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Graduate School of Medical and Dental Sciences

Medical and Dental Sciences

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Life Science and Technology

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Oral Pathology

Junior Associate Professor
Kei Sakamoto

Assistant Professor
Kou Kayamori

Technical Staff
Miwako Hamagaki

Graduate Students
Masita Mandasari
Nguyen Thi Kim Chi
Akane Yukimori
Sawangarun Wanlada
Yae Ohata
Yuko Ymagata (Oral and Maxillofacial Surgery)
Akane Wada
Shoko Ishida

(1) Research

- 1) Study on the molecular mechanisms of oral cancer development.
- 2) Study on molecular markers useful for pathology diagnosis of oral premalignancies.
- 3) Study on the molecular mechanisms of odontogenic tumor development.
- 4) Clinico-pathological research on oral and maxillofacial regions
- 5) Molecular mechanism of bone formation and bone regeneration
- 6) Roles of Notch signaling in skeletal formation and regeneration
- 7) Molecular mechanism of bone destruction by oral cancers
- 8) Evolutional changes in skeletal formation

(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. Harazono Y, Yamashiro M, Yoshitake H, Kayamori K, Izumo T, Harada K. A case of highly suspected small cell osteosarcoma in the mandible. *Journal of Oral and Maxillofacial Surgery, Medicine, and pathology.* 2015; 27; 38-40
2. Yamada T, Yamashiro M, Kawamata A, Katsuki Y, Uezono-Honda A, Kayamori K, Harada K. Transparotid excision of rhabdomyosarcoma in masseter muscle, A case report. *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology.* 2015; 27; 45-48
3. Hiroyuki Yoshitake, Kou Kayamori, Ryosuke Nakamura, Sou Wake, Kiyoshi Harada. Pseudotumor in the temporomandibular joint: A case report. *Int J Surg Case Rep.* 2015; 15; 5-9
4. Zayer Lin, Iimura T, Kasugai S, Yamaguchi A. Oral mucosal fibroblasts that overexpress BMP-2 differentiate into osteoblasts and participate in new bone formation during bone regeneration. *J Oral Biosciences* . 2015; 57; 118-123
5. Wu S, Lin Z, Yamaguchi A, Kasugai S. The effects of periosteum removal on the osteocytes in mouse calvaria *Dent Oral Craniofac Res* . 2015;
6. Yuriko Nishiyama, Tsutomu Matsumoto, Ji-Won Lee, Takashi Saitou, Takeshi Imamura, Keiji Moriyama, Akira Yamaguchi, Tadahiro Iimura. Changes in the spatial distribution of sclerostin in the osteocytic lacuno-canalicular system in alveolar bone due to orthodontic forces, as detected on multimodal confocal fluorescence imaging analyses. *Arch. Oral Biol.* 2015.01; 60(1); 45-54
7. Ryosuke Nakamura, Kou Kayamori, Erika Oue, Kei Sakamoto, Kiyoshi Harada, Akira Yamaguchi. Transforming growth factor- β synthesized by stromal cells and cancer cells participates in bone resorption induced by oral squamous cell carcinoma. *Biochem. Biophys. Res. Commun.* 2015.03; 458(4); 777-782
8. Tanaka K, Harada H, Kayamori K, Omura K. Chronic sclerosing sialadenitis of the submandibular gland as the initial symptom of IgG4-related disease: a case report. *Tohoku J Exp Med.* 2015.07; 236(3); 193-198
9. Rei Tohyama, Kou Kayamori, Kiyoshi Sato, Miwako Hamagaki, Kei Sakamoto, Hisataka Yasuda, Akira Yamaguchi. 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. *J. Oral Pathol. Med.* 2015.10;
10. So Wake, Hiroyuki Yoshitake, Kou Kayamori, Toshiyuki Izumo, Kiyoshi Harada. Expression of CD90 decreases with progression of synovial chondromatosis in the temporomandibular joint. *Cranio.* 2015.12; 1-7

[Conference Activities & Talks]

1. Sakamoto K. Diagnostic pathology of oral cancer and premalignant lesions.. The 19th scientific congress and dental exhibition 2015.05.14 HoChiMinh city, Vietnam

Bacterial Pathogenesis

Professor SUZUKI Toshihiko

(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. Kazuhito Satou, Makiko Shimoji, Hinako Tamotsu, Ayaka Juan, Noriko Ashimine, Misuzu Shinzato, Claudia Toma, Toshitsugu Nohara, Akino Shiroma, Kazuma Nakano, Kuniko Teruya, Yasunobu Terabayashi, Shun Ohki, Nobuo Koizumi, Shou Okano, Toshihiko Suzuki, Takashi Hirano. Complete Genome Sequences of Low-Passage Virulent and High-Passage Avirulent Variants of Pathogenic *Leptospira interrogans* Serovar Manilae Strain UP-MMC-NIID, Originally Isolated from a Patient with Severe Leptospirosis, Determined Using PacBio Single-Molecule Real-Time Technology. *Genome Announc.* 2015; 3(4);
2. Yohei Yamaguchi, Tomoko Kurita-Ochiai, Ryoki Kobayashi, Toshihiko Suzuki, Tomohiro Ando. Activation of the NLRP3 inflammasome in *Porphyromonas gingivalis*-accelerated atherosclerosis. *Pathog Dis.* 2015.06; 73(4);
3. M Sugiyama, A Saeki, A Hasebe, R Kamesaki, Y Yoshida, Y Kitagawa, T Suzuki, K Shibata. Activation of inflammasomes in dendritic cells and macrophages by *Mycoplasma salivarium*. *Mol Oral Microbiol.* 2015.07;

[Books etc]

1. Toshihiko Suzuki. G.I. Research Inflammasome and digestive disorder. Sentan Igaku-sha, 2015.10
2. Toshihiko Suzuki. New medicine Infectious gastroenteritis. Saishin Igaku-sha, 2015.11

[Conference Activities & Talks]

1. Noboru Nakasone, Naomi Higa, Claudia Toma, Giichi Takaesu, Toshihiko Suzuki. The mechanisms of inhibition of the secretion of EspB via type III secretion system by extracts from Guava. The 88th Annual Meeting Japanese Society for Bacteriology 2015.03.27 Gifu
2. Ryosuke Kamesaki, Ayumi Saeki, Ami Abe, Akira Hasebe, Yoshimasa Kitagawa, Toshihiko Suzuki, Ken-ichiro Shibata. Inflammasome activation by *Aggregatibacter actinomycetemcomitans*. The 82th Lodge Meeting of Hokkaido Japanese Society for Bacteriology 2015.09.05 Sapporo
3. Ayumi Saeki, Akira Hasebe, Ryosuke Kamesaki, Futoshi Nakazawa, Toshihiko Suzuki, Ken-ichiro Shibata. Induction of IL-1alpha in dendritic cells and macrophages by *Streptococcus sanguinis* infection. The 82th Lodge Meeting of Hokkaido Japanese Society for Bacteriology 2015.09.05 Sapporo
4. Giichi Takaesu, Noboru Nakasone, Claudia Toma, Naomi Higa, Toshihiko Suzuki. TAK1-binding protein 2 (TAB2) negatively regulates the processing of pro-interleukin-1beta. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo

Molecular Immunology

Professor	Miyuki Azuma
Associate Professor	Shigenori Nagai
Assistant Professor	Tatsukuni Ohno
Adjunct instructor	Hiroshi Kiyono
	Yuzo Takahashi
	Takeshi Azuma
Graduate Students (Doctor)	Arundhati C. Bhingare(∼ Sept.)
	Siwen Kang
	Yuta Kondo
	Hirunwidchayarat Worawalun
	Niken Adiba Nadya
	Naoto Nishii(Apr. ∼)
	Yulong Xia(Oct. ∼)
Research Student	Xin Jin((Oct. ∼)

(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. McAlees JW, Lajoie S, Dienger K, Sproles AA, Richgels PK, Yang Y, Khodoun M, Azuma M, Yagita H, Fulkerson PC, Wills-Karp M, Lewkowich IP. Differential control of CD4(+) T-cell subsets by the PD-1/PD-L1 axis in a mouse model of allergic asthma. *Eur. J. Immunol.* 2015.04; 45(4); 1019-1029
2. Morita, H., Arae, K., Unno, H., Nambu, A, Oboki, K., Ohno, T., Matsuda, A., Toyama, S., Miyauchi, K., Yamaguchi, S., Narushima, S., Kajiwara, N., Iikura, M., Suto, H., McKenzie, A., Takahashi, T., Karasuyama, H., Okumara, K., Azuma, M., Galli, SJ., Moro, K., Akdis, C., Koyasu, S., Kubo, M., Sudo,

K., Saito, H., Matsumoto, K., and Nakae, S.. An Interleukin-33-Mast Cell-Interleukin-2 Axis Suppresses Papain-Induced Allergic Inflammation by Promoting Regulatory T Cell Numbers. *Immunity*. 2015.07; 43(1); 175-186

3. Ooi JD, Li M, Kourkoutzelos K, Yagita H, Azuma M, Holdsworth SR, Kitching AR. Programmed death 1 and its ligands do not limit experimental foreign antigen-induced immune complex glomerulonephritis. *Nephrology (Carlton)*. 2015.12; 20(12); 892-898

[Misc]

1. Patcharee R, Azuma M. Intrinsic and extrinsic control of expression of the immunoregulatory molecule PD-L1 in epithelial cells and squamous cell carcinoma. *Oral Oncol*. 2015.03; 51(3); 221-228

Advanced Biomaterials

Professor UO Motohiro
Associate Professor
HONGO Toshio
Assistant Professor
NAKAMURA Hideo
Assistant Professor
WADA Takahiro
Visiting Lecturer
Masuno Atsunobu

(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. Imamura T, Kanno Z, Imai H, Sugiyama T, Wada T, Yoshida M, Sakama M, Ono T, Honda E, Uo M. Infiltration of trace metal ions in the oral mucosa of a rat analyzed using SRXRF, XAFS, and ICP-MS. Dent Mater J. 2015; 34(6); 814-821
2. Tomoko Sugiyama, Motohiro Uo, Takahiro Wada, Daisuke Omagari, Kazuo Komiyama, Tadahide Noguchi, Yoshinori Jinbu, Mikio Kusama. Estimation of trace metal elements in oral mucosa specimens by using SR-XRF, PIXE, and XAFS Biometals. 2015.01; 28; 11-20
3. Motohiro Uo, Tomoko Sugiyama, Takahiro Wada, Toshio Hongo, Noriyuki Takashi. Distribution and chemical state analysis of eroded metallic elements from various dental alloys The Journal of the Japanese Society for Dental Materials and Devices. 2015.01; 34(1); 41-47

4. Minami Maekawa, Zusei Kanno, Takahiro Wada, Toshio Hongo, Hisashi Doi, Takao Hanawa, Takashi Ono and Motohiro Uo. Mechanical properties of orthodontic wires made of super engineering plastic Dental Materials Journal. 2015.01; 34(1); 114-119
5. Oto Aramaki, Rena Takahashi, Takahiro Wada, Motohiro Uo, Junji Tagami. Effect of Time after Light-curing of Composite Resin Crown on the Bonding Property of Resin Cement The Japanese Journal of Conservative Dentistry. 2015.02; 58(1);
6. Takahiro Wada, Naoyoshi Murata, Hiromitsu Uehara, Takuya Suzuki, Makoto Kobayashi, Yukari Okada, Yasuhiro Niwa, Hiroaki Nitani, Motohiro Uo, Kiyotaka Asakura. Improvement of A Real Gas-Sensor for the Origin of Methane Selectivity Degradation by μ -XAFS investigation Nano-Micro Letters. 2015.02; 7(3); 255-260
7. Motohiro UO, Takahiro WADA, Tomoko SUGIYAMA, Ikuo NAKANO, Kiyonobu KIMURA, Natsuko TANIGUCHI, Takashi INOMATA, Satoshi KONNO, Masaharu NISHIMURA. Elemental Analysis of Histopathological Specimens of Tungsten Carbide Lung Disease Using Synchrotron Radiation XRF and XAFS Advances in X-ray Chemical Analysis. 2015.03; 46; 177-186
8. Naoyoshi Murata, Makoto Kobayashi, Yukari Okada, Takuya Suzuki, Hiroaki Nitani, Yasuhiro Niwa, Hitoshi Abe, Takahiro Wada, Shingo Mukai, Hiromitsu Uehara, Hiroko Ariga, Satoru Takakusagi, Kiyotaka Asakura. A high-temperature in situ cell with a large solid angle for fluorescence X-ray absorption fine structure measurement Review of Scientific Instruments. 2015.03; 86; 034102
9. Sugiyama T., Uo M., Wada T, Omagari D, Komiyama K, Miyazaki S, Numako C, Noguchi T, Jinbu Y, Kusama M, Mori Y.. Detection of trace metallic elements in oral lichenoid contact lesions using SR-XRF, PIXE, and XAFS Scientific Reports. 2015.06; 5(10672); 1-12
10. Sugiyama T., Uo M., Mizoguchi T., Wada T., Omagar D, Komiyama K., Mori Y.. Copper accumulation in the sequestrum of medication-related osteonecrosis of the jaw Bone Reports. 2015.08; 3; 40-47

[Books etc]

1. Motohiro Uo. New Research Trends of Fluorite-Based Oxide Materials: From Basic Chemistry and Materials Science to Engineering Applications. NOVA Science Publishers, 2015.01 (ISBN : 978-1-63117-350-9)

[Misc]

1. Motohiro Uo, Takahiro Wada, Tomoko Sugiyama. Applications of X-ray fluorescence analysis (XRF) to dental and medical specimens Japanese Dental Science Review. 2015.01; 51; 2-9
2. Motohiro Uo. Analysis of Biomedical Specimens Containing Metal and Ceramics Using Synchrotron Radiation XRF and XAFS Bulletin of the Ceramic Society of Japan. 2015.01; 50(1); 27-31
3. Motohiro Uo. Nanotechnology The Journal of Dental Engineering. 2015.01; 34(1); 1-4
4. Tomoko SUGIYAMA, Takahiro WADA, Motohiro UO. Preparation of film shaped concentration calibration specimens for SR-XRF - Application for the trace elemental analysis in the biological tissues using SR-XRF and development of the diagnostic material- 2015.08; 33(2); 16-21

[Conference Activities & Talks]

1. Application of SR-XRF and XAFS for the Clinical Diagnosis. The 74th Okazaki Conference, "Frontier of X-ray Absorption Spectroscopy and Molecular Science" 2015.02.03
2. H.NAKAMURA, K.MOTOMURA, Y.Michi, M.YAMAMOTO, T.YOSHIOKA, S.TANAKA. Monitoring Pressure and Temperature in Dental Cavity Through Micro Sensors.. 93rd General Session & Exhibition of the IADR, 44th Annual Meeting of the AADR, 39th Annual Meeting of the CADR. 2015.03.13 Boston, USA
3. Takahiro Wada, Naoyoshi Murata, Hiromitsu Uehara, Takuya Suzuki, Makoto Kobayashi, Yukari Okada, Yasuhiro Niwa, Hiroaki Nitani, Motohiro Uo, Kiyotaka Asakura. Study of Micro Gas Sensor Using Micro XAFS - The reason for a Decrease of Methane Selectivity -. 2015.03.17

4. Effects of composition on photoluminescence and chemical states of Cu-doped tin phosphate glasses. 2015.03.17
5. Takahiro Wada, Naoyoshi Murata, Hiromitsu Uehara, Takuya Suzuki, Yasuhiro Niwa, Hiroaki Nitani, Motohiro Uo, Kiyotaka Asakura. μ -XAFS Investigation of a Real μ -Gas Sensor to Reveal the Origin of Methane Selectivity Degradation. XAFS16 2015.08.24 Karlsruhe, Germany
6. Tomoya Konishi, Yuuki Ooka, Nobutomo Uehara, Masaru Kamano, Takahiro Wada, Motohiro Uo. Effects of Composition on Luminescence Properties of Copper-doped Tin Phosphate Glasses. ICG Annual Meeting 2015.09.20
7. Inokoshi M, Tanimoto H, Zhao H, Uo M, Minakuchi S. Time dependence of the degree of conversion for a self-adhesive cement- influence of all ceramic restorations . The 66th General Session of the Japanese Society for Dental Materials and Devices 2015.10.03 Tokyo
8. Takahiro Wada, Naoyoshi Murata, Takuya Suzuki, Hiromitsu Uehara, Hiroaki Nitani, Yasuhiro Niwa, Motohiro Uo, Kiyotaka Asakura. μ -X-ray Absorption Fine Structure Analysis of Changes of Pd/Al₂O₃ catalyst in a Degradation Real μ -Gas Sensor. 1st International Symposium of Institute for Catalysis 2015.10.14 Sapporo, Japan
9. Takahiro Wada, Naoyoshi Murata, Hiromitsu Uehara, Takuya Suzuki, Yasuhiro Niwa, Hiroaki Nitani, Motohiro Uo, Kiyotaka Asakura. Multi-points XAFS Analysis of the Pd/Al₂O₃ Catalyst Overlay in an Actual Degraded Micro Gas Sensor. PACIFICHEM2015 2015.12.16 Honolulu, Hawaii, USA

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. Uzawa N, Suzuki M, Miura C, Tomomatsu N, Izumo T,. Primary ameloblastic carcinoma of the maxilla: A case report and literature review. *Oncology Letters*.. 2015.01; 9(1); 459-467
2. Harazono Y, Yamashiro M, Yoshitake H, Kayamori K, Izumo T, Harada K.. A case of highly suspected small cell osteosarcoma in the mandible. *Journal of Oral and Maxillofacial Surgery, Medicine, and pathology*. . 2015.01; 27; 38-40
3. Wake S, Yoshitake H, Kayamori K, Izumo T, Harada K.. Expression of CD90 decreases with progression of synovial chondromatosis in the temporomandibular joint. *CRANIO*. 2015.08; 21; 215

[Books etc]

1. Izumo T. Surgical Pathology of Oral Cancer: in Oral Cancer: Diagnosis and Therapy. Springer, 2015.04
(ISBN : 978-4431549376)

Oral Radiation Oncology

Professor	Masahiko MIURA
Assistant Professor	Atsushi KAIDA
Clinical Fellow	Yoichiro HASEGAWA
	Satoshi SATO
Graduate Students	Tatuaki GOTOU
	Chisato YAMADA
	Eri TSUCHIDA
	Kouhei OKUYAMA
	Hiroyuki ONOZATO
	Nisha GOWRI MANILA
	Sirimanas JIARANUCHART
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) Radiosensitization mechanism by novel anti- microtubule agents
- 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. Chisato Yamada, Atsushi Kaida, Kohei Okuyama, Kiyoshi Harada, Masahiko Miura. Effects of Chk1 inhibitor or paclitaxel on cisplatin-induced cell-cycle kinetics and survival in parental and cisplatin-resistant HeLa cells expressing fluorescent ubiquitination based cell cycle indicator (Fucci). *Integr Cancer Sci Therap.* 2015; 2; 87-92
2. Jesus Izaguirre-Carbonell, Hirofumi Kawakubo, Hiroshi Murata, Atsushi Tanabe, Toshifumi Takeuchi, Tomoe Kusayanagi, Senko Tsukuda, Takeshi Hirakawa, Kazuki Iwabata, Yoshihiro Kanai, Keisuke Ohta, Masahiko Miura, Kengo Sakaguchi, Sachihito Matsunaga, Hiroeki Sahara, Shinji Kamisuki, Fumio Sugawara. Novel anticancer agent, SQAP, binds to focal adhesion kinase and modulates its activity. *Sci Rep.* 2015; 5; 15136
3. Lian Xue, Yoshiya Furusawa, Ryuichi Okayasu, Masahiko Miura, Xing Cui, Cuihua Liu, Ryoichi Hirayama, Yoshitaka Matsumoto, Hirohiko Yajima, Dong Yu. The complexity of DNA double strand break is a crucial factor for activating ATR signaling pathway for G2/M checkpoint regulation regardless of ATM function. *DNA Repair (Amst.).* 2015.01; 25; 72-83
4. Eri Tsuchida, Atsushi Kaida, Endrawan Pratama, Masa-Aki Ikeda, Keiji Suzuki, Kiyoshi Harada, Masahiko Miura. Effect of X-Irradiation at Different Stages in the Cell Cycle on Individual Cell-Based Kinetics in an Asynchronous Cell Population. *PLoS ONE.* 2015.06; 10(6); e0128090
5. Yugo Sawada, Kazuya Omoto, Naoki Kohei, Kengo Sakaguchi, Masahiko Miura, Kazunari Tanabe. Sulfoquinovosylacylpropanediol is a novel potent radiosensitizer in prostate cancer. *Int. J. Urol.* 2015.06; 22(6); 590-595
6. Atsushi Kaida, Masahiko Miura. Unusual prolongation of radiation-induced G2 arrest in tumor xenografts derived from HeLa cells. *Cancer Sci.* 2015.10; 106(10); 1370-1376
7. Tatsuaki Goto, Atsushi Kaida, Masahiko Miura. Visualizing cell-cycle kinetics after hypoxia/reoxygenation in HeLa cells expressing fluorescent ubiquitination-based cell cycle indicator (Fucci). *Exp. Cell Res.* 2015.12; 339(2); 389-396
8. Kohei Okuyama, Atsushi Kaida, Yoshiki Hayashi, Yoshio Hayashi, Kiyoshi Harada, Masahiko Miura. KPU-300, a Novel Benzophenone-Diketopiperazine-Type Anti-Microtubule Agent with a 2-Pyridyl Structure, Is a Potent Radiosensitizer That Synchronizes the Cell Cycle in Early M Phase. *PLoS ONE.* 2015.12; 10(12); e0145995

[Conference Activities & Talks]

1. Kohei Okuyama, Atsushi Kaida, Kiyoshi Harada, Masahiko Miura. A novel type of anti-microtubule agent, KPU-300, is a potent radiosensitizer through synchronization of the cell cycle at M-phase. 15th International Congress of Radiation Research 2015.05.27 Kyoto
2. Tatsuaki Goto, Atsushi Kaida, Masahiko Miura. Cell cycle kinetics in HeLa cells expressing Fucci under hypoxia and after reoxygenation. 15th International Congress of Radiation Research 2015.05.27 Kyoto
3. Atsushi Kaida, Masahiko Miura. Visualizing the effects of tumor microenvironments on cell cycle kinetics in HeLa cells following X-irradiation. 15th International Congress of Radiation Research 2015.05.28 Kyoto

4. Masahiko Miura. Visualizing Cell cycle kinetics in HeLa cell in vitro and in vivo following X irradiation. 15th International Congress of Radiation Research 2015.05.29 Kyoto
5. Masahiko Miura. Basics of Radiation Biology with a Focus on 4Rs. 12th International Stereotactic Radiosurgery Society Congress 2015.06.07 Yokohama
6. Nisha Gowri Manila, Atsushi Kaida, Masahiko Miura. Inhibition of IGF-IR retards release from radiation-induced G2 arrest. TMDU Student Symposium 2015, 7th TMDU International Symposium Program 2015.08.29 Tokyo
7. Kohei Okuyama, Atsushi Kaida, Yoshiki Hayashi, Yoshio Hayashi, Kiyoshi Harada, Masahiko Miura. A novel type of anti-microtubule agent, KPU-300, is a potent radiosensitizer through synchronization of the cell cycle in M-phase. 22nd International Conference on Oral and Maxillofacial Surgery 2015.10.27 Melbourne, Australia
8. Masahiko Miura, Atsushi Kaida. Radiobiology for stereotactic radiotherapy. The 28th Annual Meeting of the Japanese Society for Radiation Oncology, Workshop 2015.11.19 Maebashi
9. Taito Asahina, Atsushi Kaida, Keisuke Sasai, Ryoichi Yoshimura, Masahiko Miura. Temporo-spatial cell cycle kinetics in HeLa cells by Ir-192 HDR-RALS. The 28th Annual Meeting of the Japanese Society for Radiation Oncology, Workshop 2015.11.20 Maebashi
10. Nisha Gowri Manila, Atsushi Kaida, Masahiko Miura. IGF-1 receptor influences radiation-induced G2 arrest in HeLa cells expressing fluorescent ubiquitination-based cell cycle indicator (Fucci). ISAJ 6th Symposium on Recent Advances and Technology 2015.12.04 Tokyo
11. Nisha Gowri Manila, Atsushi Kaida, Masahiko Miura. Effect of IGF-IR-inhibition on the radiation – induced cell kinetics and DNA repair. 80th Annual Meeting of the Stomatological Society 2015.12.26 Tokyo

Oral and Maxillofacial Surgery

Professor Hiroyuki HARADA

Junior Associate Professor Yuji KABASAWA, Eriko MARUKAWA

Assistant Professor Minoru IKUTA, Hiroaki SHIMAMOTO,

Keiichi MORITA, Fumihiko TSUSHIMA

Hirofumi TOMIOKA, Hideaki HIRAI

Graduate Student

Namiaki TAKAHARA, Seiichiro ODA, Dilruba AKTER, Yu OIKAWA,

Yusuke ONOZATO, Toru TAKEMOTO, Yuko YAMAGATA, Naoto NISHII,

Shuhei HUKUDA, Ruri KOMIYA

(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 β -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. Mochizuki Y, Harada H, Ikuta M, Shimamoto H, Tomioka H, Tanaka K, Hirai H, Omura K. Clinical characteristics of multiple primary carcinomas of the oral cavity. *Oral Oncol.* 2015.02; 51(2); 182-189
2. Tomioka H, Kaneoya A, Mochizuki Y, Harada H. Primary diffuse large B-cell lymphoma arising in the tongue accompanied by ataxia-telangiectasia: a case report. *J Clin Diagn Res.* 2015.06; 9(6); ZD25-ZD27
3. Tanaka K, Harada H, Kayamori K, Omura K. Chronic sclerosing sialadenitis of the submandibular gland as the initial symptom of IgG4-related disease: a case report. *Tohoku J Exp Med.* 2015.07; 236(3); 193-198
4. Mochizuki Y, Harada H, Sakamoto K, Kayamori K, Nakamura S, Ikuta M, Kabasawa Y, Marukawa E, Shimamoto H, Tushima F, Omura K. Malignant lymphoma with initial symptoms in the mandibular region. *J Cancer Ther.* 2015.07; 6(7); 554-565
5. Kudo M, Harada H, Matsumoto K, Sato Y, Omura K, Ishii Y. Massive neurilemoma of the hard plate in which preoperative diagnosis was difficult. *Case Rep Surg.* 2015.08; 2015; 638025
6. Tsushima F, Sakurai J, Harada H. A case of upper gingiva carcinoma with chronic graft-versus-host disease after allogenic bone marrow transplantation. *Aust Dent J.* 2015.09; 60(3); 404-407
7. Kuribayashi Y, Tsushima F, Morita K, Matsumoto K, Sakurai J, Uesugi A, Sato K, Oda S, Sakamoto K, Harada H. Long-term outcome of non-surgical treatment in patients with oral leukoplakia. *Oral Oncol.* 2015.11; 51(11); 1020-1025
8. 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. *PLOS One.* 2015.11; 10(11); e0140480
9. Fukuda S, Hayashi R, Nishimura Y, Nakamizo M, Ota Y, Chazono H, Nakamura K, Harada H, Fujimoto Y, Yoshimoto S. Report of head and neck cancer registry of Japan clinical statistics of registered patients, 2013. *Japanese Journal of Head and Neck Cancer.* 2015.11; 41(supplement);
10. Kudoh M, Harada H, Sato Y, Omura K, Ishii Y. Massive odontameloblastoma arising in the maxilla: a case report. *J Medical Case Rep.* 2015.12; 9; 278

[Conference Activities & Talks]

1. Harada H. Prediction of cervical lymph node and distant metastasis in oral carcinoma. TMU-TMDU Joint Symposium 2015 2015.03.14 Tokyo, Japan
2. Morita K. Distraction osteogenesis for patients with cleft lip and palate at Tokyo Medical and Dental University. The 56th Congress of the Korean Association of Oral and Maxillofacial Surgeons. Symposium II: DO & Deformity 2015.04.24 Goyang, Korea
3. Daiphong Lam, Ami Kuribayashi, Junichiro Sakamoto, Shin Nakamura, Hiroyuki Harada, Tohru Kurabayashi. A case report of B-cell lymphoblastic lymphoma in the mental region. 2015.06.06
4. Shinya Kotaki, Junichiro Sakamoto, Shin Nakamura, Takahide Taguchi, Hiroyuki Harada, Akira Toriihara, Tohru Kurabayashi. Perineural spread of malignant tumor : a case of Diffuse large B-cell lymphoma. 2015.06.07
5. Morita K, Oikawa Y, Kayamori K, Sakamoto K, Ishikawa S, Inazawa J, Harada H. Targeted resequencing of cancer-related genes in oral cancer. The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan
6. Takada J, Ogawa T, Sato C, Uezono M, Morita M, Moriyama K. A case of Holoprosencephaly with unilateral cleft lip and palate treated with maxillary distraction osteogenesis in adolescence. The 8th International Orthodontic Congress 2015.09.28 London, UK

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, Tetsu SATO

Graduate Student: Lam Dai PHONG, Shinya KOTAKI, Ngamsom SUPAK, Hiroko ISHII, Noriko SUZUKI, Chutamas DEEPHO, Tran Thi Xuan LAN

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. Nunthayanon K, Honda E, Shimazaki K, Ohmori H, Inoue-Arai MS, Kurabayashi T, Ono T. A pilot study on characterization of articulatory movements during fricative/s/sound in an anterior open-bite subject: a tooth-visualized 3-T magnetic resonance imaging video evaluation. J World Fed Orthod. 2015; 4; 71-77
2. Suzuki M, Yoshino N, Shimada M, Tetsumura A, Matsumura T, Fukayama H, Kurabayashi T. Trigeminal neuralgia: differences in magnetic resonance imaging characteristics of neurovascular compression between

symptomatic and asymptomatic nerves. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015.01; 119(1); 113-118

3. Nunthayanon K, Honda E, Shimazaki K, Ohmori H, Inoue-Arai MS, Kurabayashi T, Ono T. Differences in velopharyngeal structure during speech among asians revealed by 3-tesla magnetic resonance imaging movie mode. *Biomed Res Int.* 2015.03; 2015; 126264
4. Lam PD, Kuribayashi A, Imaizumi A, Sakamoto J, Sumi Y, Yoshino N, Kurabayashi T.. Differentiating benign and malignant salivary gland tumours: diagnostic criteria and the accuracy of dynamic contrast-enhanced MRI with high temporal resolution. *The British Journal of Radiology.* 2015.05; 88(1049);
5. Nunthayanon K, Honda E, Shimazaki K, Ohmori H, Inoue-Arai MS, Kurabayashi T, Ono T. Use of an advanced 3-T MRI movie to investigate articulation. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015.06; 119(6); 684-694
6. Yumi Mochizuki, Hiroyuki Harada, Kei Sakamoto, Kou Kayamori, Shin Nakamura, Minoru Ikuta, Yuji Kabasawa, Eriko Marukawa, Hiroaki Shimamoto, Fumihiko Tsushima, Ken Omura, . Malignant Lymphoma with Initial Symptoms in the Mandibular Region *Journal of Cancer Therapy.* 2015.07; 6; 554-565
7. Kuppusamy M, Watanabe H, Kasugai S, Kuroda S. Effects of abutment removal and reconnection on inflammatory cytokine production around dental implants. *Implant Dentistry.* 2015.12; 24; 730-734

[Conference Activities & Talks]

1. Kurabayashi T. MRI: basics and clinical application in dentistry. 37th Annual Scientific Conference on Dental Research 2015.04.13 Ho-Chi-Minh City, Viet Nam
2. Nakamura S. Perineural spread of head and neck malignancy. 37th Annual Scientific Conference on Dental Research 2015.04.13 Ho Chi Minh City, Viet Nam
3. Junichiro Sakamoto, Shinya Kotaki, Tadanobu Aragaki, Ami Kurabayashi, Tohru Kurabayashi. Diffusion kurtosis imaging (DKI): Analysis of the odontogenic cystic lesions. 2015.06.06
4. Mamiko Fujikura, Keiichi Nishikawa, Akiko Imaizumi, Yoshinori Sasaki, Junichiro Sakamoto, Mika Otonari, Tsukasa Sano, Kenji Mishima, Tohru Kurabayashi. Signal intensity of cortical bone and TMJ disc on MR images (Part 2). 2015.06.06
5. Akiko Imaizumi, Yoshinori Sasaki, Mika Otonari Yamamoto, Keiichi Nishikawa, Mamoru Wako, Natsuko Nagura, Mamiko Fujikura, Junichiro Sakamoto, Tohru Kurabayashi. T1 and T2 relaxation times of normal tissues in the head and neck regions: comparisons between 1.5T and 3.0T. 2015.06.06
6. Daiphong Lam, Ami Kuribayashi, Junichiro Sakamoto, Shin Nakamura, Hiroyuki Harada, Tohru Kurabayashi.. A case report of B-cell lymphoblastic lymphoma in the mental region.. 2015.06.06
7. Yosuo Okumura, Maki Izawa, Kazuo Iwai, Naoto Ohbayashi, Kenichi Gotoh, Kenji Sato, Yoshito Sugihara, Keiichi Nishikawa, Masakazu Notsu, Yasuo Harada, Kazuo Maruhasi, Akira Mishima. Dose measurement of intra-oral technique to define diagnostic level. 56th Meeting of Japanese Society for Oral and Maxillo-facial Radiology 2015.06.06 Sendai city
8. Shinya Kotaki, Junichiro Sakamoto, Shin Nakamura, Takahide Taguchi, Hiroyuki Harada, Akira Toriihara, Tohru Kurabayashi. Perineural spread of malignant tumor : a case of Diffuse large B-cell lymphoma. 2015.06.07
9. Watanabe H, Nomura Y, Sumi Y, Honda E, Kurabayashi T. An experience of using SEDENTEXCT IQ phantom and Radia software to analyze the spatial resolution of cone-beam computed tomography for dental use. The 20th International Congress of Dento-maxillo-facial Radiology 2015.08.26 Santiago, Chile
10. Shin Nakamura, Norio Yoshino, Tohru Kurabayashi. 2 cases of mandibular gingival squamous cell carcinoma with the perineural spread along the lingual nerve. 2015.10.24 Fukuoka
11. Iku Shibata, Haruki Imai, Zusei Kanno, Akemi Tetsumura, Takao Hanawa, Takashi Ono. Three-dimensional quantification of the influences of form factors on MRI artifacts. The 74th Annual Meeting of the Japanese Orthodontic Society 2015.11.18 Fukuoka

[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(Sept)
Assistant Professors
Tomoyuki Miyamoto,
Tomoka Matsumura(Jan),
Kazumasa Kubota(Apr),
Hospital Staffs
Yukiko Baba(Dec),
Atsushi Najima,
Manami Yajima,
Fumiko Hasuike,
Hiroko Hagihara,
Yasuha Hayashi,
Kotomi Ota
Graduate Students
Takutoshi Inoue,
Kaeko Araki,
Asami Izumida,
Chihiro Suzuki
Research Students
Hidetaka Murata
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 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. Suzuki M, Yoshino N, Shimada M, Tetsumura A, Matsumura T, Fukayama H, Kurabayashi T. Trigeminal neuralgia: differences in magnetic resonance imaging characteristics of neurovascular compression between symptomatic and asymptomatic nerves. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015.01; 119(1); 113-118
2. Fujii-Abe K, Uriu K, Kawahara H. Case of Vasovagal Syncope With Asystole Associated With Propofol Sedation Anesthesia Progress . 2015.12; 62(00); 159-161

[Conference Activities & Talks]

1. Fukayama H. Safe and comfortable dentistry for patients and doctors. 35th Myanmar Dental Conference & 16th FDI-MDA joint Educational Meeting 2015.01.09 Yangon, Myanmar
2. Haruhisa Fukayama. Safe and comfortable dentistry for patients and doctors. 35th Myanmar Dental Conference & 16th FDI-MDA joint Educational Meeting 2015.01.09 Yangon, Myanmar

3. T. Matsumura, R. Wakita, K. Kamiya, N. Seino, Y. Ikeda, H.Fukayama.. Hands-free Vascular Imaging System (Veinsite®) for Dental Trainees.. 93rd General Session & Exhibition of the IADR 2015.03.13
4. Tomoka Matsumura, Ryo Wakita, Kiyoshi Kamiya, Nanako Seino, Yoriko Ikeda, Haruhisa Fukayama. Hands-free Vascular Imaging System (Veinsite®) for Dental Trainees. IADR general session 2015.03.13 Boston, Mass, USA
5. Gene T. Yocum¹, Ryo Wakita¹, Michael R Stephen², James M. Cook², Charles W. Emala¹, George Gallos¹ (AUA Sponsor). Selective Pharmacologic Targeting of the GABAA α 4 Subunit in Airway Smooth Muscle to Alleviate Bronchospasm. AUA 62nd Annual Meeting 2015.04.25 Nashville, Tennessee
6. Haruhisa Fukayama. Painless local anesthesia. Dies Forum, International Dental Scientific Conference & Expo 2015.09.18
7. Haruhisa Fukayama. Painless local anesthesia. Pain VS Anesthesia 2015.09.20

Orofacial Pain Management

Professor	Masahiko SHIMADA
Assistant Professor	Akira NISHIYAMA, Yoko YAMAZAKI
Hospital Staff	Hiroko KIMURA, Yuko ANDOH, Daisuke TOMIZAWA Hiroko IMURA, Masako TOBE, Natsuko OOTOMO
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 multivariate 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 pberipheral 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 pberipheral 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. Suzuki M, Yoshino N, Shimada M, Tetsumura A, Matsumura T, Fukayama H, Kurabayashi T.. Trigeminal neuralgia: differences in MRI characteristics of neurovascular compression between symptomatic and asymptomatic nerves Oral Surg Oral Med Oral Pathol Oral Radiol.. 2015.01; 119(1); 113-118
2. Niimi, T.; Yamazaki, Y.; Shimada, M.. Effectiveness of Rikkosan for Intractable Intraoral Pain: a case report Traditional & Kampo Medicine. 2015.03; 2(1); 27-29
3. Tomoko Niimi, Yoko Yamazaki and Masahiko Shimada. Effectiveness of Rikkosan for intractable intraoral pain 2015.03; 2(1); 27-29
4. H. Imura, M. Shimada, Y. Yamazaki, K. Sugimoto. Characteristic changes in saliva and taste in burning mouth syndrome patients Journal of Oral Pathology and Medicine. 2015.08; online(DOI: 10.1111/jop.12350); DOI: 10.1111/jop.12350

[Conference Activities & Talks]

1. M. Shimada. Orofacial Pain Management in Japan. Special Lecture, University of Dental Medicine, Yangon 2015.02.06 Yangon, Myanmar
2. M.Shimada. Contemporary Orofacial Pain Management in Japan. The 11th biennial Anaesthesiology and Intensive Care conference, Myanmar society of Anaesthesiologist 2015.02.07 Yangon, Myanmar
3. Hiroko Imura, Masahiko Shimada, Yoko Yamazaki, Kumiko Sugimoto. Saliva and taste in burning mouth syndrome patients. International Association for Dental Research 2015.03.12
4. Kaori Tsukagoshi, Akira Nishiyama. The effects of mouth opening exercises for 2 cases of patient with the temporomandibular disorders with anterior disk displacement without reduction. 4th Asian Academic Congress for Temporomandibular Joint 2015.11.17
5. Nguyen Ho Quynh Anh, Yamazaki Yoko, Imura Hiroko, Taira Masato, Kurabayashi Tohru, Shimada Masahiko. GREY MATTER VOLUME CHANGES IN TRIGEMINAL NEURALGIA. The 80th Annual Meeting of The Stomatological Society 2015.12.26 Tokyo

Pediatric Dentistry

Associate Professor Michio MIYASHIN
Junior Associate Professor Yoshiaki Ono(~ Mar.),
Zenzo MIWA(~ Mar.)
Assistant Professor Yoshiaki HASHIMOTO, Haruko FUJITA,
Mizuho MOTEGI, Satoko KAKINO
Clinical Professor Youichirou SHIMADA(~ Mar.),
Keiichi TAKEI(Apr. ~)
Adjunct Lecturer Yoshiharu MUKAI(~ Mar.),
Mitsurou TANAKA(~ Mar.),
Hitoyata SHIMOKAWA, Hiroaki NAGAI,
Nobutaka ISOGAWA, Yuki IMAMURA,
Mitsuko INOUE(Apr. ~)
Naoko UEHARA(Apr. ~), Makiko TAKASHI
Syuko MURATA(Apr. ~)
Hospital staff Naoko UEHARA(~ Mar.), Yukie NAKAJIMA,
Atsushi OISHI, Sachi GOTOH, Taki SEKIYA,
Kanae WADA(Apr. ~), Sachiko ITOH(Apr. ~)
Graduate Student Sachiko ITOH(~ Mar.), Tomoki UEHARA,
Kuniomi NAKAMURA, Shizuka TANAKA(~ Mar.),
SHEN Dong He, GANBOLD Khongorzul,
Erika KUBOTA, IJBARA Manhal M.A.,
ZUMULAITI Shaokelati,
WIT Yee Wint(Oct. ~),
Satomi FURUSAWA(Apr. ~),
Kousuke MAEDA(Apr. ~ Aug.)
Research Student Ayako NAKANE(~ Mar.), Shuko MURATA(~ Mar.),
Mami AOKI, Miki IIDA, Anri OHTA,
Chikako SATOH, Aoi AKAIKE,
Chika INOHARA(Apr. ~), Maya KATAOKA(Apr. ~)
International Research Student WIT Yee Wint(~ Sep.)
Enrolled dentist Ayako TOKUDA(Aug. ~), Gaku SHIMADA(Oct. ~)

(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. Sekiya T, Miwa Z, Tsuchihashi N, Uehara N, Sugimoto K. Analysis of physiological responses associated with emotional changes induced by viewing video images of dental treatments. *Journal of Medical and Dental Sciences*. 2015.03; 62(1); 11-18
2. Sasazawa S, Kakino S, Matsuura Y . Optical-fiber-based laser-induced breakdown spectroscopy for detection of early caries. *Journal of Biomedical Optics*. 2015.06; 20(6); 165002
3. Wada K, Miyashin M. New techniques for producing aesthetic, direct full-crown composite resin restorations for primary molars: a 24-month follow-up study of eight cases. *Eur J Paediatr Dent*. 2015.09; 16(3); 205-209
4. Nakajima N and Miyashin M. Application of OCT for pediatric dentistry *The Journal of the Japanese Society for Dental Materials and Devices*. 2015.11; 34(6); 441-444

[Misc]

1. Haga N, Kubota M, Miwa Z. Hereditary sensory and autonomic neuropathy types IV and V in Japan. *Pediatrics International* . 2015.02; 57(1); 1-13

[Conference Activities & Talks]

1. Yamada A, Kakino S, Matsuura Y. Photo-acoustic analysis of dental pulp using NIR laser light. 2015.01.12 Tokyo
2. Yamada A, Kakino S, Matsuura Y. Photo-acoustic signal detection from dental pulp for pulp vitality test.. The Joint Symposium of 9th International Symposium on Medical, Bio- and Nano-Electronics, and 6th International Workshop on Nanostructures & Nanoelectronics 2015.03.02 Sendai
3. Kakino S, Miwa Z, Miyashin M ,Sakota D, Matoba K. Quantitative diagnosis for dental pulp viability relevant to blood.. 2015.03.14 Boston, USA
4. Yamada A, Kakino S, Matsuura Y. Photo-acoustic analysis of dental pulp using near infrared laser light.. 5th Asian and Pacific RIm Symposium on Biophotonics (APBP) 2015.04.22 Yokohama
5. Uehara T, et al. A rankl-binding peptide accelerates BMP-induced bone regeneration in murine maxilla by subperiosteal injections. 13th Congress of the Internatitonal Society of Bone Morphometry 2015.04.27 Tokyo
6. Miyashin M, Zumuraiti S, Aoki M, Nakajima Y, Wada K. Ultrasonic device for extraction of primary teeth with ankylosis, a report of a case. 53th Annual Conference of the Japanese Society of Pediatric Dentistry 2015.05.21 Hiroshima
7. Nakajima N, Aoki M, Miyashin M. Pathological study for progressive root and bone resorption in replanted permanent incisors after traumatic avulsion. 53th Annual Conference of the Japanese Society of Pediatric Dentistry 2015.05.22 Hiroshima
8. Yamada A, Kakino S, Matsuura Y. Detection of blood in dental root canal by using time-frequency analysis of photo acoustic signal. Technical Meeting on Optical and Quantum Devices, IEE Japan 2015.09.28 Tokyo
9. Shen D, Horiuchi N, Nozaki K, Nakamura M, Nagai A, Yamashita K, Miyashin M. Osteoblastic responses to OCP and carbonate-containing OCP in vitro. The 37th annual meeting of the japanese 2015.11.09 Kyoto
10. Shen D, Horiuchi N, Nozaki K, Nakamura M, Nagai A, Yamashita K, Miyashin M. Carbonate-containing octacalcium phosphate enhanced osteoblast proliferation and differentiation. Asian bioceramics symposium 2015.12.10 Tokyo

[Awards & Honors]

1. Uehara T, et al. : New Investigator Award "A RANKL-binding peptide accelerates BMP-induced bone regeneration in murine maxilla by subperiosteal injections.", International Sociesty of Bone Morphometry, 2015.04
2. SHEN Donghe, et al. : Best Student of ABC Awards "Carbonate-containing octacalcium phosphate enhanced osteobalst proliferation and differentiation" , Asian bioceramics symposium, 2015.12

Orthodontic Science

Professor	Takashi ONO
Associate Professor	
Junior Associate Professor	Yoshiro MATSUMOTO, Zuipei 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	Yasuhiro SHIMIZU, Hiroko OMORI, Risa USUMI, Chiho KATO, Haruki IMAI (-Mar), Sarina KOIKE (-Mar), Hidemasa OKIHARA (Apr-)
Graduate Students	Jui-Chin HSU (-Mar), Yuhei IKEDA (-Mar), Toshihiro IMAMURA (-Mar) Minami MIYASAKA (-Mar), Mutsumi MIYAZAKI (-Mar), Asuka OKITO(-Mar) Kulthida NUNTHAYANON(-Sep), Shuji OISHI, Soma KITA Yoichiro KUMA, Tomomi SAKAGUCHI, Mio MAKIGUCHI Hiroyuki YAMAGUCHI, Jin-Gyu AN, Wei-Jen LAI 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 (Apr-), Erika OZAWA (-Mar) Moe SATO (Apr-), Kasumi HATANO (Apr-), Keiko FUKINO (Apr-) Shin-Sheng Yang (Apr-), Lu ZAHO (Apr-), Thi kim Uyen DONG (Oct-) Meshari Faleh H ALRESHIDI (Oct-)
Graduate School Research Students	Takeru KYURAGI (-Mar), Hidemasa OKIHARA (-Mar), Yukiha FUNAKI, Ayako KAWABE, Rieko ONO, Arisa SAWADA Emina WAKASUGI, Yuhei IKEDA(Apr-), Toshihiro IMAMURA(Apr-) Minami MIYASAKA(Apr-), Mutsumi MIYAZAKI(Apr-), Asuka OKITO(Apr-) Ayako KIRII, Syusuke UESUGI, Tomonari MATSUMURA Junpei SUZUKI, Kyohei YAMADA, Misako KOKETSU Takahiro SHIMAMINE, Katsuhiko SUZUKI, Mirei HAGIWARA Chiho SATOKAWA, Asuka MANABE, Shuntaro SAWAZAKI (Apr-) Makiko OKUZAWA (Apr-), Sena OKANO (Apr-Dec), Preska KEO (Apr-) Xiyuan GUO (Apr-), Wu YANG (Oct-), Sun-min KIM (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. Okito A, Nakahama K, Akiyama M, Ono T, Morita I. Involvement of the G-protein-coupled receptor 4 in RANKL expression by osteoblasts in an acidic environment. *Biochem Biophys Res Commun.* 2015; 458(2); 435-440
2. Nunthayanon K, Honda E, Shimazaki K, Ohmori H, Inoue-Arai MS, Kurabayashi T, Ono T. A pilot study on characterization of articulatory movements during fricative /s/ sound in an anterior open bite subject: a tooth-visualized 3-T MRI movie evaluation. *J World Feder Orthod.* 2015; 4; 71-77
3. Ono R, Watari I, Kubono-Mizumachi M, Ono T. GLP-1R expression in the major salivary glands of rats. *J Oral Biosci.* 2015; 57(4); 200-204
4. Imamura T, Kanno Z, Imai H, Sugiyama T, Wada T, Yoshida M, Sakama M, Ono T, Honda E, Uo M. Infiltration of trace metal ions in the oral mucosa of a rat analyzed using SRXRF, XAFS, and ICP-MS. *Dent Mater J.* 2015; 34(6); 814-821
5. Kokai S, Fukuyama E, Sato Y, Hsu JC, Takahashi Y, Harada K, Ono T. Comprehensive treatment approach for bilateral cleft lip and palate in an adult with premaxillary osteotomy, tooth autotransplantation, and 2-jaw surgery. *Am J Orthod Dentofacial Orthop.* 2015.01; 147(1); 114-126
6. Maekawa M, Kanno Z, Wada T, Hongo T, Doi H, Hanawa T, Ono T, Uo M. Mechanical properties of orthodontic wires made of super engineering plastic. *Dent Mater J.* 2015.01; 34(1); 114-119
7. Kita S, Shimazaki K, Yajima Y, Omura S, Ono T, Oshima M. Computational fluid dynamics study on the nasal respiratory function before/after maxillo-mandibular orthognathic surgery SEISAN KENKYU. 2015.01; 67(1); 55-58
8. Takada J, Miyamoto JJ, Yokota T, Ono T, Moriyama K. Comparison of the mandibular hinge axis in adult patients with facial asymmetry with and without posterior unilateral crossbite. *Eur J Orthod.* 2015.02; 37(1); 22-27
9. Nunthayanon K, Honda E, Shimazaki K, Ohmori H, Inoue-Arai MS, Kurabayashi T, Ono T. Differences in velopharyngeal structure during speech among asians revealed by 3-tesla magnetic resonance imaging movie mode. *Biomed Res Int.* 2015.03; 2015; 126264
10. Sawada A, Usui N, Shimazaki K, Taira M, Ono T. The effects of cognitive behavioral therapy on experimental orthodontic pain. *Orthod Waves.* 2015.05; 74(1); 10-14
11. Uchima Koecklin KH, Kato C, Funaki Y, Hiranuma M, Ishida T, Fujita K, Yabushita T, Kokai S, Ono T. Effect of unilateral nasal obstruction on tongue protrusion forces in growing rats. *J Appl Physiol.* 2015.05; 118(9); 1128-1135
12. Abbassy MA, Watari I, Bakry AS, Hamba H, Hasan AH, Tagami J, Ono T. Diabetes detrimental effects on enamel and dentin formation. *J Dent.* 2015.05; 43(5); 589-596
13. Nunthayanon K, Honda E, Shimazaki K, Ohmori H, Inoue-Arai MS, Kurabayashi T, Ono T. Use of an advanced 3-T MRI movie to investigate articulation. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015.06; 119(6); 684-694

