients with Down syndrome with a previous history of acute myeloid leukemia. *Pediatr Blood Cancer*. 2016.12;

#### [Conference Activities & Talks]

1. Koji Otabe, Ken Watanabe, Norio Shimizu, Takeshi Muneta, Ichiro Sekiya. High Sensitivity Virus / Mycoplasma Screening Test Reveals High Prevalence of Parvovirus B19 Infection In Synovial Tissues and Bone Marrow. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
2. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Nobutake Ozeki, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya. PDGF-AA/AB In Human Serum Are Potential Indicators Of The Proliferative Capacity Of Human Synovial Mesenchymal Stem Cells. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
3. Mitsuru Mizuno, Hisako Katano, Yo Mabuchi, Yusuke Ogata, Shizuko Ichinose, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Nobutake Ozeki, Kunikazu Tsuji, Chihiro Akazawa, Takeshi Muneta, Ichiro Sekiya. Properties of MSCs Derived From Surface, Stroma, and Perivascular Synovium Of Oa Patients. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
4. Kenta Katagiri, Takeshi Muneta, Koji Otabe, Yu Matsukura, Hisako Katano, Ichiro Sekiya. Fibrous Synovium Releases Higher Number Of MSCs Than Adipose Synovium in a Suspended Synovium Culture Model. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
5. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya. Interleukin-1  $\beta$  Promotes In Vitro Chondrogenesis Of Synovial Mesenchymal Stem Cells. Orthopaedic Research Society 2016 Annual Meeting 2016.03.06 Orlando, USA
6. Nobutake Ozeki, Junpei Matsuda, Takeshi Muneta, Hideyuki Koga, Kunikazu Tsuji, Kenta Katagiri, Mitsuru Mizuno, Tomoyuki Saito, Ichiro Sekiya. Biomechanical Analysis of Centralization With an Anchor for Meniscus Extrusion in a Porcine Model. Orthopaedic Research Society 2016 Annual Meeting 2016.03.07 Orlando, USA
7. Yusuke Nakagawa, Hideyuki Koga, Takeshi Muneta, Shinji Kiuchi, Hideo Ono, Tsuyoshi Nagata, Toshifumi Watanabe, Masafumi Horie, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Hisako Katano, Ichiro Sekiya. Three-Dimensional Reconstructed MRI Evaluation of Arthroscopic Centralization Technique for Extruded Lateral Meniscus. Orthopaedic Research Society 2016 Annual Meeting 2016.03.07 Orlando, USA
8. Ichiro Sekiya. Adult stem cell-based approaches (Intraarticular delivery, model systems vs humans) Overview. ICRS Summit 2016.04.10 Kyoto, JAPAN

9. Haruna Shibayama, Ken-ichi Imadome, Chizuko Sakashita, Ken Watanabe, Norio Shimizu, Takatoshi Koyama, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. In vitro and in vivo effects of proteasome inhibitor bortezomib on Epstein-Barr virus-positive T- or NK-cell lymphoproliferative diseases. 17th International Symposium on Epstein-Barr virus (EBV) and Associated Diseases 2016.08.10 Zurich
10. Shiho KOBAYASHI, Naoki OTOMO, Kaoru OKUYAMA, Shihoko SUWA, Michiko KAJIWARA. Study of the performance and usefulness of "ORTHO VISION Max" in TMDU. The 32nd World Congress of Biomedical Laboratory Science 2016.09.02 Kobe International Conference Center, JAPAN
11. Mitsui-Sekinaka K, Imai K, Tsujita Y, Mitsui N, Asano T, Sekinaka Y, Kanegane H, Yoshida K, Miyano S, Kojima S, Ogawa S, Ohara O, Okada S, Kobayashi M, Takagi M, Morio T, Nonoyama S.. Activated PI3 Kinase Delta Syndrome (APDS)-Like Immunodeficiency Caused by PTEN Mutation. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Barcelona, Spain
12. Hoshino A, Okada S, Yoshida K, Nishida N, Yamashita M, Okano T, Tsumura M, Nishimura S, Sakata S, Takagi M, Imai K, Miyano S, Ogawa S, Kojima S, Nonoyama S, Morio T, Kanegane H. . Abnormal Hematopoiesis and Autoimmunity in Humans with Germline IKZF1 Mutations. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Barcelona, Spain
13. Leiding J, Okada S, Shcherbina A, Abinun M, Pulsipher M, Hagin D, Linemans C, Sullivan K, Bunin N, Kilic S, De La Calle-Martin O, Roiman C, Aldave J.C, Iguchi A, Imai K, Ohkawa T, Gennery A, Slatter M, Ochs H, Mori T, Torgerson T. Hematopoietic Stem cell Transplantation in Patients with Gain of Function STAT1 Mutation. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Barcelona, Spain
14. Sekinaka Y, Mitsui N, Imai K, Yabe M, Mitsui-Sekinaka K, Honma K, Arai A, Yoshida K, Miyano S, Seiji K, Hira A, Takata M, Ohara O, Ogawa S, Morio T, Nonoyama S. Common Variable Immunodeficiency Caused by Fanc Mutations. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.22 Brcelona, Spain
15. Ichiro Sekiya. Scientific update: the synovial joint milieu - implications for cartilage repair. ICRS World Congress 2016.09.23 Naples, Italy
16. Okano T, Watanabe E, Takashima T, Nishikawa T, Kawano Y, Tomoda T, Tanaka-Kubota M, Miyamoto S, Yeh T, Yamashita M, Tanaka K, Mitusiki N, Ohara O, Takagi M, Imai K, Kanegane H, Morio T.. IGG1 Gammopathy in X-SCID Caused by Maternal T and B cell Engraftment. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.23 Barcelona, Spain
17. Moriya K, Tanita K, Ohnishi H, Niizuma H, Rikiishi T, Nishikomori R, Ishige T, Imai K, Kanegane H, Sasahara Y, Arakawa H, Kure S, Morio T. I < kappa> B- $\alpha$  S32 Mutations Underly Ectodermal Dysplasia with Immunodeficiency Manifestations and Correlation with Immunological Parameters.. 17th Biennial Meeting of the European Society for Immunodeficiencies 2016.09.23 Brcelona, Spain
18. Haruna Shibayama, Ken-ichi Imadome, Chizuko Sakashita, Ken Watanabe, Fuyuko Kawano, Norio Shimizu, Takatoshi Koyama, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. In vitro and in vivo effects of bortezomib on EBV-T/NK-LPDs. The 78th Annual Meeting of the Japanese Society of Hematology 2016.10.14 Yokohama
19. Akihiro Hoshino, Satoshi Okada, Kenichi Yoshida, Naonori Nishida, Yusuke Okuno, Hiroo Ueno, Motoi Yamashita, Tsubasa Okano, Miyuki Tsumura, Shiho Nishimura, Sonoko Sakata, Masatoshi Takagi, Kohsuke Imai, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Seishi Ogawa, Seiji Kojima, Shigeaki Nonoyama, Tomohiro Morio, Hirokazu Kanegane. ABNORMAL HEMATOPOIESIS AND AUTOIMMUNITY IN HUMANS WITH GERMLINE IKZF1 MUTATIONS. 2016.10.21
20. Marie Scully, Paul Knoebl, MD, Karim Kentouche, Lawrence Rice, Jerzy Windyga, Reinhard Schneppenheim, Johanna A Kremer Hovinga, Michiko Kajiwara, Caterina Maggiore, Jennifer Doralt, Leah Martell, and Bruce M. Ewenstein. Pharmacodynamic Profile of a Recombinant ADAMTS13 (BAX930) in Hereditary Thrombotic Thrombocytopenic Purpura (Upshaw-Schulman Syndrome (USS)). American Society of Hematology, 58th Annual Meeting 2016.12.03 San Diego, CA, USA
21. Akihiro Hoshino, Satoshi Okada, Kenichi Yoshida, Yusuke Okuno, Miyuki Tsumura, Shiho Nishimura, Sonoko Sakata, Masatoshi Takagi, Kohsuke Imai, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru

Miyano, Seishi Ogawa, Seiji Kojima, Shigeaki Nonoyama, Tomohiro Morio, Hirokazu Kanegane. AB-NORMAL HEMATOPOIESIS AND AUTOIMMUNITY IN HUMANS WITH GERMLINE IKZF1 MUTATIONS. 2016.12.16

**[Awards & Honors]**

1. Ichiro Sekiya, The Japanese Society for Regenerative Medicine Award (Clinical Category), The Japanese Society for Regenerative Medicine, 2016.03
2. Koji Otabe, Excellence in Translational Science Award from Journal of Orthopaedic Research, Orthopaedic Research Society, 2016.03
3. Mitsuru Mizuno, Young Investigator Award, The Japanese Tissue Culture Association, 2016.05
4. Yusuke Nakagawa, Grant for Study Abroad by Mitsukoshi Health and Welfare Foundation, Mitsukoshi Health and Welfare Foundation, 2016.08

## Cleanroom

Associate Professor SUNAKAWA Mitsuhiro  
Assistant Professor MATSUMOTO Hiroyuki

### ( 1 ) Research

- 1) The development of disposable hygienic materials for dental use.
- 2) The survey for the oral diseases in patients with HIV.
- 3) The survey for the relationship between the consciousness of the staff and students and the needle stick accident in the hospital.