14. Ishida T, Ikemoto S, Ono T. Nasomaxillary hypoplasia with a congenitally missing tooth treated with Le Fort II osteotomy, autotransplantation and nickel-titanium alloy wire. *Am J Orthod Dentofacial Orthop.* 2015.09; 148(3); 479-492
15. Kato G, Shimizu Y, Sugamori Y, Maeda M, Takahashi M, Tamura Y, Murali R, Ono T, Ohya K, Aoki K. The inhibitory effects of a RANKL-binding peptide on articular and periarticular bone loss in a murine model of collagen-induced arthritis: A bone histomorphometric study. *Arthritis Res Ther.* 2015.09; 17; 251
16. Park Y, Hosomichi J, Ge C, Xu J, Franceschi R, Kapila S. Immortalization and characterization of mouse temporomandibular joint disc cell clones with capacity for multi-lineage differentiation. *Osteoarthritis Cartil.* 2015.09; 23(9); 1532-1542
17. Ayano Dei, Jun J Miyamoto, Jun-Ichi Takada, Takashi Ono, Keiji Moriyama. Evaluation of blood flow and electromyographic activity in the perioral muscles. *Eur J Orthod.* 2015.11;
18. Kokai S, Kanno Z, Koike S, Uesugi S, Takahashi Y, Ono T, Soma K. Retrospective study of 100 auto-transplanted teeth with complete root formation and subsequent orthodontic treatment. *Am J Orthod Dentofacial Orthop.* 2015.12; 148(6); 982-989

[Books etc]

1. Watari I, Abbassy MA, Podyma-Inoue KA, Ono T. Major Topics in Type 1 Diabetes. INTECH, 2015.11 (ISBN : 978-953-51-2204-3)

[Conference Activities & Talks]

1. Koike-Hamba S, Hamba H, Shimazaki K, Tagami J, Ono T. Micro-CT analysis of inhibited demineralization around brackets with fluoride-releasing adhesives. The 93rd General Session & Exhibition of the IADR 2015.03 Boston, USA
2. Kita S, Shimazaki K, Yajima Y, Iwai T, Omura S, Oshima M, Ono T. Computational fluid dynamics study on the nasal respiratory function before/after maxillo-mandibular orthognathic surgery. 37th Annual Scientific Conference on Dental Research 2015.04.13 Ho Chi Minh City, Vietnam
3. Abe Y, Kato C, Funaki Y, Okihara H, Fujita K, Ishida T, Yabushita T, Kokai S, Ono T. Development of the motor representation within the face primary motor cortex in growing rats. 37th Annual Scientific Conference on Dental Research 2015.04.13 Ho Chi Minh City, Vietnam
4. Oishi S, Shimizu Y, Hosomichi J, Kuma Y, Usumi-Fujita R, Maeda H, Nagai H, Kaneko S, Suzuki J, Yoshida K, Ono T. The effects of intermittent hypoxia on the microstructure of growing craniofacial bones. SLEEP 2015 2015.06.06 Seattle, USA
5. Kuma Y, Usumi-Fujita R, Hosomichi J, Oishi S, Nagai H, Shimizu Y, Kaneko S, Suzuki J, Yoshida K, Ono T. Impairment of nasal airway under intermittent hypoxia during growth period in rats. SLEEP 2015 2015.06.06 Seattle, USA
6. Hosomichi J, Kuma Y, Oishi S, Usumi-Fujita R, Shimizu Y, Maeda H, Nagai H, Shitano C, Kaneko S, Ishida Y, Suzuki J, Yoshida K, Ono T. Up-regulation of inflammatory pathway through interleukins and NOS in the geniohyoid muscle. SLEEP 2015 2015.06.08 Seattle, USA
7. Yamaguchi H, Ishida Y, Suzuki J, Isobe M, Ono T. Transfection Efficiency of Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells Decoy in Periodontium by Using Ultrasound Microbubble. 91st Congress of the European orthodontic society 2015.06.13
8. Watari I, Podyma-Inoue KA, Yonemitsu I, Miyazaki M, Ono T. Altered craniofacial morphogenesis in offspring of rats with gestational diabetes. 91st Congress of the European Orthodontic Society 2015.06.13 Venice, Italy
9. Ohmori H, Kirimoto H, Shioya Y, Ono T. Relationship between gum chewing rate and autonomic nervous system activity. 91th Congress of the European Orthodontic Society 2015.06.17 Venice, Italy

10. Makiguchi M, Funaki Y, Kato C, Kokai S, Ono T. Effects of increased occlusal vertical dimension on the jaw-opening reflex in adult rats. 91st Congress of the European Orthodontic Society 2015.06.17 Venice, Italy
11. Sakaguchi-Kuma T, Fujishiro H, Shimazaki K, Yamaguchi K, Ono T, Akita K. The anatomic study of the ridge on condylar process of mandible. International Congress of Clinical Anatomy 2015.06.24 Rouen, France
12. Kokai S, Kanno Z, Koike S, Uesugi S, Ono T. Retrospective study of 100 autotransplanted teeth with complete root formation and subsequent orthodontic treatment. 8th International Orthodontic Congress 2015.09.27 London, UK
13. Uchima Koecklin KH, Kato C, Funaki Y, Hiranuma M, Ishida T, Fujita K, Yabushita T, Kokai S, Ono T. Increase in force and changes in the contractile characteristics of the tongue-protruding muscles after nasal obstruction in growing rats. 8th International Orthodontic Congress 2015.09.27 London, UK
14. Matsumoto Y, Hosomichi J, Ishida Y, Ohmori H, Shimizu Y, Kyuragi T, Shitano C, Kawabe A, Maekawa M, Ikeda Y, Kirii A, Kita S, Sakaguchi T, An J, Yamada K, Suzuki K, Ono T. Root resorption of maxillary incisors associated with ectopically erupting canines: predisposing factors, diagnosis and prognosis of orthodontic treatment. 8th International Orthodontic Congress 2015.09.27 London, UK
15. Oishi S, Shimazaki K, Sakai K, Matsumura T, Kita S, Lai W, Nunthayanon K, Uchima K, Ono T. Two cases treated with distal movement of unilateral maxillary molars using the distalizing appliance. 48th Scientific Congress of Korean Association of Othodontsts 2015.10.30 Gwangju Metropolitan City, Korea
16. Hosomichi J, Nakai Y, Maeda H, Kuma Y, Oishi S, Usumi-Fujita R, Shimizu Y, Kaneko S, Ishida Y, Shibutani N, Yoshida K, Ono T. Intermittent hypoxia triggers inflammatory pathway with down-regulated myofibrillar and mitochondrial biogenesis in the geniohyoid muscle. The 74th Annual Meeting of the Japanese Orthodontic Society 2015.11.20 Fukuoka, Japan

[Awards & Honors]

1. Hosomichi J, Nakai Y, Maeda H, Kuma Y, Oishi S, Usumi-Fujita R, Shimizu Y, Kaneko S, Ishida Y, Shibutani N, Yoshida K, Ono T. Japanese Orthodontic Society Award of Excellence, The 74th Annual Meeting of the Japanese Orthodontic Society, 2015.11

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, Go Inoue, Keiichi Hosaka, Tomohiro Takagaki, Rena Takahashi

Specially Appointed Junior Associate Professor: Syozi Nakashima (∼ March)

Specially Appointed Assistant Professor: Noriko Hiraishi, NHM Khairul Matin

Hospital Staff: Masahiro Takahashi, Oto Aramaki, Hidenori Hamba (∼ September) , Miho Tsujimoto (∼ March) , Yukiko Tanno, Naoko Matsui (April ∼) , Ikumi Wada (April ∼)

Foreign Researcher: Md. Sofiqul ISLAM, Mohammad Issa Michael Nassar

Clinical Professor: Katsufumi Nakamura

Guest Clinical Professor: Kouzou Nishimura

Secretary: Shiori Ogi, Takako Nakagawa

Graduate Student: Shigeyuki Nagai (∼ March) , Naoko Matsui (∼ March) , Ikumi Wada (∼ March) ,

Nariaki Yoshimine (∼ March) , Megumi Oshima (∼ March) , Ornnicha Thanatvarakorn (∼ March) ,

Alaa Turkistani, Teerapong Mamane (∼ September) , Sahar Jameel Khunkar (∼ September) ,

Ka Kyou (∼ September) , Ehab Zaki Alsayed (∼ September) , Junichi Shinagawa, Rena Oguro,

Takahide Ibusuki, Asami Aida, Ayaka Chiba, Kei Horie, Tomoka Ueno, Hiroki Tezuka,

Kento Sato, Takaaki Sato, Masami Arai, Maria Nakamura, Ritsuko Mashiko, Kong Kalyan,

Baba Bista, Maria Jacinta Rosario Hernandez Romero, Zaher Bukhari,

Patrycja Zakilna Majkut, Rui Guan, Ayaka Kusanagi, 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,

Yuan Zhou, 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 (April ∼),

Nao Takahashi (April ∼), Yuna Kanamori (April ∼), Yukina Ochiai (April ∼),

Kurumi Ide (April ∼), Yusuke Kuno (April ∼), Yuki Ito (April ∼), Shigeki Uchinuma (April ∼),

Daiki Nagano (April ∼), Yusuke Kakinuma (April ∼), Akira Nakane (April ∼)

Research Student: Shinji Ogura, Mineo Kijima, Marina Abe (April ∼), Yukiko Tanno (∼ September)

(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) 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.

5) 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), which has shown a great potential for such assessment.

6) 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.

7) 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.

8) 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.

9) 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.

10) Characterization of polymerization characteristics of light-cured resin composites

Aiming to establish appropriate clinical techniques to overcome polymerization shrinkage stress of composite resins, we have investigated the influence of the adhesives, composite resins, light irradiation methods and cavity configuration (C-factor) on the development of polymerization shrinkage stress using various techniques such as optical coherence tomography (OCT) and micro-focus X-ray computed tomography (micro-CT).

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. Hy Marghalani, T Bakhsh, A Sadr, J Tagami. Ultramorphological assessment of dentin-resin interface after use of simplified adhesives. *Oper Dent.* 2015; 40(1); E28-E39
2. Takako YOSHIKAWA, Makoto MORIGAMI, Alireza SADR, Junji TAGAMI. Environmental observation of enamel crack and resin-tooth cavity gap formation *Asian Pacific Journal of Dentistry.* 2015; 15; 13-19
3. Hua Qiao, Rena Takahashi, Toru Nikaido, Syozi Nakashima, Alireza Sadr, Masaomi Ikeda, Junji Tagami. Change of dentin permeability in different storage media after resin coating *Asian Pacific Journal of Dentistry.* 2015; 15(2); 33-40
4. Hamid Nurrohmah, Syozi Nakashima, Tomohiro Takagaki, Alireza Sadr, Toru Nikaido, Yuya Asakawa, Motohiro Uo, Sally J Marshall, Junji Tagami. Immobilization of phosphate monomers on collagen induces biomimetic mineralization. *Biomed Mater Eng.* 2015.01; 25(1); 89-99
5. Rubens Garcia, Tomohiro Takagaki, Takaaki Sato, Naoko Matsui, Toru Nikaido, Junji Tagami. Effect of Dentin Desensitizers on Resin Cement Bond Strengths. *RSBO.* 2015.01; 12(1); 14-22
6. Mohannad Nassar, Noriko Hiraishi, Yukihiko Tamura, Masayuki Otsuki, Kazuhiro Aoki, Junji Tagami. Phytic Acid: An Alternative Root Canal Chelating Agent. *J Endod.* 2015.02; 41(2); 242-247
7. Oto Aramaki, Rena Takahashi, Takahiro Wada, Motohiro Uo, Junji Tagami. Effect of Time after Light-curing of Composite Resin Crown on the Bonding Property of Resin Cement *The Japanese Journal of Conservative Dentistry.* 2015.02; 58(1);
8. A Tanaka, M Nakajima, N Seki, R M Foxton, J Tagami. The effect of tooth age on colour adjustment potential of resin composite restorations. *J Dent.* 2015.02; 43(2); 253-260
9. Alsayed EZ, Hariri I, Sadr A, Nakashima S, Bakhsh TA, Shimada Y, Sumi Y, Tagami J. Optical coherence tomography for evaluation of enamel and protective coating *Dental Materials Journal.* 2015.02; 34(1); 98-107
10. Akihiko Shimizu, Takatsugu Yamamoto, Syozi Nakashima, Toru Nikaido, Toyotaro Sugawara, Yasuko Momoi. Measurement of surface hardness of primary carious lesions in extracted human enamel -Measurement of Knoop hardness using Cariotester- *Dent Mater J.* 2015.02;
11. Naoko Matsui, Tomohiro Takagaki, Alireza Sadr, Masaomi Ikeda, Shizuko Ichinose, Toru Nikaido, Junji Tagami. The role of MDP in a bonding resin of a two-step self-etching adhesive system. *Dent Mater J.* 2015.02;
12. Espigares J, Sadr A, Hamba H, Shimada Y, Otsuki M, Tagami J, Sumi Y.. Assessment of natural enamel lesions with optical coherence tomography in comparison with microfocus x-ray computed tomography *Journal of Medical Imaging.* 2015.02; 2(1);
13. Yuichi Kitasako, Yoshiyuki Sasaki, Tomohiro Takagaki, Alireza Sadr, Junji Tagami. Age-specific prevalence of erosive tooth wear by acidic diet and gastroesophageal reflux in Japan. *J Dent.* 2015.04; 43(4); 418-423
14. M A Abbassy, I Watari, A S Bakry, H Hamba, Ali H Hassan, J Tagami, T Ono. Diabetes detrimental effects on enamel and dentine formation. *J Dent.* 2015.05; 43(5); 589-596
15. Maria J R H Romero, Syozi Nakashima, Toru Nikaido, Shizuko Ichinose, Alireza Sadr, Junji Tagami. Inhibition of hydroxyapatite growth by casein, a potential salivary phosphoprotein homologue. *Eur. J. Oral Sci.* 2015.06;
16. Megumi Oshima, Hidenori Hamba, Alireza Sadr, Toru Nikaido, Junji Tagami. Effect of polymer-based desensitizer with sodium fluoride on prevention of root dentin demineralization. *Am J Dent.* 2015.06; 28(3); 123-127
17. Turki A Bakhsh, Alireza Sadr, Mona M Mandurah, Yasushi Shimada, Osama Zakaria, Junji Tagami. In situ characterization of resin-dentin interfaces using conventional vs. cryofocused ion-beam milling. *Dent Mater.* 2015.07; 31(7); 833-844

18. Takahide Ibusuki, Yuichi Kitasako, Alireza Sadr, Yasushi Shimada, Yasunori Sumi, Junji Tagami. Observation of white spot lesions using swept source optical coherence tomography (SS-OCT): in vitro and in vivo study. *Dent Mater J.* 2015.07; 34(4); 545-552
19. Kalyan Kong, Md Sofiqul Islam, Mohannad Nassar, Noriko Hiraishi, Masayuki Otsuki, Cynthia K Y Yiu, Junji Tagami. Effect of phytic acid etchant on the structural stability of demineralized dentine and dentine bonding. *J Mech Behav Biomed Mater.* 2015.08; 48; 145-152
20. Nariaki Yoshimine, Yasushi Shimada, Junji Tagami, Alireza Sadr. Interfacial Adaptation of Composite Restorations Before and After Light Curing: Effects of Adhesive and Filling Technique. *J Adhes Dent.* 2015.08; 17(4); 329-336
21. A Turkistani, S Nakashima, Y Shimada, J Tagami, A Sadr. Microgaps and Demineralization Progress around Composite Restorations. *J. Dent. Res..* 2015.08; 94(8); 1070-1077
22. Patrycja Majkut, Alireza Sadr, Yasushi Shimada, Yasunori Sumi, Junji Tagami. Validation of Optical Coherence Tomography against Micro-computed Tomography for Evaluation of Remaining Coronal Dentin Thickness. *J Endod.* 2015.08; 41(8); 1349-1352
23. Toru Nikaido, Hamid Nurrohman, Tomohiro Takagaki, Alireza Sadr, Shizuko Ichinose, Junji Tagami. Nanoleakage in Hybrid Layer and Acid-Base Resistant Zone at the Adhesive/Dentin Interface. *Microsc. Microanal..* 2015.09; 1-7
24. Patricia Makishi, Suppason Thitthaweerat, Alireza Sadr, Yasushi Shimada, Adriano Luis Martins, Junji Tagami, Marcelo Giannini. Assessment of current adhesives in class I cavity: Nondestructive imaging using optical coherence tomography and microtensile bond strength. *Dent Mater.* 2015.09; 31(9); e190-e200
25. Ikumi Wada, Yasushi Shimada, Masaomi Ikeda, Alireza Sadr, Syozi Nakashima, Junji Tagami, Yasunori Sumi. Clinical assessment of non carious cervical lesion using swept-source optical coherence tomography. *J Biophotonics.* 2015.10; 8(10); 846-854
26. Teerapong Mamanee, Masahiro Takahashi, Masatoshi Nakajima, Richard M Foxton, Junji Tagami. Initial and long-term bond strengths of one-step self-etch adhesives with silane coupling agent to enamel-dentin-composite in combined situation. *Dent Mater J.* 2015.10; 34(5); 663-670
27. Maria Nakamura, Yuichi Kitasako, Syozi Nakashima, Alireza Sadr, Junji Tagami. Impact of toothpaste on abrasion of sound and eroded enamel: An in vitro white light interferometer study. *Am J Dent.* 2015.10; 28(5); 268-272
28. Y Kitasako, A Sadr, M F Burrow, J Tagami. Thirty six-month clinical evaluation of a highly-filled flowable composite for direct posterior restorations. *Aust Dent J.* 2015.11;
29. Patricia Makishi, Rafael R Pacheco, Alireza Sadr, Yasushi Shimada, Yasunori Sumi, Junji Tagami, Marcelo Giannini. Assessment of Self-Adhesive Resin Composites: Nondestructive Imaging of Resin-Dentin Interfacial Adaptation and Shear Bond Strength. *Microsc. Microanal..* 2015.12; 21(6); 1523-1529
30. Marcelo Giannini, Tomohiro Takagaki, Renata Bacelar-Sá, Paulo Moreira Vermelho, Gláucia Maria Bovi Ambrosano, Alireza Sadr, Toru Nikaido, Junji Tagami. Influence of resin coating on bond strength of self-adhesive resin cements to dentin. *Dent Mater J.* 2015.12; 34(6); 822-827
31. Nagai S, Otsuki M, Sadr A, Shimada Y, Hayashi J, Tagami J, Sumi Y. Effect of erbium-doped: yttrium-aluminum-garnet laser preparation on resin-cavity interface using a universal adhesive evaluated by swept source optical coherence tomography *Asian Pac J Dent.* 2015.12; 15(2); 41-50

[Misc]

1. Toru Nikaido, Go Inoue, Tomohiro Takagaki, Rena Takahashi, Alireza Sadr, Junji Tagami. . Resin Coating Technique for Protection of Pulp and Increasing Bonding in Indirect Restoration. *Curr Oral Health Rep.* 2015; 2(2); 81-86
2. Yasushi Shimada, Alireza Sadr, Yasunori Sumi, Junji Tagami. Application of Optical Coherence Tomography (OCT) for Diagnosis of Caries, Cracks, and Defects of Restorations. *Curr Oral Health Rep.* 2015; 2(2); 73-80

3. Marcelo Giannini, Patrícia Makishi, Ana Paula Almeida Ayres, Paulo Moreira Vermelho, Bruna Marin Fronza, Toru Nikaido, Junji Tagami. Self-etch adhesive systems: a literature review. *Braz Dent J.* 2015.01; 26(1); 3-10
4. Sahar J Khunkar, Sachiko Utaka, Ilnaz Hariri, Alireza Sadr, Masaomi Ikeda, Syozi Nakashima, Toru Nikaido, Junji Tagami. Formation and characterization of hypermineralized zone beneath dentine lesion body induced by topical fluoride in-vitro. *Arch. Oral Biol.* 2015.04; 60(4); 574-581
5. Yuichi Kitasako. Dental Erosion: Clinical appearance and Management 2015.04; 7(2); 142-147

[Conference Activities & Talks]

1. Kong K, Islam MS, Nassar M, Hiraishi N, Otsuki M, Yiu CK, Tagami J. Effect of Phytic Acid on the Stability of Demineralized Dentin . 2015.01 Bangkok
2. Keiichi Hosaka. Esthetic and functional composite restorations -material selection and technique-. 9th Iranian General Dentists Association Congress 2015.01.15 Tehran
3. Sadr Alireza, Keiichi Hosaka. Science meets practice. 9th Iranian General Dentists Association Congress 2015.01.15 Tehran
4. Keiichi Hosaka. “From Fillings toward Restorations” Great Potentials of Direct Composite Restorations. 9th Iranian General Dentists Association Congress 2015.01.16 Tehran
5. Otsuki M. Caries diagnosis for minimal invasive dentistry. The 1st Interdisciplinary Oral Science International Symposium, BK-Korea21 2015.01.16 Seoul, Republic of Korea
6. Yuan Zhou, Yasushi Shimada . Assessment of Biofilm-induced Enamel and Dentin Demineralization around Composite Restoration by Swept Source Optical Coherence Tomography. The 6th International Congress on Adhesive Dentistry 2015.01.30 Bangkok, Thailand
7. Ueno T, Shimada Y, Matin K, Alireza S, Tagami J, Sumi Y. Optical evaluation of enamel and dentin demineralization by cariogenic biofilm using SS-OCT. 6th IAD 2015.01.31 Bangkok, Thailand
8. Zhou Y, Shimada Y, Matin K, Sadr A, Tagami J, Sumi Y. Assessment of biofilm-induced enamel and dentin demineralization around composite restoration by swept source optical coherence tomography (SS-OCT). 6th International Congress on Adhesive Dentistry 2015.01.31 Bangkok, Thailand
9. Nikaido T. Hosaka K., Kubo S., Maseki T., Rikuta A., Sasazaki H., Satoh K, Shinkai K., Uno S., Yamamoto T., Yoshikawa K., Yatani H., Momoi Y.. Three-year Evaluation of Direct Composite Restorations in a Multicenter Prospective Trial.. 6th IAD 2015.01.31 Bangkok
10. Makishi P, Thitthaweerat S, Sadr A, Shimada Y, Giannini M, Tagami J, Sumi Y.. 3D Leakage Pathway and Bond Strength of Current Adhesive Systems in Class-I Cavity.. The 6th International Congress of Adhesive Dentistry 2015.01.31 Bangkok, Thailand
11. Inoue G, Mashiko R, Atomura J, Tagami J. Morphological Assessment of the Effect of Calcium-Containing Primer System. 6th International congress on Adhesive Dentistry 2015.01.31 Bangkok, Thailand
12. Hayashi J, Sadr A, Espigares J, Shimada Y, Tagami J, Sumi Y. Gap Formation during Placement of Bulk-fill Composites in Deep Cavities. 2015.01.31
13. Bista Baba, Nakashima S, Nikaido T, Sadr A, Takagaki T, Tagami J. Adsorption Behavior of Adhesive Functional Monomer MDP to Apatite Surface at Neutral pH. the 6th International Congress on Adhesive Dentistry 2015.02.01
14. Otsuki M. Qray in Clinical Dentistry. Japanese Conference on Qray (JCQ) 2015.02.15 Tokyo, Japan
15. Takaaki Sato, Tomohiro Takagaki, Naoko Matsui, Hidenori Hamba, Toru Nikaido, Alireza Sadr, Nobuhiko Yui, Junji Tagami . Morphological and mechanical evaluation of enamel-adhesive interface of self-etch systems. the IADR/AADR/CADR General Session 2015.03
16. Rui Guan, Naoko Matsui, Takaaki Sato, Tomohiro Takagaki, Alireza Sadr, Toru Nikaido, Junji Tagami . Morphological Characteristics of ABRZ of Newly-developed Dentin Adhesives . the IADR/AADR/CADR General Session 2015.03

17. Horie K, Shimada Y, Matin K, Sadr A, Tagami J, Sumi Y. Monitoring of cariogenic demineralization at adhesive interface using SS-OCT. IADR General Session 2015.03.01 Boston, USA
18. Tezuka H, Shimada Y, Matin K, Sadr A, Tagami J, Sumi Y. Assessment of cervical tooth demineralization induced by *Streptococcus mutans* using SS-OCT. IADR General Session 2015.03.01 Boston, USA
19. Junichi SHINAGAWA, Go INOUE, Toru NIKAIDO, Junji TAGAMI. Early Bond Strengths of 4-META/MMA-TBB Cements to CAD/CAM Resin Composite. IADR General Session 2015 2015.03.11 Boston, Mass., USA
20. T. Yoshikawa, M. Morigami, A. Sadr . Effects of Light-Curing Method and Resin Composite Composition on Composite/Wall-Adaptation. 93rd, IADR 2015.03.11 Boston
21. Tsuda Y, Kitasako Y, Sadr A, Nakashima S, Tagami J. Toothbrushing timing after acidic drinks affects enamel loss in-situ. 93rd General Session & Exhibition of the IADR 2015.03.12 Boston, USA
22. Sarina Koike, Hidenori Hamba, Kazuo Shimazaki, Junji Tagami, Takashi Ono. Inhibitory demineralization around brackets by fluoride releasing adhesives using micro-CT. 93rd General Session & Exhibition of the IADR 2015.03.12
23. Hidenori Hamba, Alireza Sadr, Shoji Nakashima, Toru Nikaido, Junji Tagami. Micro-CT Mineral Density and Nanoindentation Mechanical Properties in Carious Dentin. 93rd General Session & Exhibition of the IADR 2015.03.12
24. Tsuda Y, Kitasako Y, Sadr A, Nakashima S, Tagami J. Toothbrushing timing after acidic drinks affects enamel loss in situ. 93rd General Session & Exhibition of the IADR 2015.03.12 Boston, USA
25. Takaaki Sato; Tomohiro Takagaki; Naoko Matsui; Hidenori Hamba, Toru Nikaido, Alireza Sadr, Nobuhiko Yui, Junji Tagami. Morphological and mechanical evaluation of enamel-adhesive interface of self-etch systems. 93rd General Session & Exhibition of the IADR 2015.03.12
26. Mamanee T, Takahashi M, Nakajima M, Tagami J. Bond Strength Durability of Self-etch Adhesives to Combined Enamel-dentin-composite Substrates. 93rd IADR 2015.03.12
27. Turkistani A, Sadr A, Shimada Y, Nakashima S, Tagami J, Sumi Y.. Effect of adhesives on caries lesion progress around composite restorations. IADR General Session 2015.03.14 Boston, USA
28. Noda Yukari, Takahashi Masahiro, mamane Teerapong, Nakajima Masatoshi, Ikeda Masaomi, Takagaki Tomohiro, Hosaka Keiichi, Tagami Junji. Effect of universal primer/thermocycling on bond strength to ceramics. American Association for Dental Research 2015.03.16 Los Angeles
29. Hiraishi N, Otsuki M, Tagami J. Influence of HEMA on Monomer-collagen Interaction Studied by NMR. . IADR general session 2015.03.21 Boston
30. Junji Tagami. Esthetic restoration with innovative technology. Russian Ministry of Health and Welfare Seminar 2015.04.12 Indigo Hotel(St.Petersburg)
31. Junji Tagami. Esthetic restoration with innovative technology . Russian Ministry of Health and Welfare Seminar 2015.04.14 Russian dental maxillofacial surgery central laboratory(Moscow)
32. Noriko Hiraishi, Masayuki Otsuki, Daisaku Kaneko, Junji Tagami. In vitro Cytotoxicity of Mussel-Mimetic Bio-adhesive Polymers in Comparison with Conventional Dental Materials. . The 4th Tri-University Consortium on Oral Science and Education 2015.05.21 Bangkok
33. Junji Tagami. Harmonization in Dental Education in Asia:SEAN-Japan information Sharing. ASEAN Dental Forum:Cooperation on Establishment of Common Competencies for ASEAN Dentists 2015.05.22 Than Pu Ying Petchara Auditorium
34. Junji Tagami. Optical coherence tomograph:Application to detection of caries,cracks and defects of restoration. The 10th IDCMR Congress(International Dental Collaboration of the Mekong River Region) 2015.06.08 Mahidol University, Faculty of Dentistry
35. Naoko Matsui, Tomohiro Takagaki, Ji-Hun Seo, Toru Nikaido, Nobuhiko Yui, Junji Tagami. The relationship between the concentration of MDP of bonding and penetration depth into dentin.. The 142nd meeting of Japanese Society for Conservative Dentistry 2015.06.09

36. Akifumi Takahashi, Tomohiro Takagaki, Takaaki Sato, Masaomi Ikeda, Toru Nikaido, Junji Tagami. The effect of phosphoric acid etching on the treatment of zirconium ceramics. 2015.06.09
37. Naoko Matsui. A confocal fluorescence microscopic analysis on the effect of the MDP concentration in bonding agent. the 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25
38. TAGUCHI Keita, HATAYAMA Takashi, SATO Kento, YOSHIMINE Nariaki, TAKAHASHI Masahiro, HOSAKA Keiichi, NAKAJIMA Masatoshi, TAGAMI Junji. The effect of warm air-blowing on the microtensile bond strength of one-step self-etch adhesive systems to root canal dentin. 2015.06.25
39. Aramaki O, Kawashima N, Shimada Y, Okiji T, Tagami J. The 3D analysis of Iba1+ macrophages in human dental pulp by whole mount immunostaining. The 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25 Kitakyushu
40. ARAOKA Daisuke, SATO Kento, TAKAHASHI Masahiro, IKEDA Masaomi, HOSAKA Keiichi, NAKAJIMA Masatoshi, TAGAMI Junji. The effect of light curing of universal primer on the bond strengths of dual cure resin cement. 2015.06.25 Kitakyushu
41. Yasushi Shimada, Ikumi Sanda, Hiroki Tezuka, Kei Horie, Oto Aramaki, Junji Tagami . Effect of application time of a newly developed one-step selfetch adhesive on microshear bond strength. 2015.06.25
42. Luong Dao Minh Nguyet, Yasushi Shimada, Alireza Sadr, Junji Tagami, Yasunori Sumi. Effect of microtensile bond strength crosshead speed and flowable composite on bond test results using optical coherence tomography. The 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25 Kitakyushu
43. Atsuko Tagami, Rena Takahashi, Toru Nikaido, Junji Tagami. Effect of curing mode and restoration thickness on tensile bond strength of a dual-cure resin cement to dentin. 7th TMDU International Summer Program (ISP2015) 2015.08 Tokyo, Japan
44. N. Hiraishi, M. Otsuki, J. Tagami, I Morio. 44Ca doped pH-cycling study on Dentin Remineralization by Isotope Microscopy. IADR-SEA 2015.08.13 Bali, Indonesia
45. Junji Tagami. Inheritance and evolution in cariology and operative dentistry. Honorary doctorate memorial lecture 2015.09.04 Mahidol University, Faculty of Dentistry
46. Yasushi Shimada. Application of bacteriostatic dental materials for caries management. Annual Conference of Academic of Operative Dentistry of the Republic of China 2015.09.06 Taipei
47. Yasushi Shimada. Application of swept-source optical coherence tomography (SS-OCT) for diagnosis of caries, cracks and defects of restorations . Annual Conference of Academic of Operative Dentistry of the Republic of China 2015.09.06 Taipei
48. Junji Tagami. Long term stability of Bonded Interfaces. IAAD, International Academy for adhesive Dentistry, first Biennial meeting 2015.09.11 Renaissance Orland
49. Junji Tagami. PHI Leader Ship Course. PHI Leader Ship Course 2015.09.20 Boston
50. T. Yoshikawa, M. Morigami, A. Sadr . Effects of Light-Curing Method and Bonding on Different-Type Composite/Wall Adaptation. Academy of dental materials 2015.10.07
51. Nakajima M, Takahashi M, Mamanee T, Thitthaweerat S, Seki N, Hosaka K, Tagami J. Bond Strengths of Dual-Cure Adhesive Resin Cements to Dentin. Academy of Dental Materials 2015 Annual Meeting 2015.10.08 Lahaina, Maui, HI
52. I.Wada, Y. Shimada, A.Sadr, S.Nakashima, J. Tagami, Y Sumi. Assessment of non carious cervical lesion using swept-source optical coherence tomography. The Academy of Dental Materials Annual Meeting 2015.10.08
53. Yasushi Shimada, Juri Hayashi, Oto Aramaki, Ikumi Sanda, Alireza Sadr, Yasunori Sumi, Junji Tagami. 3D assessment of dental caries using swept-source optical coherence tomography. The Academy of Dental Materials Annual Meeting 2015.10.08
54. Aramaki O, Takahashi R, Wada T, Uo M, Tagami J. Bonding Property of Resin Cement to Composite Resin Crown. Academy of Dental Materials 2015.10.08 Maui

55. Hatayama T, Nakajima M, Hosaka K, Kainose K, Wakabayashi N, Tagami J. Stress Distribution in Resin-Core Build-Up Tooth under Different Load Directions. Academy of Dental Materials 2015 Annual Meeting 2015.10.08 Lahaina, Maui, HI
56. CR will change Clinical future - For good composite resin restoration -. 2015.11.01
57. WADA Ikumi, SHIMADA Yasushi, SADR Alireza, NAKASHIMA Syozi, TAGAMI Junji, SUMI Yasunori. Cross-sectional assessment of Non Carious Cervical Lesion using SS-OCT. 2015.11.13
58. Junji Tagami. Combined restoration with self-etching Adhesive and Flowable composite resin . Composite resin bonding restoration technique forum 2015.11.14 Beijing
59. Joun A.Sorensen . New research frontiers in Material Systems and Digital Technology at the University of Washington. Oral pathology Society special meeting 2015.11.17 TMDU
60. ARAOKA Daisuke, TAKAHASHI Masahiro, HOSAKA Keiichi, OTSUKI Masayuki, TAGAMI Junji. The effect of various food to tooth discoloration.. 2015.11.22 Tokyo
61. ARAOKA Daisuke, TAKAHASHI Masahiro, HOSAKA Keiichi, OTSUKI Masayuki, TAGAMI Junji. The effect of various food to tooth discoloration.. 2015.11.22 Tokyo
62. ARAOKA Daisuke, TAKAHASHI Masahiro, HOSAKA Keiichi, OTSUKI Masayuki, TAGAMI Junji. The effect of various food to tooth discoloration.. 2015.11.22 Tokyo
63. Cariology and Operative Dentistry-Summary of 20 years-. 20th anniversary lecture of the Prof Tagami's Cariology and Operative Dentistry 2015.12.10
64. Toru Nikaido. Clinical application of advanced adhesive materials and technology. Special lecture program, Faculty of Dentistry, Masaryk University 2015.12.14 Brno, Czech Republic
65. Yasushi Shimada. Assessment of dental caries and adhesive restoration using optical coherence tomography. 34th congress of Japanese Society for Adhesive Dentistry 2015.12.20 Tokyo
66. Adhesive dentistry :its science and clinical application . 2015.12.29 Yangon

[Awards & Honors]

1. The third place winner for presentation., International Adhesive Dentistry, 2015.01
2. Outstanding Poster Award, First Prize Poster Award Competition, The 6th International Congress on Adhesive Dentistry, 2015.02
3. Complimentary Award for Outstanding Research, 6th International Adhesive Dentistry, 2015.02
4. Research Category Awards (Cariology and Mineralised Tissues), IADR-SEA , 2015.08
5. Honorary doctorate, Mahidol University, Faculty of Dentistry, 2015.09

Fixed Prosthodontics

Professor
Hiroyuki MIURA

Associate Professor
Kenichi YOSHIDA

Junior Associate Professor
Daizo OKADA
Wataru KOMADA

Assistant Professor
Chiharu SHIN
Shiho OTAKE
Reiko OGURA
Satoshi OMORI
Reina NEMOTO

Attending Staff
Tasuku INAGAKI
Yoji UEDA
Rie FUJITA
Tazuko MAKIYAMA
Ayaka NODA
Hiroyuki OKAMOTO
Miho SATO
Kyoshi MATSUKAWA
Fujino OSHIMA
Yoko ISHIKAWA
Mariko KUBO
Kazuhisa FUJITA
Hideto MATSUI
Risa YAMADA
Luo Siyang
Michika MINAMIFUCHI
Ayana URABA
Izumi FUKUMOTO
Bakhit Mohammed Yassin M
Paisankobrit Vibul
Rana Asano
Saika Shirasaki
Mina Takita
Shiro Rikitoku
Kai Shibakuchi

(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-Br 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. Inoue M, Nakajima H, Akiba N, Hibino Y, Nagasawa Y, Sumi Y, Minakuchi S. Influence of monomer content on the viscoelasticity, water sorption and solubility of experimental fluorinated soft lining materials Dental Materials Journal. 2015.02; 34(1); 70-77
2. Tamura A, Fukumoto I, Yui N, Matsumura M, Miura H.. Increasing the repeating units of ethylene glycol-based dimethacrylates directed toward reduced oxidative stress and co-stimulatory factors expression in human monocytic cells. J Biomed Mater Res A. 2015.03; 103(3); 1060-1066
3. Miho Sato, Hitoshi Kato, Daizo Okada, Reiko Ogura, Kyoshi Matsukawa, Hiroyuki Miura. Investigation of the location of the Main Occluding Area in upper and lower dentitions The Journal of Japanese Society of Stomatognathic Function. 2015.09; 22(1); 14-22
4. Okamoto H, Tsutsumi Y, Watanabe M, Yamakage K, Ashida M, Chen P, Doi H, Miura H, Matsumura M, Hanawa T. Evaluation of release and accumulation of metal ions from titanium and nickel by accelerated dissolution test in simulated body environments Electrochemistry. 2015.12; 83(12); 1048-1052

[Conference Activities & Talks]

1. Sato A, Ogura R, Sato M, Kato H, Okada D, and Miura H. Occlusal sensation and bite force on the main occluding area.. 93rd General Session & Exhibition of the IADR 2015.03.11
2. Minamifuchi M, Otake S, Uraba A, Miura H. Bond Strengths of Cements to a New Cements to a New Ceramic-based Restorative Material. 93rd General Session & Exhibition of the IADR 2015.03.12
3. Uraba A, Otake S, Minamifuchi M, Miura H. Tensile Bond Strengths of New Resin Cement to bovine teeth. The 124th scientific meeting of Japan Prosthodontic Society 2015.05.30 Saitama
4. Nozaki K, Fujita K, Ebe N, Miura H, Yamashita K, Nagai A. Bioresorbable and osteoconductive properties of porous carbonated apatite implanted in cortical and cancellous bone tissues. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09
5. Iwata N, Nozaki K, Miura H, Yamashita K, Nagai A. The effect of titania nanotube surfaces on osteoblast behavior. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09
6. Nozaki K, Fujita K, Yamashita K, Miura H, Nagai A. Evaluation of bone formation and degradation of porous carbonated apatite block. 2015.10.03
7. Luo S, Okada D., Mohammed Y.B., Matsukawa K., Shin C., Ogura R., Miura H. Stress Distribution in Cement with Different Post and Core System.. The 63rd JADR Annual Meeting & Exhibition 2015.10.31 Fukuoka, Japan
8. Okada D, Luo S, Mohammed YB, Matsukawa K, Shin C, Ogura R, Miura H.. Stress Distribution in Crowns with Different Crown Materials and Thickness.. The 63rd JADR Annual Meeting & Exhibition 2015.10.31 Fukuoka, Japan
9. Bakhit M Y, Okada D, Luo S, Matsukawa K. Shin C, Ogura R, Miura H. The Stress Distribution within Dentin with Different Crown Materials.. The 63rd JADR Annual Meeting & Exhibition 2015.10.31 Fukuoka, Japan
10. Oshima F, Okada D, Ogura R, Shin C, Miura H. Stress distribution in root restored with different post and core systems.. 2015.11.29 Tokyo, Japan
11. Natsuko Iwata, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. The effect of titania nanotube surfaces on osteoblast behavior. 15th Asian Bioceramics Symposium 2015.12.10
12. Risa Yamada, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita and Akiko Nagai. Study on antimicrobial activity by silver doped yttria-stabilized zirconia. 15th Asian Bioceramics Symposium 2015.12.10

13. Kazuhisa Fujita, Kosuke Nozaki, Kimihiro Yamashita, Hiroyuki Miura, and Akiko Nagai. Alkaline Phosphatase Activity of Periodontal Ligament Cell on Hydroxyl- and Carbonated-Apatites. 15th Asian Bioceramics Symposium 2015.12.10

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) Properties of oral tissue-derived mesenchymal stem cells/ Horizon of dental pulp regeneration
- 2) Crosstalk between pulpal inflammation and regeneration
- 3) Evaluation of newly developed endodontic sealers
- 4) Evaluation of endodontic technique using computational fluid dynamics(CFD)

- 5) Application of laser to endodontics
- 6) Application of optical coherence tomography
- 7) Analysis of nickel-titanium endodontic instruments
- 8) Electrophysiological approach to cell-to-cell couplings between odontoblasts
- 9) Diffusion through enamel and dentin
- 10) Lymphangiogenesis in the dental pulp
- 11) Influence of sympathetic nervous control on dentinogenesis of odontoblasts
- 12) Neuro-scientific research for dental pain
- 13) Diagnosis using CBCT & Diagnosis of vertical root fractures by analyzing reconstructed three-dimensional models obtained from CBCT images

(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. Ohsumi T, Takenaka S, Wakamatsu R, Sakaue Y, Narisawa N, Senpuku H, Ohshima H, Terao Y, Okiji T. Residual structure of *Streptococcus mutans* biofilm following complete disinfection favors secondary bacterial adhesion and biofilm re-development PLoS One. 2015.01; 10(1); e0116647
2. Han L, Kodama S, Okiji T. Evaluation of calcium-releasing and apatite-forming abilities of fast-setting calcium silicate-based endodontic materials. International Endodontic Journal. 2015.02; 48(2); 124-130
3. Ebihara A, Iino Y, Yoshioka T, Hanada T, Sunakawa M, Sumi Y, Suda H. Apices of maxillary premolars observed by swept source optical coherence tomography. SPIE Lasers in Dentistry XXI. 2015.02; 9306; 93060J-93060J-5

4. Wadachi R, Yoshioka T, Harada N, Ebihara A, Suda H. The present situation and problems of tooth fracture -the present demands of dental practice revealed through a survey of new patients of an endodontic outpatient clinic- The Japanese Journal of Conservative Dentistry. 2015.02; 58(1); 1-9
5. Han L, Okiji T. Dentinal tubule-occluding ability of S-PRG filler extract solutions on artificially demineralized bovine dentin Japanese Journal of Conservative Dentistry. 2015.02; 58(1); 17-25
6. Iino Y, Yoshioka T, Hanada T, Ebihara A, Sunakawa M, Sumi Y, Suda H. Observation of the pulp horn by swept source optical coherence tomography and cone beam computed tomography. SPIE Lasers in Dentistry XXI. 2015.02; 9306; 93060I-93060I-5
7. Watanabe H, Kazama R, Asai T, Kanaya F, Ishizaki H, Fukushima M, Okiji T. Efficiency of the dual-cured resin cement polymerization induced by high-intensity LED curing units through ceramic material. Operative Dentistry. 2015.04; 40(2); 153-162
8. Han L, Okiji T. Dentin tubule occluding ability of dentin desensitizers. American Journal of Dentistry. 2015.04; 28(2); 90-94
9. Zhou M, Kawashima N, Suzuki N, Yamamoto M, Ohnishi K, Katsube K, Tanabe H, Kudo A, Saito M, Suda H. Periostin is a negative regulator of mineralization in the dental pulp tissue. Odontology. 2015.05; 103(2); 152-159
10. Shigetani Y, Yoshida K, Kuratate M, Takei E, Yoshida N, Yamanaka Y, Ohshima H, Okiji T. Temporospacial localization of dentine matrix protein 1 following direct pulp capping with calcium hydroxide in rat molars. International Endodontic Journal. 2015.06; 48(6); 573-581
11. Yoshida N, Yoshida K, Ohkura N, Takei E, Edanami N, Oda Y, Hosoya A, Nakamura H, Okiji T. Correlation between fibrillin-1 degradation and mRNA downregulation and myofibroblast differentiation in cultured human dental pulp tissue. Journal of Histochemistry & Cytochemistry. 2015.06; 63(6); 438-448
12. Gu J, Ikeda H, Suda H. Sympathetic regulation of tertiary dentinogenesis via beta-2 adrenergic receptor on rat odontoblasts Journal of Endodontics. 2015.07; 41(7); 1056-1060
13. Sueyama Y, Kaneko T, Ito T, Okiji T. Effects of lipopolysaccharide-stimulation on CD146 mRNA expression in dental pulp stem cells and dental pulp tissues Japanese Journal of Conservative Dentistry. 2015.08; 58(4); 282-289
14. Suzuki N, Takimoto K, Kawashima N. Cathepsin K inhibitor regulates inflammation and bone destruction in experimentally induced rat periapical lesions. Journal of Endodontics. 2015.09; 41(9); 1474-1479
15. Jamleh A, Komabayashi T, Ebihara A, Nassar M, Watanabe S, Yoshioka T, Miyara M, Suda H. Root surface strain during canal shaping and its influence on apical microcrack development: a preliminary investigation. International Endodontic Journal. 2015.12; 48(12); 1103-1111
16. Watanabe S, Okiji T. Application of Er:YAG laser for root-end cavity preparation in intentional replantation: a case report Journal of Japanese Society for Laser Dentistry. 2015.12; 26(3); 130-135

[Books etc]

1. Sunakawa M, Suda H. Physiological function of dentin/pulp complex and periodontal membrane. Okiji T, Suda H, Nakamura H ed. Textbook of Endodontics. Nagasueshoten, 2015.04

[Misc]

1. Okiji T. Physicochemical and biological properties of mineral trioxide aggregate as a pulp capping material The Journal of the Stomatological Society, Japan. 2015.11; 82(3); 88-93
2. Ebihara A. Application of OCT to endodontics DE. 2015.11; 195; 425-428
3. Komabayashi T, Ebihara A, Aoki A. The use of lasers for direct pulp capping. Journal of Oral Science. 2015.12; 57(4); 277-286

[Conference Activities & Talks]

1. Watanabe H, Kazama R, Asai T, Ishizaki H, Fukushima M, Okiji T. Effects of irradiation distance and thickness of machinable ceramic on the irradiance of LED Curing-units. The 6th International Congress on Adhesive Dentistry 2015.01.30 Bangkok, Thailand
2. Watanabe S, Hanada T, Kobayashi C, and Suda H. Root canal irrigation activated by new diode laser system and Er:YAG laser. Academy of Laser Dentistry conference 2015.02.07 Palm Springs, CA
3. Ebihara A, Iino Y, Yoshioka Y, Hanada T, Sunakawa M, Sumi Y, Suda H. Apices of maxillary premolars observed by swept source optical coherence tomography. SPIE 2015.02.08 San Francisco, CA
4. Iino Y, Yoshioka T, Hanada T, Ebihara A, Sunakawa M, Sumi M, Suda H. Observation of the pulp horn by swept source optical coherence tomography and cone beam computed tomography. SPIE 2015.02.08 San Francisco, CA
5. Yao K, Watanabe S, Ebihara A, Kobayashi C. Apical extrusion of root canal irrigants during root canal irrigation activated by Diode Laser and Er:YAG Laser. Academy of Laser Dentistry Conference 2015.02.09 Palm Springs, CA
6. Hashimoto K, Kawashima N, Bakhit A, Yamamoto M, Koizumi Y, Takahashi S, Ohi C, Suzuki N. ALPase activity of pulp cells on EDTA and NaClO-treated dentin. 93rd General Session and Exhibition of the IADR 2015.03.11 Boston, MA
7. Kawashima N, Hashimoto K, Bakhit A, Yamamoto M, Koizumi Y, Takahashi S, Ohi C, Suzuki N. Mineralizing properties of gingiva-derived mesenchymal stem cells cultured in 3D-condition. 93rd General Session and Exhibition of the IADR 2015.03.11 Boston, MA
8. Ohkura N, Ohkura M, Yoshiba N, Yoshiba K, Ida-Yonemochi H, Ohshima H, Okiji T. Immunolocalization and gene-expression of multidrug resistance-associated protein-4 in human pulp. 93rd General Session and Exhibition of the IADR 2015.03.11 Boston, MA
9. Yoshiba N, Yoshiba K, Ohkura N, Takei E, Edanami N, Oda Y, Hosoya A, Nakamura H, Okiji T. Fibrillin-1 degradation and myofibroblasts induction in cultured human dental pulp. 93rd General Session and Exhibition of the IADR 2015.03.11 Boston, MA
10. Yoshiba K, Takei E, Edanami N, Hinata G, Yoshiba N, Shigetani Y, Okiji T. Reparative dentinogenesis after pulp-capping with a light-cured calcium silicate-based material. 93rd General Session and Exhibition of the IADR 2015.03.11 Boston, MA
11. Takei E, Shigetani Y, Yoshiba K, Hinata G, Yoshiba N, Okiji T. M2-macrophage accumulation after pulpotomy with a light-cured resin-modified calcium-silicate material. 93rd General Session and Exhibition of the IADR 2015.03.11 Boston, MA
12. Ohkura M, Ohkura N, Yoshiba N, Yoshiba K, Ida-Yonemochi H, Ohshima H, Saito I, Okiji T. Prostaglandin I2 receptor expression in orthodontic force-applied rat dental pulp. 93rd General Session and Exhibition of the IADR 2015.03.11 Boston, MA
13. Gu J, Ikeda H, Suda H. Immunohistochemical analysis of beta-2 adrenergic receptor on odontoblasts and its association with tertiary dentin formation. 93rd General Session and Exhibition of the IADR 2015.03.13 Boston, MA
14. Kawashima N. Intracanal medicament. The 18th APEC congress 2015.04.08 Amman, Jordan
15. Han L, Yamamoto S, Okiji T. Biomineralization of calcium silicate-based endodontics materias: Effect of an extract solution on demineralized dentin surface. The 65th General Session of the Japanese Society for Dental Materials and Devices 2015.04.11 Sendai
16. Uraba S, Komatsu K, Ebihara A, Ohbayashi N, Okiji T. Detection of apical periodontitis using cone-beam computed tomography and periapical radiography. The 4th Tri-University Consortium 2015.05.20
17. Kawamura J, Kaneko T, Yamanaka Y, Ito T, Sunakawa M, Okiji T. Immunohistochemical and gene-expression analysis of pulp injury-induced glial cell activation in the rat thalamus. The 4th Tri-University Consortium 2015.05.20 Thai

18. Okiji T. Root canal preparation: Current concepts and techniques. Health Science University of Mongolia 2015.06.02 Ulaanbaator
19. Okiji T. Root canal preparation: Current concepts and techniques. Ulaanbaator Dental Center 2015.06.03 Ulaanbaator
20. Hinata G, Yoshiba K, Edanami N, Takei E, Shigetani Y, Yoshiba N, Okiji T. Immunohistochemical analysis of rat subcutaneous tissue reactions to calcium silicate-based pulp capping materials. The 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25 Kitakyushu
21. Ito T, Kaneko T, Yamanaka Y, Sueyama Y, Yoshiba K, Okiji T. Dental pulp tissue engineering using three-dimensional scaffolds with stem cells in rat molars. The 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25 Kitakyushu
22. 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. The 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25 Kitakyushu
23. Aramaki O, Kawashima N, Shimada Y, Okiji T, Tagami J. The 3D analysis of Iba1+ macrophages in human dental pulp by whole mount immunostaining. The 142rd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25 Kitakyushu
24. Tazawa K, Ikeda H, Okiji T. Changes in lymphatic localization in the rat dental pulp after cavity preparation. The Japanese Society of Conservative Dentistry 2015.06.25 Kitakyushu, Fukuoka
25. Sueyama Y, Kaneko T, Ito T, Okiji T. Influence of lipopolysaccharide-stimulation on CD146 mRNA expression in dental pulp stem cells. The 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.26 Kitakyushu
26. Ebihara A. Save the teeth, current endodontics part 5. Kosaka seminar in 2015 2015.07.09 Tokyo
27. Kaneko T, Maeda T, Okiji T. Introduction of the use of dental operating microscope to preclinical practice and preliminary clinical practice of endodontics. The 34th Annual Meeting of the Japanese Dental Education Association 2015.07.10 Kagoshima
28. Kawamura J, Ebihara A, Wadachi R, Tsuruta J, Kinoshita A, Okiji T. Inflection of e-learning in the clinical clerkship -Part I: the introduction of the system-. 2015.07.10
29. Han L, Yamamoto S, Okiji T. Evaluation of in vitro bioactivity of a prototype calcium-silicate-based endodontic material. The 36th Annual Scientific Meeting of Japan Endodontic Association 2015.07.11 Yokohama
30. Kaneko T, Ito T, Sueyama Y, Okiji T. Engineering of the coronal dental pulp tissue using rat mesenchymal stem cells in rat molars. The 36th Annual Scientific Meeting of Japan Endodontic Association 2015.07.11 Yokohama
31. Hinata G, Yoshiba K, Han L, Edanami N, Takei E, Yoshiba N, Okiji T. Bioactivity of calcium silicate-based endodontic materials: Ultrastructure of the material surface after subcutaneous implantation in rats. The 36th Annual Scientific Meeting of Japan Endodontic Association 2015.07.11 Yokohama
32. Sueyama Y, Kaneko T, Ito T, Okiji T. Influence of lipopolysaccharide stimulation on CD146 and MAP1B mRNA expression in dental pulp stem cells. The 36th Annual Scientific Meeting of Japan Endodontic Association 2015.07.11 Yokohama
33. Ito T, Kaneko T, Sueyama Y, Okiji T. Cell proliferation and CD146 mRNA expression of rat mesenchymal stem cells stimulated by lipopolysaccharide. The 36th Annual Scientific Meeting of Japan Endodontic Association 2015.07.11 Yokohama
34. Ohkura N, Yoshiba N, Yoshiba K, Okiji T. Effect of prostaglandin EP4 receptor agonist on the expression of various genes in cultured human dental pulp tissue. The 36th Annual Scientific Meeting of Japan Endodontic Association 2015.07.11 Yokohama
35. Okiji T. Vital pulp therapy after traumatic tooth injury: Biological basis and current concepts. The 7th Congress of Asian International Association of Dental Traumatology 2015.07.11 Kitakyushu

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37. Nishijo M, Tokita D, Miyara K, Ebihara A, Okiji T. Shaping ability of a new automatic root canal preparation device in simulated root canals performed by students. The 36th Annual Scientific Meeting of JEA 2015.07.12 Tsurumi
38. Ikeda H. Odontoblasts as a functional syncytium. Pulp biology symposium in Queen's University Belfast 2015.09.03 Belfast, UK
39. Sueyama Y, Kaneko T, Ito T, Okiji T. Histochemical and gene expression analysis of lipopolysaccharide-stimulated stem cells in dental pulp. The 57th Symposium of the Society for Histochemistry 2015.09.05 Vienna, Austria
40. Ohkura N, Edanami N, Yoshida N, Yoshida K, Ida-Yonemochi H, Ohshima H, Okiji T. Immunohistochemical analysis of prostaglandin transporter in pulpotomized rat molars. The 57th Annual Meeting of Japanese Association for Oral Biology 2015.09.11 Niigata
41. Komatsu K, Abe Y, Toshihiko T, Ishimura H, Ebihara A, Suda H, Okiji T. Diagnosis of vertical root fractures by analyzing reconstructed three-dimensional models obtained from CBCT images: a case series. European Society of Endodontology 2015.09.19 Barcelona, Spain
42. Yamamoto M, Hashimoto K, Bakhit A, Suzuki N, Kawashima N, Okiji T. Effects of short-period three-dimensional (3D) spheroid culture for odonto-/osteoblastic differentiation of dental pulp cells. European Society of Endodontology 2015.09.19 Barcelona, Spain
43. Sueyama Y, Kaneko T, Ito T, Okiji T. Effects of lipopolysaccharide-stimulation on CD146 and MAP1B mRNA expression in dental pulp stem cells. FDI Annual World Dental Congress 2015.09.22 Bangkok, Thailand
44. Ito T, Sueyama Y, Kaneko T, Okiji T. Dental pulp tissue-engineering with stem cells in rat molars. FDI Annual World Dental Congress 2015.09.22 Bangkok, Thailand
45. Sueyama Y, Kaneko T, Ito T, Okiji T. Lipopolysaccharide-stimulation causes proliferation of stem cells of the dental pulp: Double immunoperoxidase labeling analysis. The 56th Meeting of the Japan Society for Histochemistry and Cytochemistry 2015.10.03 Osaka
46. Han L, Yamamoto S, Okiji T. Evaluation of newly-developed one-bottle one-step adhesive systems: Ultrastructural analysis of treated tooth surfaces and adhesive interfaces. The 66th General Session of the Japanese Society for Dental Materials and Devices 2015.10.03 Tokyo
47. Sueyama Y, Kaneko T, Ito T, Okiji T. Lipopolysaccharide-stimulated stem cells show increases of CD146 mRNA expression and cell proliferation. The 63rd Annual Meeting of Japanese Association for Dental Research 2015.10.30 Fukuoka
48. Kaneko T, Sueyama Y, Ito T, Okiji T. Macrophage-like cells are differentiated from stem cells in engineered pulp tissues. The 63rd Annual Meeting of Japanese Association for Dental Research 2015.10.30 Fukuoka
49. Nara K, Kawashima N, Hashimoto K, Bakhit A, Noda S, Okiji T. Expression of microRNA21 in a macrophage cell line and experimentally-induced rat pulpal inflammation. 2015.11.12
50. Watanabe S, Yao K, Satake K, Hongo T, Ebihara A, Kobayashi C, Okiji T. Pressure generated outside the apex during root canal irrigation activated by diode laser and Er:YAG laser. The 17th JSCD/KACD Joint-Scientific Meeting 2015.11.12 Tokyo
51. Bakhit A, Kawashima N, Hashimoto K, Noda S, Nara K, Okiji T. Cytotoxic effects of new calcium silicate-based sealers on an osteoblastic cell line. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.12 Tokyo
52. Hongo T, Watanabe S, Yao K, Satake K, Ebihara A, Kobayashi C, Okiji T. Kinetics of Vaporized Cavitation Bubbles during Root Canal Irrigation Activated by Diode Laser. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo

53. Wakamatsu R, Takenaka S, Ohsumi T, Sakaue Y, Okiji T. Penetration of sodium hypochlorite into dentinal tubules. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo
54. Ohkura N, Yoshiba N, Yoshiba K, Oda Y, Ida-Yonemochi H, Ohshima H, Okiji T. Effect of prostaglandin EP4 receptor agonist on cultured human dental pulp tissue. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo
55. Edanami N, Yoshiba K, Takei E, Hinata G, Takeuchi R, Tohma A, Shigetani Y, Yoshiba N, Okiji T. Hard tissue barrier formation after pulp capping with calcium silicate-based cements in rat molars. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo
56. Yamamoto S, Han L, Okiji T. Surface coating and dentinal tubule-occluding ability of s-prg filler extract solutions on ground human dentin. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo
57. Ito T, Kaneko T, Sueyama Y, Okiji T. Gene expression of DSPP and IL-6 in engineered coronal pulp tissues of rat molars. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo
58. Han L, Yamamoto S, Okiji T. Effect of acidic and alcoholic drinks on the surface ultrastructure of composite resins. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo
59. Hashimoto K, Kawashima N, Noda S, Nara K, Alam B, Saito M, Okiji T. Attachment and differentiation of dental papillae cells on sodium hypochlorite- and/or EDTA-treated dentin disks. 2015.11.13
60. Kawamura J, Kaneko T, Sunakawa M, Okiji T. Experimental Pulpitis Causes Activation of Glial Cells in the Rat Thalamus. 2015.11.13
61. Ohkura M, Ohkura N, Saito I, Okiji T. Expressional analysis of prostaglandin I₂ synthase and receptor in rat molar pulp during experimental tooth-movement. The 74th Annual Meeting of Japanese Orthodontic Society 2015.11.18 Fukuoka
62. Okiji T. Defence and repair mechanisms of the dentin/pulp complex. Dalian Medical University 2015.11.19 Dalian, China
63. Ikeda H. Transduction of innocuous pulpal sensation. Pulp biology symposium in Thailand 2015.12.28 Memorial Hall of University of Chiang Mai

Removable Partial Prosthodontics

Professor WAKABAYASHI Noriyuki

Associate Professor

FUEKI Kenji

Junior Associate Professor

UENO Takeshi

Assistant Professor

INUKAI Shusuke

Assistant Professor

KOHNO Eiko

Assistant Professor

MINAMI Ichiro

Assistant Professor

MURAKAMI Natsuko

Assistant Professor

WADA Junichiro

Assistant Professor

WADACHI Juro

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ARAI Yuuki

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HAYAMA Hironari

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HIRASAWA Masahiro

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INAGAWA Hideaki

Graduate Student

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Graduate Student

ISHIYAMA Hiroyuki

Graduate Student

KAJIMA Yuka

Graduate Student

KUMAGAI Hayato

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NABESHIMA Gen

Graduate Student

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Graduate Student

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Graduate Student
SATOKAWA Yuya
Graduate Student
SUZUKI Natsuki
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TAKAKUSAKI Kensuke
Graduate Student
TSUTSUMI Chiaki
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WATANABE Chie
Graduate Student
YAMAZAKI Toshiki
Graduate Student
YOGO Yoshiaki
Graduate Student
YOSHIHARA Chie
Dental Resident
TSUBOTA Yasuhiro
Dental Resident
KATSUKI Azusa
Dental Resident
SEKINISHI Takashi
Dental Resident
SHIOZAWA Maho
Dental Resident
TAKAICHI Atsushi
YATABE Masaru

(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 Biomaterials to Prosthodontics
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

Introduction to Clinical Dentistry

Tooth Carving

Observation and assistance at clinic term I and II

Basic Occlusal Reconstruction

Year 4

Research Project

Removable Partial Prosthodontics

Advanced knowledge and skill with occlusion

Years 5 and 6

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. Genki Kato, Yasuhiro Shimizu, Yuki Arai, Natsuki Suzuki, Yasutaka Sugamori, Miki Maeda, Mariko Takahashi, Yukihiko Tamura, Noriyuki Wakabayashi, Ramachandran Murali, Takashi Ono, Keiichi Ohya,

- Setsuko Mise-Omata, Kazuhiro Aoki. The inhibitory effects of a RANKL-binding peptide on articular and periarticular bone loss in a murine model of collagen-induced arthritis: a bone histomorphometric study. *Arthritis Res. Ther.* 2015; 17(1); 251
2. Yusuke Toyoshima, Noriyuki Wakabayashi. Load limit of mini-implants with reduced abutment height based on fatigue fracture resistance: experimental and finite element study. *Int J Oral Maxillofac Implants.* 2015.01; 30(1); e10-e16
3. Wada J, Fueki K, Yatabe M, Takahashi H, Wakabayashi N. A comparison of the fitting accuracy of thermoplastic denture base resins used in non-metal clasp dentures to a conventional heat-cured acrylic resin. *Acta Odontologica Scandinavica.* 2015.01; 73(1); 33-37
4. E Yoshida, K Fueki, N Wakabayashi. Influence of intra-oral sensory impairment by anaesthesia on food comminution and mixing in dentate subjects. *J Oral Rehabil.* 2015.01; 42(6); 401-406
5. Junichiro Wada, Masayuki Hideshima, Shunsuke Inukai, Hiroshi Matsuura, Noriyuki Wakabayashi. Influence of the Width and Cross-Sectional Shape of the Major Connector of Maxillary Dentures on the Accuracy of Speech Production. *Folia Phoniatrica et Logopaedica.* 2015.02; 66; 227-236
6. Shiozawa M, Takahashi H, Asakawa Y, Iwasaki N. Color stability of adhesive resin cements after immersion in coffee *Clinical Oral Investigations.* 2015.03; 19(2); 309-317
7. Wakabayashi N, Wada J. Structural factors affecting prosthodontic decision making in Japan. *Japanese Dental Science Review.* 2015.05; 51(4); 96-104
8. Keisuke Katayama, Ayako Mochizuki, Takafumi Kato, Minako Ikeda, Yasuha Ikawa, Shiro Nakamura, Kiyomi Nakayama, Noriyuki Wakabayashi, Kazuyoshi Baba, Tomio Inoue. Dark/light transition and vigilance states modulate jaw-closing muscle activity level in mice. *Neurosci. Res.* 2015.07; 101; 24-31
9. 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 oral health-related quality of life in patients with shortened dental arches: a multicentre study. *J Oral Rehabil.* 2015.09; 42(9); 701-708
10. Yuka Kajima, Atsushi Takaichi. Future Prospects of Zr-14nb Alloy as a Next-Generation Dental Prosthesis Material *Health Care Current Reviews.* 2015.09; 3(1); 137
11. Natsuki Suzuki, Kazuhiro Aoki, Petr Marcián, Libor Borák, Noriyuki Wakabayashi. A threshold of mechanical strain intensity for the direct activation of osteoblast function exists in a murine maxilla loading model. *Biomech Model Mechanobiol.* 2015.11; 14(71); 1-10
12. Chiaki Tsutsumi, Kazuo Takakuda, Noriyuki Wakabayashi. Reduction of *Candida* biofilm adhesion by incorporation of prereacted glass ionomer filler in denture base resin. *J Dent.* 2015.12; 44(1); 37-43

[Books etc]

1. Masaru Yatabe. *Non-metal Clasp Denture.* 2015 (ISBN : 978-4-7812-0437-6)
2. Masaru Yatabe. *Best Denture Design.* 2015 (ISBN : 978-4-8851-0317-9)
3. Ichiro Minami and Alex Wirianski. *Accelerometers: Principles, Structure and Applications.* (ISBN : 978-1-62808-128-2)

[Misc]

1. Noriyuki Wakabayashi. Flipped classroom as a strategy to enhance active learning *Kokubyo Gakkai Zasshi.* 2015.03; 82(1); 1-7

[Conference Activities & Talks]

1. Akimoto T, Ueno T, Tsutsumi Y, Doi H, Hanawa T, Wakabayashi N. The corrosion resistance of Ti-Zr binary alloy with compositional change. IADR (The International Association for Dental Research) 2015.03.11 Boston, USA
2. N. Murakami, T. Sekinishi, S. Inukai, N. Wakabayashi. Denture tooth thickness influences the fracture mode of denture base. 2015 IADR General Session & Exhibition 2015.03.13 Boston, Mass., USA
3. Yuka Kajima, Atsushi Takaichi, Tohru Yasue, Hisashi Doi, Hidekazu Takahashi, Takao Hanawa, Noriyuki Wakabayashi. Evaluation of the shear bond strength of dental porcelain to Zr-14Nb alloy with low magnetic susceptibility . TRI 4th university consortium 2015.05.20 Thailand
4. Junichiro Wada. Basic Study focused on Fitting Accuracy of Thermoplastic resin for Non-metal clasp denture. 4th TRI University Consortium 2015.05.20 Chulalongkorn University
5. Wakabayashi N. Recent challenges in mechanical stress analyses for optimization of restorative and prosthodontic biomaterials. The 4th Tri-University Consortium on Oral Science and Education 2015.05.20 Bangkok, Thailand
6. Kumagai H, Kohno E, Fueki K, Wakabayashi N. Risk Factors for Denture-Related Mucosal Pain in Removable Partial Denture Wearers. 2015.05.30
7. Wadachi J, Wakabayashi N. Utilization of E-learning to a partial denture prosthodontics model training course. Preparation by the contents even a smart device can use.. 2015.07.11
8. Takaichi A, Kajima Y, Nakamoto T, Ashida M, Doi H, Nomura N, Hanawa T, Takahashi H, Wakabayashi N. Fatigue resistance of Co-Cr-Mo alloy clasps fabricated by selective laser melting process.. 2015.10.03
9. Wakabayashi N. Future Perspectives of Dental Education and Research in Globalized Society. 80th Anniversary Celebration Ceremony of School of Stomatology, the Fourth Military Medical University 2015.10.17 Xi'an, China
10. Yasuha Nogawa, Ayako Mochizuki, Keisuke Katayama, Minako Ikeda, Yuka Abe, Shiro Nakamura, Kiyomi Nakayama, Masaaki Kiyomoto, Takafumi Kato, Kazuyoshi Baba, Noriyuki Wakabayashi, Tomio Inoue. The effects of citalopram on masseter and neck muscle activities in mice. Neuroscience 2015 2015.10.18 Chicago
11. Atsushi Takaichi. Anisotropy of fatigue strength of the clasp prepared by Selective Laser Melting. 2015.12.05
12. Kajima Y, Takaichi A, Nakamoto T, Kimura T, Ashida M, Doi H, Nomura N, Hanawa T, Takahashi H, Wakabayashi N. . Fatigue resistance of Co-Cr-Mo alloy clasps fabricated by selective laser melting process. 6th International Conference on Mechanics of Biomaterials and Tissues (ICMOBT) 2015.12.07 waikoloa, Hawaii, USA
13. Takaichi A, Kajima Y, Yasue T, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Evaluation of the shear bond strength of dental porcelain to Zr-14Nb alloy with low magnetic susceptibility . 6th International Conference on Mechanics of Biomaterials and Tissues 2015.12.08 Hawaii, USA

[Others]

1. A case rehabilitated with fixed bridge and clasp-retained removable partial dentures for a partially edentulous patient with cosmetic disturbance and severe periodontal disease, 2015.01
Ann Jpn Prosthodont Soc 7 : 73-76, 2015

Oral Implantology and Regenerative Dental Medicine

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Maho KON, Yuki DATE, Akiko FURUICHI, Takahiro NAKAMURA, 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. Hidemi Nakata, *Shinji Kuroda, Hisafumi Takushima, Shohei Kasugai. Prosthetic recovery utilizing residual dental implants: A case report involving a unilateral milled-bar-magnet attachment combination Journal of Dental Implants. 2015; 5(1); 82-86
2. Kuppusamy Maheswari, Jia Hao, Zayar Lin, Hidemi Nakata, Shohei Kasugai, *Shinji Kuroda. Cytokines Levels in Peri-implant Crevicular Fluid in The Initial Stages of Dental Implant Treatment - A Preliminary Clinical Study Journal of Oral Tissue Engineering. 2015;
3. Yukawa Ken, Tachikawa Noriko, Kasugai Shohei. Attitude Survey of Patients visited our Dental Implant Clinic with the difference of sex 2015;
4. Yamaguchi Y, Shiota M, Munakata M, Kasugai S and Ozeki M. Effect of implant design on primary stability using torque-time curves in artificial bone International Journal of Implant Dentistry. 2015; 1(21);
5. Fueki K, Igarashi Y, Maeda Y, Baba K, Koyano K, Sasaki K, Akagawa Y, Kuboki T, Kasugai S, Garrett N. Effect of prosthetic restoration on oral health-related quality of life in patients with shortened dental arches: a multicentre study. Journal of Oral Rehabilitation. 2015; 42(9); 701-708
6. J Hao, A Acharya, K Chen, J Chou, S Kasugai, N P Lang. Novel bioresorbable strontium hydroxyapatite membrane for guided bone regeneration. Clin Oral Implants Res. 2015.01; 26(1); 1-7

7. Warunee Pluemsakunthai, Bach Le, Shohei Kasugai. Effect of buccal gap distance on alveolar ridge alteration after immediate implant placement: a microcomputed tomographic and morphometric analysis in dogs. *Implant Dent.* 2015.02; 24(1); 70-76
8. Ken Yukawa, Noriko Tachikawa, Shohei Kasugai. Three-dimensional finite elemental analysis of bone stress near an implant placed at the border between mandible and fibular graft in mandibular reconstruction. *Open Journal of Regenerative Medicine.* 2015.11; 4; 35-45
9. Munemitsu Miyasaka, Hidemi Nakata, Jia Hao, You-kyoung Kim, Shohei Kasugai, *Shinji Kuroda. Low-intensity pulsed ultrasound stimulation enhances HSP90 and mineralized nodule formation in mouse calvaria derived osteoblasts *Tissue Engineering Part A.* 2015.12; 21(23, 24); 2829-2839
10. Kuppusamy M, Watanabe H, Kasugai S, Kuroda S. Effects of abutment removal and reconnection on inflammatory cytokine production around dental implants. *Implant Dentistry.* 2015.12; 24; 730-734
11. 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. Makoto Shiota. Different diagnosis and the treatment for peri-implant disease. 35th Myanmar Dental Conference 2015.01.08
2. Kasugai S. How to avoid and/or solve problems in dental implant treatment. Bangkok Implant Symposium 2015 2015.02.10 Askra Theater, Bangkok, Thailand
3. Makoto Shiota. 3D Diagnosis for Implant Surgery. WCUPS2015 2015.05.02
4. Makoto Shiota. Utility of Static Computer Guided Surgery for Implant Prosthesis. 7th Annual International Symposium of Advanced Protocols in Oral Implantology 2015.05.15
5. Manabu Kanazawa, Maiko Iwaki, Daisuke Sato, Yuri Omura, Anna Miyayasu, Shohei Kasugai, Shunsuke Minakuchi. Immediate Loading of Two-Implant Mandibular Overdentures: 3-year Prospective Study. 16th meeting of the International College of Prosthodontists 2015.09.17 Seoul, Korea
6. A Miyayasu, M Kanazawa, Y Omura, D Sato, S Kasugai, S Minakuchi. Immediately loaded mandibular two-implant overdentures: Cost analysis. The 16th International College of Prosthodontists Biennial Meeting 2015.09.17 Seoul, Korea
7. Miyahara T, Fuji M, Hagaguchi J, Fujimori T, Shiota M, Kasugai S. Extraction site management with apatite fiber material. Clinical study.. The 24th Annual Scientific Meeting of European Association for Osseointegration (EAO) 2015.09.24 Stockholmsmässan, Stockholm, Sweden
8. Htet M, Madi M, Zakaria O, Miyahara T, Wang X, Lin Z, Aoki K, Kasugai S. Peri-implantitis treatment with laser or titanium bur.. The 24th Annual Scientific Meeting of European Association for Osseointegration (EAO) 2015.09.24 Stockholmsmässan, Stockholm, Sweden
9. Nguyen VO N T, Hao J, Ohshima M, Kuroda S, Kasugai S. Tissue destruction and inflammatory progression of experimentally induced peri-implantitis in a novel murine model.. The 24th Annual Scientific Meeting of European Association for Osseointegration (EAO) 2015.09.24 Stockholmsmässan, Stockholm, Sweden
10. Wu S, Lin Z, Yamaguchi A, Kasugai S. The effects of periosteum removal on the osteocytes in mouse calvaria. . The 24th Annual Scientific Meeting of European Association for Osseointegration (EAO) 2015.09.24 Stockholmsmässan, Stockholm, Sweden
11. Wang X, Zakaria O, Madi M, Kasugai S. Induced vertical bone augmentation by sputtered hydroxyapatite coated mini titanium implants after dura mater elevation in rabbit calvarial model. . The 24th Annual Scientific Meeting of European Association for Osseointegration (EAO) 2015.09.24 Stockholmsmässan, Stockholm, Sweden
12. Makoto Shiota. Contemporary approach for overcoming the implant prosthetic complications. Korean Academy of Osseointegration 2015 Symposium 2015.10.11

13. Kasugai S. How to avoid problems in dental implant treatments.. The 18th ICOI Asia-Pacific Section Congress 2015.11.13 Angkor Miracle Resort & Spa, Seam Reap, Cambodia
14. Yukawa Ken,Tachikawa Noriko,Kasugai Shohei. Attitude Survey of Patients visited our Dental Implant Clinic with the difference of sex. 2015.11.28

Organic Biomaterials

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. J.-H. Seo, S. Kakinoki, T. Yamaoka, N. Yui.. Directing stem cell differentiation by changing the molecular mobility of supramolecular surfaces. *Advanced Healthcare Materials*. 2015; in press
2. J.-H. Seo, Y. Tsutsumi, A. Kobari, M. Shimojo, T. Hanawa, N. Yui.. Modulation of friction dynamics in water by changing the combination of the loop- and graft-type poly(ethylene glycol) surfaces *Soft Matter* . 2015; 11; 936-942
3. S. Kakinoki, J.-H. Seo, Y. Inoue, K. Ishihara, N. Yui, T.Yamaoka.. Mobility of the Arg-Gly-Asp (RGD) ligand on the outermost surface of biomaterials suppresses integrin-mediated mechanotransduction and subsequent cell functions. *Acta Biomaterialia*. 2015.02; 13(1); 45-51
4. A. Tamura, I. Fukumoto, N. Yui, M. Matsumura, H. Miura. Increasing the repeating units of ethylene glycol-based dimethacrylates directed towards reduced oxidative stress and co-stimulatory factor expression in human monocytic cells. *Journal of Biomedical Materials Research Part A*. 2015.03; 103(3); 1060-1066
5. A. Tamura, N. Yui. β -Cyclodextrin-threaded biocleavable polyrotaxanes ameliorate impaired autophagic flux in Niemann-Pick type C disease. *Journal of Biological Chemistry*. 2015.04; 290(15); 9442-9454

6. S. Yamada, Y. Sanada, A. Tamura, N. Yui, K. Sakurai. Chain architecture and flexibility of α -cyclodextrin/PEG polyrotaxanes in dilute solutions. *Polymer Journal*. 2015.06; 47(6); 464-467
7. K. Nishida, A. Tamura, N. Yui. Acid-labile polyrotaxane exerting endolysosomal pH-sensitive supramolecular dissociation for therapeutic applications. *Polymer Chemistry*. 2015.06; 6(21); 4040-4047
8. M. Terauchi, G. Ikeda, K. Nishida, A. Tamura, S. Yamaguchi, K. Harada, N. Yui. Supramolecular polyelectrolyte complexes of bone morphogenetic protein-2 with sulfonated polyrotaxanes to induce enhanced osteogenic differentiation. *Macromolecular Bioscience*. 2015.07; 15(7); 953-964
9. A. Tamura, G. Ikeda, K. Nishida, N. Yui. Cationic polyrotaxanes as a feasible framework for the intracellular delivery and sustainable activity of anionic enzymes: a comparison study with methacrylate-based polycations. *Macromolecular Bioscience*. 2015.08; 15(8); 1134-1145

[Conference Activities & Talks]

1. Atsushi Tamura. Polyrotaxane-based intracellular delivery of cyclodextrins for intractable disease therapies. . Joint Conference of 8th Asian Cyclodextrin Conference and 32nd Cyclodextrin Symposium 2015.05.16 Kumamoto
2. Naoko Matsui. A confocal fluorescence microscopic analysis on the effect of the MDP concentration in bonding agent. the 142nd Meeting of the Japanese Society of Conservative Dentistry 2015.06.25

Functional Material

Tsuyoshi KIMURA

(1) Research

1) Decellularization of native tissue for regenerative medicine

In order to obtain a novel scaffold, which can be applied for regenerative tissue, ultra-high pressurization method was developed for the complete elimination of the cells and inactivation of the viruses.

2) Inducing molecular aggregation using ultra-high pressurization

The basic and applied science on molecular aggregation triggered by hydrogen bonding at over 6,000 atm is studied. This technique is being applied for hybridization of DNA with polymer for drug delivery system.

3) Bio-interface

To investigate how the materials interact with biological cues such as phospholipids, proteins, or cells, precisely controlled surface via atomic transfer radical polymerization was prepared. The basic research on physical and biological properties of this surface is being investigated.

4) Specific capture of Treg cells

In order to remove Treg cells, which induce immunotolerance, a device of capturing of Treg cells is developed.

(2) Education

In order to develop technology, which may contribute to the advance in the medical science, lectures on functional molecules from basic to advanced knowledge on molecular design for specific purpose, mainly concentrated on medical application would be executed. Theories on functional molecules and overviews on medical system would be lectured in Graduate School of Medical and Dental Sciences. Students would have chances to learn about Genomics and Bio-intelligent system in Graduate School of Biomedical Science.

(3) Clinical Services & Other Works

The development of functional molecules can provide novel materials for the clinical application such as blood vessel, cornea, skin, or bone. Unlike the conventional materials which have been used in clinics so far, it would be possible to promote or suppress specific biological response using functionalized materials. Furthermore, the screening essential drug compound for certain purpose, it would help the patients to be treated with higher efficiency and less pain.

(4) Publications

[Original Articles]

1. A. Matsushashi, K. Nam, T. Kimura, A. Kishida. Fabrication of fibrillized collagen microspheres with microstructure resembling extracellular matrix *Soft Matter*. 2015.04; 11(14); 2844-2851
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 PartB*. 2015.05;

3. Y. Hashimoto, S. Funamoto, S. Sasaki, J. Negishi, T. Honda, S. Hattori, K. Nam, T. Kimura, M. Mochizuki, H. Kobayashi, A. Kishida. Corneal regeneration by deep anterior lamellar keratoplasty (DALK) using decellularized corneal matrix PLOS ONE. 2015.07; 10(7); e0131989
4. P. Wu, N. Nakamura, T. Kimura, K. Nam, T. Fujisato, S. Funamoto, T. Higami, A. Kishida. Decellularized porcine aortic intima-media as a potential cardiovascular biomaterial Interact Cardiovasc Thorac Surg. 2015.08; 21(2); 189-194
5. Jun Negishi, Seiichi Funamoto, Tsuyoshi Kimura, Kwangwoo Nam, Tetsuya Higami, Akio Kishida. Porcine radial artery decellularization by high hydrostatic pressure. J Tissue Eng Regen Med. 2015.11; 9; E114-E151

[Conference Activities & Talks]

1. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. Preparation and physical properties of a small diameter decellularized vascular graft covered with electrospun fibers. SFB 2015 Annual Meeting and Exposition 2015.04.15 Charlotte, USA
2. N. Nakamura, A. Ito, K. Nam, T. Kimura, T. Fujisato, T. Tsuji, A. Kishida. Preparation of decellularized mandible bone with periodontal membrane for periodontal reconstruction. SFB 2015 Annual Meeting and Exposition 2015.04.15 Charlotte, USA
3. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. Preparation of a small diameter decellularized vessel covered with nanofibers by electrospinning. The 5th Asian Biomaterials Congress 2015.05.06 Taipei, Taiwan
4. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. Preparation of a small diameter decellularized blood vessel covered with electrospun nanofibers. Biomaterials International 2015 2015.06.01 Kenting, Taiwan
5. N. Nakamura, T. Kimura, A. Ito, T. Fujisato, T. Tsuji, A. Kishida. Acellular periodontal ligament matrix for artificial tooth implant. 27th European Conference on Biomaterials 2015.08.30 Krakow, Poland
6. A. Kishida, N. Nakamura, A. Ito, K. Nam, T. Kimura, T. Fujisato, T. Tsuji. Periodontal reconstruction using decellularized periodontal tissue combined with artificial tooth. 4th TERMIS World Congress 2015.09.08 Boston, USA
7. N. Nakamura, T. Kimura, K. Nam, T. Fujisato, T. Tsuji, H. Iwata, A. Kishida. Artificial microenvironment of decellularized bone marrow induced hematopoiesis. 4th TERMIS World Congress 2015.09.08 Boston, USA
8. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. A small-diameter decellularized vascular graft covered with electrospun fibers. 4th TERMIS World Congress 2015.09.08 Boston, USA
9. Y. Zhang, K. Nam, T. Kimura, A. Kishida. Preparation of gradient decellularized dermis-polymer complex for tissue interlinking device. 4th TERMIS World Congress 2015.09.08 Boston, USA
10. T. Kimura, N. Nakamura, N. Sasaki, S. Sakaguchi, S. Kimura, A. Kishida. Preparation of interface for specific capture of target cells. Bio4Apps 2015 2015.12.09 Fukuoka, Japan
11. T. Kimura, N. Nakamura, H. Morita, P. Wu, K. Nam, T. Fujisato, A. Kishida. Fabrication of decellularized aorta with electrospun fibers for small-diameter vascular grafts. Pacifichem 2015 2015.12.15 Hawaii, USA

Plastic and Reconstructive Surgery

Professor: Mutsumi Okazaki

Junior Associate Professor: Hiroki Mori

Assistant Professor (Hospital Staff): Noriko Uemura

Project Assistant Professor (Hospital Staff) : Tanaka Kentaro

Graduate Student: Yuhki Wakimura, Makiko Inoue, Takuya Higashino, Katsuya Gorai, Aki Takada,
Yoko Maruyama, Tsutomu Homma, Satoshi Usami, Mayuko Hamanaga

(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 remolding 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. Nipple reconstruction with banked costal cartilage after vertical-type skin-sparing mastectomy and deep inferior epigastric artery perforator flap. *Breast Cancer*. 2015; 22(1); 95-97
2. Okazaki M, Tanaka K, Uemura N, Usami S, Homma T, Okubo A, Hamanaga M, Mori H. One-stage dual latissimus dorsi muscle flap transfer with a pair of vascular anastomoses and double nerve suturing for long-standing facial paralysis. *Journal of Plastic, Reconstructive & Aesthetic Surgery*. 2015; 68; e113-e119
3. Tanaka K, Okazaki M, Yano T, Miyashita H, Homma T, Tomita M. Quantitative Evaluation of Blood Perfusion to Nerves Included in the Anterolateral Thigh Flap using Indocyanine Green Fluorescence Angiography: A Different Contrast Pattern between the Vastus Lateralis Motor Nerve and Femoral Cutaneous Nerve. *Journal of Reconstructive Microsurgery*. 2015; 31; 163-170
4. Usami S, Okazaki M, Wakimura Y. Extensor Digiti Minimi Transfer for the Treatment of an Unstable Metacarpophalangeal Joint in Thumb Polydactyly Without Thenar Atrophy. *Journal of Hand and Microsurgery*. 2015; 7; 110-111
5. Usami S, Kawahara S, Yamaguchi T, Hirase Y. Homodigital artery flap reconstruction for fingertip amputation: a comparative study of the oblique triangular neurovascular advancement flap and the reverse digital artery island flap. *Journal of Hand Surgery*. 2015; 40; 291-297
6. Usami S, Kodaira S, Homma T, Okazaki M. Postoperative voluminal flap reduction after fingertip reconstruction using the reverse digital artery island flap. *Hand Surgery*. 2015; 20; 133-136
7. Wakimura Y, Wang W, Itoh S, Okazaki M, Takakuda K. An Experimental Study to Bridge a Nerve Gap with a Decellularized Allogeneic Nerve. *Plastic and Reconstructive Surgery*. 2015; 136(3); 319e-327e

[Conference Activities & Talks]

1. Tanaka K, Okazaki M, Yano T, Suesada N. Postoperative Complications after Skull Base Reconstruction. The 16th Congress of International Society of Craniofacial Surgery 2015.09.17 Urayasu
2. Homma T, Yano T, Tanaka K, Hamanaga M, Okazaki M. A rare case of 14 consecutive surgeries, including 4 free flap reconstructions performed on the same patient. The 16th Congress of International Society of Craniofacial Surgery 2015.09.18 Urayasu
3. Hamanaga M, Yano T, Tanaka K, Suesada N, Homma T, Okazaki M. Review of our reconstructive procedures for a trigeminal nerve sheath tumor. The 16th Congress of International Society of Craniofacial Surgery 2015.09.18 Urayasu

Head and Neck Surgery

Professor Takahiro Asagkage
Junior associate professor Takuro Sumi, Taro Sugimoto
Project professor Seiji Kishimoto
Assistant professor Yusuke Kiyokawa
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 anatomy of the skull base.
- Surgical approaches to the skull base and deep area of the face.
- Clinical application of new device of endoscopic examination.
- Establishment of the standard neck dissection.
- Treatment of pediatric head and neck tumor.
- Human papilloma virus infection and head and neck cancer.

(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. T Sasaki, S Kishimoto, K Kawabata, et al. Risk factors for cervical lymph node metastasis in superficial head and neck squamous cell carcinoma J Med Dent Science. 2015; 62; 19-24

2. M Sugawara, M Aoyagi, S Kishimoto, et al. Extended orbital exenteration for sinonasal malignancy with orbita Journal of Neurosurgery. 2015.01; 123(1); 1-7
3. K Misawa , Y Misawa, H Fukushima, et al. Aberrant methylation inactivates somatostatin and somatostatin receptor type 1 in head and neck squamous cell carcinoma. PLoS One. 2015.03; 10(3); e0118588
4. T Kanazawa , K Misawa , H Fukushima, et al. Next Generation Therapeutic Targets in Head and Neck Cancer? Toxins. 2015.08; 7(8); 2959-2984
5. R Kamiyama , H Mitani, H Fukushima, et al. A Clinical Study of Pharyngolaryngectomy with Total Esophagectomy: Postoperative Complications, Countermeasures, and Prognoses. Otolaryngol Head Neck Surgery. 2015.09; 153(3); 392-399
6. A Yamashita, K Ichikura, S Sugimoto, S Kishimoto, Shimozuma E, Matsushima E. Reliability and validity of the Head and Neck Cancer Inventory (HNCI) in Japanese patients Palliative and Supportive Care . 2015.10; 13(5); 1373-1380
7. T Yano, M Okazaki, S Kishimoto, et al. Indication for and Limitation of the Facial Dismasking Flap Approach for Skull Base Surgery to Achieve the Best Esthetical and Functional Results Annals of Plastic Surgery. 2015.12; 75(7); 662-667
8. K. Nakagawa, R Yoshimura, Skishimoto, 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. S Kishimoto. Symposium :Management of sinonasal cancer. "Craniofacial surgery for advanced juvenile angiofibromas with intracranial extension". 13th Asia-Oceania ORL-HNS Congress 2015.03.21 Taipei, Taiwan
2. Sugimoto T, Asakage T, Kawada K, Kiyokawa Y, et al.. Salvage Endoscopic Transoral Surgery for the Recurrent Hypopharyngeal Cancer after Chemoradiotherapy and Bioradiotherapy.. 2015 International Congress of Korean Society of Otorhinolaryngology-Head and Neck Surgery 2015.04 Seoul (Korea)
3. A Tasaki, T Sugimoto, T Sumi, F Nomura, Y Kiyokawa, Y Inayoshi, N Hattori, S Kishimoto. Adverse Events of Cisplatin, Fluorouracil and Docetaxel in Head and Neck Cancer. The joint meeting of 4th congress of Asian society of head and neck oncology and 39th annual meeting of Japan society for head and neck cancer 2015.06 Kobe, JAPAN
4. Sumi T, S Kishimoto, F Nomura, Y Kiyokawa, Y Inayoshi, A Tasaki, N Hattori, T Sugimoto. Treatment Result of Surgery for Infant Sarcoma of Stomato-pharyngeal Area. . The joint meeting of 4th congress of Asian society of head and neck oncology and 39th annual meeting of Japan society for head and neck cancer 2015.06 Kobe, JAPAN
5. K Miwa, Y Kiyokawa, T Sumi, K Tanaka, N Suesada, M Okazaki, S Kishimoto. Mandibulectomy for Intraoral Sarcoma in an Infant: A Case Report.. The joint meeting of 4th congress of Asian society of head and neck oncology and 39th annual meeting of Japan society for head and neck cancer 2015.06 Kobe, JAPAN
6. F Nomura, T Sugimoto, K Kawada, T Sumi, Y Inayoshi, Y Kiyokawa, A Tasaki, N Hattori, T Kawano, S Kishimoto. The Salvage Transoral Surgery after the Radiotherapy with Cetuximab for the Hypopharyngeal Cancer.. The joint meeting of 4th congress of Asian society of head and neck oncology and 39th annual meeting of Japan society for head and neck cancer 2015.06 Kobe, JAPAN
7. T Sugimoto, K Kawada, S Kishimoto, T Sumi, Y Kiyokawa, F Nomura, Y Inayoshi, N Hattori, A Tasaki, T Kawano. Subcutaneous Neck Emphysema after the Transoral Surgery for the Patients with Hypopharyngeal Cancer.. The joint meeting of 4th congress of Asian society of head and neck oncology and 39th annual meeting of Japan society for head and neck cancer 2015.06
8. A Toriihara, M Nakadate, T Fujioka, J Oyama, A Tsunoda, T Sumi, U Tateishi. Pretherapeutic evaluation of cancer of the external auditory canal using FDG-PET/CT.. 2015 annual meeting of Society of nuclear medicine and molecular imaging. 2015.06 Baltimore, United States

9. T Asakage. Symposium 4 Oral Cancer -Oral Cancers in Asian Countries-. The joint meeting of 4th congress of Asian society of head and neck oncology & 39th annual meeting of Japan society for head and neck cancer Kobe 2015.06 Kobe, JAPAN
10. G Omura, M Ando, T Asakage. Under40 symposium1 Basic science Comorbidities predicts poor prognosis for surgical treated advanced head and neck cancer pateints. . The joint meeting of 4th congress of Asian society of head and neck oncology & 39th annual meeting of Japan society for head and neck cancer 2015.06 Kobe, JAPAN
11. Y Saito, G Omura, T Asakage. Under40 symposium6 nasopharynx, sinonasal cavity A retrospective analysis and prognostic factors of maxillary squamous cell carcinoma.. The joint meeting of 4th congress of Asian society of head and neck oncology & 39th annual meeting of Japan society for head and neck cancer 2015.06 Kobe
12. M Ando, Y Saito, T Asakage. Identification of a MET mutation by next generation sequencing. Identification of a MET mutation by next generation sequencing.. The joint meeting of 4th congress of Asian society of head and neck oncology & 39th annual meeting of Japan society for head and neck cancer 2015.06
13. T Nomura, M Kishimoto, H Iwaki, S Kishimoto, et al. Maxillary swing approach for removal of the palatal carcinoma. 4th Asia Society of Head and Neck Oncology 2015.06.04 Kobe
14. S Kishimoto. Chair of Academic Siminar 4: Therapeutic Approaches in Soft Tissue Sarcomas of the Head and Neck Region by K Miura. 4th Asia Society of Head and Neck Oncology 2015.06.04 kobe
15. S Kishimoto. Chair of Symposium 2: Skull Base tumor: Comprehensive management of skull base tumors. 4th Asia Society of Head and Neck Oncology 2015.06.04 Kobe
16. T Asakage. Chairman Oral (English) case report 1 . The joint meeting of 4th congress of Asian society of head and neck oncology & 39th annual meeting of Japan society for head and neck cancer 2015.06.04 Kobe
17. B Takeshi, T Tokumaru et al. Daily QOL evaluation after long period from CCRT treatment for hypopharyngeal cancer. 4th Asian society Head and Neck Congress 2015.06.05 Kobe
18. H Fukushima . Is It Really Safe: Secondary T-E(J) Puncture Subsequent to Jejunum Transplant?. 4th Congress of Asian Society of Head and Neck Oncology, 39th Annual Meeting of Japan Society for Head and Neck Cancer, 2015.06.05 Kobe
19. T Fujikawa, A Hatanaka, T Tokumaru, et al. Slow but Favorable Recovery of Swallowing in Elderly Head and Neck Cancer Patients After Reconstructive Surgery. 3rd Congress of European ORL-HNS, 2015.06.07 Prague, Czech Rep.
20. T Asakage. Chairman Update of head and neck cancer treatment point of view of a French otolaryngologist expert.. Expect Meeting at Head & Neck Cancer 2015.07 Tokyo
21. A case of mucinous adenocarcinoma from buccal mcosa. 2015.09.11
22. T Yano, M Okazaki, K Tanaka, S kishimoto, et al. Indication for and aesthetical results of a facial dismasking flap approach in skull base surgery. 16th Biennial Congress of the International Society of Craniofacial Surgery 2015.09.14 Chiba
23. Sugimoto T, Asakage T, Kawada K. Challenging Cases of Flexible Endoscopic Surgery for Laryngo-Hypopharyngeal Cancer.. 5th International robotic surgery symposium 2015.10 Seoul (Korea)
24. K Ichikawa, J Ishimaru, M Uchiyama, K Igarashi, A Ochi, S Kishimoto. The distribution of SUVs in the light accumulation lesions of the larynx on PET-CT. 2015.12.01 Tokyo
25. S Kishimoto. Lecture "Three topics on the skull base surgery". Kaohsiung Chang Gung Memorial Hospital 2015.12.18 Taipei, Taiwan

Radiation Therapeutics and Oncology

Professor Ryoichi Yoshimura

Lecturers Kazuma Toda

Research Associates Keiji Hayashi, Keiko Nakagawa

Hospital Staff members Rikiya Sato(∼ Mar), Hirohumi Kuwabara

Resudent Takuya Nagano(Apr ∼)

(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 710 patients, including 172 head and neck cancer patients, 125 urological cancer patients, 110 breast cancer patients, 85 lung cancer patients, and 50 esophageal cancer patients, were treated by external beam radiotherapy at our hospital in 2014. Moreover, high-dose-rate brachytherapy was performed in 44 patients with uterine cancer, and low-dose-rate brachytherapy in 34 patients with oral cancer.