### ( 2 ) Education

The improvement of the nosocomial infection control system in the University Hospital, Faculty of Dentistry, Tokyo Medical and Dental University and the education of the actual infection control method to all staff and clinical course students.

### ( 3 ) Publications

#### [Misc]

1. Sunakawa M. Infection Control in Dentistry Carlisle. 2016.12; 21(3); 1-3

#### [Conference Activities & Talks]

1. Iino Y, Yoshioka T, Hanada T, Ebihara A, Sunakawa M, Sumi Y, Okiji T. Visualization of substructures of resected apical root surface by swept-source optical coherence tomography. The 15th Congress of the World Federation for Laser Dentistry 2016.07.17 Nagoya
2. Rashed BA, Ebihara A, Iino Y, Yoshioka T, Hanada T, Sunakawa M, Sumi Y, Okiji T. Evaluation of root canal anatomy of maxillary premolars using swept source optical coherence tomography in comparison with dental operating microscope and cone beam computed tomography. The 15th Congress of the World Federation for Laser Dentistry 2016.07.18 Nagoya
3. Kagaya N, Sawa E, Kobayashi N, Hanaoka S, Kobayashi M, Matsumoto H, Suzuki H. Patient's attitude survey to "harmful rumor" of HIV/AIDS. The 33rd Annual Meeting of The Japan Society for Disability and Oral Health 2016.10.02 Omiya
4. Iino Y, Ebihara A, Yoshioka T, Hanada T, Sunakawa M, Sum Y, Okiji T. Application of optical coherence tomography in endodontics. The 23rd General Meeting of the Japanese Association for Dental Science 2016.10.21 Fukuoka
5. Sunakawa M. Sterilization and disinfection methods of the used instruments in the dental clinic -actuals at the dental hospital, Tokyo Medical and Dental University-. Instrument Management & Infection Prevention Symposium 2016.10.30 Tokyo

# Center for Development of Devices and Drugs in Dentistry

Director Junji TAGAMI  
Co-Director Hidekazu TAKAHASHI  
Hideki HARASAWA  
Naoko HARADA  
Member Miwako WAGAI (CRC)  
Kazuko KOJIMA (CRC)

## ( 1 ) Outline

Center for development of devices and drugs in dentistry was established in April, 2004 and is committed to a wide range of activities, such as education, consultation for new devices and drugs application, and support for clinical trials in University Hospital of Dentistry.

## ( 2 ) Education

We provide a program for the 3rd year students of the School of Dentistry, also for the 2nd year students of the School of Oral Health Care Sciences majoring in Oral Health Engineering to help them to gain fundamental knowledge of Pharmaceutical Affairs Act which is required for development and application of dental devices. Collaborating with the Institute of Biomaterials and Bioengineering, we lecture the 1st year students in Master's Program at Graduate School of Medical and Dental Sciences on issues and systems related to the mission that many outcomes from studies about innovative dental devices and materials will be put into use without "device-lag" .

## ( 3 ) Clinical Services & Other Works

### 1. Clinical trial supporting Services

In order to accomplish clinical trials successfully, we manage and support from planning, paper work to patient care as a main office of clinical trials in University Hospital of Dentistry.

### 2. Consultation Services

We provide consultation services about various issues concerning the Pharmaceutical Affairs Act, not only for pharmaceutical and dental companies but also for dentists and researchers in our University.

By the supporting services of clinical trials, we hope that applicant will be able to form a protocol adequately and effectively, and to start the clinical trial swiftly.

## ( 4 ) Clinical Performances

### · Consultation achievements

We managed and supported one clinical trial for dental device in 2016.

The 37 consultation services concerning dental devices were performed in 2016.

## ( 5 ) Publications

### [Original Articles]

1. Miho Sugiura, Yuichi Kitasako, Alireza Sadr, Yasushi Shimada, Yasunori Sumi, Junji Tagami. White spot lesion remineralization by sugar-free chewing gum containing bio-available calcium and fluoride: A double-blind randomized controlled trial. *Journal of Dentistry*. 2016.11; 54; 86-91

### [Books etc]

1. Junji Tagami. Quarterly dental care. First publication, 2016.04
2. ryo imai,ritu aoki,reiko kaduki,hiko hyakusoku. rehabilitation makeup-To be visible makeup therapy option-. kokuseidou publishing company, 2016.06
3. nico. Quintessence publishing, 2016.08

### [Misc]

1. Hidekazu TAKAHASHI. Outlook of CAD/CAM resin blocks approved by social insurance system *Journal of Japan Academy of Digital Dentistry*. 2016.07; 6(1); 3-6

### [Conference Activities & Talks]

1. Hidekazu TAKAHASHI. General information for CAD/CAM composite resin blocks.. Project seminar of Japanese Academy of Digital Dentistry 2016.02.21 Tokyo
2. Yuan Zhou, Khairul Matin. Evaluation of Resin Infiltration to Prevent Progression of Root Caries. American Association for Dental Research (AADR) Annual Meeting 2016.03.16 Los Angeles, Calif, USA
3. Chihiro MATSUURA, Yasushi SHIMADA, Alireza SADR, Junji TAGAMI, Yasunori SUMI . 3D assessment of dentin caries under composite restorations using SS-OCT . 45th annual meeting of AADR 2016.03.17 Los Angeles
4. Tomoko TABATA, Yasushi SHIMADA, Alireza SADR, Junji TAGAMI, Yasunori SUMI. Assessment of Enamel Crack at Cavo-surface Margin Using 3D SS-OCT. 45th annual meeting of AADR 2016.03.17 Los Angeles
5. Yuki Naruse, Tomohiro Takagaki, Naoko Matsui, Takaaki Sato, Toru Nikaido, Masaomi Ikeda, Junji Tagami. Effects of alumina-blasting for a CAD/CAM resin block on adhesion. 45th Annual meeting of American Association for Dental Research 2016.03.17 Los Angeles
6. Masatoshi Nakajima, Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Keiichi Hosaka, Junji Tagami. Effect of smear layer-deproteinizing on dentin bonding of self-etch adhesives. 45th AADR 2016.03.18 Los Angeles, Calif
7. Taweesak Prasansuttiorn, Ornnicha Thanatvarakorn, Junji Tagami, Masatoshi Nakajima. Bonding durability of dental adhesive to smear layer-deproteinized dentin. 45th AADR 2016.03.18 Los Angeles, Calif
8. Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Masahiro Takahashi, Suppason Thittaweerat, Junji Tagami, Masatoshi Nakajima. Scrubbing effect of one-step self-etch adhesives on dentin bonding. 45th AADR 2016.03.18 Los Angeles, Calif
9. David Pashley, Ayaka Chiba, Jianfeng Zou, Masatoshi Nakajima, Jianguo Tan, Junji Tagami, Debora Scheffel, Josimeri Hebling, Kelli Agee, Lorenzo Breschi, Genevieve Gregorie, Seung Jang, Franklin Tay. Effect of ethanol on size-exclusion characteristics of dentin-collagen to monomer. 45th AADR 2016.03.18 Los Angeles, Calif.
10. Inoue G, Mashiko R, Nakashima S, Tagami J. Surface assessment on artificial caries-affected dentin with FCP-COMPLEX. 45th Annual Meeting of American Association for Dental Research 2016.03.19 Los Angeles, USA

11. Prof. Nairn H F Wilson. History and reasons behind current trends in dentistry in the UK. 2016.04.04 Tokyo medical and dental university
12. Junji Tagami. About composite resin restration. 2016.05.18
13. Microtensile bond strength to dentin of a newly developed one-step self-etch system containing hydrophilic amide monomer. 2016.06.09
14. Sae AKEHASHI, Rena TAKAHASHI, Toru NIKAIDO, Junji TAGAMI. Enhancement of Dentin Bond Strength of Resin Cement using New Resin Coating Materials. The 144th Meeting of the Japanese Society of Conservative Dentistry 2016.06.10 Tochigi, Japan
15. Aramaki O, Kawashima N, Shimada Y, Okiji T, Tagami J . Three-dimensional analysis of Iba1+ macrophages in human dental pulp using whole mount immunostaining. 94th General session & exhibition of the IADR 2016.06.22 Seoul, Korea
16. Rena Takahashi, Yasushi Shimada, Yu-Chih Chiang, Ikumi Wada, Yasunori Sumi, Junji Tagami. Comparison of light-cured pit and fissure sealants on enamel demineralization using swept-source optical coherence tomography. 94th General Session & Exhibition of the IADR 2016.06.24 Seoul, Korea
17. Yu-Jung Lai, Ting-Chen Liu, Szu-Ying Huang, Rena Takahashi, Yasushi Shimada, Junji Tagami, Yu-Chih Chiang. Effects of S-PRG Fillers-containing Composite on Demineralization Inhibition of Enamel Surface: Optical Coherence Tomography (OCT) and Micro Computed Tomography (Micro CT) Approaches. 94th General Session & Exhibition of the IADR 2016.06.24 Seoul, Korea
18. Effect of cavity depth on Ultimate Tensile Strength of bulk fill flowable resin. 2016.09.10
19. Nakajima Y, Iwasaki N, Takahashi H, Yoshida M, Honda E, Kurabayashi T. MRI Artifacts and Radiopacity of CAD/CAM Composite Resin Blocks. The 2016 Academy of Dental Materials Annual Meeting 2016.10.13 Chicago
20. Takahashi H, Iwasaki N, Sumi Y. Effect of Cavity Design on Gap Formation Observed by OCT. The 2016 Academy of Dental Materials Annual Meeting 2016.10.14 Chicago
21. Takahashi H, Iwasaki N, Yasue T, Sumi Y. Observation of dental restoration gap formation using optical coherence tomography. 1st International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher 2016.10.17 Suita, Osaka, Japan
22. Junji Tagami. Creating a future dentistry with the adhesive dentistry. Research Day with CU,UI,UMPandTMDU Dental Students 2016 2016.10.18 Akio Suzuki memorial Hall in TMDU
23. Yuna KANAMORI, Rena TAKAHASHI, Toru NIKAIDO, Junji TAGAMI. The effect of light irradiation on dentin bond strengths of dual-cure resin cements. The 145th Meeting of Japanese Society of Conservative Dentistry 2016.10.27 Nagano, Japan
24. Junji Tagami. New trend of dental materials, adhesive resin and composite resin. 2016.11.23 Study medicine in Czech Republic
25. The evaluation of bond strength of calcium containing adhesive system to artificial demineralized dentin.