(6) Clinical Performances

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

(7) Publications

[Conference Activities & Talks]

1. Yoshimura R. SAVI. Japanese Society for Radiation Oncology 2015.11.20 Maebashi
2. Toda K, Sato R, Hoshi A, Yasuhiro S, Tamaki M, Yoshimura R. intrafractional movement during frameless stereotactic radiosurgery and radiotherapy. the 28th annual meeting of the Japanese Society for Radiation Oncology 2015.11.21
3. Yuasa-Nakagawa K, Yoshimura R, Watanabe H, Kaida A, Miura M. Brachytherapy for the very elderly with oral and oropharyngeal cancers. ESMO-ASIA 2015 2015.12.20 Singapore

Maxillofacial Anatomy

Professor	Shunichi SHIBATA
Assistant Professor	Shun-ichi SHIKANO
Graduate Student	Tsuyoshi MORITA
Graduate Student	Kaoru FUJIKAWA
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. Tanaka M, Watanabe M, Yokomi I, Matsumoto N, Sudo K, Satoh H, Igarashi T, Seki A, Amano H, Ohura K, Kakei R, Shibata S, Nagayama M, Tanuma J. Establishment of a novel dwarf rat strain: cartilage calcification insufficient (CCI) rats. *Experimental Animals*. 2015.05; 64(2); 121-128
2. Shibata S, Morita T, Yokohama-Tamaki T, Murakami G, Cho BH. An immunohistochemical study of matrix components in early-stage vascular canals within mandibular condylar cartilage in midterm human fetuses. *Anatomical Record*. 2015.09; 298; 1560-1571
3. Fujikawa K, Yokohama-Tamaki T, Morita T, Baba O, Qin C, Shibata S. An in situ hybridization study of perlecan, DMP1, and MEPE in developing condylar cartilage of the fetal mouse mandible and limb bud cartilage. *European Journal of Histochemistry*. 2015.09; 59; 2553
4. Yokohama-Tamaki T, Otsu K, Harada H, Shibata S, Obara N, Irie K, Taniguchi A, Nagasawa T, Aoki K, Caliar SR, Weisgerber DW, Harley BAC. CXCR4/CXCL12 signaling impacts enamel progenitor cell proliferation and motility in the dental stem cell niche. *Cell and Tissue Research*. 2015.12; 362(3); 633-642

[Books etc]

1. Shun-ichi Shikano. Awa Segoro's Anatomy. 2015 (ISBN : 978-4-8446-0835-6)

[Conference Activities & Talks]

1. Shibata S. An immunohistochemical study of matrix components in early-stage vascular canals within mandibular condylar cartilage in midterm human fetuse. 2014 Frontier Meeting in Tokyo Medical and Dental University 2015.02.14 TMDU Tokyo
2. Shibata S. Changes in education in dental school of TMDU. 33th annual meeting of the dental society of health sciences university of Hokkaido 2015.03.07 Asty Sapporo Sapporo
3. Fijikawa K, Morita T, Yokohama-Tamaki, T, Shibata S. Expression of MEPE in mouse cartilage. The 57th Annual Meeting of Japanese Association for Oral Biology 2015.09.12 Toki Messe Niigata
4. Masahiro Noda, Akira Aoki, Koji Mizutani, Taichen Lin, Motohiro Komaki, Shunichi Shibata, Yuichi Izumi. Effect of low-level laser therapy on early stage of wound healing of tooth extraction socket. The 58th Autumn Meeting of the Japanese Society of Periodontology 2015.09.13 Hamamatsu
5. Morita T, Fujikawa K, Shibata S. Expression of Hyaluronan Synthase (Has) in Developing Mouse Tooth Germ. The 62th Annual Meeting of JADR 2015.10.30 Fukuoka International Convnetion Center Fukuoka

Cognitive Neurobiology

Professor Masato Taira
Adjunct Professor Kumiko Sugimoto
Junior Associate Professor Hisayuki Ojima
Assistant Professor Narumi Katsuyama
Research Associate Nobuo Usui
Part-time Instructor Mari Kumashiro
Post-doctoral fellow Juri Fujiwara
Research fellow Rui Watanabe
Graduate Student Eriko Kikuchi(Tachi)
Yuko Imai
Kono Youko
Saneyuki Mizutani
Maki Okada

(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. Akiko Kamada, Daisuke Yoshino, Nobuo Usui . Relation between impression evaluation and choice behavior for merchandise : An examination using the semantic differential method and paired comparisons. *Bulletin of Human Science*. 2015.03; (36); 133-143
2. Yuki Ohara, Naomi Yoshida, Yoko Kono, Hirohiko Hirano, Hideyo Yoshida, Shiro Mataka, Kumiko Sugimoto. Effectiveness of an oral health educational program on community-dwelling older people with xerostomia. *Geriatr Gerontol Int*. 2015.04; 15(4); 481-489
3. Sawada A, Usui N, Shimazaki K, Taira M, Ono T. The effects of cognitive behavioral therapy on experimental orthodontic pain. *Orthod Waves*. 2015.05; 74(1); 10-14
4. Mizutani S, Usui N, Yokota T, Mizusawa H, Taira M, Katsuyama N.. Depth perception from moving cast shadow in macaque monkey. *Behavioural Brain Research*. 2015.07; 288; 63-70
5. Hisayuki Ojima and Junsei Horikawa. Recognition of modified conditioning sounds by competitively trained guinea pigs *Frontiers in Behavioral Neuroscience*. 2015.12;

[Misc]

1. Haga N, Kubota M, Miwa Z. Hereditary sensory and autonomic neuropathy types IV and V in Japan. *Pediatrics International* . 2015.02; 57(1); 1-13

[Conference Activities & Talks]

1. Ojima H. Mechanisms of cortical suppression evoked by the reversed form of a damping natural sound.. 38th ARO Annual Midwinter Meeting 2015.02.21 Baltimore, USA
2. Ojima H, Ishida T, Taira M, Horikawa J. Contrast in processing of sounds played forward and reversely and learning effects on this contrast.. NIH Science Events 2015.02.25 Bethesda, MD, USA
3. Fujiwara J., Usui N., Eifuku S., Iijima T., Taira M., Tsutsui K., and Tobler P.N.. Ventrolateral prefrontal activity reflects increases in object value induced by larger choice sets. The 38th Annual Meeting of the Japan Neuroscience Society 2015.07.29

4. Katsuyama N, Usui N, Okabe S, Kajiya R, Taira M. Activation of the posterior inferior temporal sulcus by motion in depth induced by cast shadow. . 2015.08.20
5. FUJIWARA J., USUI N., EIFUKU S., IJIMA T., TAIRA M., TSUTSUI K., and TOBLER P.N. . Ventrolateral prefrontal activity reflects increases in object value induced by larger choice sets.. 45th annual meeting of the Society for Neuroscience 2015.10.17
6. A. IKEDA, J. MIYAMOTO, N. USUI, M. TAIRA and K. MORIYAMA. Effect of mastication on satiety using an attentional bias task.. The 63rd International Association for Dental Research. JADR· Annual Meeting 2015.10.30

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

Endrawan Pratama,
Zhang Kui (Oral Implantology
and Regenerative Dental
Medicine),
Toshiko Furutera, Mya Nandar,
Charoenlarp Ponkawee,
Norisuke Yokoyama,
Erika Kubota (Pedodontics),
Tian Xiaohui (Oral Implantology
and Regenerative Dental
Medicine)
Rajendran Arun Kumar (Oct-)
Kaori Morinaka (Apr-Jun),
Nao Naohara (Jul-Oct)

Secretary

(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. Taro Kitazawa, Masaki Takechi, Tatsuya Hirasawa, Noritaka Adachi, Nicolas Narboux-Nême, Hideaki Kume, Kazuhiro Maeda, Tamami Hirai, Sachiko Miyagawa-Tomita, Yukiko Kurihara, Jiro Hitomi, Giovanni Levi, Shigeru Kuratani, Hiroki Kurihara. Developmental genetic bases behind the independent origin of the tympanic membrane in mammals and diapsids. *Nat Commun.* 2015; 6; 6853
2. Michiko Yoshida, Kenji Hata, Rikako Takashima, Koichiro Ono, Eriko Nakamura, Yoshifumi Takahata, Tomohiko Murakami, Sachiko Iseki, Teruko Takano-Yamamoto, Riko Nishimura, Toshiyuki Yoneda. The transcription factor *Foxc1* is necessary for *Ihh*-*Gli2*-regulated endochondral ossification. *Nat Commun.* 2015; 6; 6653

3. Hiroshi Nagashima, Fumiaki Sugahara, Masaki Takechi, Noboru Sato, Shigeru Kuratani. On the homology of the shoulder girdle in turtles. *J. Exp. Zool. B Mol. Dev. Evol.*. 2015.05; 324(3); 244-254
4. Thanit Prasitsak, Mya Nandar, Shigeru Okuhara, Shizuko Ichinose, Masato S Ota, Sachiko Iseki. Foxc1 is required for early stage telencephalic vascular development. *Dev. Dyn.*. 2015.05; 244(5); 703-711
5. R Arun Kumar, A Sivashanmugam, S Deepthi, Sachiko Iseki, K P Chennazhi, Shantikumar V Nair, R Jayakumar. Injectable Chitin-Poly(ϵ -caprolactone)/Nanohydroxyapatite Composite Microgels Prepared by Simple Regeneration Technique for Bone Tissue Engineering. *ACS Appl Mater Interfaces*. 2015.05; 7(18); 9399-9409
6. Eri Tsuchida, Atsushi Kaida, Endrawan Pratama, Masa-Aki Ikeda, Keiji Suzuki, Kiyoshi Harada, Masahiko Miura. Effect of X-Irradiation at Different Stages in the Cell Cycle on Individual Cell-Based Kinetics in an Asynchronous Cell Population. *PLoS ONE*. 2015.06; 10(6); e0128090
7. Yayoi Ikeda, Masa-Aki Ikeda. Cyclin E marks quiescent neural stem cells and caspase-3-positive newborn cells during adult hippocampal neurogenesis in mice. *Neurosci. Lett.*. 2015.10; 607; 90-96
8. Endrawan Pratama, Xiaohui Tian, Widya Lestari, Sachiko Iseki, Solachuddin J A Ichwan, Masa-Aki Ikeda. Critical role of ARID3B in the expression of pro-apoptotic p53-target genes and apoptosis. *Biochem. Biophys. Res. Commun.*. 2015.12; 468(1-2); 248-254
9. Yayoi Ikeda, Yuko Matsunaga, Masahito Takiguchi, Masa-Aki Ikeda. Expression of cyclin E in postmitotic neurons during development and in the adult mouse brain. *Gene Expr. Patterns*. 11(1-2); 64-71

[Misc]

1. Masaki Takechi, Taro Kitazawa, Hiroki Kurihara, Shigeru Kuratani. Evo-devo study of the mammalian middle ear *Seitai no Kagaku*. 2015.06; 66(3); 234-239

[Conference Activities & Talks]

1. Sachiko Iseki. Opposing effects of FGF18 and FGF2 on postnatal bone healing and fetal bone formation. Indo-Australian Conference on Biomaterials, Tissue Engineering, Drug Delivery System & Regenerative Medicine (BiTERM 2015) 2015.02
2. Masaki Takechi, Taro Kitazawa, Junko Takei, Yukiko Kurihara, Sachiko Iseki, Hiroki Kurihara, Shigeru Kuratani. Comparative developmental analysis of middle ear formation in mouse and chicken embryos. The 120th Annual Meeting of The Japanese Association of Anatomists 2015.03 Kobe
3. Ikeda, MA. Simple and efficient long-term culture method to maintain multipotent differentiation potential of mesenchymal stem/stromal cells. Seminar 2015.03.27 Kuantan, Malaysia
4. Masaki Takechi, Taro Kitazawa, Sachiko Iseki, Yukiko Kurihara, Hiroki Kurihara, Shigeru Kuratani. Why do only mammals have three ossicles in the middle ear?. The 55th Annual Meeting of the Japanese Tetsyolohy Society 2015.07
5. Masaki Takechi, Taro Kitazawa, Yukiko Kurihara, Sachiko Iseki, Hiroki Kurihara, Shigeru Kuratani. Developmental genetic bases behind the independent origin of the tympanic membrane in mammals and diapsids. 17th Annual Meeting of Society of Evolutionary Studies, Japan 2015.08 Chuo University
6. Saadat Khandakar Asm, Arman Kaiffee, Arslan Ahmet, Sachiko Iseki, Kiyoshi Ohtani, Masa-Aki Ikeda. Expression study of E2F-target genes in osteosarcoma (U2OS) and glioblastoma (T98G) cell lines after knocking down ARID3A and ARID3B. XIV. National Congress of Medical Biology and Genetics 2015.10.27 Fethiye, Turkey
7. Saadat Khandakar Asm, Arman Kaiffee, Arslan Ahmet, Kiyoshi Ohtani, Masa-Aki Ikeda. Overexpression of ARID3 facilitates E2F-dependent apoptosis. XIV. National Congress of Medical Biology and Genetics 2015.10.27
8. Sachiko Iseki. Shh functions in oropharyngeal region. Oral intractable disease project, Osaka University, International Symposium 2015 2015.12
9. Endrawan Pratama, Khandakar A S M Saadat, Widya Lestari, Solachuddin J. A. Ichwan, Sachiko Iseki, Kiyoshi Ohtani, Masa-Aki Ikeda. ARID3B promotes gene expression critical for E2f-mediated cell cycle progression and p53-mediated apoptosis. Biochemistry and Molecular Biology (BMB2015) 2015.12.01 Kobe

[Awards & Honors]

1. Poster Prize (Masaki Takechi), Japanese Teratology Society, 2015.07

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama

Junior Associate Professor Hiroshi Fujita, Yasuki Ishizaki, Masao Saito

Research Student Mizuki Nagata, Asuka Okito,
Syun Nishihara

(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.

Biodesign

Professor Kazuo TAKAKUDA
Specially Appointed Professor
Yoshihiro TAKEMOTO
Visiting Professor Kazuko IRIMURA
Assistant Professor Shigeru ITO
Hisashi DOI
Wei WANG
Mari YUASA
Research Assistants Shukan OKANO
Hiroyuki MASUNO
Noriko NAKAISHI
Graduate Students (Doctoral coarse)
Tetsuro WATANABE, Kimihiro OKANO,
Ryoichi SUZUKI, Katsunari MURAKAMI,
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. Ryo Kokubun, Wei Wang, Shengli Zhu, Guoqiang Xie, Shizuko Ichinose, Soichiro Itoh, Kazuo Takakuda. In vivo evaluation of a Ti-based bulk metallic glass alloy bar Biomed Mater Eng. 2015; 26(1-2); 9-17
2. Yusuke Nakagawa, Takeshi Muneta, Shinpei Kondo, Mitsuru Mizuno, Kazuo Takakuda, Shizuko Ichinose, Takeshi Tabuchi, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Synovial mesenchymal stem cells promote healing after meniscal repair in microminipigs. Osteoarthritis Cartilage. 2015.06; 23(6); 1007-1017
3. Yuki Wakimura, Wei Wang, Soichiro Itoh, Mutsumi Okazaki, Kazuo Takakuda. An Experimental Study to Bridge a Nerve Gap with a Decellularized Allogeneic Nerve. Plast. Reconstr. Surg.. 2015.09; 136(3); 319e-327e

4. Chiaki Tsutsumi, Kazuo Takakuda, Noriyuki Wakabayashi. Reduction of Candida biofilm adhesion by incorporation of prereacted glass ionomer filler in denture base resin. J Dent. 2015.12; 44(1); 37-43

Maxillofacial Surgery

Professor: Kiyoshi HARADA

Junior Associate Professor: Masashi YAMASHIRO, Satoshi YAMAGUCHI, Narikazu UZAWA

Assistant Professor: Yutaka SATO, Hiroyuki YOSHITAKE, Yasuyuki MICHI, Kazuto KUROHARA
Kouichi NAKAKUKI, Yoshio OHYAMA

Hospital Staff: Itaru SONODA, Kunihiro MYO, Nobuyoshi TOMOMATSU, Keiko MAEDA, Chieko MICHIKAWA
Yoshinori INABA,

(from April)Chie AKATSU,Ryousuke NAGAOKA,
Tomomi SAKUMA, Jun SUMINO, Takasi WATANABE

Graduate Student:Takuma MORITA, Hirokazu KACHI, Kouhei OKUYAMA, Chihiro YOSHIDA,
Takeshi OKAMURA, Sou WAKE, Yuuta KONDOU, Masahiko TERAUCHI, Uyannga ENKHBOLD,
Reiko HOSHI, Sakie KATSUMURA, Tomoki KANEMARU, Syun NISHIHARA, Erina TONOUCHI,
Takasuke INADA (from April) Durugu-nn BATBO-RUDO,Eri SONE,Narumi OSIBE,
Keiitiro NAKAZATO,Hirosi KATO Takahiko YAMADA, Yusun KIMU
Student: Akiyo NORIME, Ami TSUYUZAKI, (from April)Rika AKAMINE,
Hiroyasu HAYASI

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, Yasushi NIINAKA, Takao WATANABE
Testuo SUZUKI, Masayuki YAMANE, Takashi MISHIMAGI, Narihiro ABE,Erika OUE,Norihiro ENDO,
(from April) Yasuhiro KURASAWA

(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, facical 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. Yamada C, Kaida A, Okuyama K, Harada K, Miura M. Effects of Chk1 inhibitor or paclitaxel on cisplatin-induced cell-cycle kinetics and survival in parental and cisplatin-resistant HeLa cells expressing fluorescent ubiquitination-based cell cycle indicator (Fucci) Integr Cancer Sci Therap. . 2015; 2(1); 87-92
2. Okuyama K, Kaida A, Hayashi Y, Hayashi Y, Harada K, Miura M . KPU-300, a novel benzophenone-diketopiperadine-type anti-microtubule agent with a 2-pyridine structure, is a potent radiosensitizer that synchronizes the cell cycle in early M phase. PLoS One. . 2015;
3. Tsuchida E, Kaida A, Pratama E, Ikeda MA, Suzuki K, Harada K, Miura M. Effect of X-Irradiation at Different Stages in the Cell Cycle on Individual Cell-Based Kinetics in an Asynchronous Cell Population. PLoS One. 2015.01; 10(6); e0128090
4. Uzawa N, Miura C, Suzuki M, Tomomatsu T, Izumo N, Harada K. Ameloblastic Carcinoma of Primary Type in the maxilla: a report of a case and review of literatures. Oncology Letters. 2015.01; 9 (1); 459-467
5. Moriya Y, Uzawa N, Morita T, Mogushi K, Miyaguchi K, Takahashi K, Michikawa C, Sumino J, Tanaka H, Harada K. The high-temperature requirement factor A3 (HtrA3) is associated with the acquisition of the invasive phenotype of oral squamous cell carcinoma cells. Oral Oncology. 2015.01; 51(1); 84-9

[Conference Activities & Talks]

1. Okuyama K, Kaida A, Hayashi Y, Hayashi Y, Harada K, Miura M . A novel type of anti-microtubule agent, KPU-300, is a potent radiosensitizer through synchronization of the cell cycle at M-phase. . 15th International Congress of Radiation Research 2015.03.25 Kyoto, Japan
2. Masahiko Terauchi, Go Ikeda, Kei Nishida, Atsushi Tamura, Satoshi Yamaguchi, Kiyoshi Harada, Nobuhiko Yui. Design of sulfonated polyrotaxane mimicked the heparin and evaluation of osteoinductive ability with BMP-2. The 5th Asian Biomaterials Congress 2015.05.06 Taipei
3. Narikazu Uzawa, Yoshio Ohyama, Kunihiro Myo, Miho Suzuki, Yasuyuki Michi, Masashi Yamashiro, Kiyoshi Harada. Head and neck reconstruction with radical forearm, rectus abdominis, and scapula

flaps.. The Joint Meeting of 4th Congress of Asian Society of Head and Neck Oncology & 39th Annual Meeting of Japan society for Head and Neck Cancer. 2015.06.04

4. Kondo Y, Ohno T, Bhingare AC, Yagita H, Harada K, Azuma M. VISTA and CTLA-4 combination blockade enhances multifunctionality of tumor infiltrating CD8+ T cells. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08 Nagoya, Japan
5. Okuyama K, Kaida A, Hayashi Y, Hayashi Y, Harada K, Miura M. A Novel benzophenone-diketopiperadine-type anti-microtubule agent with a 2-pyridine structure, KPU-300, is a potent radiosensitizer through synchronization of the cell cycle at M-phase. . 22nd International Conference on Oral and Maxillofacial Surgery 2015.10.27 Melbourne
6. Masahiko Terauchi, Satoshi Yamaguchi, Kiyoshi Harada.. Design of sulfonated polyrotaxane mimicked the heparin and evaluation of osteoinductive ability with BMP-2. International Conference on Oral and Maxillofacial Surgery 2015 2015.10.27 Melbourne
7. Nishi N, Bhingare A, Ohno T, Kondo Y, Azuma M. Combinational immune checkpoint blockade with VISTA and CTLA-4 enhances anti-tumor responses. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo
8. Nishi N, Bhingare A, Ohno T, Kondo Y, Azuma M. Endogenous and exogenous IL-33 promotes antitumor immunity. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo
9. Masahiko Terauchi, Takasuke Inada, Tomoki Kanemaru, Kei Nishida, Atsushi Tamura, Satoshi Yamaguchi, Kiyoshi Harada, Nobuhiko Yui. Heparin-mimicking supramolecules for enhancing osteoinduction ability of bone morphogenetic protein-2. The 2015 International Chemical Congress of Basin Societies 2015.12.15 Honolulu

[Awards & Honors]

1. 15th International Congress of Radiation Research. Young Investigators Travel Award. , ICRR, 2015.03
2. 15th International Congress of Radiation Research. Excellent Poster Award, ICRR, 2015.03

Maxillofacial Orthognathics

Professor	Keiji MORIYAMA
Associate Professor	Shoichi SUZUKI
Junior Associate Professor	Takuya OGAWA
Assistant Professor	Michiko TSUJI, Norihisa HIGASHIHORI, Jun MIYAMOTO, Yukiho KOBAYASHI, Naoko HARADA, Yosuke ITO
Clinical Fellow	Junichi TAKADA, Rina HIKITA, Tsutomu MATSUMOTO, Yuko KOMAZAKI, Naomi YAMAMOTO, Kenji OGURA, Yuki TAKAHASHI
Post-doctoral Fellow	Masayoshi UEZONO, Chiho WATANABE
Graduate Student	Keiko MURAMOTO, Akitsu IKEDA, Naoki KOUDA, Tsasan Tumurkhuu, Maki MORISHITA, Kouhei YAHIRO Ayumi SHOJI, Taizo HIRATSUKA Entei RIN, Miyu ARAKI, Takeshi OGASAWARA, Kousuke TSUJI, Yoshihiro YAMAGATA, Aung Bhone Myat Hiroyuki KAMIMOTO, Kyoko HIRABAYASHI, Kenta FUNAHASHI, Hideyuki YOSHIZAWA
Graduate International Research Student	Takayuki UMEZAWA, Sakiko AKIYAMA, Takuya ASAMI, Sahori MATSUNO, Rie KINOSHITA, Ruriko NAKAMURA, Misato HANDA, Syuhei AKIYAMA, Asuka TAMURA, Cheng Shih-wei Eric, Kenjiro MATSUMURA, Yuki NAKAZAWA, Naomi KAWAKUBO, Michiyo IKEDA
Resident	Yuri BABA

(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. Naomi Yamamoto, Masamitsu Oshima, Chie Tanaka, Miho Ogawa, Kei Nakajima, Kentaro Ishida, Keiji Moriyama, Takashi Tsuji. Functional tooth restoration utilising split germs through re-regionalisation of the tooth-forming field. *Sci Rep.* 2015; 5; 18393
2. Takuya Ogawa, Chiemi Sato, Naomi Kawakubo, Keiji Moriyama. Orthodontic treatment of a patient with hypoglossia. *Cleft Palate Craniofac. J.* 2015.01; 52(1); 102-109
3. Yumiko Nakayama, Yoshiyuki Baba, Michiko Tsuji, Hiroki Fukuoka, Takuya Ogawa, Mizue Ohkuma, Keiji Moriyama. Dentomaxillofacial characteristics of ectodermal dysplasia. *Congenit Anom (Kyoto).* 2015.02; 55(1); 42-48
4. Kitasako Y, Sasaki Y, Takagaki T, Sadrc A, Tagami J. Age-specific prevalence of erosive tooth wear by acidic diet and gastroesophageal reflux in Japan *Journal of Dentistry.* 2015.02;
5. Reiko Wadachi, Toshihiko Yoshioka, Takahiro Hanada, Naoko Harada, Arata Ebihara, Hideaki Suda. The Present Situation and Problems of Tooth Fravture -The Present Demands of Dental Practice Revealed through a Survey of New Patients of an Endodontic Clinic- *The Japanese Journal of Conservative Dentistry.* 2015.02; 58 (1); 1-9
6. Nozomi Ahiko, Yoshiyuki Baba, Michiko Tsuji, Shoichi Suzuki, Tsuyoshi Kaneko, Junko Kindaichi, Keiji Moriyama. Investigation of maxillofacial morphology and dental development in hemifacial microsomia. *Cleft Palate Craniofac. J.* 2015.03; 52(2); 203-209
7. Shiyang Liu, Norihisa Higashihori, Kohei Yahiro, Keiji Moriyama. Retinoic acid inhibits histone methyltransferase Whsc1 during palatogenesis. *Biochem. Biophys. Res. Commun.* 2015.03; 458(3); 525-530

8. Wanting Lin, Yoichi Ezura, Yayoi Izu, Arayal Smriti, Makiri Kawasaki, Chantida Pawaputanon, Keiji Moriyama, Masaki Noda. Profilin Expression Is Regulated by Bone Morphogenetic Protein (BMP) in Osteoblastic Cells. *J. Cell. Biochem.* 2015.08;
9. Momotoshi Shiga, Takuya Ogawa, Issareeya Ekprachayakoon, Keiji Moriyama. Orthodontic Treatment and Long-Term Management of a Patient With Marfan Syndrome. *Cleft Palate Craniofac. J.* 2015.08;
10. Erika Suzuki-Okamura, Norihisa Higashihori, Tatsuo Kawamoto, Keiji Moriyama. Three-dimensional analysis of hard and soft tissue changes in patients with facial asymmetry undergoing 2-jaw surgery. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015.09; 120(3); 299-306
11. Umezawa T, Chen P, Tsutsumi Y, Doi H, Ashida M, Suzuki S, Moriyama K, Hanawa T. Calcification of MC3T3-E1 cells on titanium and zirconium Dental Materials Journal. 2015.10; 34(5); 713-718
12. Thunyporn Surapornsawasd, Takuya Ogawa, Keiji Moriyama. Identification of nuclear localization signals within the human BCOR protein. *FEBS Lett.* 2015.10; 589(21); 3313-3320
13. Simon Poelmans, Tatsuro Kawamoto, Francesca Cristofoli, Constantinus Politis, Joris Vermeesch, Isabelle Bailleul-Forestier, Greet Hens, Koenraad Devriendt, Anna Verdonck, Carine Carels. Genotypic and phenotypic variation in six patients with solitary median maxillary central incisor syndrome. *Am. J. Med. Genet. A.* 2015.10; 167A(10); 2451-2458
14. Ayano Dei, Jun J Miyamoto, Jun-Ichi Takada, Takashi Ono, Keiji Moriyama. Evaluation of blood flow and electromyographic activity in the perioral muscles. *Eur J Orthod.* 2015.11;

[Conference Activities & Talks]

1. Keiji Moriyama. Treatment of Surgical and Non-surgical Class IIIs. Association of Orthodontists (Singapore) Congress (AOSC) 2015 2015.02.06 Singapore
2. Moriyama K. Can TADs Replace Surgery For The Skeletally Compromised Patient?. Association of Orthodontists (Singapore) Congress (AOSC) 2015 2015.02.06 Singapore
3. N. Yamamoto, M. Oshima, K. Moriyama, T. Tsuji. Multiplied Tooth Regeneration by Transplantation of a Cleaved tooth germ. 93rd General Session & Exhibition of the IADR 2015.03.11 Boston, Mass., USA
4. Maki Morishita, Tomoki Muramatsu, Shin Hayashi, Momoki Hirai, Yumiko Suto, Teruaki Konishi, Keiji Moriyama, Johji Inazawa. Exploring mechanisms for chromothripsis by irradiation. American Association for Cancer Research Annual Meeting 2015 2015.04.21 Philadelphia
5. Wanting Lin, Yoichi Ezura, Yayoi Izu, Keiji Moriyama, Masaki Noda. Deletion of Pfn1 have an effect on bone formation. 13th Congress of the International Society of Bone Morphometry 2015.04.29 Tokyo
6. Keiji Moriyama. "Give Thy Thoughts with Tongue" -The Tongue is An Eloquent Organ in Orthodontics. 2015 Annual Session, American Association of Orthodontists. 2015.05.15 San Francisco CA
7. Keiji Moriyama. TMDU Faculty of Dentistry, Cultivating Professionals with Knowledge and Humanity, hereby Contributing to People's Well-Being.. Tri-university Consortium on Oral Science and Education 2015.05.20 Bangkok, Thailand
8. N. Yamamoto, M. Oshima, C. Tanaka, K. Moriyama, T. Tsuji. Tooth regenerative therapy by utilizing a split tooth germ. The 4th Tri-university Consortium on Oral Science and Education 2015.05.20 Bankok
9. Chiho Watanabe, Norihisa Higashihori, Rina Hikita, Tsutomu Matsumoto, Yosuke Ito, Tatsuo Kawamoto and Keiji Moriyama. Long-term Observations After Surgical Orthodontic Treatment For Mandibular Prognathism With Facial Asymmetry. International Seminar on Cleft Lip and/or Plate and Related Craniofacial Anomalies 2015.06.08 Tokyo
10. Jun-ichi Takada, Takuya Ogawa, Chiemi Sato, Masayoshi Uezono, Kei-ichi Morita, Keiji Moriyama. A Case of Holoprosencephaly with Unilateral Cleft Lip and Palate Treated with Maxillary Distraction Osteogenesis in Adolescence. International Seminar on Cleft Lip and/or Plate and Related Craniofacial Anomalies 2015.06.08 Tokyo

11. Takuya Ogawa. Measurement of distraction force in maxillary distraction osteogenesis for cleft lip and palate. International Seminar on Cleft Lip and/or Plate and Related Craniofacial Anomalies 2015.06.08 Tokyo
12. Maki Morishita, Tomoki Muramatsu, Shin Hayashi, Momoki Hirai, Yumiko Suto, Teruaki Konishi, Keiji Moriyama, Johji Inazawa. Exploring mechanisms for chromothripsis by irradiation. The 34th Sapporo International Cancer Symposium 2015.06.25 Hokkaido
13. Chinatsu MATSUKAWA, Naoko SEKI, Yoshiyuki SASAKI, Ikuko MORIO. Investigation on the curriculum of professional training colleges for dental hygienists. 2015.07.11
14. Keiji Moriyama. Dental education in super-aging society in Japan. 26th SEAADE Annual Scientific Meeting 2015.08.13 Indonesia
15. Tsasan Tumurkhuu, Takuya Ogawa, Yuko Komazaki, Ganjargal Ganburged, Amarsaikhan Bazar, Takeo Fujiwara, Keiji Moriyama. Association between Maternal Education and Malocclusion in Mongolian Adolescents. IADR-SEAADE SEA Division 2015 2015.08.15 Indonesia
16. Keiji Moriyama. Non-surgical and Surgical Orthodontic Treatment for the Patients of Mandibular Prognathism.. SWU 21st Foundation Anniversary Celebration 2015.08.24 Bangkok, Thailand
17. Tsuji M, Naganishi H, Torikai K, Moriyama K. A case of Apert syndrome treated by bimaxillary orthognathic surgery after Le Fort III distraction. The 16th Congress of International Society of Craniofacial Surgery 2015.09.14 Chiba
18. Ogawa T, Sawada H, Kataoka K, Baba Y, Moriyama K. Measurement of distraction force in maxillary distraction osteogenesis for cleft lip and palate. The 16th Congress of International Society of Craniofacial Surgery 2015.09.14 Chiba
19. Y. Komagamine, M. Kanazawa, Y. Sasaki, S. Minakuchi. Prognosis of new complete dentures from Patient's Denture Assessment (PDA) of existing dentures. International College of Prosthodontists, 16th Biennial Meeting 2015.09.17 Souel, Korea
20. Michiyo IKEDA, Jun J MIYAMOTO, Jun-ichi TAKADA, Keiji MORIYAMA. Association between volumetric measurements of mandibular morphology and condylar movement in facial asymmetry subjects. 8th International Orthodontic Congress 2015.09.27 London
21. Morita J, Tsuji M, Uezono M, Moriyama K. Characteristic orofacial phenotypes in a patient diagnosed with orofaciogigital syndrome. 8th International Orthodontic Congress 2015.09.27 London
22. Chiho Watanabe, Norihisa Higashihori, Rina Hikita, Tsutomu Matsumoto, Yosuke Ito, Tatsuo Kawamoto, Keiji Moriyama. Long-term observations after surgical orthodontic treatment for mandibular prognathism with facial asymmetry. 8th International Orthodontic Congress 2015.09.27 London
23. Tsutomu Matsumoto, Norihisa Higashihori, Rina Hikita, Chiho Watanabe, Jun Miyamoto, Tatsuo Kawamoto, Shoichi Suzuki, Keiji Moriyama. Three-dimensional analysis of lower lip movement during articulation in patients with mandibular prognathism by motion capture system. 8th International Orthodontic Congress 2015.09.27 London
24. Jun-chi Takada, Takuya Ogawa, Chiemi Sato, Masayoshi Uezono, Kei-ichi Morita, Keiji Moriyama. A Case of Holoprosencephaly with Unilateral Cleft Lip and Palate Treated with Maxillary Distraction Osteogenesis in Adolescence. 8th International Orthodontic Congress 2015.09.27 London
25. Sakiko Akiyama, Michiko Tsuji, Taizo Hiratsuka, Rina Hikita, Tsutomu Matsumoto and Keiji Moriyama. An orthodontic management case of Williams syndrome with severe crowding in lower arch. 8th International Orthodontic Congress 2015.09.27 London
26. Takuya Asami, Rina Hikita, Ayumi Shoji, Tsutomu Matsumoto, Mao Sato, Michiko Tsuji, Yoshiyuki Baba, Keiji Moriyama. Clinical study of Williams syndrome patients-Intraoral characteristics-. 8th International Orthodontic Congress 2015.09.27 London
27. Sahori Matsuno, Rina Hikita, Wanting Lin, Tsutomu Matsumoto, Mao Sato, Michiko Tsuji, Yoshiyuki Baba, Keiji Moriyama. Clinical study of Williams syndrome patients: Part 1, General findings and characteristics of craniofacial morphology. 8th International Orthodontic Congress 2015.09.27 London

28. Maki Morishita, Tomoki Muramatsu, Shin Hayashi, Momoki Hirai, Yumiko Suto, Teruaki Konishi, Keiji Moriyama and Johji Inazawa. Chromothripsis-like pattern in cancer-cell genome after irradiation by a focused vertical micro-beam system, SPICE. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08 Aichi
29. Kenji Ogura, Toshinori Ishizuya, Keiji Moriyama, Akira Yamaguchi. Intermittent administration of parathyroid hormone facilitates osteogenesis by different mechanisms in cancellous and cortical bone. ASBMR Annual Meeting 2015.10.09 Washington
30. Akitsu Ikeda, Jun J Miyamoto, Nobuo Usui, Masato Taira, Keiji Moriyama. Effect of mastication on satiety using an attentional bias task. The 63rd Annual Meeting of Japanese Association for Dental Research 2015.10.30 Fukuoka
31. Kenji Ogura, Toshinori Ishizuya, Keiji Moriyama, Akira Yamaguchi. PTH Facilitates Osteogenesis by Different Mechanisms between Cancellous- and Cortical-bones. The 63rd Annual Meeting of Japanese Association for Dental Research 2015.10.30 Fukuoka
32. Keiji Moriyama. Therapeutic effect of nanogel-based delivery of soluble FGFR2 with S252W mutation on craniosynostosis. The 34th Annual Academic Session of KADR 2015.11.14 Seoul, Korea
33. Kazuo TAKAKUDA, Hazuki KOSHITOMAE, Naoko HARADA, Kazuko IRIMURA. Failure Rate Estimation of Medical Devices by Bayesian statistics. Oromaxillofacial Biomechanics Association 2015.11.16
34. Yuki Takahashi, Norihisa Higashihori, Keiji Moriyama. Correction of a high-angle class II malocclusion with condylar resorption using a skeletal anchorage system. 2015 APOS (Asian Pacific Orthodontic Society) Resident Forum 2015.12.04 Taiwan
35. Keiji Moriyama. Consideration of soft tissue in treatment of case with dentoskeletal discrepancies. The 28th TAO annual meeting & 2015 APOS residents forum 2015.12.06 Taiwan

[Others]

1. Evaluation of Community Dental Health Activities in Hiraizumi-cho(IWATE pref.) 1985-
2. Study on Structure of Oral-Medical-Informatics-System. 1991-
3. Study on the Arch Length Discrepancy of Children in Kanagawa 1991-

Maxillofacial Prosthetics

2015

Professor
TANIGUCHI Hisashi

Junior Associate Professor
SUMITA Yuka

Assistant Professor
HATTORI Mariko
OTOMARU Takafumi

Clinical Staff
HARAGUCHI Mihoko
MURASE Mai
NAGAI Hana

Graduate Student
YOSHI Shigen
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ELBASHTI Mahmoud Ellarousi
YANAGI Ayaka
SAID Mohamed Moustafa
ASWEHLEE Amel Mohamed
LI Na
Kamiyanagi Ayuko
KELIMU Shajidan
YEERKEN Yesiboli

Part-time Special Student
WATANABE Mao
AIMAIJIANG Yiliyaer

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 Yiliyaer, OTOMARU Takafumi, TANIGUCHI Hisashi. 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*. 2015;
2. Takafumi Otomaru ,Yuka I. Sumita, Yiliyaer Aimaijiang, Motohiro Munakata, Noriko Tachikawa, Shohei Kasugai, Hisashi Taniguchi. Rehabilitation of a bilateral maxillectomy patient with a free fibula osteocutaneous flap and with an implant-retained obturator: a clinical report *Journal of Prosthodontics*. 2015;
3. 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*. 2015;
4. Elbashti ME, Aswehlee A, Hattori M, Sumita YI , Taniguchi H. The future of maxillofacial prosthetics in Libya: A call to establish the field *Libyan Dental Journal*. 2015;
5. 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 *The International Journal of Prosthodontics*. 2015;
6. Hattori Mariko, Sumita Yuka I, Taniguchi Hisashi. Sound analysis of a musical performance to evaluate prosthodontic treatment for a clarinet player. *J Prosthodont*. 2015.01; 24(1); 71-77
7. Elbashti ME, Hattori M, Sumita YI , Taniguchi H. Evaluation of articulation simulation system using artificial maxillectomy models. *J Oral Rehabil*. 2015.05; 42; 678-684
8. Kanazaki A, Otomaru T, Sumita YI, Kosaka M, Haraguchi M, Hattori M, Murase M, Taniguchi H. Long-term Observation of Definitive Prostheses in Cleft Lip and Palate Patients *J. Jpn. Cleft Palate Assoc*. 2015.10; 40(3); 233-242
9. Yuka SUMITA. Prosthetic Treatment for Oropharyngeal Defect *Maxillofacial Prosthetics*. 2015.12; 38(2); 33-36

[Conference Activities & Talks]

1. Aimaijiang Y, Otomaru T, Sumita YI, Said M, Munakata M, Taniguchi H.. Prosthodontic Rehabilitation of a Mandibulectomy Patient with an Implant-Retained Overdenture. Biennial joint congress of JPS-CPS-KAP 2015.04
2. Otomaru T, Aimaijiang Y, Said M, Taniguchi H. Investigation of factors affecting food mixing ability in maxillectomy patients. Biennial joint congress of JPS-CPS-KAP 2015.04 Kanagawa, JAPAN
3. Said M. Functional Outcomes of Implant-Prosthetic Treatment Treatment in Oral Resection Patients: A Systemic Review. The 4th international dental congress 2015.04.08 Egypt
4. Sato Y, Mikishima T, Katsuki Y, Mibu M, Sano H, Sone E, Yoshimasu H, Harada K. A study on cases following pharyngeal flap operation in our department. The 69th annual meeting of the Japanese stomatological society 2015.05

5. Haraguchi M, Sumita YI, Iida T, Taniguchi H.. Prosthodontic treatment for 2 cleft lip and palate patients with amelogenesis imperfecta. 39th meeting of Japanese cleft palate association 2015.05 Tokyo, JAPAN
6. Haraguchi M, Sumita YI, Taniguchi H. Surgical prostheses aimed improvement of oral form in postoperative oral cancer patients -Two stent cases-. The Joint Meeting of 4th Congress of Asian Society of Head and Neck Oncology & 39th Annual Meeting of Japan Society for Head and Neck Cancer 2015.06 Kobe
7. Haraguchi M, Sumita YI, Taniguchi H. Prosthetic rehabilitation for a patient with extensive hemangioma/vascular malformation in the head and neck region. The 32nd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2015.06.19 Tokyo
8. Murase M, Yanagi A, Sumita YI, Taniguchi H. Nutrition assessment for a patient with recurrent advanced carcinoma of maxilla. The 32nd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2015.06.19 Tokyo
9. Aswehlee A, Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Modified surgical stent improved a mandibulectomy patient's QOL in the early stage of the postoperative rehabilitation. The 32nd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2015.06.19 Tokyo
10. Hoshiai T, Kosaka M, Oki M, Shinozuka O, Taniguchi H. Modal analysis of the maxillary dentition with maxillary obturator prostheses comparing different retainer types of metal frameworks. 2015.06.19 Tokyo
11. Kanazaki A, Oki M, Yoshi S, Yanagi A, Taniguchi T. A case report of long-term use of a hollow type obturator - A copy hollow-type obturator production. 2015.06.19 Tokyo
12. Nomura K, Otomaru T, Kosaka M, Yoshi S, Said M, Taniguchi H. Prosthodontic rehabilitation of adolescent patient with maxillary resection up to 7 years A case report. The 32nd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2015.06.20 Tokyo
13. Yanagi A, Sumita YI, Otomaru T, Yoshi S, Kanazaki A, Hattori M, Haraguchi M, Murase M, Kosaka M, Oki M, Taniguchi H. Clinical study on maxillofacial prosthetic patients in our clinic for 35 years. The 32nd Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2015.06.20 Tokyo
14. Sumita YI. Current status of prosthetic treatment for oropharyngeal area. 2015.06.20
15. Yanagi A, Murase M, Sumita YI, Taniguchi H. Evaluation of Nutritional Status using Mini Nutritional Assessment-Short Form in Patients under Maxillofacial Treatments . The 16th Congress of the Parenteral and Enteral Nutrition Society of Asia (PENSA 2015) 2015.07.24 Aichi, JAPAN
16. Murase M, Yanagi A, Sumita YI, Taniguchi H. Nutritional assesment of multiple oral cancer patients with maxillofacial prosthesis. The 16th Congress of the Parenteral and Enteral Nutrition Society of Asia (PENSA 2015) 2015.07.24 Nagoya
17. Shrestha A, Churei H, Sumita YI, Suzuki T, Matsubara H, Taniguchi H, Ueno T. Fabrication of Obturator Type of Sports Mouthguard for Maxillectomy Patient and its Speech Intelligibility Assessment : A Case Study. 7th TMDU International Summer Program 2015.08
18. Said M. An Overview about Maxillofacial Prosthetics in TMDU. 7th TMDU International Summer Program 2015.08
19. Said M, Otomaru T, Aimaajian Y, Taniguchi H. Masticatory function and health-related quality of life in maxillectomy patients. 16 th biennial meeting of the international college of prosthodontists 2015.09 Korea
20. Otomaru T, Aimaajian Y, Said M, Munakata M, Tachikawa N, Kasugai S, Taniguchi H. Prosthodontic rehabilitation of a maxillectomy patient with an implant-retained overdenture. 16 th biennial meeting of the international college of prosthodontists 2015.09 Korea
21. Elbashti ME, Aswehlee A, Hattori M, Sumita YI, Taniguchi H. The role of digital technology in overseas maxillofacial prosthetic collaboration. 27th Biennial Scientific Congress of the Institute of Maxillofacial Prosthetists and Technologists IMPT 2015.09.10 London
22. Elbashti ME, Aswehlee A, Hattori M, Sumita YI, Taniguchi H. A mono-block brachytherapy prosthesis for the treatment of mandibular lesions: A case report. 27th Biennial Scientific Congress of the Institute of Maxillofacial Prosthetists and Technologists IMPT 2015.09.11 UK

23. Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Digital treatment planning in maxillofacial prosthetics: a case report. 16 th biennial meeting of the international college of prosthodontists 2015.09.17 Korea
24. Hattori M, Sumita YI, Aswehlee A, Elbashti ME, Taniguchi H. Facial prosthesis made by dental materials on exposed reconstruction plate. 16 th biennial meeting of the international college of prosthodontists 2015.09.17 Korea
25. Elbashti ME, Aswehlee A, Hattori M, Sumita YI, Taniguchi H. The role of digitization in rapid reproduction of obturators. 16 th biennial meeting of the international college of prosthodontists 2015.09.17 Korea
26. Aswehlee A, Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Prosthodontic rehabilitation of a patient with osteomyelitis: a case report. 16 th biennial meeting of the international college of prosthodontists 2015.09.17 Korea
27. Kosaka M, Sumita YI, Taniguchi H. Influence of dento-maxillary prosthesis adjustment on salivary cortisol levels. Annual Scientific Meeting of Japan Prosthodontic Society Tohoku-Hokkaido Branch 2015.10 Morioka
28. Sumita YI. Current Maxillofacial Prosthetic Treatment and Research in TMDU. 43rd Indian prosthodontic society conference 2015.12.05
29. Kanazaki A, Otomaru T, Taniguchi H. The effect of occlusal reconstruction on body sway in patients wearing dento-maxillary prosthesis after head and neck tumor resection. 80th Stomatological Society Meeting 2015.12.26

[Awards & Honors]

1. Excellence in Research 2014(Hattori M), Faculty of Dentistry, Tokyo Medical and Dental University (TMDU), 2015.01
2. Tokyo Medical and Dental University postgraduate study abroad award (Elbashti ME), 2015.05

Metals

Takao HANAWA Prof
Yusuke TSUTSUMI Senior Assoc Prof
Maki ASHIDA Assist Prof
Peng CHEN Assist Prof
Hisashi DOI Assist Prof
Toshie NAKANISHI Secretary
Tomoko SETOGUCHI 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) Education

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. Maekawa M, Kanno Z, Wada T, Hongo T, Doi H, Hanawa T, Ono T, Uo M. Mechanical properties of orthodontic wires made of super engineering plastic Dental Materials Journal. 2015.02; 34(1); 114-119
2. Seo JH, Tsutsumi Y, Kobari A, Shimojo M, Hanawa T, Yui N. Modulation of friction dynamics in water by changing the combination of the loop- and graft-type poly(ethylene glycol) surfaces Soft Mater. 2015.02; 11(5); 936-942