#### **[Awards & Honors]**

1. Best Poster Award (3rd prize), International Academy for Digital Dental Medicine, 2016.09



## Clinical Center for Sports Medicine and Sports Dentistry

### Clinical Center of Sports Medicine

Center Chief and Junior Associate Professor ; Kazuyoshi YAGISHITA

Junior Associate Professor ; Mitsuhiro ENOMOTO

Tokunin Assistant; Tomomasa NAKAMURA

Chief of Athletic Rehabilitation; Junya AIZAWA

Physiotherapist; Kenji HIROHATA, Takehiro OHMI, Shunsuke OHJI

Secretary; Kiyomi ITOH

### Sports Medicine/Dentistry

Associate Professor; Toshiaki UENO

Assistant Professor; Toshiyuki TAKAHASHI, Hiroshi CHUREI

Hospital Staff; atsuhide KUROKAWA

Graduate Student; Akihiro MITSUYAMA, Sintaro FUKASAWA,

Abhishekhi SHRESTHA, Mai IKEGAWA, Takahiro SHIRAKO,

Yuriko YOSHIDA, Nana SHIOTA, Hajime TANABE

### (1) Outline

Center of Sports Medicine and Sports Dentistry was established as a bridgehead for sports medical science and sports dental science which deals the clinical management of trauma and disorder for athletes and sports-active people, and the safety measures and prevention of sports-related traumatic injuries and disorders. Center of Sports Medicine and Sports Dentistry is consisted of Clinical Center of Sports Medicine in University Hospital of Medicine and Sports Medicine/Dentistry and Sports dentistry clinic in University Hospital of Dentistry.

### (2) Research

#### ○ Clinical Center of Sports Medicine

- 1) Athletic rehabilitation for rapid recovery from injury and high performance in athletes.
  - 1)-a Intervention of core strength in patients with anterior cruciate ligament reconstruction.
  - 1)-b Treatment from the aspect of core function in patients with overuse and fatigue fracture.
- 2) Evaluation methods for core function.
- 3) Development of dynamic stability.
- 4) Hyperbaric oxygen treatment
  - 4)-a Soft tissue injuries related with sports activities.
  - 4)-b Conditioning in sports activities

#### ○ Sports Medicine/Dentistry

- 1) Oral health promotion of athletes and sports-active people
  - 1)-a Field survey of oral health conditions in athletes and sports-active people
  - 1)-b Changes of oral environment associated with physical and sporting activities
  - 1)-c Influences of sports drinks and supplements on oral health
- 2) Safety measures of sports-related dental and maxillofacial traumatic injuries
  - 2)-a Diagnosis and treatment techniques for sports-related dental and maxillofacial injuries
  - 2)-b Development and innovation of sports mouthguard

- 2)-c Development and innovation of sports faceguard
- 2)-d Development and innovation of scuba diving mouthpiece
- 3) Correlations between occlusion and general motor functions
- 3)-a Biomechanical assessment of motor performance associated with occlusion
- 3)-b Electrophysiological analysis of neuromuscular function associated with occlusion
- 4) Correlations between occlusion and body posture
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

### (3) Clinical Services & Other Works

Center of Sports Medicine and Sports Dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered traumatic injuries, overuse disorders, disorders related with internal medicine, and dental diseases.

○ Clinical Center of Sports Medicine

Number of patients (From January 2015 to December 2015)

Section of out-patient clinic: 4,480

Section of athletic rehabilitation: 3,747

○ Sports Medicine/Dentistry, Sports dentistry clinic

Sports dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered dental diseases and traumatic injuries. Custom-fitted protective gears such as mouthguard and face-guard against sports-related dental and maxillofacial trauma are also handled for participants in contact sports such as a boxing, American football, rugby football, hockey, lacrosse, and martial art.

### (4) Publications

#### [Original Articles]

1. Takashi Ikeda, Tetsuya jinnno, Junya Aizawa, Tadashi Masuda, Kazuo Hirakawa, Kazunari Ninomiya, Kouji Suzuki, Sadao Morita. Effects of perioperative factors and hip geometry on hip abductor muscle strength during the first 6 months after anterolateral total hip arthroplasty. *Journal of Physical Therapy Science*. 2016; in press;
2. T Nakamura, Y Yoshida, H Churei, J Aizawa, K Hirohata, T Ohmi, S Ohji, T Takahashi, M Enomoto, T Ueno, K Yagishita. The effect of teeth clenching on dynamic balance at jumplanding: a pilot study *Journal of Applied Biomechanics*. 2016;
3. Saya Watanabe, Junya Aizawa, Manabu Shimoda, Mitsuhiro Enomoto, Tomomasa Nakamura, Atushi Okawa, Kazuyoshi Yagishita. Effect of short-term fatigue, induced by high-intensity exercise, on the profile of the ground reaction force during single-leg anterior drop-jumps. *J Phys Ther Sci*. 2016; 28(12); 3371-3375
4. Toshifumi Watanabe, Takeshi Muneta, Kazuyoshi Yagishita, Kenji Hara, Hideyuki Koga, Ichiro Sekiya. Closed Suction Drainage Is Not Necessary for Total Knee Arthroplasty: A Prospective Study on Simultaneous Bilateral Surgeries of a Mean Follow-Up of 5.5 Years. *J Arthroplasty*. 2016.03; 31(3); 641-645
5. YASUSHI KOJIMA, MITSUHIRO ENOMOTO, TAKUYA OYAIZU, KAZUYOSHI YAGISHITA. What is the optimal management of decompression illness?: Treatment at Medical Hospital of Tokyo Medical and Dental University *The Japanese Journal of Hyperbaric and Undersea Medicine*. 2016.03; 51(1); 14-18
6. Hayashi K, Takahashi T, Tanabe M, Horie M, Oyaizu T, Enomoto M, Shibata S, Yagishita K, Ueno T. The facilitatory effects of hyperbaric oxygen treatment on membrane bone wound healing in a rat calvarial defect model *Undersea Hyperb Med*. 2016.03; 43(2); 135-142
7. Kairi Hayashi, Toshiyuki Takahashi, Mai Ikegawa, Masaki Horie, Takuya Oyaizu, Mitsuhiro Enomoto, Shunichi Shibata, Kazuyoshi Yagishita, Toshiaki Ueno. The facilitatory effects of hyperbaric oxygen