3. Shinonaga T, Tsukamoto M, Kawa T, Chen P, Nagai A, Hanawa T. Formation of periodic nanostructures using a femtosecond laser to control cell spreading on titanium *Applied Physics B*. 2015.03; 119; 493-496
4. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Superplasticity in the Ti-6Al-7Nb alloy processed by high-pressure torsion *Mater. Sci. Eng. A*. 2015.06; 640; 449-453
5. Ashida M, Sugimoto T, Nomura N, Tsutsumi Y, Chen P, Doi H, Hanawa T. Microstructure and mechanical properties of large-scale ingots of the Zr-1Mo alloy *Mater. Trans.* 2015.07; 56(9); 1544-1548
6. Jang SH, Lee DH, Ha JY, Hanawa T, Kim KH, Kwon TY. Preliminary evaluation of mechanical properties of Co-Cr alloys fabricated by three new manufacturing processes *Int J Prosthodont*. 2015.07; 28(4); 396-398
7. Umezawa T, Chen P, Tsutsumi Y, Doi H, Ashida M, Suzuki S, Moriyama K, Hanawa T. Calcification of MC3T3-E1 cells on titanium and zirconium *Dental Materials Journal*. 2015.10; 34(5); 713-718
8. Fukuhara Y, Kyuzo M, Tsutsumi Y, Nagai A, Chen P, Hanawa T. The effect of different component ratios in block polymers and processing conditions on electrodeposition efficiency onto titanium *Applied Surface Science*. 2015.11; 355; 784-791
9. Nozaki K, Shinonaga T, Ebe N, Horiuchi N, Nakamura M, Tsutsumi Y, Hanawa T, Tsukamoto M, Yamashita K, Nagai A. Hierarchical periodic micro/nano-structures on nitinol and their influence on oriented endothelialization and anti-thrombosis *Mater Sci Eng C Mater Biol Appl*. 2015.12; 57; 1-6
10. Okamoto H, Tsutsumi Y, Watanabe M, Yamakage K, Ashida M, Chen P, Doi H, Miura H, Matsumura M, Hanawa T. Evaluation of release and accumulation of metal ions from titanium and nickel by accelerated dissolution test in simulated body environments *Electrochemistry*. 2015.12; 83(12); 1048-1052
11. Tsutsumi Y, Nishisaka T, Doi H, Ashida M, Chen P, Hanawa T. Reaction of calcium and phosphate ions with titanium, zirconium, niobium, and tantalum *Surf Interface anal*. 2015.12; 47(13); 1148-1154

[Books etc]

1. Hanawa T. Biofunctionalization of metals with polymers, *Advances in metallic biomaterials: Processing and applications*. Springer, New York, 2015.06
2. Hanawa T. Biofunctionalization of metallic materials: Creation of biosis-abiosis intelligent interface, *Interface Oral Health Science 2014*. Springer, New York, 2015.09

[Conference Activities & Talks]

1. Akimoto T, Ueno T, Tsutsumi Y, Doi H, Hanawa T, Wakabayashi N. The corrosion resistance of Ti-Zr binary alloy with compositional change. IADR (The International Association for Dental Research) 2015.03.11 Boston, USA
2. Hanawa T, Ashida M, Chen P, Doi H, Tsutsumi Y, Horita Z. Strengthening of Ti-6Al-7Nb alloy for dental narrow implants. Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015) 2015.04.15 NC, USA
3. Chen P, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Cellular and gene expression responses in osteoblast-like cells to metals. Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015) 2015.04.15 NC, USA
4. Tsutsumi Y, Niizeki N, Chen P, Ashida M, Doi H, Noda K, Hanawa T. Micro-arc oxidation treatment for improvement of antibacterial property of titanium. Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015) 2015.04.15 NC, USA
5. Chen P, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Extension, locomotion, and proliferation of osteoblast-like cells on metals. Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015) 2015.04.15 NC, USA
6. Chen P, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Osteogenic activity of MC3T3-E1 cells on sputter-deposited metals. The 5th Asian Biomaterials Congress (ABMC5) 2015.05.06 Taipei, Taiwan

7. Tsutsumi Y, Niizeki N, Chen P, Ashida M, Doi H, Noda K, Hanawa T. Development of multi-biofunctional surface on Ti by simple electrochemical treatment. The 5th Asian Biomaterials Congress (ABMC5) 2015.05.06 Taipei, Taiwan
8. Kajima Y, Takaichi A, Yasue T, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Evaluation of the shear bond strength of dental porcelain to Zr-14Nb alloy with low magnetic susceptibility . 4th TRI university consortium 2015.05.20 Thailand
9. Hanawa T, Fukuhara Y, Tsutsumi Y, Chen P, Doi H, Ashida M, Inoue Y, Ishihara K. Biofunctionalization of titanium with electrodeposited MPC polymer. Biomaterials International 2015 (BMI 2015) 2015.06.01 Kenting, Taiwan
10. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Improvement of bioactivity of zirconium by combination of anodic and cathodic polarization method. Biomaterials International 2015 (BMI 2015) 2015.06.01 Kenting, Taiwan
11. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T. Influence of heat treatment on mechanical properties of Ti-6Al-7Nb processed by severe plastic deformation. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09 Tokyo, Japan
12. Chen P, Ashida M, Tsutsumi Y, Doi H, Hanawa T. Effect of sputter-deposited metals on osteogenic potential of preosteoblast cells. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09 Tokyo, Japan
13. Tsutsumi Y, Chen P, Ashida M, Doi H, Nakai M, Niinomi M, Hanawa T. Micro-arc oxidation treatment for improvement of antibacterial property of titanium and its alloy. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09 Tokyo, Japan
14. Tsutsumi Y, Niizeki N, Chen P, Ashida M, Doi H, Noda K, Hanawa T. Electrochemical surface treatment for achieving both hard-tissue compatibility and antibacterial property on Ti. The 13th World Conference on Titanium (Ti-2015) 2015.08.16 San Diego, California, USA
15. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Effects of grain refinement by high-pressure torsion on mechanical properties of Ti-6Al-7Nb. The 13th World Conference on Titanium (Ti-2015) 2015.08.16 San Diego, California, USA
16. Hanawa T, Nomura N, Ashida M, Tsutsumi Y, Doi H, Chen P, Itoh M. Decrease of MRI artifact in spinal instruments of zirconium alloy. 27th European Conference on Biomaterials (ESB2015) 2015.08.30 Krakow, Poland
17. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Effects of initial microstructure on the resultant microstructure and mechanical properties of Ti-6Al-7Nb alloy after HPT processing. International workshop on giant straining process for advanced materials (GSAM2015) 2015.09.03 Fukuoka, Japan
18. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Superplasticity of biocompatible Ti-6Al-7Nb alloy after processing by high-pressure torsion. 12th International Conference on Superplasticity in Advanced Materials (ICSAM) 2015 2015.09.08 Tokyo, Japan
19. Biological properties of a-BC:H films prepared by pulsed plasma CVD. 2015.09.13
20. Hanawa T. Biomedical application of Ti and its alloys. 16th KIM-JIM Symposium 2015.09.16 Fukuoka, Japan
21. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Electrochemical surface treatments on metallic biomaterials for improvement of antibacterial property and hard tissue compatibility. XIV Brazil MRS Meeting (SBPMat2015) 2015.09.27 Rio de Janeiro, Brazil
22. Hanawa T, Tsutsumi Y, Fukuhara Y, Chen P, Ashida M, Doi H. Biofunctionalization of titanium with electrodeposited functional molecules. XIV Brazil MRS Meeting (SBPMat2015) 2015.09.27 Rio de Janeiro, Brazil

23. Nomura N, Suyalatu, Nakamoto T, Kimura T, Doi H, Tsutsumi Y, Hanawa T. Mechanical properties of selective laser melted Co-Cr-Mo alloys for biomedical applications. XIV Brazil MRS Meeting (SBPMat2015) 2015.09.27 Rio de Janeiro, Brazil
24. Washio K, Tsutsumi Y, Tsumanuma Y, Supreda S, Yano K, Ichinose S, Yamato M, Okano T, Hanawa T, Ishikawa I . New periodontal-like tissue formation on the modified titanium surface. 11th Asian Pacific Society of Periodontology Meeting (11th APSP) 2015.10.08 Bali, Indonesia
25. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Formation of multi-biofunctional surface layer on titanium by simple electrochemical treatment. International Symposium on EcoTopia Science 2015 (ISETS '15) 2015.11.27 Nagoya
26. Hanai M, Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Microstructures and mechanical properties of bi-modal Ti-6Al-7Nb alloy processed by high-pressure torsion. International Symposium on EcoTopia Science 2015 (ISETS '15) 2015.11.27 Nagoya
27. Tsutsumi Y, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T. Formation of bioactive and antibacterial ceramic layer on titanium by simple electrochemical surface treatment. 15th Asian BioCeramics Symposium (ABC 2015) 2015.12.10 Tokyo
28. Tsutsumi Y, Nishisaka T, Doi H, Ashida M, Chen P, Hanawa T. Reaction of calcium and phosphate ions with titanium, zirconium, niobium, and tantalum. 15th Asian BioCeramics Symposium (ABC 2015) 2015.12.10 Tokyo
29. Hanai M, Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Strengthening of bi-modal Ti-6Al-7Nb alloy using high-pressure torsion. Twenty-Fourth International Symposium on Processing and Fabrication of Advanced Materials (PFAM XXIV) 2015.12.18 Osaka
30. Hanawa T, Ashida M, Tsutsumi Y, Doi H, Chen P. Zr-1Mo alloy to decrease of MRI Artifact. Twenty-Fourth International Symposium on Processing and Fabrication of Advanced Materials (PFAM XXIV) 2015.12.18 Osaka
31. Tsutsumi Y, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T. Optimization of silver ion release from electrochemically-treated titanium surface. Twenty-Fourth International Symposium on Processing and Fabrication of Advanced Materials (PFAM XXIV) 2015.12.18 Osaka

Cell Biology

Professor	Takao Nakata
Associate Professor	Akihiro Inoue
Assistant 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 with in the cells and we observe the cell phenotypes by time-laps 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 or 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

[Original Articles]

1. Tomohiro Ishii, Koji Sato, Toshiyuki Kakumoto, Shigenori Miura, Kazushige Touhara, Shoji Takeuchi, Takao Nakata. Light generation of intracellular $\text{Ca}(2+)$ signals by a genetically encoded protein BACCS. Nat Commun. 2015; 6; 8021

2. Toshifumi Asano, Toru Ishizuka, Keisuke Morishima, Hiromu Yawo. Optogenetic induction of contractile ability in immature C2C12 myotubes Sci Rep. 2015.02; 5; 8317
3. Toshifumi Asano, Toru Ishizuka, Hiromu Yawo, Keisuke Morishima. Development of biotransducers driven by photostimulation Solid-State Sensors, Actuators and Microsystems (TRANSDUCERS2015). 2015.06; 1605-1608

[Conference Activities & Talks]

1. Toshifumi Asano, Toru Ishizuka, Hiromu Yawo, Keisuke Morishima. Optical myogenic differentiation of skeletal muscle cell. The 14th Congress of the Japanese Society for Regenerative Medicine 2015.03.19 Pacifico Yokohama
2. Takao Nakata. Study of secretory pathway using optogenetic tools. The 120th Annual Meeting of The Japanese Association of Anatomists 2015.03.21 Kobe
3. Toshifumi Asano, Toru Ishizuka, Hiromu Yawo, Keisuke Morishima. Development of biotransducers driven by photostimulation. 18th International Conference on Solid-State Sensors, Actuators and Microsystems Transducers 2015 2015.06.21 Alaska, USA
4. Koji Sato, Tomohiro Ishii, Shoji Takeuchi, Takao Nakata. Expression of light-activated calcium channel in the mouse olfactory sensory neurons. The 49th Annual Meeting of the Japanese Association for the Study of Taste and Smell 2015.09.24 Gifu
5. Tomohiro Ishii, Koji Sato, Toshiyuki Kakumoto, Shigenori Miura, Kazushige Touhara, Shoji Takeuchi, Takao Nakata. Optogenetic tool for controlling intracellular Ca^{2+} signals (Tomohiro Ishii). BMB2015 2015.12.01 Kobe

Medical Biochemistry

Professor Yutaka Hata

Assistant Professor Hiroaki Iwasa

Assistant Professor Kyoko Matsuzaki-Arimoto

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. Kodaka M, Yang Z, Nakagawa K, Maruyama J, Xu X, Sarkar A, Ichimura A, Nasu Y, Ozawa T, Iwasa H, Ishigami-Yuasa M, Ito S, Kagechika H, Hata Y.. A new cell-based assay to evaluate myogenesis in mouse myoblast C2C12 cells. *Experimental Cell Research*. 2015; 336; 171-181
2. Kawano S, Maruyama J, Nagashima S, Inami K, Qiu W, Iwasa H, Nakagawa K, Ishigami-Yuasa M, Kagechika H, Nishina H, Hata Y.. A cell-based screening for TAZ activators identifies ethacridine, a widely used antiseptic and abortifacient, as a compound that promotes dephosphorylation of TAZ and inhibits adipogenesis in C3H10T1/2 cells. *Journal of Biochemistry*. 2015; 158; 413-423
3. Lefebvre J, Clarkson M, Massa F, Bradford ST, Charlet A, Buske F, Lacas-Gervais S, Schulz H, Gimpel C, Hata Y, Schaefer F, Schedl A.. Alternatively spliced isoforms of WT1 control podocyte-specific gene expression. *Kidney International*. 2015; 88; 321-331
4. Ohshima D, Arimoto-Matsuzaki K, Tomida T, Takekawa M, Ichikawa K.. Spatio-temporal Dynamics and Mechanisms of Stress Granule Assembly. *PLoS Computational Biology*. 2015.06; 11(6);
5. Manami Kodaka, Zeyu Yang, Kentaro Nakagawa, Junichi Maruyama, Xiaoyin Xu, Aradhan Sarkar, Ayana Ichimura, Yusuke Nasu, Takeaki Ozawa, Hiroaki Iwasa, Mari Ishigami-Yuasa, Shigeru Ito, Hiroyuki Kagechika, Yutaka Hata. A new cell-based assay to evaluate myogenesis in mouse myoblast C2C12 cells. *Exp. Cell Res.*. 2015.08; 336(2); 171-181
6. Shodai Kawano, Junichi Maruyama, Shunta Nagashima, Kazutoshi Inami, Wenzhe Qiu, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiroshi Nishina, Yutaka Hata. A cell-based screening for TAZ activators identifies ethacridine, a widely used antiseptic and abortifacient, as a compound that promotes dephosphorylation of TAZ and inhibits adipogenesis in C3H10T1/2 cells. *J. Biochem.*. 2015.11; 158(5); 413-423

[Misc]

1. Kodaka M, Hata Y.. The mammalian Hippo pathway: regulation and function of YAP1 and TAZ. *Cellular and molecular life sciences*. 2015; 72; 285-306
2. Iwasa H, Jiang X, Hata Y. . RASSF6; the Putative Tumor Suppressor of the RASSF Family. *Cancers*. 2015; 9; 2415-2426
3. Nagashima S, Kodaka M, Iwasa H, Hata Y.. MAGI2/S-SCAM outside brain. *Journal of Biochemistry*. 2015; 157; 177-184
4. Kodaka M, Hata Y.. The mammalian Hippo pathway: regulation and function of YAP1 and TAZ. *Cell Molecular Life Science*. 2015; 72; 285-306
5. Takanobu Shimizu, Yutaka Hata. Hippo signal SEITAI No KAGAKU. 2015.10; 66(5); 444-445
6. Yutaka Hata, Takanobu Shimizu. The Hippo signal as drug targets in cancer and other diseases *Experimental Medicine*. 2015.11; 33(18); 2946-2952

[Conference Activities & Talks]

1. Yutaka Hata. Transcriptional coactivator with PDZ-binding motif (TAZ), a potential target for interventions against muscle-wasting disorders. *Neuroscience Symposium 2015* 2015.10.23

Joint Surgery and Sports Medicine

Takeshi Muneta
Tetsuya Jinno
Hideyuki Koga

Department of Joint Reconstruction

Tomoyuki Mochizuki

Department of Cartilage Regeneration

Kunikazu Tsuji
Toshifumi Watanabe

Yusuke Nakagawa, Yu Matsukura, Yoshie Seki, Enichi Nakatsuru,
Shinpei Kondo, Mio Udo, Ryusuke Saito, Katsuaki Yanagisawa, Makiko Inoue, Toshiyuki Ohara,
Akimasa Kimura, Mikio Shioda, Kaori Nakamura, Kanehiro Hiyama,
Kim Minde, Etsuko Matsumura, Mari Uomizu,
Takashi Hoshino, Mai Katakura, Shinji Hagio, Takashi Kondo, Hiroko Ueki, Kei Inomata, Naoko Shintani

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 section of Orthopedic and Neurosurgery 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-meniscectomy 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. Hideyuki Koga, Takeshi Muneta, Roald Bahr, Lars Engebretsen, Tron Krosshaug. Video Analysis of ACL Injury Mechanisms Using a Model-Based Image-Matching Technique Sports Injuries and Prevention. 2015; 109-120

2. Shinji Takahashi, Wakaba Fukushima, Takuaki Yamamoto, Tetsuya Jinno, Yukihide Iwamoto, Toshikazu Kubo, Nobuhiko Sugano, Yoshio Hirota, . Temporal Trends in Characteristics of Newly Diagnosed Non-traumatic Osteonecrosis of the Femoral Head From 1997 to 2011: A Hospital-Based Sentinel Monitoring System in Japan. *J Epidemiol.* 2015; 25(6); 437-444
3. Koji Otabe, Hiroyuki Nakahara, Akihiko Hasegawa, Tetsuya Matsukawa, Fumiaki Ayabe, Naoko Onizuka, Masafumi Inui, Shuji Takada, Yoshiaki Ito, Ichiro Sekiya, Takeshi Muneta, Martin Lotz, Hiroshi Asahara. Transcription factor Mohawk controls tenogenic differentiation of bone marrow mesenchymal stem cells in vitro and in vivo. *J. Orthop. Res.* 2015.01; 33(1); 1-8
4. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura Koji, Otabe, Ichiro Sekiya. Mid- to Long-term Results of Single-Bundle Versus Double-Bundle Anterior Cruciate Ligament Reconstruction: Randomized Controlled Trial. *Arthroscopy.* 2015.01; 31(1); 69-76
5. Gaku Koyano, Tetsuya Jinno, Daisuke Koga, Chisato Hoshino, Takeshi Muneta, Atsushi Okawa. Is closed suction drainage effective in early recovery of hip joint function? Comparative evaluation in one-stage bilateral total hip arthroplasty. *J Arthroplasty.* 2015.01; 30(1); 74-78
6. Yu Matsukura, Takeshi Muneta, Kunikazu Tsuji, Kazumasa Miyatake, Jun Yamada, Kahaer Abula, Hideyuki Koga, Makoto Tomita, Ichiro Sekiya. Mouse synovial mesenchymal stem cells increase in yield with knee inflammation. *J. Orthop. Res.* 2015.02; 33(2); 246-253
7. Mitsuru Aizawa, Tetsuya Jinno, Hideki Nanke, Kenshi Ishii, Sadaomi Kawachi. Femoral fracture caused by removal of femoral intramedullary nail made of stainless steel *J Med Cases.* 2015.03; 6(3); 105-108
8. Ichiro Sekiya, Takeshi Muneta, Masafumi Horie, Hideyuki Koga. Arthroscopic Transplantation of Synovial Stem Cells Improves Clinical Outcomes in Knees With Cartilage Defects. *Clin Orthop Relat Res.* 2015.04; 473(7); 2316-2326
9. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Posterolateral Bundle Graft Fixation Angles on Clinical Outcomes in Double-Bundle Anterior Cruciate Ligament Reconstruction: A Randomized Controlled Trial. *Am J Sports Med.* 2015.05; 43(5); 1157-1164
10. Kahaer Abula, Takeshi Muneta, Kazumasa Miyatake, Jun Yamada, Yu Matsukura, Makiko Inoue, Ichiro Sekiya, Daniel Graf, Aris N Economides, Vicki Rosen, Kunikazu Tsuji. Elimination of BMP7 from the developing limb mesenchyme leads to articular cartilage degeneration and synovial inflammation with increased age. *FEBS Lett.* 2015.05; 589(11); 1240-1248
11. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Initial Graft Tension on Knee Stability and Graft Tension Pattern in Double-Bundle Anterior Cruciate Ligament Reconstruction. *Arthroscopy.* 2015.05; 31(9); 1756-1763
12. Yusuke Nakagawa, Takeshi Muneta, Shinpei Kondo, Mitsuru Mizuno, Kazuo Takakuda, Shizuko Ichinose, Takeshi Tabuchi, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Synovial mesenchymal stem cells promote healing after meniscal repair in microminipigs. *Osteoarthritis Cartilage.* 2015.06; 23(6); 1007-1017
13. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Evaluation of a behind-remnant approach for femoral tunnel creation in remnant-preserving double-bundle anterior cruciate ligament reconstruction - Comparison with a standard approach. *Knee.* 2015.06; 22(3); 249-255
14. Nobutake Ozeki, Takeshi Muneta, Seiya Matsuta, Hideyuki Koga, Yusuke Nakagawa, Mitsuru Mizuno, Kunikazu Tsuji, Yo Mabuchi, Chihiro Akazawa, Eiji Kobayashi, Tomoyuki Saito, Ichiro Sekiya. Synovial mesenchymal stem cells promote meniscus regeneration augmented by an autologous Achilles tendon graft in a rat partial meniscus defect model. *Stem Cells.* 2015.06; 33(6); 1927-1938
15. Yusuke Ogata, Yo Mabuchi, Mayu Yoshida, Eriko Grace Suto, Nobuharu Suzuki, Takeshi Muneta, Ichiro Sekiya, Chihiro Akazawa. Purified Human Synovium Mesenchymal Stem Cells as a Good Resource for Cartilage Regeneration. *PLoS ONE.* 2015.06; 10(6); e0129096

16. Takeshi Muneta. Twenty-Year Experience of a Double-Bundle Anterior Cruciate Ligament Reconstruction. *Clin Orthop Surg.* 2015.06; 7(2); 143-151
17. Ryohei Takada , Tetsuya Jinno , Daisuke Koga , Masanobu Hirao , Takeshi Muneta , Atsushi Okawa . Is Drain Tip Culture Prognostic of Surgical Site Infection? Results of 1380 Drain Tip Cultures in Total Hip Arthroplasty. *J Arthroplasty.* 2015.08; 30(8); 1407-1409
18. Tomoko Araki, Tadashi Masuda, Tetsuya Jinno, Sadao Morita. Incidence of floating toe and its association with the physique and foot morphology of Japanese children. *J Phys Ther Sci.* 2015.10; 27(10); 3159-3162
19. Toshifumi Watanabe, Takeshi Muneta, Ichiro Sekiya, Scott A Banks. Intraoperative joint gaps and mediolateral balance affect postoperative knee kinematics in posterior-stabilized total knee arthroplasty. *Knee.* 2015.12; 22(6); 527-534
20. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Shizuka Fujii, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Akifumi Matsuyama, Ichiro Sekiya. Platelet-derived growth factor (PDGF)-AA/AB in human serum are potential indicators of the proliferative capacity of human synovial mesenchymal stem cells. *Stem Cell Res Ther.* 2015.12; 6(1); 243
21. 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.* 2015.12; 1-19
22. Kazumasa Miyatake, Tetsuya Jinno, Daisuke Koga, Yuki Yamauchi, Takeshi Muneta, Atsushi Okawa. Comparison of Different Materials and Proximal Coatings Used for Femoral Components in One-Stage Bilateral Total Hip Arthroplasty. *J Arthroplasty.* 2015.12; 30(12); 2237-2241

[Conference Activities & Talks]

1. Toshiyuki Ohara, Takeshi Muneta, Yu Matsukura, Kunikazu Tsuji, Ichiro Sekiya. Hypoxia enhances colony formation and proliferation with chondrogenic potential in passage 0 human synovial mesenchymal stem cells.. Orthopaedic Research Society 2015 Annual Meeting 2015.03.28
2. Ryusuke Saito, Ichiro Sekiya, Nobutake Ozeki, Yusuke Nakagawa, Mio Udo, Katsuaki Yanagisawa, Kunikazu Tsuji, Takeshi Muneta. Strenuous Running Enhances Degeneration Of Articular Cartilage In A Rat Mia-induced Arthritis Model. ORS 2015 Annual Meeting 2015.03.28 Las Vegas, USA
3. Mio Udo, Ichiro Sekiya, Kunikazu Tsuji, Nobutake Ozeki, Yusuke Nakagawa, Toshiyuki Ohara, Ryusuke Saito, Katsuaki Yanagisawa, Takeshi Muneta. In Vivo Evaluation Of Arthritis By Mmp Activatable Probe In A Rat Mia-Induced Model. ORS 2015 Annual Meeting 2015.03.28 Las Vegas, USA
4. Mio Udo, Ichiro Sekiya, Kunikazu Tsuji, Nobutake Ozeki, Yusuke Nakagawa, Toshiyuki Ohara, Ryusuke Saito, Katsuaki Yanagisawa, Takeshi Muneta. Low Dosage Of Monoiodoacetic Acid Induces Arthritis Without Bone Defect In A Rat Model. ORS 2015 Annual Meeting 2015.03.28 Las Vegas, USA
5. Kaori Nakamura, Hideyuki Koga, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya, Takeshi Muneta. Evaluation of pivot-shift phenomenon in different maneuvers using triaxial accelerometer in pre/postoperative ACL reconstruction. 2015 Summit of Asia-Pacific Knee, Arthroscopy and Sports Medicine Society (APKASS) 2015.05.08 Taipei, Taiwan
6. Takeshi Muneta. Behind-remnant arthroscopic observation of anterior cruciate ligament and a new remnant-preserving reconstruction. APKASS Summit 2015.05.08 Taipei
7. Takeshi Muneta. Centralization method for lateral meniscus damages using anchor device. Lunch Seminar APKASS Summit 2015.05.09 Taipei
8. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Takeshi Muneta, Atsushi Okawa. Drain tip culture cannot be prognostic of surgical site infection after total hip arthroplasty. 16th EFORT 2015.05.27
9. Yuko Tokunaga Segawa, Makoto Kamegaya, Takashi Saisu, Jun Kakizaki, Mitsuaki Morita, Yasuhiro Oikawa, Reiko Tanaka, Yuta Tsukagoshi, Tetsuya Jinno, Atsushi Okawa. Treatment outcome of poor prognostic group of patients with Legg-Calvé-Perthes disease. The Asia Pacific Paediatric Orthopaedic Society (APPOS) 2015 2015.06.05 China, Hong Kong

10. Takeshi Muneta. ACL Reconstruction Approaching the Femoral Remnant from Behind. 10th Biennial ISAKOS Congress The Different Aspects of an Anatomical ACL Reconstruction 2015.06.08 Lyon, France
11. Yusuke Nakagawa, Koga H, Nagata T, Takashi T, Sekiya I, Muneta T. 3D reconstructed image analysis of effect on extruded lateral meniscus using centralization. 43th Japanese Society for Magnetic Resonance in Medicine 2015.09.10
12. Mari Uomizu, Keiichi Akita, Kumiko Yamaguchi . Anatomical variants in the insertion of the pectoralis minor tendon associated with the coracohumeral ligament. 4th Argentine congress of clinical anatomy 2015.09.24 Buenos aires, Argentina
13. Takeshi Muneta. Notchplasty for Anatomic Double-bundle Anterior Cruciate Ligament Reconstruction. 4th Asia Arthroscopy Congress 2015.10.02 Seoul, Korea
14. Hideyuki Koga, Takeshi Muneta. Importance of posterior oblique ligament in medial collateral ligament reconstruction based on biomechanics. 42nd Japanese congress of clinical biomechanics 2015.11.13

Biostructural Science

Professor : Yoshiro TAKANO (- Mar)
 Associate Professor: Makoto TABATA
 Technician: Makoto SUGIURA
 Secretary: Haruno KURODA (- Mar)
 Tomoko YAMAMOTO (April -)
 Graduate Student: Takafumi NAKANO (June -)

(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 section and microscopy. This skills work is a good opportunity to know the variation and the finesse of the human body in histology.

(4) Publications

[Original Articles]

1. Masahiro Chatani, Akiko Mantoku, Kazuhiro Takeyama, Dawud Abduweli, Yasutaka Sugamori, Kazuhiro Aoki, Keiichi Ohya, Hiromi Suzuki, Satoko Uchida, Toru Sakimura, Yasushi Kono, Fumiaki Tanigaki,

Masaki Shirakawa, Yoshiro Takano, Akira Kudo. Microgravity promotes osteoclast activity in medaka fish reared at the international space station. Sci Rep. 2015; 5; 14172

Pharmacology

Staffs and Students(April, 2015)

Associate Professor Kazuhiro AOKI
Assistant Professor Yukihiro TAMURA
Technologist Mariko TAKAHASHI

Researchers
Nobuyoshi TOMOMATSU (Maxillofacial Surgery)
Yasuhiro SHIMIZU (Orthodontic Science)

Graduate Students
Yasutaka SUGAMORI
Md. Haque Bhuyan ZAHIRUL
Tomoki UEHARA (Pediatric Dentistry)
Yuki ARAI (Removable Prosthodontics)
Toru TAKEMOTO(Oral and Maxillofacial Surgery)
Hideaki Inagawa(Removable Prosthodontics)

Lecturers
Keiichi OHYA
Akira NIFUJI
Etsuko TAKAHASHI
Nozomi HASEGAWA
Eiichi KUBOMURA
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. Toshimi Sato, Neil Alles, Masud Khan, Kenichi Nagano, Mariko Takahashi, Yukihiro Tamura, Asako Shimoda, Keiichi Ohya, Kazunari Akiyoshi, Kazuhiro Aoki. Nanogel-crosslinked nanoparticles increase the inhibitory effects of W9 synthetic peptide on bone loss in a murine bone resorption model. *Int J Nanomedicine*. 2015; 10; 3459-3473
2. Genki Kato, Yasuhiro Shimizu, Yuki Arai, Natsuki Suzuki, Yasutaka Sugamori, Miki Maeda, Mariko Takahashi, Yukihiro Tamura, Noriyuki Wakabayashi, Ramachandran Murali, Takashi Ono, Keiichi Ohya, Setsuko Mise-Omata, Kazuhiro Aoki. The inhibitory effects of a RANKL-binding peptide on articular and periarticular bone loss in a murine model of collagen-induced arthritis: a bone histomorphometric study. *Arthritis Res. Ther*. 2015; 17(1); 251
3. Masahiro Chatani, Akiko Mantoku, Kazuhiro Takeyama, Dawud Abduweli, Yasutaka Sugamori, Kazuhiro Aoki, Keiichi Ohya, Hiromi Suzuki, Satoko Uchida, Toru Sakimura, Yasushi Kono, Fumiaki Tanigaki, Masaki Shirakawa, Yoshiro Takano, Akira Kudo. Microgravity promotes osteoclast activity in medaka fish reared at the international space station. *Sci Rep*. 2015; 5; 14172
4. Mohannad Nassar, Noriko Hiraishi, Yukihiro Tamura, Masayuki Otsuki, Kazuhiro Aoki, Junji Tagami. Phytic Acid: An Alternative Root Canal Chelating Agent. *J Endod*. 2015.02; 41(2); 242-247
5. Natsuki Suzuki, Kazuhiro Aoki, Petr Marcián, Libor Borák, Noriyuki Wakabayashi. A threshold of mechanical strain intensity for the direct activation of osteoblast function exists in a murine maxilla loading model. *Biomech Model Mechanobiol*. 2015.11; 14(71); 1-10

[Conference Activities & Talks]

1. Uehara T, Mise S, Arai Y, Sugamori Y, Kato G, Tamura Y, Tabata Y, Murali R, Wakabayashi N, Miyashin M, Aoki K. A rankl-binding peptide accelerates BMP-induced bone regeneration in murine maxilla by subperiosteal injections.. 13th Congress of the Internatitonal Society of Bone Morphometry 2015.04.27 Tokyo(Tokyo Garden Palace Hotel)
2. Md. Zahirul Haque Bhuyan, Yoshinari Y, Kawasaki M, Sugamori Y, Kato G, Takahashi M, Tamura Y, Aoki K. The preliminary results on the effects of RANKL-binding peptide of cartilage destruction.. 12th Bone Biology Forum 2015.08.21 Chiba (Cross Wave Makuhari)

[Awards & Honors]

1. New Investigator Award(Uehara T), 13th Congress of the Internatitonal Society of Bone Morphometry, 2015.04

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 transcription factors necessary for the maintenance of chondrogenic phenotype.
2. 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

[Conference Activities & Talks]

1. Kazuo Ito, Tamayuki Shinomura. Quantitative analysis of enhancer activities essential for the high-level expression of type II collagen gene. The 28th Annual Meeting of the Japanese Society of Cartilage Metabolism 2015.03.06
2. T. Shinomura. Strength of enhancer elements found in type II collagen gene.. Gordon Research Conference on Cartilage Biology & Pathology 2015.03.22 Galveston, TX, USA

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 Hiroko Yamanokuchi
 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 EndMT which is involved in cancer progression
 Epithelial-mesenchymal transition (EMT) plays important roles in various physiological and pathological processes, and is regulated by signaling pathways mediated by cytokines including transforming growth factor (TGF)- β . Endothelial cells also 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- β (TGF- β) family play pivotal roles on in angiogenesis and lymphangiogenesis, and that abnormalities in TGF- β 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- β family signals regulate angiogenesis and lymphangiogenesis in tumor microenvironment.

(3) Structural and functional mapping of lysosomal membranes
 Lysosomes are ubiquitous organelles rich in hydrolytic enzymes, responsible for the degradation of macromolecules 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. 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.

Although the hydrolytic enzymes within lysosomes are mainly involved in the degradation processes, versatility of lysosomes depends on architecture of lysosomal membranes. Lysosomal membrane proteins act at several crucial steps of the lysosome life cycle, including lumen acidification, metabolite export, molecular motors recruitment, fusion with other organelles, and regulation of lysosomal biogenesis and autophagy by sensing energy metabolism. However, the mechanism coordinating the interaction of the lysosomal membrane proteins has not been sufficiently elucidated. Accordingly, we aim to uncover the structural and functional characteristics of assembly of membrane proteins on lysosomal membranes.

Lysosome-associated membrane proteins (LAMPs) regulate intracellular positioning of mitochondria in MC3T3-E1 cells

Lysosome associated membrane proteins-1 and -2 (LAMPs) are major protein components of the lysosomal membrane. They are type I transmembrane proteins composed of a large, heavily glycosylated luminal domain, a transmembrane domain and a short C-terminal cytoplasmic tail. LAMPs were initially considered to act as a barrier to protect the structural integrity of lysosomal membranes from the lytic luminal environment, by forming a glycocalyx. However, the deficiency of LAMPs does not affect the integrity of lysosomes. The deficiency of LAMPs in mouse embryonic fibroblasts affects the intracellular positioning of both phagosomes and lysosomes, by reducing their transport along microtubules towards the microtubule-organizing center. Since two organelles should approach each other before fusion, it is conceivable that the LAMPs-mediated regulation of the intracellular positioning of lysosomes and phagosomes is the role fulfilled by LAMPs in phagocytosis.

Accumulating evidence suggests that lysosomes are important in the bone-forming activity of osteoblasts. However, the roles of LAMPs in osteoblasts have not been elucidated. We investigated the role of LAMPs in the pre-osteoblastic cell line MC3T3-E1 and the osteocytic cell line MLO-Y4. We demonstrated that the downregulation of LAMPs promotes the perinuclear localization of mitochondria in MC3T3-E1 cells. Our findings are the first evidence suggesting the involvement of LAMPs in regulating the cellular positioning of mitochondria. Considering the facts that calcium phosphate deposits reside as granules in mitochondria, the LAMPs-mitochondria axis may be involved in the regulation of the mineralization process (reported in the “Experimental Cell Research”).

(4) Heparan sulfate proteoglycan-dependent cellular logistics

Heparan sulfate proteoglycans (HSPGs) are one of the basic constituents of plasma membranes where it interacts with a number of extracellular ligands. However, in addition to the extracellular function, HSPGs have been also suggested to mediate the trafficking of a variety of macromolecules from the cell surface. Growth factors, cytokines, lipoproteins, cell penetrating peptides, polycation-nucleic acid complexes, exosomes, and pathogens enter cells through HSPG-dependent endocytosis stressing the importance of the identification of HSPG species that participate in a formation of various endocytotic complexes.

The other subject, which is necessary to understand the biological significance of the HSPG-dependent transport pathway, is the role of HSPGs in the intracellular transport to cell surface. Elucidation of the molecular basis of the HSPG-mediated vesicles formation and its trafficking will be a breakthrough in the matrix biology.

Heparan sulfate proteoglycan and its putative role in trafficking of transglutaminase 2

Transglutaminase 2 (TG2) is a calcium-dependent enzyme that catalyzes a formation of covalent bonds between certain proteins, resulting in formation of aggregates. Activity of TG2 has been correlated with various physiological and pathological states. Although TG2 does not possess the secretory signal, it is also found on the cell surface where it cross-links ECM proteins and modulates the interactions of cells with the ECM. The details regarding the TG2 trafficking to the cell surface are still unclear, but the roles of both phospholipids and HSPGs have been suggested.

We have studied the putative role of HSPGs in trafficking of TG2 to and from the cells surface in mouse C6 glioma cell line model. At first we have characterized HSPGs expressed by glial cell lines. Staining with 10E4 antibodies showed high expression of HSPGs on cell surface. Immunoblotting using the antibodies recognizing HS-derived epitope revealed several bands suggesting the presence of multiple types of transmembrane-type proteoglycans, various syndecan and glypican species are the putative candidates for interaction with TG2. Subcellular fractionation and immunocytochemical analyses showed that TG2-specific compartments were also specific for HSPGs suggesting possible interactions between those molecules (presented at The 87th Annual Meeting of Japanese Biochemical Society).

(5) 3D microfocus X-ray movie system

We have developed a 3D microfocus X-ray movie system for the first time. By using this cineradiographic

system, the respiratory function in a murine model mimicking the initial stages of Parkinson's Disease (PD) can be examined in details besides the primary symptoms (resting tremor, muscle rigidity, slowness of movements). Respiratory function (diaphragm displacement and ribcage volume) showed mild alterations in the PD group. The jaw-opening reflex was observed during gravity deceleration, and we found that the magnitude of jaw-postural responses was associated positively with the gravity deceleration rate, "Jerk" rather than gravity. These results will contribute to understanding the PD symptoms in-depth.

3D microfocus X-ray movie system

We have developed a 3D microfocus X-ray movie system for the first time. By using this cineradiographic system, the respiratory function in a murine model mimicking the initial stages of Parkinson's Disease (PD) was analyzed. As a result, parameters of respiratory function (diaphragm displacement and ribcage volume) showed mild alterations in the PD group. The results suggest that respiratory alterations in PD may emerge simultaneously to other motor symptoms, and not as a consequence of the latter. The initial phase of gravity deceleration produced coordinated and generalized extension of the head, spine, and hindlimbs. The jaw-opening reflex was observed during gravity deceleration, and the magnitude of jaw-postural responses was associated positively with the gravity deceleration rate, "Jerk". The cineradiographic system contributes to the study of jaw-opening reflex in dentistry as well.

(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 "Enzymology of serine-palmitol transferase" (May 21, 2015) and "Selective secretion pathway in salivary gland" (November 18, 2015). Our graduate student investigated the role of lysosome-associated proteins in osteoblastic cells.

(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. Anupama R Rajapakshe, Katarzyna A Podyma-Inoue, Kazue Terasawa, Katsuya Hasegawa, Toshimitsu Namba, Yasuhiro Kumei, Masaki Yanagishita, Miki Hara-Yokoyama. Lysosome-associated membrane proteins (LAMPs) regulate intracellular positioning of mitochondria in MC3T3-E1 cells. *Exp. Cell Res.* 2015.02; 331(1); 211-222
2. Kazue Terasawa, Anupama R Rajapakshe, Katarzyna A Podyma-Inoue, Chiemi Mishima-Tsumagari, Masaki Yanagishita, Miki Hara-Yokoyama. Preferential recognition of isocitrate dehydrogenase by a rabbit monoclonal antibody (ab124797) against the C-terminal peptide of RANKL. *J. Immunol. Methods.* 2015.05;
3. P S de Campos, K Hasegawa, Y Kumei, J L Zeredo. Cineradiographic analysis of respiratory movements in a mouse model for early Parkinson's disease. *Respir Physiol Neurobiol.* 2015.11; 218; 40-45

4. 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

[Books etc]

1. Watari I, Abbassy MA, Podyma-Inoue KA, Ono T. Major Topics in Type 1 Diabetes. INTECH, 2015.11 (ISBN : 978-953-51-2204-3)

[Conference Activities & Talks]

1. Takashi Ode, Katarzyna A. Podyma-Inoue, Shinichi Arakawa, Miki Yokoyama, Yuichi Izumi. Intracellular cholesterol trafficking is involved in osteoblastic differentiation of MC3T3-E1 cells. The 58th Spring Meeting of the Japanese Society of Periodontology 2015.05 Chiba, Makuhari
2. Anupama R. Rajapakshe, Katarzyna A. Podyma-Inoue, Takashi Ode, Miki Hara-Yokoyama. Lysosome-associated membrane proteins (LAMPs) regulate bidirectional transport of lysosomes in MC3T3-E1 cells. The 58th Spring Meeting of the Japanese Society of Periodontology 2015.05 Chiba, Makuhari
3. Ippei Watari, Katarzyna Anna Podyma-Inoue, Ikuo Yonemitsu, Mutsumi Miyazaki and Takashi Ono. Altered craniofacial morphogenesis in the offspring of rats with gestational diabetes. The 91st Congress of the European Orthodontic Society 2015.06 Venice, Italy
4. Roles of signaling networks during endothelial-mesenchymal transition. TGF- β Meeting in Uppsala 2015.08 Uppsala, Sweden
5. Miki Yokoyama. Glycosylation regulates CD38 assembly on the cell surface. GLYCOBIOLOGY 2015 2015.08.12 Philadelphia
6. Tetsuro Watabe. Roles of Signaling and Transcriptional Networks during Endothelial-to-Mesenchymal Transition. 10th World Congress for Microcirculation 2015.09
7. Miki Yokoyama. Lysosome-associated membrane proteins regulate intracellular positioning of mitochondria. The 57th Annual Meeting of Japanese Association for Oral Biology 2015.09.11 Niigata
8. Miki Hara-Yokoyama, Shizuko Ichinose, Kumiko Ishii, Hidetake Kurihara, Shozo Ichinose, Keido Tadano-Aritomi, Norihiro Tada, Kazue Terasawa, Katarzyna A. Podyma-Inoue, Toshihide Kobayashi, Koichi Furukawa, and Kazuhisa Iwabuchi. Glycosphingolipids regulate the arrangement of the tight junction strands necessary for remodeling of the blood-testis barrier. The 8th Meeting of the Japanese Society for Ceramides 2015.10 Sapporo
9. Tetsuro Watabe. Roles of signaling networks during the formation and maintenance of vascular systems. Asia-Australia Vascular Biology Meeting 2015.10 Busan, Korea
10. Tetsuro Watabe. Roles of signal networks during the formation of vascular systems. KAIST Vascular Biology Meeting 2015.10 Daejeon, Korea
11. Katarzyna A. Podyma-Inoue, Anupama R. Rajapakshe, Takuya Moriwaki, Tetsuro Watabe and Miki Yokoyama. Heparan sulfate proteoglycan and intracellular transport; clues from proteomic analysis of transport vesicles. The 88th Annual Meeting of Japanese Biochemistry Society 2015.12 Kobe
12. Tetsuro Watabe. Roles of signal network during endothelial-to-mesenchymal transition. 2015.12 Kobe
13. Watabe Tetsuro. Roles of PDGF-BB signaling during the formation of lymphatic vessels. The 23rd Meeting of The Japanese Vascular Biology and Medicine Organization 2015.12.10 Kobe

Cell Signaling

Associate Professor(Principal Investigator)Tomoki NAKASHIMA
Assistant Professor Mikihiro HAYASHI

(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. Lynett Danks, Noriko Komatsu, Matteo M Guerrini, Shinichiro Sawa, Marietta Armaka, George Kollias, Tomoki Nakashima, Hiroshi Takayanagi. RANKL expressed on synovial fibroblasts is primarily responsible for bone erosions during joint inflammation. *Ann. Rheum. Dis.* 2015.05;
2. Matteo M Guerrini, Kazuo Okamoto, Noriko Komatsu, Shinichiro Sawa, Lynett Danks, Josef M Penninger, Tomoki Nakashima, Hiroshi Takayanagi. Inhibition of the TNF Family Cytokine RANKL Prevents Autoimmune Inflammation in the Central Nervous System. *Immunity*. 2015.12; 43(6); 1174-1185

[Misc]

1. Hayashi M, Nakashima T, Takayanagi H. Semaphorins in bone homeostasis Semaphorin. 2015; 159-173
2. [Bone and Calcium Research Update 2015. Regulation of bone remodeling by osteocytes] . 2015.01; 25(1); 21-28

3. Tomoki Nakashima. Amazing function of osteocyte 2015.01; 25(6); 899-905
4. Tomoki Nakashima. Bone remodeling and alveolar bone homeostasis 2015.08; 25(8); 1220-1228

[Conference Activities & Talks]

1. Tomoki Nakashima . Regulation of bone remodeling . 3rd Seoul Symposium on Bone Health KSBMR-JSBMR joint symposium 2015.05.27 Seoul

Inorganic Materials

Professor Kimihiro Yamashita
Associate Prof. Miho Nakamura
Assistant Prof. Naohiro Horiuchi
Assistant Prof. Noriko Ebe
Research Associate Naoko Hori

(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. N. Horiuchi, J. Endo, N. Wada, K. Nozaki, M. Nakamura, A. Nagai, K. Katayama and K. Yamashita. Dielectric properties of fluorine substituted hydroxyapatite: the effect of the substitution on configuration of hydroxide ion chains Journal of Materials Chemistry B. 2015; 3(33); 6790-6797

2. N. Wada, N. Horiuchi, M. Nakamura, K. Nozaki, T. Hiyama, A. Nagai and K. Yamashita. Controlled calcite nucleation on polarized calcite single crystal substrates in the presence of polyacrylic acid J. Cryst. Growth. 2015; 415; 7-14
3. N. Horiuchi, Y. Tsuchiya, N. Wada, K. Nozaki, M. Nakamura, A. Nagai, T. Okura and K. Yamashita. Polarization-assisted surface engineering for low temperature degradation-proof in yttria-stabilized zirconia ceramics J. Asian Ceram. Soc.. 2015; 3(2); 156-159
4. Kosuke Nozaki, Hiroki Koizumi, Naohiro Horiuchi, Miho Nakamura, Toshinori Okura, Kimihiro Yamashita, Akiko Nagai. Suppression effects of dental glass-ceramics with polarization-induced highly dense surface charges against bacterial adhesion. Dent Mater J. 2015; 34(5); 671-678
5. M. Nakamura, T. Tentunen, J. Varaniemi, J. Salonen, N. Hori, K. Yamashita, . Characterization of Human Osteoclast on Different Bioceramics, Key Engineering Materials. 2015.01; 631; 363-366
6. N. Matsui, K. Nozaki, K. Ishihara, K. Yamashita,. The Effects of Fibronectin Concentration on its Configuration on Hydroxyapatite Surfaces and the Osteoblast Response Materials Science & Engineering C. 2015.01; 48; 378-383
7. M. Nakamura, N. Hori, S. Namba, T. Toyama, N. Nishimiya, K. Yamashita,. Wettability and Surface Free Energy of Polarised Ceramic Biomaterials Biomedical Materials. 2015.01; 10(1); 011001
8. A. Ito, Y. Sogo, A. Yamazaki, M. Aizawa, A. Osaka, S. Hayakawa, M. Kikuchi, K. Yamashita, Y. Tanaka, M. Tadokoro, L. Ágata de Sena, F. Buchanan, H. Ohgushi, M. Böhner. Interlaboratory Studies on in vitro Test Methods for Estimating in vivo Resorption of Calcium Phosphate Ceramics Acta Biomaterialia. 2015.06; 25; 347-355
9. K. Nozaki, H. Koizumi, N. Horiuchi, M. Nakamura, T. Okura, A. Nagai, K. Yamashita. Antibacterial Properties of Dental Glass-Ceramics with Polarization-Induced Highly Dense Surface Charges Dental Materilas Journal. 2015.10; 34(5); 671-678
10. Norio Wada, Naohiro Horiuchi, Kohei Ohta, Shintaro Urasaki, Kohei Yamauchi, Kimihiro Yamashita. Controlled in Vivo Nacre Formation in Flat Pearls with Hydroxyapatite Bioceramic Nuclei Crystal Growth & Design. 2015.12; 16(1); 167-173
11. Nozaki K, Shinonaga T, Ebe N, Horiuchi N, Nakamura M, Tsutsumi Y, Hanawa T, Tsukamoto M, Yamashita K, Nagai A. Hierarchical periodic micro/nano-structures on nitinol and their influence on oriented endothelialization and anti-thrombosis Mater Sci Eng C Mater Biol Appl. 2015.12; 57; 1-6

[Books etc]

1. K. Nozaki, N. Ebe, K. Yamashita, A. Nagai. Mineral Scales and Deposits. Elasevier, 2015.08

[Conference Activities & Talks]

1. K. Shibata, N. Horiuchi, K. Nozaki, M. Nakamura, A. Nagai, K. Yamashita. Hydrothermal synthesis of fibrous hydroxyapatite. The 5th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-5) 2015.06.09 Tokyo, Japan
2. K. Watanabe, N. Horiuchi, K. Nozaki, M. Makamura, A. Nagai, K. Yamashita. Dielectric evaluation of chlorine substituted hydroxyapatite. The 5th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-5) 2015.06.09 Tokyo, Japan
3. Nozaki K, Fujita K, Ebe N, Miura H, Yamashita K, Nagai A. Bioresorbable and osteoconductive properties of porous carbonated apatite implanted in cortical and cancellous bone tissues. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09
4. Iwata N, Nozaki K, Miura H, Yamashita K, Nagai A. The effect of titania nanotube surfaces on osteoblast behavior. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09

5. T. Masutani, N. Horiuchi, K. Nozaki, M. Nakamura, K. Yamashita, A. Nagai. Polarization influences on cell dynamics via ERK signaling pathways. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09
6. N. Horiuchi, K. Ryu, N. Yoshida, T. Okura and K. Yamashita. Sodium Ion Conducting Ceramics with Na₅YSi₄O₁₂-Type Structure Synthesized by a Polymerized Complex Method. 20th International Conference on Solid State Ionics (SSI-20) 2015.06.16 Keystone, US
7. Nozaki K, Fujita K, Yamashita K, Miura H, Nagai A. Evaluation of bone formation and degradation of porous carbonated apatite block. 2015.10.03
8. Donghe Shen, Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita, Michiyo Miyashin. Osteoblastic responses to OCP and carbonate-containing OCP in vitro. The 37th annual meeting of the Japanese society for biomaterials 2015.11.09 Kyoto, Japan
9. Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Dielectric Study on Reorientation Phenomena of Hydroxide Ion in Hydroxyapatite. 17th US-Japan Seminar on Dielectric and Piezoelectric Ceramics 2015.11.17 Matsumoto, Japan
10. Yuta Kuwamura, Naohiro Horiuchi, Hirobumi Shibata, Kazuaki Hashimoto, Kimihiro Yamashita, Akiko Nagai. Osteoclast formation on carbonate substituted apatite. 15th Asian BioCeramics symposium 2015.12.09 Tokyo, Japan
11. Naohiro Horiuchi, Norio Wada, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Dielectric Phenomena in Monoclinic and Hexagonal Hydroxyapatite. 15th Asian BioCeramics symposium 2015.12.09 Tokyo, Japan
12. Donghe Shen, Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita, Michiyo Miyashin. Carbonate-containing Octacalcium Phosphate enhanced osteoblast proliferation and differentiation. 15th Asian BioCeramics symposium 2015.12.09 Tokyo, Japan
13. Natsuko Iwata, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. The effect of titania nanotube surfaces on osteoblast behavior. 15th Asian Bioceramics Symposium 2015.12.10
14. Risa Yamada, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita and Akiko Nagai. Study on antimicrobial activity by silver doped yttria-stabilized zirconia. 15th Asian Bioceramics Symposium 2015.12.10
15. Kazuhisa Fujita, Kosuke Nozaki, Kimihiro Yamashita, Hiroyuki Miura, and Akiko Nagai. Alkaline Phosphatase Activity of Periodontal Ligament Cell on Hydroxyl- and Carbonated-Apatites. 15th Asian Bioceramics Symposium 2015.12.10
16. T. Endo, K. Nozaki, K. Hashimoto, K. Yamashita, A. Nagai. Characterization of structure stability of β -tricalcium phosphate doped Na ion by electrical analysis. 15th Asian Bioceramics Symposium 2015.12.10
17. Kazuki Igeta, Kosuke Nozaki, Mamoru Aizawa, Kimihiro Yamashita, Akiko Nagai. Comparison of cytokines secretions from macrophage cultured on hydroxyapatite and carbonated apatite dense ceramics. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.16
18. Yuta Kuwamura, Naohiro Horiuchi, Kazuaki Hashimoto, Kimihiro Yamashita, Akiko Nagai. Effect of carbonated apatite on osteoclast differentiation of RAW264. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.16

[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

Periodontology

Professor Yuichi IZUMI

Associate Professor Hisashi WATANABE

Lecturer Satsuki HAGIWARA, Akira AOKI

Research Associate

Yasuo TAKEUCHI, Koji MIZUTANI, Tomonari SUDA, Sayaka KATAGIRI, Norio AOYAMA

Graduate Students

Yasuo ITO, Kaori FUJIWARA,

Takahiko SHIBA, Shogo MAEKAWA,

Keiko AKAZAWA, Masayuki TOI,

Masahiro NODA, Takahiro IKAWA,

Ayano UEKUBO, Satoru ONIZUKA,

Makoto KANEKO, Misa GOKYU,

Yuka SHIHEIDO, Taichen Lin,

Wataru ONO, Hiroki SATO,

Takeaki SUDO, Mizuki NAGATA,

Kiichi MARUYAMA, Kosei YANO,

Chantida Pawauputanon Na Mahasarakham

Ammar Shujaa Addin, Tooru TAKAGI,

Anri OHTSU, Eri TAZAKI, Sayuri UDAGAWA,

Risako MIKAMI, Rina KOMAZAKI, Daisuke KIDO,

Takasi ODE, Masaki TSUBOKAWA, Sophannary Kong,

Thatawee Khemwong, Nay Aung, Shinta SUZUKI (April ~),

Yuto OOSUGI (April ~), Kohei TAKEDA (April ~),

Yosuke TUCHITANI (April ~), Shunsuke FUKUBA (April ~),

Naho SUZUKI (April ~), Anongwee Leewananthawet (September ~),

Prima Buranasin (September ~)

Hospital Staff: 7, Research Student: 17, Registered dentist: 53

(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. Komabayashi T, Ebihara A, Aoki A. The use of lasers for direct pulp capping. J Oral Sci. 2015; 57(4); 277-286
2. Endo A, Watanabe T, Ogata N, Nozawa T, Aikawa C, Arakawa S, Maruyama F, Izumi Y, Nakagawa I. Comparative genome analysis and identification of competitive and cooperative interactions in a polymicrobial disease. ISME J. 2015.03; 9(3); 629-642
3. Konuma K, Itoh M, Suganami T, Kanai S, Nakagawa N, Sakai T, Kawano H, Hara M, Kojima S, Izumi Y, Ogawa Y . Eicosapentaenoic acid ameliorates non-alcoholic steatohepatitis in a novel mouse model using melanocortin 4 receptor-deficient mice. PLoS One. 2015.03; 10(3); e0121528
4. Shinkai K, Oda S, Yamaguchi H, Yamada M, Yoshikawa K, Yoshimine Y, Watanabe H. A Proposal of Educational Guideline for Laser Dentistry Journal of Japanese Society for Laser Dentistry. 2015.04; 26(1); 28-31
5. Aoki A, Mizutani K, Schwarz F, Sculean A, Yukna RA, Takasaki AA, Romanos GE, Taniguchi Y, Ssaki KM, Zeredo JL, Koshy G, Coluzzi DJ, White JM, Abiko Y, Ishikawa I, Izumi Y.. Periodontal and peri-implant wound healing following laser therapy. Periodotol 2000. 2015.04; 68(1); 217-69
6. Shimizu S, Momozawa Y, Takahashi A, Nagasawa T, Ashikawa K, Terada Y, Izumi Y, Kobayashi H, Tsuji M, Kubo M, Furuichi Y. A genome-wide association study of periodontitis in a Japanese population. J. Dent. Res. 2015.04; 94(4); 555-561
7. 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 β -tricalcium phosphate: a preclinical study in dogs. J. Periodont. Res.. 2015.05;
8. Matsuura T, Akizuki T, Hoshi S, Ikawa T, Kinoshita A, Sunaga M, Oda S, Kuboki Y, Izumi Y. Effect of a tunnel-structured β -tricalcium phosphate graft material on periodontal regeneration: a pilot study in a canine one-wall intrabony defect model. Journal of Periodontal Research. 2015.06; 50(3); 347-355
9. Suzuki J, Aoyama N, Aoki M, Tada Y, Wakayama K, Akazawa H, Shigematsu K, Hoshina K, Izumi Y, Komuro I, Miyata T, Hirata Y, Isobe M. Incidence of periodontitis in Japanese patients with cardiovascular diseases: a comparison between abdominal aortic aneurysm and arrhythmia. Heart Vessels. 2015.07; 30(4); 498-502

10. Pavlić V, vujić -Aleksić V, Aoki A, Nežić L. Treatment of recurrent aphthous stomatitis by laser therapy: A systematic review of the literature. *Vojnosanit Pregl.* 2015.08; 72(8); 722-728
11. Suzuki J, Imai Y, Aoki M, Fujita D, Aoyama N, Tada Y, Akazawa H, Izumi Y, Isobe M, Komuro I, Nagai R, Hirata Y. High incidence and severity of periodontitis in patients with Marfan syndrome in Japan. *Heart Vessels.* 2015.09; 30(5); 692-695
12. 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 B-Tricalcium Phosphate Blocks: A 2-Month Histological Pilot Study in Beagle Dogs. *J. Periodontol.* 2015.09; 1-14
13. Pawaputanon Na Mahasarakham C, Ezura Y, Kawasaki M, Smriti A, Moriya S, Yamada T, Izu Y, Nifuji A, Nishimori K, Izumi Y, Noda M. BMP-2 Enhances Lgr4 Gene Expression in Osteoblastic Cells *J. Cell. Physiol.* 2015.09; (e-pub);
14. Ogita M, Tsuchida S, Aoki A, Satoh M, Kado S, Sawabe M, Nanbara H, Kobayashi H, Takeuchi Y, Mizutani K, Sasaki Y, Nomura F, Izumi Y. Increased cell proliferation and differential protein expression induced by low-level Er:YAG laser irradiation in human gingival fibroblasts: proteomic analysis. *Lasers in Medical Science.* 2015.09; 30(7); 1855-1866
15. Suda T, Kobayashi H, Akiyama T, Takano T, Gokyu M, Sudo T, Khemwong T, Izumi Y. Desensitizing Agent Reduces Dentin Hypersensitivity During Ultrasonic Scaling: A Pilot Study. *J Clin Diagn Res.* 2015.09; 9(9); ZC46-ZC49
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17. Kitamura M, Akamatsu M, Kawanami M, Furuichi Y, Fujii T, Mori M, Kunimatsu 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.* 2015.11; (e-pub);
18. Thanakun S, Izumi Y. Effect of Periodontitis on Adiponectin, C-Reactive Protein and Immunoglobulin G to Porphyromonas Gingivalis in Overweight or Obese Thai People. *J. Periodontol.* 2015.12; 1-16
19. 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.* 2015.12; e-pub
20. Khamaisi Mogher, Katagiri Sayaka, Keenan Hillary, Park Kyoungmin, Maeda Yasutaka, Li Qian, Qi Weier, Thomou Thomas, Eschuk Danielle, Tellechea Ana, Veves Aris, Huang Chenyu, Orgill Dennis Paul, Wagers Amy, King George L. PKCdelta inhibition normalizes the wound-healing capacity of diabetic human fibroblasts *J Clin Invest.*

[Books etc]

1. Watanabe H (Supervise), Yokose S, Togaya N, Gomi K et al.. Introduction of laser dentistry. Dental Diamond Publisher, 2015.04
2. evolution : contemporary protocols for anterior single-tooth implants. 2015.11 (ISBN : 978-4-7812-0460-4)

[Misc]

1. Nagpal Y, Yamashiro Y, Izumi Y. The Two-Way Association of Periodontal Infection with Systemic Disorders: An Overview. *Mediators Inflamm.* 2015; (e-pub);
2. Suzuki J, Aoyama N, Izumi Y, Isobe M, Komuro I, Hirata Y. Effect of periodontitis on cardiovascular manifestations in Marfan syndrome. Critical common role of TGF- β . *Int Heart J.* 2015; 56(2); 121-124
3. Aoki A, Mizutani K, Izumi Y. A novel Comprehensive periodontal pocket therapy using the Er:YAG laser The Journal of the Stomatological Society. 2015; 82(3); 14

4. Izumi Y, Aoyama N, Matsuura T, Mizutani K. The current evidence of dental care and oral health for achieving healthy longevity in an aging society. Japan Dental Association. 2015.03; 252-257
5. Watanabe H. Clinical application of ruscello paste MASDENT F Journal of GC Membership Society . 2015.05; (153); 29-35
6. Watanabe H, Nagai S. Novel dental treatments developed by laser, LED and light The Journal of The Japan Dental Association. 2015.07; 68(4); 284-293
7. Aoki A, Tsubokawa M, Kakizaki S, Lin T, Mizutani K, Izumi Y. Application of dental OCT in periodontal therapy Dental Materials Journal. 2015.11; 34(6); 433-436
8. Watanabe H. Biological function of various factors related to periodontal disease and development of novel therapy The Japanese Journal of Conservative Dentistry. 2015.12; 58(6); 439-442

[Conference Activities & Talks]

1. Lin T, Aoki A, Saito N, Yumoto M, Nakajima S, Nagasaki K, Wada S, Izumi Y . Dental hard tissue ablation with pulsed Cr: CdSe laser . 35th Annual Meeting of the Laser Society of Japan 2015.01.11 Tokyo
2. Watanabe H. Basis of periodontal diseases and its treatment procedure. GC Dental College Seminar 2015.01.27 Tokyo
3. Suwannarong W, Tangwanichgapong K, Sumanonta G, Takeuchi Y, Nagasawa T, Izumi Y, Dasanayake A. Periodontopathic bacterial burden in pregnant Thai women. 93rd General Session and Exhibition of the International Association of Dental Research 2015.03.12 Boston, USA
4. Gokyu M, Kobayashi H, Kawashima N, Ikeda Y, Nanbara H, Sudo T, Suda T, Izumi Y. Bacterial evaluation in Periodontal-Endodontic lesion. The International Association for Dental Research (IADR) 2015.03.14 Boston
5. Hasegawa M, Mizutani K, Nanbara H, Kobayashi H, Izumi Y. Insulin Resistance Impairs Gingival Wound Healing Via PKC Activation. 2015 IADR General Session & Exhibition 2015.03.14 Boston, MA, USA
6. Otsu A, Sekiuchi T, Suda T, Takeuchi Y, Izumi Y. The decontamination effect of sodium hypochlorite dilution water . 16th Annual meeting of the Japan Society for Oral Functional Water 2015.03.29 Tokyo
7. Watanabe H. Lasers use in periodontology. 37th Asian Pacific Dental Congress 2015.04.02 Singapore
8. Shiheido Y, Maejima Y, Suzuki J, Aoyama N, Kobayashi N, Kaneko M, Izumi Y, Isobe MJ, Aoyama N, Kaneko M, Izumi Y, Isobe M. Infection of Periodontal Pathogen Triggers Cardiac Rupture of Infarcted Myocardium in Mice. The 79th Annual Scientific Meeting of the Japanese Circulation Society 2015.04.24 Osaka
9. Watanabe H. Effectiveness of PDGF or laser application on periodontal diseased root surfaces . 55th Annual Iranian Dental Association Congress 2015.05.11 Tehran, Iran
10. Watanabe H. Non-surgical and surgical periodontal therapy using laser and its basis and clinical outcome. WFLD Symposium in conjunction with 55th Annual Iranian Dental Association Congress 2015.05.12 Tehran, Iran
11. Ode T, Podyma-Inoue KA, Arakawa S, Yokoyama M, Izumi Y. Intracellular cholesterol trafficking is involved in osteoblastic differentiation of MC3T3-E1 cells. The 58th Spring Meeting of the Japanese Society of Periodontology 2015.05.15 Chiba
12. Rajapakshe A, Podyma-Inoue KA, Ode T, Yokoyama M. Lysosome-associated membrane proteins (LAMPs) regulate bidirectional transport of lysosomes in MC3T3-E1 cells. The 58th Spring Meeting of the Japanese Society of Periodontology 2015.05.15 Chiba
13. Chigasaki O, Aoyama N, Sasaki Y, Aoki A, Takeuchi Y, Mizutani K, Ikeda Y, Gokyu M, Umeda M, Izumi Y. The relationship between Red-complex bacterial counts and prevalence and severity of periodontal disease. 58th Annual spring meeting of Japanese Society of Periodontology 2015.05.15 Chiba

14. Kido A, Nagata T, Naruishi K, Tabeta K, Yamazaki K, Yoshie H, Watanabe H, Izumi Y, Suda R, Yamamoto M, Shiba H, Kurihara H, Yanagida M, Kitamura M, Mizuno M, Mishima A, Murakami S. Periodontal diagnosis by using immunocromatography for calprotectin in GCF . 58th Annual Spring Meeting of Japanese society of Periodontology 2015.05.15 Chiba
15. Nagata M, Iwasaki K, Akazawa K, Komaki M, Yokoyama N, Tooi M, Izumi Y, Morita I. The influence of concentration ratio of culture medium from periodontal ligament stem cells on periodontal regeneration. The 58th Spring Meeting of the Japanese Society of Periodontology 2015.05.15 Chiba
16. Aoyama N, Suzuki J, Kobayashi N, Yoshida A, Kaneko M, Shiheido Y, Sato H, Isobe M, Izumi Y. Prevalence of periodontal disease in patients of coronary heart disease. The 58th Spring Meeting of the Japanese Society of Periodontology 2015.05.16 Chiba
17. Akazawa K, Iwasaki K, Nagata M, Komaki M, Yokoyama N, Ayame H, Yamaki K, Tooi M, Izumi Y, Morita I. Construction of double-layered cell transferred-amnion using osteoblasts and periodontal ligament stem cells by cell transfer technology. The 58 the Spring Meeting of the Japan Society of Periodontology 2015.05.16 Chiba
18. Shiheido Y, Maejima Y, Suzuki J, Aoyama N, Kaneko M, Izumi Y, Isobe M. Infection of a Periodontal Pathogen, *Porphyromonas gingivalis*, Triggers Cardiac Rupture of Infarcted Myocardium in Mice. 4th TRI-UNIVERSITY CONSORTIUM 2015.05.20 Bangkok, Thailand
19. Gokyu M, Kobayashi H, Nanbara H, Sudo T, Ikeda Y, Suda T, Izumi Y. Thrombospondin-1 Expression by Periodontal Pathogen via Toll-like Receptor 2. 4th Tri-University Consortium 2015.05.21 Bangkok, Thailand
20. Tsumanuma Y, Iwata T, Washio K, Kuroda H, Yamato M, Okano T, Izumi Y. Comparison of canine multipotent mesenchymal stromal cells from various mesenchymal tissues. Europerio 8 2015.06.03 London, UK
21. Maruyama N, Goda A, Takeuchi Y, Shiba T, Koyanagi T, Izumi Y, Maruyama F, Nakagawa I. Bacterial activity in peri-implantitis and periodontitis. Europerio 8 2015.06.03 London, UK
22. Shiba T, Watanabe F, Maruyama F, Takeuchi Y, Koyanagi T, Maruyama N, Nakagawa I, Izumi Y. Inconsistency between abundance of 16S rRNA and mRNA in bacterial community of periodontitis and peri-implantitis. Europerio 8 2015.06.03 London, UK
23. Watanabe H. Laser will contribute the extence of health life span. 27th Annual Meeting of Japanese Association for Laser Dentistry 2015.06.06 Sapporo
24. Tsukui A, Watanabe H. A case of Er:YAG laser application for periimplatitis. 27th Annual Meeting of Japanese Association for Laser Dentistry 2015.06.07 Sapporo
25. Takeuchi Y, Katagiri S, Kobayashi H, Komazaki R, Suda T, Wakamatsu M, Takamatsu H, Hayakumo S, Takano T, Kusunoki Y, Yoshida A, Kinebuchi E, Otsu A, Sekiuchi T, Katayama S, Nakazato A, Mise T, Izumi Y. The effectiveness of bacterial test as a prognostic marker for initial preparation in aggressive periodontitis. 142th Meeting of the Japanese Society of Conservative Dentistry 2015.06.25 Fukuoka
26. Kinebuchi E, Suda T, Ikeda Y, Mizutani K, Aoyama N, Hayakumo S, Koyanagi T, Sekiuchi T, Shioyama H, Izumi Y. Relation between Systemic Diseases and Periodontal Conditions: A Clinico-statica. 2015.06.25 Fukuoka
27. Takahiro Ikawa, Tatsuya Akizuki, Takanori Matsuura, Shu Hoshi, Wataru Ono, Kiichi Maruyama, Yuichi Izumi. Ridge preservation after tooth extraction using tunnel structured β -tricalcium phosphate blocks: A 8 weeks study in beagle dogs. 1st The Japanese Society for Osteoimmunology 2015.06.30
28. Shinkai K, Oda S, Yamaguchi H, Yamada M, Yoshikawa K, Watanabe H. A Proposal of Educational Guidline for Laser Dentistry. 34th Annunal meeting of Japanese society of dental education 2015.07.10 Kagoshima
29. Tooi M, Komaki M, Iwasaki K, Yokoyama N, Ayame H, Taki A, Honda I, Morioka T, Kubota T, Izumi Y, Morita I. Mesenchymal stem cell-derived exosomes altered differentiation competence in fibroblasts. The 36th Annual Meeting of the Japanese Society of Inflammation and Regeneration 2015.07.22 Tokyo, Japan

30. Nakasato A, Ikeda Y, Takeuchi Y, Katagiri S, Suda T, Maekawa S, Matsuura T, Sekiuchi T, Ikeda E, Izumi Y. Appropriate supportive periodontal therapy interval for periodontal patients. 58th Annual autumn meeting of Japanese Society of Periodontology 2015.09.12 Shizuoka
31. Maekawa S, Kagagiri S, Komazaki R, Udagawa S, Ohtsu A, Takeuchi Y, Izumi Y. Analysis of ligature-induced periodontitis in diabetic mice. 58th Annual autumn meeting of Japanese Society of Periodontology 2015.09.12 Shizuoka
32. Sho Kakizaki, Akira Aoki, Masaki Tsubokawa, Lin Tai-Chen, Koji Mizutani, Yoichi Taniguchi, Kenichiro Ejiri, Shigeru Oda, Yasunori Sumi, Yuichi Izumi. Observation and analysis of periodontal tissue using optical coherence tomography (OCT).. The 58th Autumn Meeting of the Japanese Society of Periodontology 2015.09.12 Shizuoka
33. Lin T, Aoki A, Saito N, Yumoto M, Mizutani K, Izumi Y. Effects of wavelength-tunable nanosecond pulsed Cr: CdSe laser on dental hard tissues: examination in the spectral range of 2.76-3.00 micrometer. The 58th Autumn Meeting of the Japanese Society of Periodontology 2015.09.12 Hamamatsu
34. Masahiro Noda, Akira Aoki, Koji Mizutani, Taichen Lin, Motohiro Komaki, Shunichi Shibata, Yuichi Izumi. Effect of low-level laser therapy on early stage of wound healing of tooth extraction socket. The 58th Autumn Meeting of the Japanese Society of Periodontology 2015.09.13 Hamamatsu
35. Satsuki Hagiwara. A case report of comprehensive periodontal therapy for generalized severe chronic periodontitis patient followed up twenty-eight years . 2015.09.13
36. Lin T, Aoki A, Saito N, Yumoto M, Nakajima S, Nagasaki K, Ichinose S, Mizutani K, Wada S, Izumi Y. Dental hard tissue ablation with a wavelength-tunable pulsed Cr: CdSe laser in the range of 2.76-3.00 micrometer. 76th Japan Society of Applied Physics Autumn Meeting 2015.09.16 Nagoya
37. Akazawa K, Iwasaki K, Nagata M, Komaki M, Yokoyama N, Ayame H, Yamaki K, Tooi M, Izumi Y, Morita I. Double-layered cell transfer technology for bone regeneration. The 58 the Autumn Meeting of the Japan Society of Periodontology 2015.09.21 Shizuoka
38. Takeuchi Y. General risk factors for peri-implant disease. 45th Annual Meeting of Japanese Society of Oral Implantology 2015.09.23 Okayama
39. Aoyama N. Importance of clinical examinations based on the relationship between periodontal disease and cardiovascular disease. The 8th Annual Meeting of The Japanese Society for Evidence and the Dental Professional 2015.10.03 Yokosuka
40. Washio K, Tsutsumi Y, Tsumanuma Y, Suphanantachat S, Yano K, Ichinose S, Yamato M, Okano T, Hanawa T, Ishikawa I.. Novel Periodontal Tissue Attachment on the Modified Titanium Surface. 11th Asian Pacific Society of Periodontology Symposium 2015.10.08 Bali, Indonesia
41. Watanabe H, Wang H, Ogita M and Izumi Y. Human beta-defensin-3 promotes the fibroblasts attachment and proliferation onto periodontitis affected root surfaces. 11th APSP 2015.10.08 Bali, Indonesia
42. Sudo T, Okada Y, Kobayashi H, Gokyu M, Izumi Y, Tanaka T. Identification of a candidate gene in aggressive periodontitis by whole-exome sequencing. The 60th Meeting of the Japan Society of Human Genetics 2015.10.16 Tokyo
43. Aoyama N, Suzuki J, Izumi Y, Isobe M. Increase of lost teeth in peripheral vascular disease patients. The 56th Annual Meeting of Japanese College of Angiology 2015.10.29 Tokyo
44. Aoyama N, Suzuki J, Isobe M, Izumi Y. Increased tooth loss in peripheral vascular disease patients. 5th Buerger disease and PAD Forum 2015.11.07 Phnom Penh, Cambodia
45. Sudo T, Okada Y, Kobayashi H, Gokyu M, Tanaka T, Izumi Y. Genetic analysis of aggressive periodontitis using a massively parallel sequencer. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo
46. Nagata M, Iwasaki K, Akazawa K, Komaki M, Yokoyama N, Tooi M, Izumi Y, Morita I. Culture medium from periodontal ligament stem cells enhances periodontal wound healing. The 143rd Meeting of the Japanese Society of Conservative Dentistry 2015.11.13 Tokyo

47. Matsuura T, Ikeda Y, Kobayashi H, Gokyu M, Sakamaki Y, Tsuchiya Y, Nose S, Takahashi Y, Izumi Y. A NOVEL DIAGNOSTIC LOGIC USING SALIVA PATHOGEN AND A SELF-ADMINISTERED QUESTIONNAIRE FOR SCREENING PERIODONTITIS. 101st Annual Meeting of American Academy of Periodontology 2015.11.15 Orlando, Florida
48. Lin T, Aoki A, Saito N, Yumoto M, Nakajima S, Nagasaki K, Ichinose S, Mizutani K, Wada S, Izumi Y. Dental hard tissue ablation with a newly-developed wavelength tunable Cr: CdSe laser. 101st Annual Meeting of American Academy of Periodontology 2015.11.15 Orlando, Florida, USA
49. Taniguchi A, Aoki A, Sakai K, Izumi Y. Er:YAG laser-assisted ridge augmentation for extraction sockets with buccal dehiscence: a case report. The American Academy Of Periodontology 101st Annual Meeting 2015.11.15 Orlando, Florida, USA.
50. Watanabe H. Novel dental treatments developed by laser, LED and light . The3rd education workshop of Japanese society for laser dentistry 2015.11.29 Tokyo
51. Shiheido Y, Maejima Y, Isobe M. Invasion of a Periodontal Pathogen, *Porphyromonas gingivalis*, in Myocardium Causes Mechanical Complications after Myocardial Infarction in Mice. The 32nd Annual Meeting of the International Society for Heart Research Japanese Section (ISHR2015) 2015.12.10 Kobe
52. Ejiri K. A case report of comprehensive treatment for moderate chronic periodontitis with flare-out.. The 73rd educational workshop of Japanese Academy of Clinical Periodontology Kantoh Branch 2015.12.06 Nakano

[Awards & Honors]

1. Akazawa K. Young Investigator Award of The Japanese Society of Periodontology, The Japanese Society of Periodontology, 2015
2. Akazawa K. TERAYAMA FOUNDATION - Scholarship Program, Terayama Foundation, 2015
3. Akazawa K. Morita Scholarship Foundation Scholarship Program, Morita Scholarship Foundation, 2015
4. Watanabe H. Academic Award of The Japanese Society of Conservative Dentistry , The Japanese Society of Conservative Dentistry, 2015.06

Global Health Promotion

Associate Professor: Keiko Nakamura, MD, PhD

Junior Associate Professor: Masashi Kizuki, MD, MPH, PhD; Kaoruko Seino, MMs, PhD

Assistant Professor: Ayako Morita, MMs, PhD

Research Technical Associate: Rami Hani Al Rifai, BVM, MSc, PhD; Ghada Al-Khulaidi, HA, MPA, PhD

RONPAKU (Dissertation PhD) Program Fellow: Tayphasavanh Fengthong, MD, MPH

Graduate Student: Aya Anzai, RN, PHN; Adam Izzeldin Fadl, MSc; Huu Chau Duc Nguen, MD;

Ghada Al-Khulaidi, HA, MPA; Mosiur Rahman, MSc; Rakprasit Jutarat, MPH; Saber Al-Sobaihi, MPH;

Shagdarsuren Tserendulam, MBA; Mohammad Omar Mashal, MD; Shiro Ochi, MSc, PhD;

Dasavanh Manivong, MD, MSc; Delgermaa Doshzeveg, MPH; Isaac Maro, MD, MPH;

Yoshiko Shimozawa, PT, MMs; Hoang Thuy Linh Nguyen, MD, MPH; Ahmad Shekib Arab, MD

Graduate Research Student: Yuri Tashiro, MPhrm, MPH

(1) Outline

The department of Global Health Promotion 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

The department's research investigates local, national and international policies and programs to redress health inequalities.

Major Research Topics:

- 1) Living environmental and socio cultural factors related to the health of urban populations
- 2) Prevention and control of non-communicable diseases
- 3) The Healthy Cities Program: Comprehensive, community health programs
- 4) Health promotion paradox: measuring reduction of social gradients in health
- 5) International health workforce and trade in health services

(3) Education

Master Programs

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

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. A rich variety of educational activities are 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.

Public Health Leaders (PHL) Program

Students in the PHL program 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.

(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.

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

- Access 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 academic, public health research
- Facilitate learning of staff, students, and colleagues, and
- Practice and respect professional ethics in a socio-culturally diverse environment.

(5) Publications

[Original Articles]

1. Andrew R Greenhill, Hirokazu Tsuji, Kiyohito Ogata, Kazumi Natsuhara, Ayako Morita, Kevin Soli, Jo-Ann Larkins, Kiyoshi Tadokoro, Shingo Odani, Jun Baba, Yuichi Naito, Eriko Tomitsuka, Koji Nomoto, Peter M Siba, Paul F Horwood, Masahiro Umezaki. Characterization of the gut microbiota of papua new guineans using reverse transcription quantitative PCR. PLoS ONE. 2015; 10(2); e0117427
2. Rami Al Rifai, Keiko Nakamura, Kaoruko Seino, Masashi Kizuki, Ayako Morita. Unsafe sexual behaviour in domestic and foreign migrant male workers in multinational workplaces in Jordan: occupational-based and behavioural assessment survey. BMJ Open. 2015; 5(6); e007703
3. Rahman M, Nakamura K, Seino K, Kizuki M. Do tobacco smoking and illicit drugs/alcohol dependence increase the risk of mental disorders among men? Evidence from a national urban Bangladeshi sample. Perspect Psychiatr Care . 2015.01; 51; 16-27
4. Rahman M, Nakamura K, Seino K, Kizuki M. Sociodemographic factors and the risk of developing cardiovascular disease in Bangladesh. Am J Prev Med. 2015.01; 48; 456-461
5. Al Rifai R, Nakamura K, Seino K, Morita A, Kizuki M.. Unsafe sexual behavior of domestic and foreign migrant male workers in multinational workplaces in Jordan: occupational-based and behavioral assessment survey. BMJ Open. 2015.04; 5(6); e007703
6. Rami Al Rifai, Keiko Nakamura. Differences in breast and cervical cancer screening rates in Jordan among women from different socioeconomic strata: analysis of the 2012 population-based household survey. Asian Pac. J. Cancer Prev.. 2015.07; 16(15); 6697-6704
7. Rahman M, Nakamura K, Kizuki M. . Socioeconomic differences in the prevalence, awareness, and control of diabetes in Bangladesh. Journal of Diabetes and Its Complications. 2015.08; 29(6); 788-793

8. Mosiur Rahman, Keiko Nakamura, Masashi Kizuki. Socioeconomic differences in the prevalence, awareness, and control of diabetes in Bangladesh. *J. Diabetes Complicat.* 2015.08; 29(6); 788-793
9. Izzeldin Fadl Adam, Keiko Nakamura, Masashi Kizuki, Rami Al Rifai, Urnaa Vanching. Relationship between implementing interpersonal communication and mass education campaigns in emergency settings and use of reproductive healthcare services: evidence from Darfur, Sudan. *BMJ Open*. 2015.09; 5(9); e008285
10. 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.* 2015.10; 1-12
11. Nguyen Huu Chau Duc, Keiko Nakamura, Masashi Kizuki, Kaoruko Seino, Mosiur Rahman. Trends in inequalities in utilization of reproductive health services from 2000 to 2011 in Vietnam. *J Rural Med.* 2015.11; 10(2); 65-78
12. Yuichi I Naito, Ayako Morita, Kazumi Natsuhara, Kiyoshi Tadokoro, Jun Baba, Shingo Odani, Eriko Tomitsuka, Katsura Igai, Takumi Tsutaya, Minoru Yoneda, Andrew R Greenhill, Paul F Horwood, Kevin W Soli, Suparat Phuanukoonnon, Peter M Siba, Masahiro Umezaki. Association of protein intakes and variation of diet-scalp hair nitrogen isotopic discrimination factor in Papua New Guinea highlanders. *Am. J. Phys. Anthropol.* 2015.11; 158(3); 359-370

[Books etc]

1. Nakamura K, Ashton ACJ. Diversities of Healthy Cities in Asia and the Pacific. In: *Healthy Cities – The Theory, Policy, and Practice of Value - Based Urban Health Planning*. Springer, 2015.12

[Conference Activities & Talks]

1. Nakamura K. Health Care System in Japan.. Yonsei University Special Lecture 2015.06.04 Wonju, ROK
2. Nakamura K. Sharing of good practices on non-communicable disease prevention. . Global Forum on Healthy Cities 2015.08.20 Marikina, Philippines
3. Nakamura K. Analysis of “health promotion paradox” featuring effective public health interventions. . 7th International Conference on Public Health-Greater Mekong Subregion 2015.09.27 Hue Vietnam
4. Nakamura K. Promotion of Healthy Cities: Health in All Policies. Seminar on Healthy Cities, Nishi Tokyo City 2015.10.02 Nishi Tokyo City

Environmental Parasitology

Professor Nobuo OHTA
 Associate Professor Nobuaki AKAO
 Lecturer Takashi KUMAGAI
 Assistant Professor Akina HINO (2015.3)、Mitsuko SUZUKI
 (SATREPS Project in Ghana, ~2015.3)
 Project Professor Takashi SUZUKI (J-GRID Project in Ghana, ~2015.3),
 Project Lecturer Mitsuko Ohashi (AMED J-GRID, 2015.5~)
 PhD Course Students : Toshio ARAI (~2015.3), Wataru KAGAYA,
 Masafumi YAMABE, Emmanuel BLAY, Kofi KWOFIE (2015.10~),
 Ripa JAMAL, Daisuke KOBAYASHI, Katsumi MAEZAWA, Nobuhide HATA
 Master Course Students: Emi WADA, Junya NAKAMICHI

(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, Dirofilaria immitis
- (2) Epidemiological survey of parasitic diseases: Toxocariasis, Angiostrongyloidiasis, Spirurine larva, Schistosomiasis
- (3) Molecular epidemiology of tropical diseases: Drug resistance of malaria parasites, Drug resistance of anopheline mosquitoes, Molecular detection of Trypanosomes in Tsetse fly.
- (4) Immunopathology of schistosomiasis: Regulation of egg-granuloma formation in schistosomiasis japonica.
- (5) Drug development against parasitic infection: New drug candidates for schistosomiasis
- (6) Regulation of gene expression in parasitic helminthes: RNAi and parasitism in schistosome parasites.
- (7) Molecular and epidemiological research on parasitic infections 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.

(6) Publications

[Original Articles]

1. Suzuki M, Tung NH, Kwofie KD, Adegle R, Amoa-Bosompem M, Sakyamah M, Ayetey F, Owusu KB, Tuffour I, Atchoglo P, Frempong KK, Anyan WK, Morinaga O, Yamashita T, Aboagye F, Appiah AA, Appiah-Opong R, Nyarko AK, Yamaoka S, Yamaguchi Y, Edoh D, Koram K, Ohta N, Boakye DA, Ayi I, Shoyama Y.. New anti-trypanosomal active tetracyclic iridoid isolated from *Morinda lucida* Benth. *Bioorg Med Chem Lett*. 2015; 25; 3030-3
2. Tong QB, Chen R, Zhang Yi, Yang GJ, Kumagai T, Furushima-Shimogawara R, Lou D, Yang K, Wen LY, Lu SH, Ohta N, Zhou XN.. A new surveillance and response tool: risk map of infected *Oncomelania hupensis* detected by Loop-mediated isothermal amplification (LAMP) from pooled samples. *Acta Tropica*. 2015.01; 141(Pt B); 170-177
3. Kobayashi T, Hayakawa K, Mawatari M, Itoh M, Akao N, Yotsu RR, Sugihara J, Takeshita N, Kutsuna S, Fujiya Y, Kanagawa S, Ohmagari N, Kato Y.. Loiasis in a Japanese traveler returning from Central Africa. *Tropical Medicine and Health*. 2015.06; 43(2); 149-153
4. Mbanefo EC, Kumagai T, Kodama Y, Kurosaki T, Furushima-Shimogawara R, Cherif MS, Mizukami S, Kikuchi M, Huy NT, Ohta N, Sasaki H, Hirayama K.. Immunogenicity and anti-fecundity effect of nanoparticle coated glutathione S-transferase (SjGST) DNA vaccine against murine *Schistosoma japonicum* infection. *Parasitol Int*. 2015.08; 64(1); 24-31
5. Suzuki M, Tung NH, Kwofie KD, Agegle R, Amoa-Bosompen M, Sakiamah M, Ayetey F, Owusu KB, Tuffor I, Atchoglo P, Frempong KK, Anyan WK, Uto T, Morinaga O, Yamashita T, Aboagye F, Appiah AA, Appiah-Opong R, Nyarko AK, Yamaoka S, Yamaguchi Y, Edoh D, Koram K, Ohta N, Boakye DA, Ayi I, Shoyama Y.. New anti-trypanosomal active tetracyclic iridoid isolated from *Morinda lucida* Benth. *Bioorg Med Chem Lett*. 2015.08; 25(15); 3030-3033
6. Kong Q, Fan L, Zhang J, Akao N, Dong K, Lou D, Ding J, Tong Q, Zheng B, Chen R, Ohta N, Lu S.. Molecular identification of *Anisakis* and *Hysterothylacium* larvae in marine fishes from the East China Sea and the Pacific coast of central Japan. *International Journal of Food and Microbiology*. 2015.08; 199(1); 1-7
7. Akao, N.. Zoological infections of medical importance *Rinsho Kensa* (Journal of Clinical Laboratory Medicine). 2015.10; 59(10); 944-947

8. Kagaya W, Miyazaki S, Yahata K, Ohta N, Kaneko O.. The cytoplasmic region of *Plasmodium falciparum* SURFIN4.2 is required for transport from Maurer's cleft to the red blood cell surface. *Tropical Medicine and Health*. 2015.12; 43(12); 265-272
9. Blay EA, Ghansah A, Otchere J, Koku R, Kwofie KD, Bimi L, Suzuki T, Ohta N, Ayi I.. Congenital toxoplasmosis and pregnancy malaria detection post-mortem: Effective diagnosis and its implication for efficient management of congenital infection. *Parasitology International*. 2015.12; 64(6); 603-608

[Books etc]

1. Nobuo Ohta. *Current Therapy* 2015. Igaku shoin Co., 2015.01
2. Nobuo Ohta. *Microbiology*. Igaku Shoin Co., 2015.02
3. Nobuo Ohta. *Handbook for Infection Control*. Japanese Association of Public Health, 2015.06
4. Nobuo Ohta. *Zoonotic Infections*. Iyaku Journal Co., 2015.12

[Misc]

1. Nobuo Ohta. Tokyo Medical and Dental University-Ghana collaboration center: 10 years report from the front-line of disease endemicity *Saishin-Igaku*. 2015.04; 70(4); 761-765
2. Nobuaki AkaO, Masahide Yoshikawa. *Toxocariasis* 2015.05; 32; 286-289

[Conference Activities & Talks]

1. Nobuo Ohta. Parasitic infections as Neglected diseases in Japan.. 2015.02.10 Matsumoto
2. Nobuo Ohta. Challenge on Schistosomiasis in Japan-from the discovery, research, elimination, and future prospect-. Peter Hotez Book Launch Event 2015.06.08 Tokyo
3. Nobuo Ohta. Development of new tools for parasite control: current situation and future prospect.. 19th Annual Meeting of the Japanese Society of Travel Medicine 2015.07.25 Shinjuku, Tokyo
4. Nobuo Ohta. Mutual dependences between hosts and helminthic parasites.. 27th Japanese Association for Developmental and Comparative Immunology 2015.08.22 Obama, Fukui
5. Takashi Kumagai, Moritoshi Iwagami, Masafumi Yamabe, Phonepadith Khattignavong, Lavy Lorphacan, Pheovaly Soundala, Bouasy Hongvanthong, Nobuo Ohta, Paul T. Brey, Shigeyuki Kano. The evaluation of the molecular diagnosis using LAMP method against the parasitic trematoda in Lao PDR. the 9th National Health Research Forum 2015.10.13 Vientiane, Lao PDR
6. Masafumi Yamabe, Takashi Kumagai, Rieko Shimogawara, Blay Emmanuel Awusah, Koichiro Ichimura, Hye-Sook Kim, Nobuo Ohta. Efficacy of N-89 and N-251 against larval stage *Schistosoma mansoni* in vitro. The 17th Japan-Korea Parasitologist's Seminar (Forum Cheju 17) 2015.11.13 Suita, Osaka
7. Takashi Kumagai, Koichiro Ichimura, Masafumi Yamabe, Rieko Shimogawara, Takenori Seki, Nobuo Ohta. The miRNA contents of the extracellular vesicles from *Schistosoma japonicum* (parasitic platelminth) after male-female pairing and/or the erythrocytes uptake. 2015.12

[Patents]

1. Novel Compound having a tetracyclic iridoid skeleton and an anti-trypanosomal, anti-leishmanial, and anti-plasmodial agents comprising the same as an active ingredient., Application Number: PCT/JP2015/050856
2. Antischistosomal Agent, Patent Number : US 8927596 B

Forensic Medicine

Professor
Koichi UEMURA

Junior Associate Professor
Toshihiko AKI
Kana UNUMA

Assistant Professor
Takeshi FUNAKOSHI

Specially Appointed Assistant Professor
Kanao NORITAKE

Graduate Student
Atsushi YAMADA
Izumi FUNAKOSHI
Naho HIRAYAMA
Yusuke FUJII
Haruka KOJIMA
Ryo WATANABE

(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. Ryohei Kuroda, Kaori Shintani-Ishida, Kana Unuma, Ken-ichi Yoshida. Immobilization Stress With α 2-Adrenergic Stimulation Induces Regional and Transient Reduction of Cardiac Contraction Through Gi Coupling in Rats. *Int Heart J.* 2015; 56(5); 537-543
2. Atsushi Yamada, Toshihiko Aki, Kana Unuma, Takeshi Funakoshi, Koichi Uemura. Paraquat induces epithelial-mesenchymal transition-like cellular response resulting in fibrogenesis and the prevention of apoptosis in human pulmonary epithelial cells. *PLoS ONE.* 2015; 10(3); e0120192
3. Hisashi Nagai, Ichiro Kuwahira, Daryl O Schwenke, Hirotsugu Tsuchimochi, Akina Nara, Sayoko Ogura, Takashi Sonobe, Tadakatsu Inagaki, Yutaka Fujii, Rutsuko Yamaguchi, Lisa Wingefeld, Keiji Umetani, Tatsuo Shimosawa, Ken-Ichi Yoshida, Koichi Uemura, James T Pearson, Mikiyasu Shirai. Pulmonary Macrophages Attenuate Hypoxic Pulmonary Vasoconstriction via β 3AR/iNOS Pathway in Rats Exposed to Chronic Intermittent Hypoxia. *PLoS ONE.* 2015; 10(7); e0131923
4. Kanako Noritake, Toshihiko Aki, Takeshi Funakoshi, Kana Unuma, Koichi Uemura. Direct Exposure to Ethanol Disrupts Junctional Cell-Cell Contact and Hippo-YAP Signaling in HL-1 Murine Atrial Cardiomyocytes. *PLoS ONE.* 2015; 10(8); e0136952
5. Kana Unuma, Toshihiko Aki, Takeshi Funakoshi, Kyoko Hashimoto, Koichi Uemura. Extrusion of mitochondrial contents from lipopolysaccharide-stimulated cells: Involvement of autophagy. *Autophagy.* 2015; 11(9); 1520-1536
6. Sayuri Okawa, Kana Unuma, Atsushi Yamada, Toshihiko Aki, Koichi Uemura. Lipopolysaccharide induces expression of collagen VI in the rat lung. *J Toxicol Pathol.* 2015.01; 28(1); 37-41
7. Mayumi Watanabe, Kana Unuma, Yusuke Fujii, Kanako Noritake, Koichi Uemura. An autopsy case of vagus nerve stimulation following acupuncture. *Leg Med (Tokyo).* 2015.03; 17(2); 120-122
8. Mayumi Watanabe, Kana Unuma, Yohsuke Makino, Kanako Noritake, Atsushi Yamada, Hirotaro Iwase, Koichi Uemura. An Autopsy Case of Acute Massive Hematochezia Caused by Superior Mesenteric Vein Thrombosis: A First Report in Forensic Medicine. *J. Forensic Sci..* 2015.08;
9. Hajime Utsuno, Toru Kageyama, Keiichi Uchida, Kazuhiko Kibayashi, Koichi Sakurada, Koichi Uemura. Pilot study to establish a nasal tip prediction method from unknown human skeletal remains for facial reconstruction and skull photo superimposition as applied to a Japanese male populations. *J Forensic Leg Med.* 2015.12; 38; 75-80
10. Kyoko Uchida, Kana Unuma, Koichi Uemura. A fatality in a child with severe fatty liver due to n-butane and isopentane poisoning resulting from long-term inhalation of an antiperspirant aerosol. *Forensic Sci Med Pathol.* 2015.12; 11(4); 631-632

[Misc]

1. Toshihiko Aki, Takeshi Funakoshi, Koichi Uemura. Regulated necrosis and its implications in toxicology. *Toxicology.* 2015.07; 333; 118-126

Health Care Management and Planning

Professor	Kazuo KAWAHARA
Assistant Professor	Makiko SUGAWA
Graduate Student	Jian CHEN
	Woonkwan HYUN
	Masakazu KIKUCHI
	Yoko KOMURA
	Daisuke KUMAZAWA
	Masao MURATA
	Hisashi OMOTE
	Masataka YANO
	Kenjiro IDE
	Daisuke IKEDA
	Takamichi KOGURE
	Takeo NIGA
	Youichi SHIMA
	Towfiqua Mahfuza Islam

(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 analyses and policy 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. 2. Md. Ismail Tareque, Yasuhiko Saito & Kazuo Kawahara. Application of Health Expectancy Research on Working Male Population in Bangladesh Asian Population Studies. 2015;
2. Towfiqua Mahfuza Islam, Md. Ismail Tareque, Makiko Sugawa, Kazuo Kawahara.. Correlates of Intimate Partner Violence Against Women in Bangladesh The Journal of Family Violence.. 2015;
3. Towfiqua Mahfuza Islam. Correlates of Intimate Partner Violence Against Women in Bangladesh The Journal of Family Violence. 2015;

Molecular Epidemiology

Professor: Masaaki MURAMATSU
Associate Professor : Noriko SATO
Assistant Professor : Shinobu IKEDA

Adjunct Instructor : Katsuko SUDO, Fumihiko SATA, Jun-ichi TAGUCHI, Kaoru MOGUSHI