- treatment on membrane bone wound healing in a rat calvarial defect model. *Undersea Hyperb Med.* 2016.03; 43(2); 135-142
8. Takashi Ikeda, Junya Aizawa, Hiroshi Nagasawa, Ikuko Gomi, Hiroyuki Kugota, Keigo Nanjo, Tetsuya Jinno, Tadashi Masuda, Sadao Morita. Effects and feasibility of exercise therapy combined with branched chain amino acid supplementation on muscle strengthening in frail and pre-frail elderly people requiring long-term care: A crossover trial. *Applied Physiology, Nutrition, and Metabolism.* 2016.04; 41(1); 438-445
9. Yoshiike T, Nishida M, Yagishita K, Nariai T, Ishii K, Nishikawa T.. Altered Sleep Spindles in Delayed Encephalopathy after Acute Carbon Monoxide Poisoning. *J Clin Sleep Med.* 2016.06; 12(6); 913-915
10. Suzuki H, Ito Y, Shinohara M, Yamashita S, Ichinose S, Kishida A, Oyaizu T, Kayama T, Nakamichi R, Koda N, Yagishita K, Lotz MK, Okawa A, Asahara H.. Gene targeting of the transcription factor *Mohawk* in rats causes heterotopic ossification of Achilles tendon via failed tenogenesis. *Proceedings of the National Academy of Sciences of the United States of America.* 2016.07; 113(28); 7840-7845
11. Hiroki Katagiri, Kaori Nakamura, Toshifumi Watanabe, Hideyuki Koga, Kazuyoshi Yagishita, Ichiro Sekiya, Takeshi Muneta. Increase of patellofemoral height has decreased maximum knee flexion after total knee arthroplasty of posterior cruciate-substituting prosthesis in a clinical series. *J Orthop Sci.* 2016.07; 21(4); 458-462
12. Fukasawa S, Churei H, Chowdhury RU, Shirako T, Shahrin S, Shrestha A, Wada T, Uo M, Takahashi H, Ueno T. Application of addition-cured silicone denture relining materials to mouthguard adjustment *Dent Mater J.* 2016.07; 35(4); 635-643
13. Junya Aizawa, Shunsuke Ohji, Hideyuki Koga, Tadashi Masuda, Kazuyoshi Yagishita. Correlations between sagittal plane kinematics and landing impact force during single-leg lateral jump-landings. *J Phys Ther Sci.* 2016.08; 28(8); 2316-2321
14. Yoko Yamamoto, Yoshihiro Noguchi, Mitsuhiro Enomoto, Kazuyoshi Yagishita, Ken Kitamura. Otological complications associated with hyperbaric oxygen therapy. *Eur Arch Otorhinolaryngol.* 2016.09; 273(9); 2487-2493
15. Ishigami T, Takahashi T, Kurokawa K, Ueno T. Effects of occlusal supporting area on dynamic posture against disturbance by electrical stimulation *Int J Sports Dent.* 2016.10; 9(1); 7-17
16. Shrestha A, Takahashi T, Kurokawa K, Mitsuyama A, Hayashi K, Ishigami T, Shahrin S, Chowdhury RU, Churei H, Ueno T. Effects of mouthguards on electromyographic activity of masticatory muscles *Int J Sports Dent.* 2016.10; 9(1); 27-37
17. Takahiro Wada, Hiroshi Churei, Toshiaki Ueno, Motohiro Uo. High shock absorbing faceguard using fiber-reinforced plastic (FRP) and elastomer *The Journal of the Japanese Society for Dental Materials and Devices.* 2016.11; 35(6); 325-328
18. Nakamura T, Yoshida Y, et al. The Effect of Teeth Clenching on Dynamic Balance at Jump-Landing: A Pilot Study. *Journal of Applied Biomechanics.* 2016.11; 19; 1-19
19. Toshitaka Yoshii, Kenichiro Sakai, Takashi Hirai, Tsuyoshi Yamada, Hiroyuki Inose, Tsuyoshi Kato, Mitsuhiro Enomoto, Shoji Tomizawa, Shigenori Kawabata, Yoshiyasu Arai, Atsushi Okawa. Anterior decompression with fusion versus posterior decompression with fusion for massive cervical ossification of the posterior longitudinal ligament with a  $\geq 50\%$  canal occupying ratio: a multicenter retrospective study. *Spine J.* 2016.11; 16(11); 1351-1357
20. Kazuyoshi Yagishita, Tetsuya Jinno, Daisuke Koga, Tsuyoshi Kato, Mitsuhiro Enomoto, Tsuyoshi Kato, Takeshi Muneta, Atsushi Okawa. Transient osteoporosis of the hip treated with hyperbaric oxygen therapy: a case series. *Undersea Hyperb Med.* 2016.11; 43(7); 847-854
21. Tomomasa Nakamura, Yuriko Yoshida, Hiroshi Churei, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Shunsuke Ohji, Toshiyuki Takahashi, Mitsuhiro Enomoto, Toshiaki Ueno, Kazuyoshi Yagishita. The Effect of Teeth Clenching on Dynamic Balance at Jump-Landing: A Pilot Study. *J Appl Biomech.* 2016.12; 1-19
22. Fukasawa S, Churei H, Chowdhury RU, Shahrin S, Shrestha A, Wada T, Uo M, Takahashi H, Ueno T. Differences among shock-absorbing capabilities of mouthguard materials *Dent Traumatol.* 2016.12; 32(6); 474-479

23. Toshitaka Yoshii, Takashi Hirai, Kenichiro Sakai, Shinichi Sotome, Mitsuhiro Enomoto, Tsuyoshi Yamada, Hiroyuki Inose, Tsuyoshi Kato, Shigenori Kawabata, Atsushi Okawa. Anterior Cervical Corpectomy and Fusion Using a Synthetic Hydroxyapatite Graft for Ossification of the Posterior Longitudinal Ligament. *Orthopedics*. 2016.12; 1-6
24. Shinichi Shirasawa, Hideyuki Koga, Masafumi Horie, Tomomasa Nakamura, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta. Forced knee extension test is a manual test that correlates with the unstable feelings of patients with ACL injury before and after reconstruction. *Knee*. 2016.12; 23(6); 1159-1163