Graduate Student: Sariya Dechamethakun, Kaung Si Thu,
Khin Thet Thet Zaw, Yuko Maeda, Fujitani,
Tay Zar Kyaw, Tadaaki Katsuta, Jyun-ya Hagiwara, Shilpa Pavethynath
Norihiko Satake, Riya Tamura, Kenji Suzuki, Hirokazu Sakamoto
Research Student: Yui Tsubota
Research Resident: Maidina Abudushataer, Ake Ko Ko Minn, 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: Clinical Informatics
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. Yamada M, Sato N, Ikeda S, Arai T, Sawabe M, Mori S, Yamada Y, Muramatsu M, Tanaka M.. Association of the chromodomain helicase DNA-binding protein 4 (CHD4) missense variation p.D140E with cancer: potential interaction with smoking. *Genes Chromosomes Cancer*.. 2015; 54; 122-128
2. Nishizawa D, Kasai S, Hasegawa J, Sato N, Yamada H, Tanioka F, Nagashima M, Katoh R, Satoh Y, Tagami M, Ujike H, Ozaki N, Inada T, Iwata N, Sora I, Iyo M, Yamada M, Kondo N, Won MJ, Naruse N, Uehara-Aoyama K, Itokawa M, Ohi K, Hashimoto R, Tanisawa K, Arai T, Mori S, Sawabe M, Nakamieno M, Yamada Y, Yamada M, Sato N, Muramatsu M, Tanaka M, Irukayama-Tomobe Y, Saito YC, Sakurai T, Hayashida M, Sugimura H, Ikeda K. Associations between the orexin (hypocretin) receptor 2 gene polymorphism Val308Ile and nicotine dependence in genome-wide and subsequent association studies. *Mol Brain*. 2015; 8; 50
3. Zhou H, Mori S, Tanaka M, Sawabe M, Arai T, Muramatsu M, Mieno MN, Shinkai S, Yamada Y, Miyachi M, Murakami H, Sanada K, Ito H.. A missense single nucleotide polymorphism, V114I of the Werner syndrome gene, is associated with risk of osteoporosis and femoral fracture in the Japanese population. *J Bone Miner Metab*. 33:694-700 (2015) *J Bone Miner Metab*. 2015; 33(6); 694-700
4. Zhou H, Mori S, Ishizaki T, Tanaka M, Tanisawa K, Mieno MN, Sawabe M, Arai T, Muramatsu M, Yamada Y, Ito H.. Genetic risk score based on the lifetime prevalence of femoral fracture in 924 consecutive autopsies of Japanese males. *J Bone Miner Metab*. 2015;
5. Maekawa K, Nakamura R, Kaniwa N, Mizusawa S, Kitamoto A, Kitamoto T, Ukaji M, Matsuzawa Y, Sugiyama E, Uchida Y, Kurose K, Ueta M, Sotozono C, Ikeda H, Yagami A, Matsukura S, Kinoshita S, Muramatsu M, Ikezawa Z, Sekine A, Furuya H, Takahashi Y, Matsunaga K, Aihara M, Saito Y; Japan Pharmacogenomics Data Science Consortium.. Development of a simple genotyping method for the HLA-A*31:01-tagging SNP in Japanese. *Pharmacogenomics*. 2015; 16(15); 1689-1699

[Conference Activities & Talks]

1. Masaaki Muramatsu. Predictive genetic tests for polygenetic diseases change health and disease perception. The 56th Annual Scientific Meeting of Japan Society of Ningen Dock 2015.07.31 Yokohama
2. Noriko Sato. Inter-individual phenotypic variation and phenotypic robustness. The 60th Annual Meeting of the Japan Society of Human Genetics 2015.10.15 Tokyo
3. Noriko Sato. Prenatal exposure to an early-gestational maternal low-protein diet affects mutational stress response in the young adult mice. BMB2015 Biochemistry and Molecular Biology 2015.12.01 Kobe
4. Sariya Dechamethakun, Noriko Sato, Shinobu Ikeda, Tomio Arai, Motoji Sawabe, Masaaki Muramatsu, Masashi Tanaka. Association of CSMD2 Gene Polymorphisms with Cancer in Japanese Population. Biochemistry and Molecular Biology BMB2015 2015.12.02

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

[Original Articles]

1. Yuko Ojio, Toshiro Kubota and Kozo Takase.. Physicians' perception of the "Guidelines for Obstetrical Practice in Japan" and the reason for different compliances. J Med Dent Sci.. 2015.09; 62(3); 69-76

Health Policy and Informatics

Professor: Kiyohide FUSHIMI
Graduate Student: Asako TUKASAKI, Kyoko SHINODA,
Ayako MATSUO, Motoko TAIMA(SANO), Toshihiro TAMAKI,
Yuya MIZUNO, Daisuke SHINJO, Hiroki AIZAWA, Tetu OHNUMA,
Akira HOMMA, Eishi UECHI, Nobuo SAKATA, Saki OHSHIMA,
Tomomitsu ICHIKAWA, Mariko KODAN

(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 care informatics is a branch of health policy science which deals with the application of information technology to health policy research. Main objective of health care 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. Takashi Tagami, Hiroki Matsui, Hiromasa Horiguchi, Kiyohide Fushimi, Hideo Yasunaga. Thoracic Aortic Injury in Japan. *Circ. J.* 2015; 79((1)); 55-60
2. Takashi Tagami, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Use of recombinant human soluble thrombomodulin in patients with sepsis-induced disseminated intravascular coagulation after intestinal perforation. *Front Med (Lausanne)*. 2015; 2; 7
3. Daisuke Shinjo, Kiyohide Fushimi. Preoperative factors affecting cost and length of stay for isolated off-pump coronary artery bypass grafting: hierarchical linear model analysis. *BMJ Open*. 2015; 5(11); e008750
4. Hiroki Aizawa, Shinobu Imai, Kiyohide Fushimi. Factors associated with 30-day readmission of patients with heart failure from a Japanese administrative database. *BMC Cardiovasc Disord*. 2015; 15; 134
5. Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Variation in Risk-Standardized Mortality of Stroke among Hospitals in Japan. *PLoS ONE*. 2015; 10(10); e0139216
6. Hiroyuki Odagiri, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Toshiro Iizuka, Mitsuru Kaise. Difference in Outcomes of Rectal Foreign Bodies between Males and Females: A Retrospective Analysis of a National Inpatient Database in Japan. *Digestion*. 2015; 92(3); 165-170

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52. 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.*. 2015.10;

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60. D Shinjo, K Fushimi. Trends in Hospital Standardized Mortality Ratios in Japan. *Value Health.* 2015.11; 18(7); A555
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64. 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.* 2015.12;
65. Takashi Tagami, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Low-dose corticosteroid treatment and mortality in refractory abdominal septic shock after emergency laparotomy. *Ann Intensive Care.* 2015.12; 5(1); 32
66. Takahiro Inoue, Kiyohide Fushimi. Weekend versus Weekday Admission and In-Hospital Mortality from Ischemic Stroke in Japan. *J Stroke Cerebrovasc Dis.* 2015.12; 24(12); 2787-2792
67. Tomoki Wada, Hideo Yasunaga, Ryota Inokuchi, Hiroki Matsui, Takehiro Matsubara, Yoshihiro Ueda, Masataka Gunshin, Takeshi Ishii, Kent Doi, Yoichi Kitsuta, Susumu Nakajima, Kiyohide Fushimi, Naoki Yahagi. Effectiveness of surgical rib fixation on prolonged mechanical ventilation in patients with traumatic rib fractures: A propensity score-matched analysis. *J Crit Care.* 2015.12; 30(6); 1227-1231
68. Yusuke Sasabuchi, Hideo Yasunaga, Hiroki Matsui, Alan K Lefor, Kiyohide Fushimi, Masamitsu Sanui. Carperitide Increases the Need for Renal Replacement Therapy After Cardiovascular Surgery. *J. Cardiothorac. Vasc. Anesth.* 2015.12; 29(6); 1426-1431

[Conference Activities & Talks]

1. Shinjo, D., Fushimi, K.. Trends In Hospital Standardized Mortality Rations In Japan. ISPOR 18th Annual European Congress 2015.11.07 Milan, Italy

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. Junko Kurokawa, Tetsuo Sasano, Masami Kodama, Min Li, Yusuke Ebana, Nobuhiro Harada, Shin-ichiro Honda, Haruaki Nakaya, Tetsushi Furukawa. Aromatase knockout mice reveal an impact of estrogen on drug-induced alternation of murine electrocardiography parameters. *J Toxicol Sci.* 2015; 40(3); 339-348
2. Matsue Y, Yoshida K, Hoshino M, Yonetsu T, Suzuki M, Matsumura A, Hashimoto Y, Yoshida M.. Clinical features and prognosis of type 2 myocardial infarction in vasospastic angina. *Am J Med.* 2015; 128; 389-395
3. Hsu P, Ai M, Kanda E, Yu NC, Chen HL, Chen HW, Cheng MH, Kohzuma T, Schaefer EJ, Yoshida M. A comparison of glycated albumin and glycosylated hemoglobin for the screening of diabetes mellitus in Taiwan Atherosclerosis. 2015; 242; 327-333
4. Nishina K, Piao W, Yoshida-Tanaka K, Sujino Y, Nishina T, Yamamoto T, Nitta K, Yoshioka K, Kuwahara H, Yasuhara H, Baba T, Ono F, Miyata K, Miyake K, Seth PP, Low A, Yoshida M, Bennett CF, Kataoka K, Mizusawa H, Obika S, Yokota T. DNA/RNA heteroduplex oligonucleotide for highly efficient gene silencing *Nat Commun.* 2015; 6; 7969
5. Murakami M, Nishina K, Watanabe C, Yoshida-Tanaka K, Piao W, Kuwahara H, Horikiri Y, Miyata K, Nishiyama N, Kataoka K, Yoshida M, Mizusawa H, Yokota T. Enteral siRNA delivery technique for therapeutic gene silencing in the liver via the lymphatic route *Sci Rep.* 2015; 5; 17035

6. Nakayama S, Kishimoto Y, Saita E, Sugihara N, Toyozaki M, Taguchi C, Tani M, Kamiya T, Kondo K. Pine bark extract prevents LDL oxidation and regulates monocytic expression of antioxidant enzymes. *Nutrition Research*. 2015.01; 35(1); 56-64
7. Yusuke Ebana, Tetsushi Furukawa. Atrial fibrillation associated genes identified through genome-wide screening analysis - A review from viewpoints of bioinformatics, basic science, and clinical study - *CARDIOANGIOLOGY*. 2015.04; 77(4); 371-378

[Books etc]

1. Schaefer EJ, Tani M. *Dyslipidemias: Pathophysiology, Evaluation and Management*. Human Press, 2015.06 (ISBN : 978-1607614234)

[Conference Activities & Talks]

1. Tani M. A role of apoA-1 containing HDL in Cardiovascular Disease. The 3rd Ochanomizu Atherosclerosis Forum 2015.02 Niwano Hotel

Forensic Dentistry

Professor Koichi Sakurada
Assistant professor Hajime Utsuno

(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. Tomoko Akutsu, Tetsushi Kitayama, Ken Watanabe, Koichi Sakurada. Comparison of automated and manual purification of total RNA for mRNA-based identification of body fluids. *Forensic Sci Int Genet.* 2015.01; 14; 11-17
2. Ken Watanabe, Mayuko Hosoya, Koichi Hirayama, Hiroshi Ikegaya, Hisako Saitoh, Hirotaro Iwase, Tomoko Akutsu, Koichi Sakurada. Development of a modified DNA chip for accurate human ABO genotyping *Jpn J Forensic Sci Tech.* 2015.01; 20(1); 41-50
3. Hajime Utsuno. Airplane crash and personal identification *International Association of Traffic and Safety Sciences Review.* 2015.06; 40(1); 55-61
4. Yasiki Iwashima, Ken Watanabe, Tetsushi Kitayama, Koji Fujii, Hiroaki Nakahara, Koichi Sakurada, Kazumasa Sekiguchi. Evaluation of washing methods to remove contaminations from hair surface for DNA analysis *Jpn J Forensic Sci Tech.* 2015.07; 20(2); 165-173
5. 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.* 2015.08;
6. Akihisa Igoh, Yusuke Doi, Koichi Sakurada. Identification and evaluation of potential forensic marker proteins in vaginal fluid by liquid chromatography/mass spectrometry. *Anal Bioanal Chem.* 2015.09; 407(23); 7135-7144
7. Hajime Utsuno, Toru Kageyama, Keiichi Uchida, Kazuhiko Kibayashi, Koichi Sakurada, Koichi Uemura. Pilot study to establish a nasal tip prediction method from unknown human skeletal remains for facial reconstruction and skull photo superimposition as applied to a Japanese male populations. *J Forensic Leg Med.* 2015.12; 38; 75-80

[Books etc]

1. Keiichi Tsukinoki, Koichi sakurada, etc.. Up-to-date Non-invasive Clinical Examination -Saliva Test and Breath Test-. CMC Publishing Co., Ltd., 2015 (ISBN : 978-4-7813-1052-7)
2. Keiji Aizawa, Koichi Sakurada, etc.. NANZANDO'S MEDICAL DICTIONARY 20th EDITION. NANZANDO Co., Ltd., 2015 (ISBN : 978-4-525-01080-5)

[Misc]

1. Koichi Sakurada. Application to individual identification of parastic virus genotypes *The Journal of the Stomatological Society, Japan.* 2015.11; 82(3); 81-87

[Conference Activities & Talks]

1. Ken Watanabe, Tomoko Akutsu, Koichi Sakurada. Development of Quantitative analyzing method of Semen-specific Unmethllated DNA Reagions using a Real-Time PCR. The 99th Congress of the Japanese Society of Legal Medicine 2015.06.11 Kochi City Culture-Plaza Cul-Port
2. Kazuhiko Kibayashi, Hajime Utsuno, Jirou Ezaki and Ayako Ro. An autopsy of bacterial meningitis caused by dental caries of maxilla 2nd molar - a case report -. The 99th congress of the Japanese Society of Legal Medicine 2015.06.11 Kochi
3. Koichi Sakurada. Forensic Science for criminal investigation. The Meeting of the Stomatological Society of Japan 2015.06.25 TMDU

4. Hajime Utsuno and Koichi Sakurada. A nasal tip prediction method for Japanese Adult population. 9th Annual meeting of Japanese society of Forensic Dental Science 2015.06.28 Tokyo
5. Hajime Utsuo, Toru Kageyama, Keiichi Uchida, Kazuhiko Kibayashi, Koichi Sakurada and Koichi Uemura. Pilot study to establish a nasal tip prediction method from unknown human skeletal remains for facial reconstruction and skull photo superimposition as applied to a Japanese female population. 16th Meeting of the International Association for Craniofacial Identification 2015.08.03 Tokyo
6. Hajime Utsuo, Toru Kageyama, Keiichi Uchida, Kazuhiko Kibayashi, Koichi Sakurada and Koichi Uemura. Pilot study to establish a nasal tip prediction method from unknown human skeletal remains for facial reconstruction and skull photo superimposition as applied to a Japanese male population. 16th Meeting of the International Association for Craniofacial Identification 2015.08.04 Tokyo
7. Koichi Sakurada. The role of body fluids for individual identification. The 28th Congress of the Japanese Society of Oral Diagnosis/Oral Medicine 2015.09.04 TMDU
8. Tomoko Akutsu, Ken Watanabe, Sairi Takamura, Hisako Saitoh, Hirotaro Iwase, Koichi Sakurada. Study of vomit identification using ELISA. The 84 Kanto District Meeting of the Japanese Society of Legal Medicine 2015.10.24 Nippon Dental university
9. Yoshihito Fujinami, Koichi Sakurada, Tomoko Akutsu, Ken Watanabe, Natsuko Mizuno. Usefulness of matrix-assisted laser desorption/Ionization time-of-flight mass spectrometry for screening of human body fluids . The 84 Kanto District Meeting of the Japanese Society of Legal Medicine 2015.10.24 Nippon Dental University

[Others]

1. 9th Annual Meeting of Japanese Society of Forensic Dental Science (Koichi Sakurada), 2015.06
A sponsor of the 9th Annual Meeting of Japanese Society of Forensic Dental Science at the University of Tokyo.
2. 16th Meeting of the International Association for Craniofacial Identification (Hajime Utsuno), 2015.08
Organized the 16th meeting of International Association for Craniofacial Identification at TMDU in '15 Aug.

[Social Contribution]

1. Individual identification using dental findings (32cases), 2015
2. Kyoto Prefecture disaster postmortem examination training program (Koichi Sakurada), Kyoto Prefectural University of Medicine, 2015.03.15
3. Tokyo metropolitan and Tachikawa city disaster prevention training programs (Koichi Sakurada), Tokyo metropolitan and Tachikawa city, Tachikawa city, 2015.09.01
4. 2015 Individual identification training program for dentist (First, Tokyo metropolitan) (Koichi Sakurada) , Bureau of Social Welfare and Public Health, Tokyo Metropolitan Government, Hachioji city, 2015.10.22

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

[Original Articles]

1. Koichi Kawabuchi, Keiko Kajitani. A comparison of Management Conditions in Japan's Dental Clinics and Medical Clinics. *Journal of Dentistry Indonesia*. 2015.08; 22(2); 37-41

[Misc]

1. Koichi Kawabuchi. A Healthcare Economist's View of Abenomics: Can "Gambling" Economic Policy Work?. *Jpn Hosp*. 2015.07; 34; 29-34

Dental Education Development

Professor MORIO Ikuko
 Assistant Professor
 SEKI Naoko
 Graduate Student
 MATSUKAWA Chinatsu
 Graduate Student
 NAITO Mio
 Graduate Student

 NGUYEN Thi Thanh Tam
 Graduate Student
 TAKINAGA Akira

(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 International Seminar, Symposium, Workshop or other events]
- 1.TMDU exhibition at the 6th International Congress on Adhesive Dentistry(IAD), Bangkok, Thailand. January 31-February 1.
 - 2.Lifelong learning seminar in Ho Chi Minh City, Vietnam. June 1-3.
 3. TMDU Dental Training Program 2015, Tokyo, Japan. October 19-23.

(4) Publications

[Original Articles]

1. A Tanaka, M Nakajima, N Seki, R M Foxton, J Tagami. The effect of tooth age on colour adjustment potential of resin composite restorations. J Dent. 2015.02; 43(2); 253-260

[Conference Activities & Talks]

1. Sunaga M, Seki N, Moross J, Fukui Y, Morio I, Kinoshita A. Implementation and Assessment of Hands-on Seminar in Thailand for Creating Clinical Simulation Learning Materials. The 9th Annual Meeting of Japan Medical e-Learning 2015.01.24 Tochigi
2. Mio Naito, Kayoko Shinada, Katsuko Taniyama. Survey on oral health literacy at newspaper printing factories. The 88th Annual Meeting of the Japan Society for Occupational Health 2015.05 Osaka
3. Seki N, Sunaga M, Miyoshi T, Hobo K, Moross J, Kinoshita A, Morio I. The demand for dental English education and application of the computer assisted simulation system. The 34th Annual Meeting of JDEA 2015.07.10 Kagoshima
4. Morio I, Seki N, Kawaguchi Y. Continuing professional development of dentists in France. the 34th Annual Meeting of JDEA 2015.07.11 Kagoshima City
5. Ishidori H, Seki N, Morio I. Result of the survey on attitudes towards studying abroad of dental students. The 34th Annual Meeting of JDEA 2015.07.11 Kagoshima
6. Chinatsu MATSUKAWA, Naoko SEKI, Yoshiyuki SASAKI, Ikuko MORIO. Investigation on the curriculum of professional training colleges for dental hygienists. 2015.07.11
7. Morio I. Global trend in dental accreditation. Osaka Dental University, Lecture 2015.08.18 Osaka
8. Nakajima M, Takahashi M, Mamanee T, Thitthaweerat S, Seki N, Hosaka K, Tagami J. Bond Strengths of Dual-Cure Adhesive Resin Cements to Dentin. Academy of Dental Materials 2015 Annual Meeting 2015.10.08 Lahaina, Maui, HI
9. Morio I. Introduction of Faculty of Dentistry, Tokyo Medical University and its strategies as 1st School of Dentistry in Japan, and 6th position in the world. Gadjah Mada University, Faculty of Dentistry, Seminar 2015.12.08 Yogyakarta, Indonesia
10. Morio I. Interprofessional collaboration between Dentist and Dental Hygiene in TMDU . Gadjah Mada University, Faculty of Dentistry, Seminar 2015.12.08 Yogyakarta, Indonesia

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 (International Exchange Center)
 Registered Resident Hiromi Nishiyama
 Takashi Tanemura(～ March)
 Graduate Student Haslina Binti Rani (～ September)
 Ei Ei Aung
 Yuri Uraoka
 Anastasiya Blizniuk
 Sachiko Komori(～ March)
 Nguyen Thi Hoang Yen
 Yuka Shizuma
 Kaung Myat Thwin
 Toshiya Kanazawa(April ～)
 Takashi Tanemura(April ～)
 Jin Aoki(April ～)
 Mitsue Kamisawa(April ～)

(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. Masayuki Ueno, Takashi Zaitzu, Satoko Ohara, FA Clive Wright, Yoko Kawaguchi. Factors influencing perceived oral health of Japanese middle-aged adults. *Asia Pacific Journal of Public Health*. 2015; 27(2); 2296-2304
2. Masayuki Ueno, Satoko Ohara, Norie Sawada, Manami Inoue, Shoichiro Tsugane, Yoko Kawaguchi. The association of active and secondhand smoking with oral health in adults: Japan public health center-based study *Tobacco Induced Diseases*. 2015; 13; 19
3. Masayuki Ueno, Takashi Zaitzu, Mari Ohnuki, Ayumi Takayama, Melissa Adiatman. Association of a visual oral health literacy instrument with perceived and clinical oral health status in Japanese adolescents *International Journal of Health Promotion and Education*. 2015; 53(6); 303-314
4. Aung EE, Ueno M, Zaitzu T, Furukawa S, Kawaguchi Y. Effectiveness of three oral hygiene regimens on oral malodor reduction: a randomized clinical trial. *Trials*. 2015; 16(13); 1-5
5. EiEi Aung, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Relationship of Oral Health Knowledge, Behavior and Status with Self-Perceived and Clinical Oral Malodor among Dental Patients. *Journal of Dental Health, Oral Disorders & Therapy*. 2015; 3(2); 83
6. A. Blizniuk, M. Ueno, T. Zaitzu, Y. Kawaguchi. Association of oral health literacy with oral health behaviour and oral health status in Belarus. *Community Dental Health*. 2015; 32; 148-152
7. Patcharaphol Samnieng, Jadesada Palasuk, Takashi Zaitzu, Masayuki Ueno, Kawaguchi Yoko. Oral Malodor and Its Related Factors in Edentate Elderly without Dentures. *Journal of Clinical Preventive Dentistry*. 2015; 11(4); 217-224
8. Haslina Rani, Masayuki Ueno, Takashi Zaitzu, Sayaka Furukawa, Yoko Kawaguchi. Factors associated with clinical and perceived oral malodor among dental students. *Journal of Medical and Dental Sciences*. 2015; 62; 33-41
9. Haslina Rani, Masayuki Ueno, Takashi Zaitzu, Yoko Kawaguchi. Oral Malodour among adolescents and its association with health behaviour and oral health status. *International Journal of Dental Hygiene*. 2015;

10. EiEi Aung,Masayuki Ueno,Takashi Zaitso,Yoko Kawaguchi. Oral Health Behaviors and Related Factors in Myanmar Population. Dental Health Current Research. 2015; 1(1);

[Conference Activities & Talks]

1. Ei Ei Aung, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Comparison of different oral hygiene procedures for oral malodor reduction . 35th Myanmar Dental Conference and 16th FDI-MDA joint education meeting, 2015.01.07 Yangon, Myanmar
2. Kaung Myat Thwin, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Comparison of Oral Health Situation between Myanmar and Japan. 35th Myanmar Dental Conference and 16th FDI-MDA joint education meeting, 2015.01.07 Yangon, Myanmar
3. Yoko Kawaguchi. Fresh Breath Clinic-Diagnosis,treatment and prevention of oral malodor. 35th Myanmar Dental Conference and 16th FDI-MDA joint education meeting, 2015.01.07 Yangon, Myanmar
4. Masayuki Ueno, Takashi Zaitso, Mari Ohnuki, Yoko Kawaguchi. Association of a Visual Oral Health Literacy Instrument with Perceived and Clinical Oral Health Status. The 93rd General Session and Exhibition of the International Association for Dental Research (IADR) 2015.03.11 Boston
5. Anastasia Blizniuk,Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Association of Oral Health Literacy with Clinical Oral Health Status. The 93rd General Session and Exhibition of the International Association for Dental Research (IADR) 2015.03.11 Boston
6. Ei Ei Aung, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Oral Health Behaviors and Related Factors in Myanmar People. The 93rd General Session and Exhibition of the International Association for Dental Research (IADR) 2015.03.11 Boston
7. Nguyen Thi Hoang Yen, Takashi Zaitso, Sachiko Takehara, Masayuki Ueno, Kawaguchi Yoko. Early childhood caries in Vietnam. 64th Annual meeting of Japanese Society for Oral Health 2015.05.27 Tsukuba
8. Ei Ei Aung, Kaung Myat Thwin, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Oral health knowledge and oral health behaviors in Myanmar population. 64th Annual meeting of Japanese Society for Oral Health 2015.05.27 Tsukuba
9. Kaung Myat Thwin, Ei Ei Aung, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Oral Health Care System and Dental Education Program in Myanmar. 64th Annual meeting of Japanese Society for Oral Health 2015.05.27 Tsukuba
10. Haslina Rani, Ei Ei Aung, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi,. Oral Malodor among High School Students. 64th Annual meeting of Japanese Society for Oral Health 2015.05.27 Tsukuba
11. Morio I, Seki N, Kawaguchi Y. Continuing professional development of dentists in France. the 34th Annual Meeting of JDEA 2015.07.11 Kagoshima City
12. Yuka Shizuma ,Takashi Zaitso, Masayuki Ueno ,Yoko Kawaguchi . New oral self-checking method for high school students. The 8th Asian Conference of Oral Health Promotion for School Children 2015.09.18 Taipei,Taiwan
13. Hitoshi Kousaka,Yukiko Nishikawaji ,Yoko Kawaguchi ,Takashi Zaitso. School image change with health education. The 8th Asian Conference of Oral Health Promotion for School Children 2015.09.18 Taipei,Taiwan
14. Yoko Kawaguchi . Effective Health Education by Application of a Visual Oral Health Literacy Instru-ment. The 8th Asian Conference of Oral Health Promotion for School Children 2015.09.18 Taipei,Taiwan
15. Yoko Kawaguchi . Current Situation and Future Perspective of Japanese Dentistry. The 8th Asian Conference of Oral Health Promotion for School Children 2015.09.18 Taipei,Taiwan
16. M.Kamisawa. Oral health promotion for people with special needs research proposal. International Seminar on Oral health 2015.10.27 TMDU
17. T.Kanazawa. A new halitosis definition. International Seminar on Oral health 2015.10.27 TMDU

18. Y.Shizuma. New oral self-checking methods for senior high school students. International Seminar on Oral health 2015.10.27 TMDU
19. T.Tanemura. Introduction of Dental health care services in Japan Ground Self-Defense Force (JGSDF). International Seminar on Oral health 2015.10.27 TMDU
20. K M Thwin. Oral health situation in Myanmar preschool children. International Seminar on Oral health 2015.10.27 TMDU
21. Y.Shizuma,T.Zaitsu,M.Ueno,M.Ohnuki,Y.Kawaguchi. The analysis of students recognition on oral health status. The 63rd Annual Meeting of Japanese Association for Dental Research 2015.10.30 Fukuoka
22. T.Zaitsu,Y.Kawaguchi:Oral Health Problems of. Oral Health Problems of Japanese Antarctic Research Expedition Team Members. The 63rd Annual Meeting of Japanese Association for Dental Research 2015.10.30 Fukuoka

[Others]

1. 2015.09
Oral Health Promotion organization International Seminar on Oral health
2. International Symposium Oral Health and Dental Education in Southeast Asia., 2015.10
International Symposium Oral Health and Dental Education in Southeast Asia.

Sports Medicine and Dentistry

[Associate Professor] Toshiaki Ueno
 [Assistant Professor] Toshiyuki Takahashi, Hiroshi Churei
 [Clinical fellow] Katsuhide Kurokawa
 [Graduate Student] Akihiro Mitsuyama, Sintaro Fukasawa, Abhishekhi Shrestha, Mai Ikegawa, Takahiro Sirako, Yuriko Yoshida, Nana Shiota, Gen Tanabe
 [Research Student] Satoshi Kawabata
 [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

(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.Dental specialist certified by JASD, 2. 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.Dental specialist certified by JASD, 2.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)
Shintaro Fukasawa (1.MG technical instructor certified by JASD)
Mai Tanabe (1. Sports dental hygienist certified by JASD)

(7) Publications

[Original Articles]

1. Kanayama T, Miyamoto H, Yokoyama A, Takahashi T, Shibuya Y. The influence of bite force strength on brain activity J Biomed Grap Comput. 2015.01; 5(1); 28-32

2. Chowdhury RU, Churei H, Takahashi H, Shahrin S, Fukasawa S, Shrestha A, Negoro T, Ueno T. Suitable design of mouthguard for sports active person with spaced dentition *Dental Traumatology*. 2015.06; 31(3); 238-242
3. Shrestha A, Takahashi T, Kurokawa K, Churei H, Chowdhury NU, Chowdhury RU, Shahrin S, Toyoshima Y, Ueno T. Physical and oral injuries and awareness of mouthguard among martial arts athletes in Nepal *Int J Sports Dent*. 2015.10; 8(1); 45-57

[Books etc]

1. Kei-ichi Ishigami, Toshiaki Ueno, Misao Kawara, Yoshinobu Maeda, Toshikazu Yasui. *Yousetsu Sports Dentistry*. Igaku Joho-Sha Ltd., 2015.01 (ISBN : 978-4-903553-53-5)

[Conference Activities & Talks]

1. Shrestha A, Churei H, Yoshida Y, Sumita Y, Taniguchi H, Ueno T. Fabrication of customized obturator type of mouthguard: a clinical approach. 7th TMDU International Summer Program (ISP2015) 2015.08.30 Tokyo, Japan
2. Chowdhury RU, Churei H, Mizobuchi, Fukasawa S, Iwasaki N, Sharika S, Shrestha A, Uo M, Takahashi H, Ueno T. Effective design of custom-made mouthguard for athletes undergoing orthodontic treatment. 103th FDI Annual World Dental Congress 2015.09.24 Bangkok, Thailand
3. Shrestha A, Takahashi T, Kurokawa K, Churei H, Chowdhury NU, Chowdhury RU, Shahrin S, Toyoshima Y, Ueno T. Oral injuries and mouthguard among martial arts athletes in Nepal. 103th FDI Annual World Dental Congress 2015.09.24 Bangkok, Thailand
4. Takahashi T, Kurokawa K, Mitsuyama A, Ueno T. Masseter muscle recruitment involved in voluntary arm movement using dumbbell. 63rd Annual Meeting of the Japanese Association for Dental Research 2015.10.30 Fukuoka, Japan

Educational System in Dentistry

Professor Kouji ARAKI

Junior Associate Professor(non-full time) Yukio NAKAMURA Hiroki KATAOKA

Graduate Student Michiyo KUROSA Moriyuki KATOH Kazuki TAKAHASHI Akitaka HATTORI Kanako TODA

Secretary Satomi ITOH

(1) Outline

Main object of educational system in dentistry in the graduate course is to provide opportunity to study evaluation method for dental education curriculum, inspection method of the validity and reliability of the evaluation system for dental education, evaluation system compared between international and Japanese education level in undergraduate or after the graduation periods, and dental clinical skills improvement by the virtual reality simulation system.

(2) Research

- 1) The development of evaluation method for dental education curriculum
- 2) The development of inspection method of the validity and reliability of the evaluation system for dental education
- 3) The development of evaluation system compared between international and Japanese education level in undergraduate or after the graduation periods
- 4) The development of the program for dental clinical skills improvement by the virtual reality simulation system

(3) Education

The education to the postgraduate students performs a lecture, practice, and Lab.

The education to the undergraduate students performs of a lecture and practice of all human general oral diagnoses.

(4) Lectures & Courses

The aim of the lecture is to understand the purpose and method about the evaluation of dental education system. In addition, it is to understand the level and inspection method of international dental education. The aim of the practice is to understand a method of data analysis provided by the evaluation system for the dental education, In addition, it is to understand the comparison with the international education level.

The aim of the Lab is to manage the teaching materials developed for simulation education and is to understand the inspection method of the evaluation for new education system.

(5) Clinical Services & Other Works

In the Clinic of Oral Diagnosis and General Dentistry, University Hospital, we performs manner and oral diagnosis education, for a student during clinical training.

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

1. Ken-ichi Tonami, Kazunobu Sano, Shizuko Ichinose and Kouji Araki . Resin–Dentin Bonding Interface After Photochemical Surface Treatment Photomedicine and Laser Surgery. 2015.01; 33(1); 1-6

[Conference Activities & Talks]

1. S.Umemori, K.Tonami, H.Nitta, K.Araki, S.Mataki. Psychological trait relates physiological stress measured by ECG frequency analysis. IADR General Session &Exhibition 2015.03.11 Boston, Massachusetts, USA, March 11-14, 2015
2. M. Iwaki, M. Kanazawa, M. Sunaga, A. Kinoshita, S. Minakuchi, S. Oda, K. Araki. Live broadcast lectures on complete denture prosthodontics: the learning effectiveness . 2015 IADR/AADR/CADR General Session & Exhibition 2015.03.12 Boston
3. Ken-ichi Tonami, Chikako Nakamura, Azusa Yamada, Sachi Umemori, Kanako Noritake, Maiko Iwaki, Masayo Sunaga, Satoko Ohara, Masayuki Hideshima, Jun Tsuruta, Hiroshi Nitta, Shigeru Oda, Atsuhiro Kinoshita, Kouji Araki, Shiro Mataki. Development of professionalism during experiential learning at welfare facilities. 26th seaade Annual Scientific Meeting, Bali, Indonesia 2015.08.12 Bali, Indonesia

[Social Contribution]

1. The Journal of Dental Education, peer reviewer

Educational Media Development

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

(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. S Hoshi, T Akizuki, T Matsuura, T Ikawa, A Kinoshita, S Oda, Y Tabata, M Matsui, Y Izumi. Ridge augmentation using recombinant human fibroblast growth factor-2 with biodegradable gelatin sponges incorporating β -tricalcium phosphate: a preclinical study in dogs. *J. Periodont. Res. Epub.* 2015.05; 51(1); 77-85
2. T Matsuura, T Akizuki, S Hoshi, T Ikawa, A Kinoshita, M Sunaga, S Oda, Y Kuboki, Y Izumi. Effect of a tunnel-structured β -tricalcium phosphate graft material on periodontal regeneration: a pilot study in a canine one-wall intrabony defect model. *J. Periodont. Res.* 2015.06; 50(3); 347-355
3. Takahiro Ikawa, Tatsuya Akizuki, Takanori Matsuura, Shu Hoshi, Shujaa Addin Ammar, Atsuhiko Kinoshita, Shigeru Oda, Yuichi Izumi. 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. *J. Periodontol. Epub.* 2015.09; 87(2); 175-183

[Conference Activities & Talks]

1. Masayo Sunaga, Hikaru Kohase, Yuji Kabasawa, Atsuhiko Kinoshita. Evaluation of Computer-assisted Education System on Clinical Simulation in Dentistry. The 93rd International Association for Dental Research General Session, 11-14 March, 2015.03.12 Boston
2. M. Iwaki, M. Kanazawa, M. Sunaga, A. Kinoshita, S. Minakuchi, S. Oda, K. Araki. Live broadcast lectures on complete denture prosthodontics: the learning effectiveness. The 93rd International Association for Dental Research General Session, 11-14 March, 2015.03.12 Boston
3. Atsuhiko Kinoshita, Masayo Sunaga, Katsuji Onoda, Naoko Seki. Introduction of TMDU SimPrac. Life-long Education with Simulation Learning Materials and Hands-on Seminar for Creating Simulation Learning Materials. University of Medicine and Pharmacy, Ho Chi Minh City 2015.06.02 Ho Chi Minh City
4. Ken-ichi Tonami, Chikako Nakamura, Azusa Yamada, Sachi Umemori, Kanako Noritake, Maiko Iwaki, Masayo Sunaga, Satoko Ohara, Masayuki Hideshima, Jun Tsuruta, Hiroshi Nitta, Shigeru Oda, Atsuhiko

Kinoshita, Kouji Araki, Shiro Mataka. Development of professionalism during experiential learning at welfare facilities. 26th Annual Scientific Meeting South East Asia Association For Dental Education (SEAADE) 12-13 August, 2015.08 Bali

Insured Medical Care Management

Professor AI Masumi
 Junior Associate Professor
 NUMAO Noboru
 Graduate Student
 KAWAMURA Hiroshi

(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 in 2014).

We welcome a new doctor course student.

(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. Inoue Masaharu, Kihara Kazunori, Yoshida Soichiro, Ito Masaya, Takeshita Hideki, Ishioka Junichiro, Matsuoka Yoh, Numao Noboru, Saito Kazutaka, Fujii Yasuhisa. A novel approach to patient self-monitoring of sonographic examinations using a head-mounted display. *J Ultrasound Med.* 2015.01; 34(1); 29-35
2. Masaya Ito, Kazunori Kihara, Soichiro Yoshida, Manabu Tatokoro, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Yasuhisa Fujii. Patient's Self-monitoring of Transurethral Surgical Images Using a Head-mounted Display *Urology Case Reports.* 2015.03; 3(2); 27-29
3. Kazunori Kihara, Fumitaka Koga, Yasuhisa Fujii, Hitoshi Masuda, Manabu Tatokoro, Minato Yokoyama, Yoh Matsuoka, Noboru Numao, Junichiro Ishioka, Kazutaka Saito. Gasless laparoendoscopic single-port clampless sutureless partial nephrectomy for peripheral renal tumors: perioperative outcomes. *Int. J. Urol..* 2015.04; 22(4); 349-355
4. Soichiro Yoshida, Masaya Ito, Manabu Tatokoro, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Multitask Imaging Monitor for Surgical Navigation: Combination of Touchless Interface and Head-Mounted Display. *Urol. Int..* 2015.04;
5. Hiroaki Ikezaki, Norihiro Furusyo, Takeshi Ihara, Takeo Hayashi, Kazuya Ura, Satoshi Hiramane, Fujiko Mitsumoto, Koji Takayama, Masayuki Murata, Takuji Kohzuma, Masumi Ai, Ernst J Schaefer, Jun Hayashi. Glycated albumin as a diagnostic tool for diabetes in a general Japanese population. *Metab. Clin. Exp..* 2015.06; 64(6); 698-705
6. Masaharu Inoue, Yasuhisa Fujii, Minato Yokoyama, Kazutaka Saito, Noboru Numao, Kazunori Kihara. Progression of hypertension after partial nephrectomy in patients with renal tumors: A preliminary report. *Int. J. Urol..* 2015.08; 22(8); 797-798
7. Powen Hsu, Masumi Ai, Eiichiro Kanda, Neng-Chun Yu, Hsiao-Lien Chen, Huan-Wen Chen, Ming-Hui Cheng, Takuji Kohzuma, Ernst J Schaefer, Masayuki Yoshida. A comparison of glycated albumin and glycosylated hemoglobin for the screening of diabetes mellitus in Taiwan. *Atherosclerosis.* 2015.09; 242(1); 327-333
8. 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..* 2015.12;

[Books etc]

1. Kazunori Kihara, Yasuhisa Fujii, Kazutaka Saito, Fumitaka Koga, Noboru Numao, Yoh Matsuoka, Junichiro Ishioka, Minato Yokoyama, Hitoshi Masuda, Tatsuya Nagai, Soichiro Yoshida, Manabu Tatokoro, Toshiki Kijima, Naoko Kawamura, Masaharu Inoue, Masaya Ito. *Gasless Single-Port RoboSurgeon Surgery in Urology.* Springer, 2015.09 (ISBN : 978-4-431-54504-0)

[Conference Activities & Talks]

1. Masaharu Inoue, Yasuhisa Fujii, Minato Yokoyama, Masaya Ito, Manabu Tatokoro, Soichiro Yoshida, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Kazunori Kihara. Progression of hypertension after partial nephrectomy in Japanese patients with renal tumors. 30th Annual EAU Congress 2015.03.21 Madrid, Spain

2. Nakayama T., Saito K., Fujii Y., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Numao N., Kihara K. Prognostic comparison of serum biomarkers for cancer-specific survival of renal cell carcinoma undergoing nephrectomy: C-reactive protein has the highest predictive ability on survival. The 30th Annual Congress of the European Association of Urology 2015.03.21 Madrid, Spain
3. Numao N., Ito M., Uchida Y., Yoshida S., Nakayama T., Inoue M., Tatokoro M., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Fujii Y., Kihara K. Optimal number of sampling cores in MRI-targeted biopsy. The 30th Annual Congress of the European Association of Urology 2015.03.21 Madrid, Spain
4. Tanaka H, Fujii Y, Ito M, Tatokoro M, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Numao N, Saito K, Yonese J, Kihara K. Novel prediction model for fat-poor angiomyolipoma in small renal masses based on radiological and clinical features. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
5. Tatokoro M., Nakanishi Y., Komai Y., Matsuoka Y., Ishioka J., Numao N., Yoshimoto K., Saito K., Fujii Y., Ogawa Y., Kihara K. Impaired glucose tolerance predicts the development of hypoglycemia after removal of pheochromocytoma. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
6. Moriyama S., Saito K., Ishioka J., Kageyama Y., Morimoto S., Arisawa C., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Matsuoka Y., Numao N., Fujii Y., Kihara K. Preoperative prediction algorithm for the selection of candidates for neoadjuvant chemotherapy in upper tract urothelial carcinomas. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
7. Fujii, Y., Kihara, K., Numao, N., Matsuoka, Y., Ishioka, J., Saito, K. Gasless single-port RoboSurgeon partial cystectomy: A hybrid technique combining an intravesical and extravesical approach. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
8. Fujii, Y., Kihara, K., Numao, N., Tanaka H., Tatokoro M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Numao N., Saito K. Selective bladder-sparing protocol consisting of low-dose chemoradiotherapy and consolidative partial cystectomy against muscle-invasive bladder cancer: oncological and functional outcome. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
9. Ishioka J, Yokoyama M, Waseda Y, Kawamura N, Ito M, Tatokoro M, Yoshida S, Matsuoka Y, Numao N, Saito K, Arisawa C, Morimoto S, Kageyama Y, Fujii Y, Kihara K. Preoperative prediction of postoperative renal function for upper tract urothelial carcinoma patients: Concerning issues of perioperative renal impairment and the use of cisplatin-based chemotherapy. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
10. Kawamura N., Yokoyama M., Fujii Y., Ishioka J., Numao N., Matsuoka Y., Saito K, Arisawa C., Okuno T., Noro A., Morimoto S., Kihara K. Longitudinal change and risk factors of severe deterioration in renal function after radical nephrectomy. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
11. Nakamura Y. , Numao N. , Yoshida S. , Komai Y. , Ito M. , Tatokoro M. , Yokoyama M. , Ishioka J. , Matsuoka Y. , Saito K. , Fujii Y. , Kihara K.. Transrectal 12-core prostate biopsy and MRI have a comparable risk of missing significant prostate cancer in men with PSA less than 10ng/ml and normal DRE. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
12. Yoshida S., Fukuyo T., Ito M., Tatokoro M., Yokoyama M, Ishioka J., Matsuoka Y., Numao N., Saito K., Fujii Y., Kihara K. A novel three-dimensional image display system for transurethral surgery. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
13. Moriyama S., Saito K., Ishioka J., Kageyama Y., Morimoto S., Arisawa C., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Matsuoka Y., Numao N., Fujii Y., Kihara K. Preoperative selection algorithm for eligible neoadjuvant chemotherapy patients in upper tract urothelial carcinomas. The 111th annual meeting of the American Urological Association 2015.05.15 New Orleans, USA
14. Tanaka H., Fujii Y., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Numao N., Saito K., Yonese J., Kihara K. Development and validation of a novel prediction model for fat-poor angiomyolipoma in small renal masses based on radiological and clinical features. The 111th annual meeting of the American Urological Association 2015.05.15 New Orleans, USA

15. Tatokoro M., Nakanishi Y., Komai Y., Matsuoka Y., Ishioka J., Numao N., Yoshimoto K., Saito K., Fujii Y., Ogawa Y., Kihara K. Impact of impaired glucose tolerance on the development of hypoglycemia following removal of pheochromocytoma. 111th annual meeting of the American Urological Association 2015.05.15 New Orleans, USA
16. Yoshida S., Fukuyo T., Ito M., Tatokoro M., Ishioka J., Matsuoka Y., Numao N., Saito K., Fujii Y., Kihara K. Development of new three-dimensional image system for transurethral surgery. The 111th annual meeting of the American Urological Association 2015.05.16 New Orleans, USA
17. Numao N., Ito M., Uchida Y., Yoshida S., Nakayama T., Inoue M., Tatokoro M., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Fujii Y., Kihara K. Optimal MRI-targeted biopsy sampling number. The 111th annual meeting of the American Urological Association 2015.05.17 New Orleans, USA
18. Kawamura N., Yokoyama M., Fujii Y., Ishioka J., Numao N., Matsuoka Y., Saito K., Arisawa C., Okuno T., Noro A., Morimoto S., Kihara K. Recovery in renal function after radical nephrectomy and its negative predictive factors: a multicenter longitudinal study. The 111th annual meeting of the American Urological Association 2015.05.18 New Orleans, USA
19. Fujii Y., Kihara K., Tanaka H., Tatokoro M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Numao N., Saito K. Oncological and functional outcomes in muscle-invasive bladder cancer patients undergoing bladder-sparing treatment consisting of low-dose chemoradiotherapy and consolidative partial cystectomy. The 111th annual meeting of the American Urological Association 2015.05.18 New Orleans, USA
20. Matsuoka Y., Numao N., Saito K., Tanaka H., Ito M., Yoshida S., Yokoyama M., Ishioka J., Fujii Y., Kihara K. Eligibility analysis for focal therapy based on prostatectomy findings: Does intermediate-risk cancer have a higher likelihood of undertreatment than low-risk cancer?. 8th International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer 2015.06.21 Amsterdam, Netherland
21. Numao N., Ito M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Fujii Y., Kihara K. Efficient sampling methods in systematic biopsy that could be performed in combination with MRI-guided biopsy. 8th International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer 2015.06.21 Amsterdam, Netherland
22. Saito K., Matsuoka Y., Numao N., Hayashi K., Yoshida S., Yokoyama M., Ishioka J., Fujii Y., Yoshimura R., Kihara K. Focal therapy for prostate cancer with hemi-gland low dose rate brachytherapy. 8th International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer 2015.06.21 Amsterdam, Netherland

[Others]

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

Geriatrics and Vascular Medicine

Professor : Kentaro SHIMOKADO

Associate Professor : Eiji KANEKO, Shohei SHINOZAKI

Assistant Professor : Yasuko ABE

Graduate Student : Kenji TOYOSIMA, Norihiko IZUMIMOTO

Yasuko USHIO, Ikeita TAKAHASHI

Hirofumi MASUTOMI, Ayumi TOBA

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. Arai Hidenori, Ouchi Yasuyoshi, Toba Kenji, Endo Tamao, Shimokado Kentaro, Tsubota Kazuo, Matsuo Seiichi, Mori Hidezo, Yumura Wako, Yokode Masayuki, Rakugi Hiromi, Ohshima Shinichi. Japan as the front-runner of super-aged societies: Perspectives from medicine and medical care in Japan. *Geriatr Gerontol Int.* 2015.06; 15(6); 673-687
2. Tsuzuki T, Shinozaki S, Nakamoto H, Kaneki M, Goto S, Shimokado K, Kobayashi H, Naito H.. Voluntary Exercise Can Ameliorate Insulin Resistance by Reducing iNOS-Mediated S-Nitrosylation of Akt in the Liver in Obese Rats. *PLoS One.* 2015.07; 10(7);

[Conference Activities & Talks]

1. Abe Y, Fushimi K, Kaneko E, Shimokado K.. Factors associated with elderly pneumonia in Japan.. 10th IAGG Chiang Mai Thailand 21 2015.10.21 Chiang Mai

Rehabilitation Medicine

Associate Professor Sadao MORITA

Graduate Student

Tomoko ARAKI,

Kashitarou HYOUDOU

Junying PIAO

Tomokazu MASAOKA

Chisato TAKADA

Maierhaba AILIXIDING

Kazuko KATSUKI

Takanori KOKUBUN

Takashi IKEDA

Masayuki HIRAO

Ryohei TAKADA

(1) Research

Research Subjects

- 1) 3-dimension motion analysis in activities of daily living
- 2) Balance and occlusion
- 3) Biomechanical analysis of artificial limb
- 4) Prevention of dislocation after total hip arthroplasty
- 5) Prevention of disuse bone atrop

(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-dimentional motion analysis in activities of daily living and molecular biological analysis of disuse atrophy.