#### [Misc]

1. Mitsuhiro Enomoto, Takashi Hirai, Hidetoshi Kaburagi, Takanori Yokota. Efficient Gene Suppression in Dorsal Root Ganglia and Spinal Cord Using Adeno-Associated Virus Vectors Encoding Short-Hairpin RNA. *Methods Mol. Biol.*. 2016; 1364; 277-290
2. Mitsuhiro Enomoto. Therapeutic effects of neurotrophic factors in experimental spinal cord injury models *Journal of Neurorestoratology*. 2016; (4); 15-22

#### [Conference Activities & Talks]

1. Ryota Shimamura, Takumi Yamada, Sadaya Misaki, Takehiro Omi, Takanobu Morozumi, Yoshinao Sato, Nami Shida, Kazutaka Sugimoto. The Gait Analysis of Patients after Bi-Cruciate Retaining TKA. The 46th Annual Meeting of the Japanese Society for Replacement Arthroplasty 2016.02.26
2. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Tomomasa Nakamura, Kazuyoshi Yagishita. Characterization of vertical and posterior ground reaction force during single leg jump-landing with body rotation. *Société Internationale de Traumatologie et Médecine des Sports d' Hiver* 2016.03
3. Yusuke Nakagawa, Hideyuki Koga, Takeshi Muneta, Kiuchi S, Ono H, Nagata T, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Hisako Katano, Ichiro Sekiya. Three-dimensional Reconstructed MRI Evaluation of Arthroscopic Centralization Technique for Extruded Lateral Meniscus. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05
4. Toshifumi Watanabe, Takeshi Muneta, Ichiro Sekiya, Hideyuki Koga, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Scott Banks. In-vivo Kinematics of Posterior-stabilized Total Knee Prosthesis Designed for Asian. *Orthopaedic Research Society 2016 Annual Meeting* 2016.03.05
5. Ikegawa M, Takahashi T, Ueno T. Effects of water gargling on changes of saliva pH and buffering capacity by taking sports drinks during exercise. 7th International Conference of Sports & Society 2016.06.02 Hawaii, U.S.A.
6. Takahiro Wada, Hiroshi Churei, Shintaro Fukasawa, Takahiro Shirako, Toshiaki Ueno, Motohiro Uo. Shock-absorbing property of face guard by incorporating a glass-fiber reinforced plastic and space. 2016.06.12
7. Shirako K, Churei H, Ueno T. Splinting by use of novel luxated tooth model and Periotest. 19th World Congress on Dental Traumatology 2016.08.11 Brisbane, Australia
8. Akiko Kawashima, Takumi Yamada, Takehiro Omi, Yoshinao Sato, Ryota Shimamura. Hip Joint Reaction Force in the Single Leg Standing and Kneeling Postures. *Asian Confederation of Physical Therapy Congress* 2016.10.07 Kuala Lumpur, Malaysia
9. Yoshinao Sato, Takumi Yamada, Takehiro Omi, Ryota Shimamura. Comparison of Foot Kinetics in the Frontal Plane during Gait Initiation between Young and Elderly Subjects. *Asian Confederation of Physical Therapy Congress* 2016.10.07 Kuala Lumpur, Malaysia
10. Takehiro Omi, Takumi Yamada, Yoshinao Sato, Ryota Shimamura. Simulation of the effect of decreasing lateral component of floorground reaction force during walking on mechanical stress of knee joint. *Asian Confederation of Physical Therapy Congress* 2016.10.07 Kuala Lumpur, Malaysia
11. Takahiro Wada, Hiroshi Churei, Haruka Takayanagi, Mako Yokose, Shitaro Fukasawa, Takahiro Shirako, Toshiaki Ueno, Naohiko Iwasaki, Hidekazu Takahashi, Motohiro Uo. Development of a faceguard using a glass-fiber reinforced thermoplastic (GFRTTP) and shock escape space. *Visual-JW 2016* 2016.10.17 Suita, Osaka, Japan

12. Takahiro Wada, Hiroshi Churei, Shintaro Fukasawa, Takahiro Shirako, Toshio Hongo, Toshiaki Ueno, Motohiro Uo. Analysis of shock absorption ability of a faceguard by incorporating a glass-fiber reinforced thermoplastic and space. International Dental Materials Congress 2016 2016.11.05 Bali, Indonesia
13. Tanabe G, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Effect of the use of commercial cleaning liquid in thermoforming process of mouthguard materials. International Dental Materials Congress 2016 2016.11.05 Bali, Indonesia
14. Hidetoshi Kaburagi, Takashi Hirai, Takanori Yokota , Atsushi Okawa,Mitsuhiro Enomoto. Role of voltage-gated sodium channels and calcium channel subunit  $\alpha$ -2/ $\delta$ -1 in the lumbar dorsal root ganglions of persistent peripheral neuropathic pain model mice.. Neuroscience2016 2016.11.15 San Diego