(3) Publications

[Original Articles]

1. Hirao M, Jinno T, Koga D, Takada R, Morita S, Ohkawa A. The effect of tranexamic acid on blood loss and coagulation markers in primary total hip arthroplasty 2015.08; 41; 804-808

[Misc]

1. Morita S. The cause and outline of the lower limb amputation Physical Therapy. 2015.04; 32(4); 292-299

[Conference Activities & Talks]

1. Yamauchi yuki, Jinno Tetsuya, Koga Daisuke, Morita Sadao, Ohkawa Atsushi. An investigation for post-operative course of metal-on-metal THA. The Japanese Society for Replacement Arthroplasty 2015.02.27 Okinawa
2. Koga Daisuke, Jinno Tetsuya, Takada Ryouhei, Hirao Masayuki, Morita Sadao, Ohkawa Atsushi. Alert point of muscle-evoked potentials in total hip arthroplasty. The Japanese Society for Replacement Arthroplasty 2015.02.27 Naha
3. Hirao Masanobu, Jinno Tetsuya, Koga Daisuke, Hoshino Chisato, Morita Sadao, Ohkawa Atsushi. The effect of tranexamic acid on blood loss and coagulation markers in primary bilateral total hip arthroplasty. The Japanese Society for Replacement Arthroplasty 2015.02.27 Naha
4. Hirao Masayuki, Jinno Tetsuya, Takada Ryouhei, Morita Sadao, Ohkawa Atsushi. The feature of the fragile femoral fracture after total hip arthroplasty. The Japanese Society of Hip Joint 2015.10.30 Oosaka

Gerodontology and Oral Rehabilitation

Professor MINAKUCHI Shunsuke

Associate Professor

OWATARI Tsuneto

Associate Professor

TOHARA Haruka

Junior Associate Professor

KOBAYASHI Ken-ichi

Junior Associate Professor

SEKITA Toshiaki

Assistant Professor

AKIBA Norihisa

Assistant Professor

INOKOSHI Masanao

Assistant Professor

KANAZAWA Manabu

Assistant Professor

KOMAGAMINE Yuriko

Assistant Professor

MOTOMURA Kazuo

Assistant Professor

NAKANE Ayako

Assistant Professor

OKUBO Mai

Assistant Professor

SATO Yusuke

Assistant Professor

TAKEUCHI Shuhei

Assistant Professor

WAKASUGI Yoko

Project Assistant Professor

HAMA Youhei

Visiting Lecturer

SUSA Chiaki

Visiting Lecturer

Satoshi Teranaka

Visiting Lecturer

Yuki Hirazima

Graduate Student

AMAGAI Noriko

Graduate Student

ARAKIDA Toshio

Graduate Student

ASAMI Mari

Graduate Student
BABA Yuuya
Graduate Student
HIROKO Namai
Graduate Student
KAGIFUKU Yuko
Graduate Student
KAIDILIYA Yalikun
Graduate Student
KAJISA Eriko
Graduate Student
KAMOCHI Gou
Graduate Student
KHAING Myat Thu
Graduate Student
KUBOTA Chieko
Graduate Student
KYOSAKA Yuka
Graduate Student
MACHIDA Nami
Graduate Student
MATSUBARA Mariko
Graduate Student
MATSUDA Yuhei
Graduate Student
MIURA Akemi
Graduate Student
MIYAYASU Anna
Graduate Student
MIZUNO Akane
Graduate Student
NAKAMURA Toshinari
Graduate Student
OBA Shoko
Graduate Student
ODA Ken
Graduate Student
OMURA Yuri
Graduate Student
OOWADA Gaku
Graduate Student
SATO Marie
Graduate Student
SHIMIZU Haruki
Graduate Student
SHINOZAKI Hiromichi
Graduate Student
SHOJI Hirotaka
Graduate Student
SOEDA Hitomi
Graduate Student
SUZUKI Hiroyuki
Graduate Student
TAGASHIRA Itoe
Graduate Student
VO Lam Thuy
Graduate Student
YAMADA Ayako

Graduate Student
YAMAGUCHI Kohei
Graduate Student
YAMAZAKI Yasuhiro
Graduate Student
YOSHII Eiji
Graduate Student
YOSHIMI Kanako
Graduate Student
YOSHIZAKI Taro
Graduate Student
ZHAO Hui Zi
Graduate Student
HIRAYAMA Daisuke
Graduate Student
JOU Ayami
Graduate Student
TANIMOTO Hiroyuki
Graduate Student
TANOUE Mariko
Graduate Student
YOSHIZUMI Yuu
Dental Resident
HIRAYAMA Daisuke
Dental Resident
HOSHINO Yoshihito
Dental Resident
INOKUCHI Nobuhiro
Dental Resident
INOUE Minoru
Dental Resident
JOU Ayami
Dental Resident
KAGAWA Tomonori
Dental Resident
KIKUCHI Keisuke
Dental Resident
Naohiko Hino
Dental Resident
TAKESHITA Shin
Dental Resident
TANOUE Mariko
Dental Resident
YAMAGA Eijirou
Dental Resident
YAMAMOTO Shinta
Dental Resident
INOUE Minoru
Dental Resident
SUSA Chiaki

(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. Kagaya H, Yokoyama M, Saitoh E, Kanamori D, Susa C, German RZ, Palmer JB. Isolated pharyngeal swallow exists during normal human feeding. *Tohoku J. Exp. Med.* 2015; 236(1); 39-43
2. Zhang F, Vanmeensel K, Inokoshi M, Batuk M, Hadermann J, Van Meerbeek B et al.. Critical influence of alumina content on the low temperature degradation of 2-3 mol% yttria-stabilized TZP for dental restorations *Journal of the European Ceramic Society.* 2015; 35(2); 741-750
3. Takeuch S, Sekita T, Kobayashi K. Adhesive Approach that uses Internal Coping for Vertical Root Fractured Teeth with Flared Root Canals *NYSDJ.* 2015; 81(4); 29-33
4. Shoji H, Nakane A, Mikushi S, Yoshida S, Yoshino H, Numasawa Y, Ishihara S, Minakuchi S. The variety of dysphagia progression in amyotrophic lateral sclerosis (ALS) *Medical Research Archives.* 2015; vol.3;
5. Susa C, Kagaya H, Saitoh E, Baba M, Kanamori D, Mikushi S, Ozaki K, Uematsu H, Minakuchi S. Classification of sequential swallowing types using videoendoscopy with high reproducibility and reliability. *Am J Phys Med Rehabil.* 2015.01; 94(1); 38-43
6. Zhang F, Inokoshi M, Vanmeensel K, Van Meerbeek B, Naert I, Vleugels J. Effect of grain boundary segregation on the hydrothermal degradation of dental 3Y-TZP ceramics *Advances in Bioceramics and Porous Ceramics VIII, Ceramic Engineering and Science Proceedings.* 2015.01; 36(5); 1-8
7. Inokoshi M, Vanmeensel K, Zhang F, De Munck J, Eliades G, Minakuchi S, Naert I, Van Meerbeek B, Vleugels J. Aging resistance of surface-treated dental zirconia. *Dent Mater.* 2015.02; 31(2); 182-194

8. Inoue M, Nakajima H, Akiba N, Hibino Y, Nagasawa Y, Sumi Y, Minakuchi S. Influence of monomer content on the viscoelasticity, water sorption and solubility of experimental fluorinated soft lining materials *Dental Materials Journal*. 2015.02; 34(1); 70-77
9. Zhang F, Vanmeensel K, Batuk M, Hadermann J, Inokoshi M, Van Meerbeek B, Naert I, Vleugels J. Highly-translucent, strong and aging-resistant 3Y-TZP ceramics for dental restoration by grain boundary segregation. *Acta Biomater*. 2015.04; 16; 215-222
10. Yoko Wakasugi, Kanji Nohara, Kentaro Okuno, Hikari Fukatsu, Nami Ueda, Haruka Tohara, Takayoshi Sakai. The relationship with aspiration on videoendoscopic evaluation of swallowing and inflammation states 2015.04; 19(1); 11-16
11. Zhang F, Inokoshi M, Vanmeensel K, Van Meerbeek B, Naert I, Vleugels J. Lifetime estimation of zirconia ceramics by linear ageing kinetics *Acta Materialia*. 2015.05; 92; 290-298
12. Jo A, Kanazawa M, Sato Y, Iwaki M, Akiba N, Minakuchi S. A randomized controlled trial of the different impression methods for the complete denture fabrication: Patient reported outcomes. *J Dent*. 2015.06;
13. Bielen V, Inokoshi M, De Munck J, Zhang F, Vanmeensel K, Minakuchi S, Vleugels J, Naert I, Van Meerbeek B. Bonding Effectiveness to Differently Sandblasted Dental Zirconia. *J Adhes Dent*. 2015.06; 17(3); 235-242
14. Yamada A, Kanazawa M, Komagamine Y, Minakuchi S. Association between tongue and lip functions and masticatory performance in young dentate adults *Journal of Oral Rehabilitation*. 2015.11; 42(11); 833-839
15. Hirayama D, Sakai Y, Akiba N, Kanazawa M, Minakuchi S. Effect of home reliner on occlusal relationships and oral mucosa: viscoelastic analyses by smoothed particle hydrodynamics simulation *Computers in Biology and Medicine*. 2015.11; 66; 20-28
16. 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*. 2015.11; 68(1); 84-89

[Conference Activities & Talks]

1. Zhang F, Inokoshi M, Vanmeensel K, Van Meerbeek B, Naert I, Vleugels J. Effect of grain boundary segregation on the hydrothermal degradation of dental 3Y-TZP ceramics. *International Conference on Advanced Ceramics and Composites* 2015.01 Florida
2. Jo A, Kanazawa M, Sato Y, Akiba N, Iwaki M, Minakuchi S. Influence of the different impression methods for complete denture fabrication on Patient Reported Outcomes. 2015.01.24
3. Haruka Tohara. Dentist role in dysphagia care team: Japanese experience. *Rehabilitation in swallowing disorders seminar* 2015.02.17
4. Haruka Tohara. Oral health care technique for non-dentist. *Rehabilitation in swallowing disorders seminar* 2015.02.17
5. Haruka Tohara. Importance of the home-visit oral care and dysphagia rehabilitation in an aged society. *Rehabilitation in swallowing disorders seminar* 2015.02.17
6. Haruka Tohara. Oral Rehabilitation for Dentist. *Rehabilitation in swallowing disorders seminar* 2015.02.18
7. Inokoshi M, Nagaoka N, Yoshihara K, De Munck J, Vanmeensel K, Zhang F, Vleugels J, Naert I, Van Meerbeek B. Microstructural and micro-Raman analysis of the zirconia-veneering ceramic interface. *Hutton Award competition, IADR General session* 2015.03 Boston
8. Y. Kaidiliya, A. Miyayasu, M. Kanazawa, Y. Omura, S. Minakuchi. Immediately loaded mandibular 2-implant overdentures retained by magnetic attachments: Marginal bone loss and survival rate. *The 14th International Conference on Magnetic Applications in Dentistry* 2015.03
9. Hitomi Soeda, Eijiro Yamaga, Yusuke Sato, Shunsuke Minakuchi. SEM Analysis of OHIP Subscales for Neurotic Complete Denture Wearers.. *International Association for Dental Research* 2015.03.12

10. M. Iwaki, M. Kanazawa, M. Sunaga, A. Kinoshita, S. Minakuchi, S. Oda, K. Araki. Live broadcast lectures on complete denture prosthodontics: the learning effectiveness . 2015 IADR/AADR/CADR General Session & Exhibition 2015.03.12 Boston
11. H.NAKAMURA, K.MOTOMURA, Y.Michi, M.YAMAMOTO, T.YOSHIOKA, S.TANAKA. Monitoring Pressure and Temperature in Dental Cavity Through Micro Sensors.. 93rd General Session & Exhibition of the IADR, 44th Annual Meeting of the AADR, 39th Annual Meeting of the CADR. 2015.03.13 Boston, USA
12. T. Arakawa, Y. Kuroki, H. Nitta, K. Toma, S. Takeuchi, T. Sekita, S. Mizukuchi, K. Mitsubayashi. Mouth guard biosensor for non-restraint monitoring of saliva glucose with telemetry system. 4th International Conference on Bio-Sensing Technology 2015.05.10 Lisbon, Portugal
13. Hiroyuki Suzuki, Manabu Kanazawa, Yuriko Komagamine, Noriko Amagai, Akemi Hosoda, Shunsuke Minakuchi. Influence of defects prosthesis by partial denture on the nutrition intake of the elderly. 12th Asian Congress of Nutrition 2015.05.17 Yokohama
14. Akemi Hosoda, Manabu Kanazawa, Yohei Hama, Yuriko Komagamine, Akiko Kojo, Shunsuke Minakuchi. The influence of the periodontal disease on dietary intake and in young females. 12th Asian Congress of Nutrition 2015.05.17 Yokohama
15. Ken Oda, Manabu Kanazawa, Shin Takeshita, Mariko Tanoue, Yuri Omura, Kaidiliya Yalikun, Anna Miyayasu, Shunsuke Minakuchi. Denture Stability of Mandibular Implant Overdentures with Locator Attachments. The 4th Tri-University Consortium on Oral Science and Education 2015.05.20 Thailand
16. Oda K,Kanazawa M,Takeshita S,Tanoue M,Omura Y,Yalikun K,Miyayasu A,Awano M,Uchida T,Minakuchi S. Denture Movement of Mandibular Implant Overdentures: Effect of Implant Number. The 124th Annual Meeting of the Japan Prosthodontic Society 2015.05.30 Omiya
17. Arakida T,Kanazawa M,Iwaki M,Yamamoto S,Nakamura T,Andou K,Minakuchi S,Handa K,Wakabayashi N. A case report of fabricating complete dentures applying optimal scanar. 2015.05.30
18. Eriko Kajisa, Yoko Wakasugi, Yuko Yamayoshi, Ayako Nakane, Haruka Tohara, Shunsuke Minakuchi. A Case Report of Progressive Supranuclea Palsy Patient Progressed Dysphagia Rapidly and Established Percutaneous Endoscopic Gastrostomy. 2015.06.13
19. Manabu Kanazawa, Maiko Iwaki, Daisuke Sato, Yuri Omura, Anna Miyayasu, Shohei Kasugai, Shunsuke Minakuchi. Immediate Loading of Two-Implant Mandibular Overdentures: 3-year Prospective Study. 16th meeting of the International College of Prosthodontists 2015.09.17 Seoul, Korea
20. A Miyayasu, M Kanazawa, Y Omura, D Sato, S Kasugai, S Minakuchi. Immediately loaded mandibular two-implant overdentures: Cost analysis. The 16th International College of Prosthodontists Biennial Meeting 2015.09.17 Seoul, Korea
21. Y. Komagamine, M. Kanazawa, Y. Sasaki, S. Minakuchi. Prognosis of new complete dentures from Patient's Denture Assessment (PDA) of existing dentures. International College of Prosthodontists, 16th Biennial Meeting 2015.09.17 Souel, Korea
22. Inokoshi M, Tanimoto H, Zhao H, Uo M, Minakuchi S. Time dependence of the degree of conversion for a self-adhesive cement- influence of all ceramic restorations . The 66th General Session of the Japanese Society for Dental Materials and Devices 2015.10.03 Tokyo
23. Manabu Kanazawa. Mandibular implant overdentures. 43rd Indian prosthodontic society conference 2015.12 Hyderabad, India

[Awards & Honors]

1. Inokoshi Masanao. Representative at Hatton Award competition for CED-IADR, 2015.03
2. Manabu Kanazawa, 2015 ICP Poster Awards, International College of Prosthodontists, 2015.09

Laboratory Medicine

Professor Shuji TOHDA

Research Associate Mai ITOH

Graduate Students Mika OHTAKA, Erika SHIRATORI, Shijun O, 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) Mechanism of abnormal growth of acute leukemia cells
- 2) Molecular diagnostic tests for cancer and infectious diseases
- 3) Mechanism of abnormal growth of lymphoma cells
- 4) Detection of minimal residual leukemia or lymphoma cells

(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

[Conference Activities & Talks]

1. Narumi J, Kanouchi T, Akaza M, Aoyagi E, Yanagi N, Ohta N, Sumi Y, Yokota T, Hagihara M, Tohda S. Study for quality control in nerve conduction study. 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.05 Osaka

Intensive Care Medicine

Associate Professor:

Koichi Nakazawa(Critical Care Medicine)(2014.4.1)

Yushi Adachi(Critical Care Medicine)(2015.4.1)

Assistant Professor:

Fumi Maruyama (Intensive Care Unit) (2014.4.1)

Takahiro Masuda (Intensive Care Unit) (2014.4.1)

Kenji Wakabayashi (Critical Care Medicine) (2015.4.1)

Akihiro Haramo (Intensive Care Unit) (2015.4.1 2016.3.31)

Nobuhiro Shiota (Anesthesiology) (2015.4.1)

Takabumi Omori (Anesthesiology) (2015.4.1)

Postgraduate students:

Mariko Senda (2014.4.1)

(1) Outline

Critical care medicine provides intensive care and treatment of critically ill patients. The role of intensivists take charge treatment of critically ill patients in the ICU. 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 attending physician. The purpose of critical care medicine is to treat and improve the serious condition by maintaining the patients' hemodynamics to be stable.

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, abnormal electrolyte, 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 Grand-in-Aid for Scientific Research C)

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

(3) Education

Undergraduate education

Lectures: Fourth-year medical students

- 1) Mechanical ventilation (Wakabayashi)
- 2) Sepsis and multiple organ dysfunction syndrome (Masuda)
- 3) Airway management (Adachi)
- 4) Respiratory physiology and monitoring (Nakazawa)
- 5) Acute respiratory distress syndrome (Wakabayashi)
- 6) Anesthesia for patients with medical complications (Haramo)
- 7) Examination of critical care medicine

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, and attending physicians get together, go round, and talk about the best treatment of the patients.

(5) Publications

[Original Articles]

1. Fletcher ME, Boshier PR, Wakabayashi K, Keun H, Smolenski RT, Kirkham PA, Adcock IM, Barton PJ, Takata M and Marczin N. Influence of glutathione-S-transferase (GST) inhibition on lung epithelial cell injury: role of oxidative stress and metabolism American Journal of Physiology - Lung Cellular and Molecular Physiology. 2015; 308(12); 1274-1285
2. Uzawa Y, Otsuji M, Nakazawa K, Fan W, Yamada Y. Derivation of recruitment function from the pressure-volume curve in an acute lung injury model. Respiratory Physiology & Neurobiology. 2015.01; 205(1); 16-20
3. Yushi U Adachi, Atsushi Numaguchi, Naoyuki Matsuda. Ultrasonography-guided radial artery catheterization and further optimal sequences. J Clin Monit Comput. 2015.02; 29(1); 201-202
4. Adachi YU, Numaguchi A.. Is it possible to identify by ultrasonography at a glance? A leaflet of valve or a flap of dissection. J Clin Anesth.. 2015.05; 27(5); 440-441
5. Numaguchi A, Adachi YU, Aoki Y, Ishii Y, Suzuki K, Obata Y, Sato S, Nishiwaki K, Matsuda N.. Radial artery cannulation decreases the distal arterial blood flow measured by power Doppler ultrasound. J Clin Monit Comput.. 2015.05; 29(5); 653-657
6. Takafumi Ohmori, Nobuhiro Shiota, Akihiro Haramo, Takahiro Masuda, Fumi Maruyama, Kenji Wakabayashi, Yushi U Adachi, Koichi Nakazawa. Post-operative cardiac arrest induced by co-administration of amiodarone and dexmedetomidine: a case report. J Intensive Care. 2015.10; 3(10); 43

[Books etc]

1. Japan-North America Medical Exchange Foundation, Wakabayashi K et al.. A passport to learning medicine abroad. Haru Shobo, 2015

[Misc]

1. Kate Tatham, Kieran O'Dea, Kenji Wakabayashi, Nandor Marczin, Masao Takata. The role of ex vivo lung perfusion in lung transplantation Journal of the Intensive Care Society. 2015.02; 16(1); 58-63

[Conference Activities & Talks]

1. Distinct inflammatory impacts between volutrauma and atelectrauma: the role of lung-marginated monocytes in ventilator-induced lung injury. Japanese Society of Intensive Care Medicine 2015.02
2. Takahiro Masuda, Chieko Mitaka, May Khin Hnin Si, Koji Kido, Yu Qi, Tokujiro Uchida, Shinya Abe, Taku Miyasho, Makoto Tomita. Polymyxin B hemoperfusion prevents renal tubular cell death in a rat model of cecal ligation and puncture. International Symposium Intensive Care Medicine and Emergency Medicine 2015.03.17 Brussels, Belgium
3. Yushi U. Adachi, Takuya Yoshida, Yuto Shioya, Kozaburo, Nakahara, Kimitoshi Nishiwaki, Naoyuki Matsuda.. Propofol anesthesia showed no effect on the dopaminergic acceleration induced by methamphetamine and nomifensine in rat striatum - in vivo microdialysis study.. International Anesthesia Research Society Annual Meeting 2015 2015.03.21 Honolulu, Hawaii, USA
4. Yushi U. Adachi, Takuya Yoshida, Naoyuki Matsuda, Koichi Nakazawa, Koshi Makita.. Lecithin decreased the hypnotic potency of intravenous anesthetics in ddY mice.. Euroanaesthesia 2015 2015.05.30 Berlin, Germany
5. Wakabayashi K, Maruyama F, Tasaka F, Ohmori T, Shinoda K, Masuda T, Nakazawa K, Mitaka C, Makita H. Pediatric ECMO for RS virus pneumonia - a case report.. Japanese Society of Respiratory Care Medicine 2015.07
6. Adachi YU.. Mixture of JM-1232(-) and propofol showed minute increases of recovery time from hypnosis after the repeated administration and the anesthesia was completely antagonized by flumazenil in ddY mice.. Annual Meeting of Japan Clinical Society of Anesthesia, Japan and China Anesthesia Conference. 2015.10.21 Yokohama, Japan
7. Yushi Adachi, Kenji Wakabayashi, Koichi Nakazawa, Koshi Makita.. Lecithin-enriched Formulation Decreases the Hypnotic Potency of Intravenous Anesthetics in ddY Mice.. Annual meeting of American Society of Anesthesiologists 2015, 2015.10.24 San Diego, CA, USA
8. Yushi Adachi, Katsuhiko Tanaka, Kazuhiko Kobayashi, Michiko Kawaguchi, Kimitoshi Nishiwaki, Koichi Nakazawa, Koshi Makita.. Droperidol Showed Greater Decreases in the Bispectral Index Values than Haloperidol During General Anesthesia With Both Desflurane and Sevoflurane.. Annual meeting of American Society of Anesthesiologists 2015 2015.10.24 San Diego, CA, USA
9. Kajikawa Y, Hosokawa S, Wakabayashi K, Maejima Y, Isobe M, Doi S. Dexmedetomidine Ameliorates Monocrotaline Induced Pulmonary Arterial Hypertension in Rats. American Heart Association Scientific Sessions 2015 2015.11.10 Orland, USA

Liaison Psychiatry and Palliative Medicine

Associate Professor Eisuke MATSUSHIMA
Junior Associate Professor Miho MIYAJIMA
Tokunin Assistant Professor
Hospital Staff
Secretary Kyoko NAKAGAWA
Graduate Student

Hirofumi NAKAMURA, Makiko KOIKE, Ako HANEKAWA, Mare NISHIURA, Mariko KOBAYASHI,
Yuhko KOHNO, Nao NAKAYAMA, Satsuki WATANABE, Aya YAMASITA, Kanako ICHIKURA,
Rie OMOYA, Takamasa NODA, Toshimi TAKANO, Noriko ISHIDUKA, Saho WADA,
Noriko YOSHIDA, Toshi KURIYAMA, Shino UMEZAWA, Hiroshi KOBO, Yoko SUZUKI, Ayasa MATSUDA,
Natsumi NAKAMURA.
Research Student Okihiko AIHARA, Ryuho IBARAKI.

(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. ICHIKURA Kanako, YAMASHITA Aya, SUGIMOTO Taro, KISHIMOTO Seiji, MATSUSHIMA Eisuke. Persistence of psychological distress and correlated factors among patients with head and neck cancer., *Palliative & Supportive Care*,. 2015;
2. ICHIKURA Kanako, MATSUDA Ayako, KOBAYASHI Mika, NOGUCHI Wataru, MATSUSHITA Toshiko, MATSUSHIMA Eisuke,. Breaking bad news to cancer patients in palliative care: A comparison of national cross-sectional surveys from 2006 and 2012., *Palliative & Supportive Care*,. 2015;
3. Soshi, T., Noda, T., Ando, K., et al.. Neurophysiological modulation of rapid emotional face processing is associated with impulsivity traits. *BMC neuroscience*,. 2015; 16(1); 1
4. Ota, M., Sato, N., Okamoto, T., Noda, T.. Neuromyelitis optica spectrum disorder and multiple sclerosis: Differentiation by a multimodal approach. *Multiple sclerosis and related disorders*,. 2015; 4(6); 515-520
5. Soshi, T., Noda, T., Ando, K. impulsivity is associated with early sensory inhibition in neurophysiological processing of affective sounds. *Frontiers in psychiatry*. 2015; 6;
6. Hattori, K., Ota, M., Noda T.. Increased cerebrospinal fluid fibrinogen in major depressive disorder. *Scientific reports*,. 2015; 5;
7. Ota, M., Noda, T. Effect of electroconvulsive therapy on gray matter volume in major depressive disorder. *Journal of Affective Disorders*,. 2015; 186; 186-191
8. Ogawa, S., Hattori, K., Noda T. Reduced cerebrospinal fluid ethanolamine concentration in major depressive disorder. *Scientific reports*,. 2015; 5;
9. Terakado A, Matsushima E. Work stress among nurses engaged in palliative care on general wards. *Psycho-oncology*. 2015; 24(1); 63-69
10. Umezawa S, Fujisawa D, Fujimori M, Ogawa A, Matsushima E, Miyashita M. Prevalence, associated factors and source of support concerning supportive care needs among Japanese cancer survivors. *Psychooncology* . 2015; 24(6); 635-642
11. Yamashita A, Ichikura K, Sugimoto T, Kishimoto S, Shimozuma K, Matsushima E. Reliability and validity of the Head and Neck Cancer Inventory (HNCI) in Japanese patients. *Palliat Support Care* . 2015; 13; 1373-1380
12. Nakagawa J, Takahashi M, Okada R, Matsushima E, Matsuda T. Women's preference for a male acquaintance enhances social reward processing of material goods in the anterior cingulate cortex *PLoS One*. 2015; 10(8);
13. Kono Y, Matsushima E, Uji M. Presenteeism among Japanese IT employees: personality, temperament and character, job strain and workplace support, and mental disturbance. *Psychology*. 2015; 6; 1971-1983
14. Umezawa S, Fujimori M, Matsushima E, Kinoshita H, Uchitomi Y. Umezawa S, Fujimori M, Matsushima E, Kinoshita H, Uchitomi Y *Cancer*. 2015; 121; 4240-4249
15. Wada S, Shimizu K, Inoguchi H, Shimoda H, Yoshiuchi K, Akechi T, Uchida M, Ogawa A, Fujisawa D, Inoue S, Uchitomi Y, Matsushima E. The association between depressive symptoms and age in cancer patients: A multicenter cross-sectional study. *J Pain Symptom Manage*.. 2015;
16. Ichikura K, Matsuda A, Kobayashi M, Noguchi W, Matsushita T, Matsushima E. Breaking bad news to cancer patients in palliative care: A comparison of national cross-sectional surveys from 2006 and 2012. *Palliat Support Care*. 2015; 13; 1623-1630
17. Nakagawa J., Takahashi M., Okada R., Matsushima E., Matsuda T. Women's Preference for a Male Acquaintance Enhances Social Reward Processing of Material Goods in the Anterior Cingulate Cortex. *PLoS One*. 2015.08; 10(8);
18. Suzuki Y, Miyajima M, Ohta K, Yoshida N, Okumura M, Nakamura M, Sasano T, Kawara T, Matsuura M, Matsushima E.. A Triphasic Change of Cardiac Autonomic Nervous System During Electroconvulsive Therapy. *J ECT*.. 2015.09; 31(3); 186-191

19. Kubota Y, Okuyama T, Uchida M, Umezawa S, Nakaguchi T, Sugano K, Ito Y, Katsuki F, Nakano Y, Nishiyama T, Katayama Y, Akechi T. Effectiveness of a psycho-oncology training program for oncology nurses: a randomized controlled trial. *Psychooncology*. 2015.10;
20. Umezawa S, Fujimori M, Matsushima E, Kinoshita H, Uchitomi Y. Preferences of advanced cancer patients for communication on anticancer treatment cessation and the transition to palliative care. *Cancer*. 2015.12; 121(23): 4240-4249
21. 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. Nakagawa J., Takahashi M., Okada R., Sue A., Watanabe M., Matsushima E., Matsuda T.. Subjective emotional effects on neural correlates of evaluation in interpersonal relationships,. The 21st Annual Meeting of the Organization for Human Brain Mapping (OHBM) 2015.06.18
2. Nakagawa J., Takahashi M., Okada R., Sue A., Watanabe M., Matsushima E., Matsuda T.. Preferences Enhance Reward Processing of Objects in the Anterior Cingulate Cortex, . he 38th Annual Meeting of the Japan Neuroscience Society, 2015.07.30
3. Miyajima M, Fujiwara K, Abe E, Suzuki Y, Sawada Y, Yamakawa T, Kano M, Maehara T, Ohta K, Sasai-Sakuma T, Sasano T, Matsuura M, Matsushima E.. Detection of Altered Heart Rate Variability Prior to Epileptic Seizure Using Multivariate Statistical Process Control.. 37TH Annual International Conference of The IEEE Engineering in Medicine and Biology Society. 2015.08.25
4. Suzuki Y, Miyajima M, Ohta K, Yoshida N, Okumura M, Nakamura M, Sawada Y, Sasano T, Kawara T, Matsuura M, Matsushima E.. Changes of cardiac autonomic nervous activity during a course of electroconvulsive therapy in depression. . 15th European Congress on Clinical Neurophysiology. 2015.09.30
5. Miyajima M, Fujiwara K, Yamakawa T, Suzuki Y, Sawada Y, Abe E, Kano M, Maehara T, Ohta K, Sasai-Sakuma T, Sasano T, Maehara M, Matsushima E. . Detection of Preictal Heart Rate Variability Alteration Using Multivariate Statistical Process Control.. 2015.10.30
6. Suzuki Y, Miyajima M, Ohta K, Yoshida N, Okumura M, Nakamura M, Sawada Y, Sasano T, Kawara T, Matsuura M, Matsushima E.. Alteration of Corrected QT Interval Associated with Generalized Tonic-Clonic Seizures induced by Electroconvulsive Therapy (ECT). . AES 69th Annual Meeting. 2015.12.04

Pharmacokinetics and Pharmacodynamics

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

(1) Research

- 1) Investigation on the membrane transport of drugs
- 2) Kinetics of drug action in disease states
- 3) Therapeutic drug monitoring and clinical pharmacokinetics
- 4) Development of new drug delivery systems

(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. Nagata M, Ishiwata Y, Takahashi Y, Takahashi H, Saito K, Fujii Y, Kihara K, Yasuhara M.. Pharmacokinetic-pharmacodynamic analysis of sunitinib-induced thrombocytopenia in Japanese patients with renal cell carcinoma Biol. Pharm. Bull.. 2015.03; 38; 402-410
2. Y. Yoshiyama, M. Kawakami, M. Narukawa, Y. Abe, M. Mori, N. Yamamoto, H. Sasaki, M. Yasuhara. Questionnaire survey on the ideal roles of community pharmacies Japanese Journal of Pharmaceutical Health Care and Sciences. 2015.06; 41(6); 424-434
3. K. Furuta, F. Mizokami, H. Sasaki and M. Yasuhara. Active topical therapy by “Furuta method” for effective pressure ulcer treatment: a retrospective study. J. Pharm. Health Care Sci.. 2015.07; 1(21); 1-9

[Conference Activities & Talks]

1. Hematopoietic stem cell transplantation using fludarabine and busulfan regimen for 10 patients with primary immunodeficiency. 2015.03.05
2. M. Yasuhara, M. Nagata, M. Nakajima, Y. Ishiwata, H. Takahashi. Hyperglycemia induced by a single dose of olanzapine in rats. 2015AAPS Annual Meeting and Exposition 2015.10.27 Orland
3. Masato Yasuhara. Progress and Future of Pharmaceutical Health Care and Sciences for the Next Quarter of Century. The 25th Annual Meeting of the Japanese Society of Pharmaceutical Health Care and Sciences 2015.11.21 Yokohama

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 Takako WATANABE
Senior Resident Miyako NURAKAWA

(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. Igari K, Kudo T, Uchiyama H, Toyofuku T, Inoue Y.. Progression of perianeurysmal inflammation after endovascular aneurysm repair for inflammatory abdominal aortic and bilateral common iliac artery aneurysms. *Ann Vasc Surg.* 2015.02; 29(364); e1-e4
2. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y.. Comparison between endovascular repair and open surgery for isolated iliac artery aneurysms. *Surg Today.* 2015.03; 45; 290-296
3. Igari K, Kudo T, Toyofuku T, Inoue Y.. Surgical Treatment for Profunda Femoris Artery Aneurysms: Five Case Reports. *Case Rep Vasc Med.* 2015.04; 375278
4. Igari K, Kudo T, Toyofuku T, Inoue Y.. Controlled antegrade and retrograde subintimal tracking technique for endovascular treatment of the superficial femoral artery with chronic total occlusion. *Ann Vasc Surg.* 2015.08; 29(1320); e7-e10
5. Igari K, Kudo T, Toyofuku T, Inoue Y.. Surgical Treatment of Cystic Adventitial Disease of the Popliteal Artery: Five Case Reports. *Case Rep Vasc Med.* 2015.08; 984681
6. Igari K, Kudo T, Toyofuku T, Inoue Y.. Bilateral Axillary Artery Aneurysms Presenting as Upper Limb Ischemia. *Ann Vasc Surg.* 2015.11; 29(1659); e7-e12

[Conference Activities & Talks]

1. Igari K, Kudo T, Toyofuku T, Inoue Y.. Crossing of infrapopliteal arterial chronic total occlusions with the Crosser™system.. 64th International congress of the European Society for Cardiovascular and Endovascular Surgery. 2015.03.26 Turkey (Istanbul)
2. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Otani, Miki Taniguchi, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Shinji Tanaka , Minoru Tanabe, Nobuyuki Enomoto and Mamoru Watanabe. Gene alterations in TERT promoter, CTNNB1, and TP53 are closely associated with development and prognosis of hepatocellular carcinoma : Comprehensive analyses by next generation sequencing technology. The 3rd JSGE International Topic Conference 2015.04.24 Sendai
3. Igari K, Kudo T, Nakamura M, Nishizawa M, Uchiyama H, Koizumi S, Toyofuku T, Inoue Y.. The snorkel technique for endovascular aneurysm repair with challenging neck anatomy . Cardiovascular Summit TCTAP 2015 2015.04.28 Seoul (Republic of Korea)
4. Kudo T.. The Current Situation of the Treatment for Peripheral Arterial Disease in Japan. . The 9th Japan-Korea Joint Meeting for Vascular Surgery. 2015.06.05 Yokohama (Japan)
5. Katsui S, Igari K, Yamamoto Y, Nakamura M, Nishizawa M, Koizumi S, Toyofuku T, Kudo T, Inoue Y. . Crossing of infrapopliteal arterial chronic total occlusions with the Crosser™system.. The 9th Japan-Korea Joint Meeting for Vascular Surgery 2015.06.05 Yokohama (Japan)
6. Igari K, Kudo T, Toyofuku T, Inoue Y.. The assessment of peripheral perfusion for the patients with isolated infrapopliteal arterial lesions by indocyanine green angiography.. 46th World Congress of Surgery WCS 2015. 2015.08.23 Bangkok (Thailand)
7. Nishizawa M, Igari K, Toyofuku T, Kudo T, Inoue Y. . A novel technique to infrainguinal arterial occlusions using the Crosser™system. . 46th World Congress of Surgery WCS 2015. 2015.08.23 Bangkok (Thailand)
8. Igari K, Kudo T, Toyofuku T, Inoue Y.. A case of arteriovenous fistula after endovenous laser ablation for varicose vein. . UIP Capter Meeting: Seoul UIP 2015 2015.08.27 Seoul (Republic of Korea)
9. Ichinose T, Kudo T, Yamamoto Y, Nakamura M, Katsui S, Nishizawa M, Igari K, Toyofuku T, Inoue Y.. A case of deep vein thrombosis due to iliac vein compression treated by catheter directed thrombolysis and iliac vein stenting.. 12th Tokyo-Shanghai International Symposium for Vascular Diseases. 2015.11.14 Shanghai (China)

10. Yamamoto Y, Kudo T, Ichinose T, Nakamura M, Katsui S, Nishizawa M, Igari K, Koizumi S, Toyofuku T, Inoue Y. . A case of surgically rescued in-stent occlusion of the SFA with jailed profunda orifice.. 12th Tokyo-Shanghai International Symposium for Vascular Diseases. 2015.11.14 Shanghai (China)

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. Gando Satoshi, Otomo Yasuhiro. Local hemostasis, immunothrombosis, and systemic disseminated intravascular coagulation in trauma and traumatic shock. *Crit Care*. 2015; 19; 72
2. Yamanouchi Satoshi, Sasaki Hiroyuki, Tsuruwa Miho, Ueki Yuzuru, Kohayagawa Yoshitaka, Kondo Hisayoshi, Otomo Yasuhiro, Koido Yuichi, Kushimoto Shigeki. Survey of preventable disaster death at medical institutions in areas affected by the Great East Japan Earthquake: a retrospective preliminary investigation of medical institutions in Miyagi Prefecture. *Prehosp Disaster Med*. 2015.04; 30(2); 145-151
3. Ushizawa Hiroto, Yahata Yuichiro, Endo Takeo, Iwashima Tomoko, Misawa Michiyo, Sonobe Makoto, Yamagishi Takuya, Kamiya Hajime, Nakashima Kazutoshi, Matsui Tamano, Matsui Mari, Suzuki Satowa, Shibayama Keigo, Doi Mikio, Irie Fujiko, Yamato Shinichi, Otomo Yasuhiro, Oishi Kazunori. An Epidemiological Investigation of a Nosocomial Outbreak of Multidrug-resistant *Acinetobacter baumannii* in a Critical Care Center in Japan, 2011-2012. *Jpn J Infect Dis*. 2015.06;

4. Mikami Saori, Aiboshi Junichi, Kobayashi Tetsuyuki, Kojima Mitsuaki, Morishita Koji, Otomo Yasuhiro. Discrete roles of intracellular phospholipases A2 in human neutrophil cytotoxicity. *J Trauma Acute Care Surg.* 2015.08; 79(2); 238-246
5. Kojima Mitsuaki, Aiboshi Junichi, Shibata Masahiro, Kobayashi Tetsuyuki, Otomo Yasuhiro. Novel role of group VIB Ca²⁺-independent phospholipase A2gamma in leukocyte-endothelial cell interactions: An intravital microscopic study in rat mesentery. *J Trauma Acute Care Surg.* 2015.11; 79(5); 782-789

[Books etc]

1. Asensio JA, Petrone P, Perez-Alonso A, Osmolak A, Loden J, Gracia G, Ksycki M, Joseph D, Fujita T, Otomo Y. *Current Therapy of Trauma and Surgical Critical Care*, 2nd Edition. Elsevier, 2015.06 (ISBN : 978-0323079808)

[Misc]

1. Shoko T, Otomo Y, Tomioka M. The earthquake in Nepal: Surgeons' dispatch from Barhabise thebmj. 2015.07;

[Conference Activities & Talks]

1. Otomo Y. LESSONS LEARNED FROM THE JAPAN TSUNAMI DISASTER. 19th World Congress on Disaster and Emergency Medicine 2015.04.23
2. Shiraishi A, Otomo Y. DERIVATION AND EXTERNAL VALIDATION OF A NOVEL PREDICTION SCORE FOR EARLY TRAUMA CARE. 19th World Congress on Disaster and Emergency Medicine 2015.04.23
3. Ushizawa H, Shiraishi A, Otomo Y. CHARACTERISTICS OF MORTALITY IN GREAT EAST JAPAN EARTHQUAKE, 2011. 19th World Congress on Disaster and Emergency Medicine 2015.04.23
4. Shiraishi A, Otomo Y, Murata K, Kato H, Sasaki J, Ogura H, Matsuoka T, Uejima T, Morimura T, Ishikura H, Hayakawa M, Hagiwara A, Takeda M, Kaneko N, Saitoh D, Yokota H, Sakamoto T, Tanaka T, Kushimoto S. Effect of Tranexamic Acid in the Real World –A Propensity Score Matching Analysis of Data from Japan Observational Study for Coagulation and Thrombolysis in Early Trauma (J-OCTET). The 16th European Congress of Trauma & Emergency Surgery 2015.05.10 Amsterdam
5. Shiraishi A, Watanabe T, Kawahara N, Otomo Y. Decompressive craniotomy can improve mortality in patients with putaminal or subcortical intracerebral hemorrhage –A propensity score analysis. 24. European Stroke Conference 2015.05.14 Vienna, Austria
6. Otomo Y. "chairman IATSIC POSTER WALK Group 2: CLINICAL TRAUMA CARE – 1 ". 46TH WORLD CONGRESS OF SURGERY WCS 2015, Bangkok, Thailand 2015.08.24 Bangkok, Thailand
7. Nakatsutsumi K, Otomo Y, Shiraishi A. "RISKS OF COMPUTED TOMOGRAPHY BEFORE EMERGENCY THORACOTOMY OR LAPAROTOMY IN SEVERELY INJURED TRAUMA VICTIMS: A NATIONWIDE OBSERVATIONAL STUDY Travel award ". 46TH WORLD CONGRESS OF SURGERY WCS 2015, Bangkok, Thailand 2015.08.24 Bangkok, Thailand
8. Otomo Y. "chairman IATSIC Free Papers "Trauma Surgery" ". 46TH WORLD CONGRESS OF SURGERY WCS 2015, Bangkok, Thailand 2015.08.25 Bangkok, Thailand
9. Otomo Y. "Invited lecture Symposium 17 Critical Care in Disaster and War: Field Report Industrial Accident (Fukushima)". "12th Congress of the World Federation of Societies of Intensive and Critical Care Medicine, Seoul, South Korea" 2015.08.29
10. Otomo Y. "Chairman Symposium 17 Critical Care in Disaster and War: Field Report". "12th Congress of the World Federation of Societies of Intensive and Critical Care Medicine, Seoul, South Korea" 2015.08.29
11. 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 2015.09.09 Las Vegas, NV, United States

12. Atsushi Shiraishi, Keita Nakatsutsumi, Yasuhiro Otomo. UNDERGOING TRUNCAL TRAUMA SURGERY BEFORE CT SCAN MAY IMPROVE IN-HOSPITAL MORTALITY IN HYPOTENSIVE OR COMATOSE TRAUMA PATIENTS. 74th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery 2015.09.09 Las Vegas, NV, United States
13. Otomo Y. "Posters Session Shock/Transfusions I". the 74th annual meeting of American Association for the Surgery of Trauma, Las Vegas 2015.09.09 Las Vegas
14. Inoue J, Shiraishi A, Yoshiyuki A, Haruta K, Otomo Y. "RESUSCITATIVE ENDOVASCULAR BALLOON OCCLUSION OF THE AORTA (REBOA) MIGHT BE DANGEROUS IN PATIENTS WITH SEVERE TORSO TRAUMA — A PROPENSITY SCORE ANALYSIS SAYS". the 74th annual meeting of American Association for the Surgery of Trauma, Las Vegas 2015.09.12 Las Vegas
15. Otomo Y. "INFORMAL EXPERT CONSULTATION ON STRENGTHENING NATIONAL AND FOREIGN MEDICAL TEAMS IN RESPONSE TO DISASTERS How to build strong domestic and international emergency medical teams capacities: the case of Japan". INFORMAL EXPERT CONSULTATION ON STRENGTHENING NATIONAL AND FOREIGN MEDICAL TEAMS IN RESPONSE TO DISASTERS, REGIONAL OFFICE FOR THE WESTERN PACIFIC, Manila 2015.09.22 Manila
16. Otomo Y. "Global EMT Registry – Lead Mentor & Verification program workshop 12-13th November 2015, WHO HQ Geneva, Switzerland ". 2015.11.12 Geneva, Switzerland

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
Hiroyuki ISHIKAWA
Yohei TAKEUCHI
Syoei TAMURA
Moriyuki NAKAMURA

Assistant Professor
Yasuka KUSUMOTO

Hospital Staff
Tomo SUZUKI
Naoki HAYASHI
Taiji HOSHIAI
Ayana NATORI

Graduate International Research Student
Hirotoshi YAMAWAKI
Shohei TAKAHASHI
Visiting Clinical
Junior Associate Professor
Seiji SAKURAI

(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. Arai T, Kinoshita Y, Senpuku H. Persistent colonization of *Candida albicans* yeast on the tongue in NOD/SCID.e2f1-/- mice *Journal of Infection and Chemotherapy*. 2015.05; 21(5); 370-375

[Conference Activities & Talks]

1. SHINOZUKA Osamu. Certification System of The Japanese Society for Disability and Oral Health. 2015 Spring Session & Annual Meeting of Korean Association for Disability and Oral Health 2015.04.04 Seoul

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 Maiko IWAKI
 Assistant Professor Sachi UMEMORI
 Assistant Professor Kanako NORITAKE
 Hospital Staff Maiko IWAKI
 Hospital Staff Yuko MITSUMA
 Hospital Staff Mina GOTO
 Hospital Staff Naoko BANDO
 Hospital Staff Yasuyuki KIMURA
 Hospital Staff Shota HAYASHI

(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 Phase1, Phase 2. (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. Ken-ichi Tonami, Kazunobu Sano, Shizuko Ichinose and Kouji Araki . Resin–Dentin Bonding Interface After Photochemical Surface Treatment Photomedicine and Laser Surgery. 2015.01; 33(1); 1-6
2. Narumi Saitou, Hiroaki Kobayashi, Yoshiko Namba, Fumi Kenmochi, Yuko Sogo, Shigeru Oda, Toshiko Adachi, Yuichi Izumi. Importance of SPT Deduced from the Treatment of Patients with Aggressive Periodontitis Journal of Japanese Society of Periodontology. 2015.03; 57(1); 41-48
3. Koichi Shinkai, Shigeru Oda, Hiroshi Ymaguchi, Mitsuyoshi Ymada, Kazushi Yoshikawa, Yoshito Yoshimine, Hisashi Watanabe. A Proposal of Educational Guideline for Laser Dentistry Journal of Japanese Society of Laser Dentistry. 2015.04; 26(1); 28-31
4. 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 β -tricalcium phosphate: a preclinical study in dogs Journal of Periodontal Research. 2015.05;
5. Jo A, Kanazawa M, Sato Y, Iwaki M, Akiba N, Minakuchi S. A randomized controlled trial of the different impression methods for the complete denture fabrication: Patient reported outcomes. J Dent. 2015.06;
6. Matsuura T, Akizuki T, Hoshi S, Ikawa T, Kinoshita A, Sunaga M, Oda S, Kuboki Y, Izumi Y . Effect of a tunnel-structured β -tricalcium phosphate graft material on periodontal regeneration: a pilot study in a canine one-wall intrabony defect model Journal of Periodontal Research. 2015.06; 50(3); 347-355
7. 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 2015.09; 1-14

[Conference Activities & Talks]

1. Ken-ichi Tonami , Azusa Yamada , Sachi Umemori , Kanako Noritake , Maiko Iwaki , Satoko Ohara , Masayuki Hideshima , Jun Tsuruta , Hiroshi Nitta , Shigeru Oda , Atsuhiko Kinoshita , Kouji Araki , Shiro Mataka.. Development of professionalism during experiential learning at welfare facilities.. South East Asia Association For Dental Education 2015
2. Jo A,Kanazawa M,Sato Y,Akiba N,Iwaki M,Minakuchi S. Influence of the different impression methods for complete denture fabrication on Patient Reported Outcomes. 2015.01.24
3. M. Iwaki, M. Kanazawa, M. Sunaga, A. Kinoshita, S. Minakuchi, S. Oda, K. Araki. Live broadcast lectures on complete denture prosthodontics: the learning effectiveness . 2015 IADR/AADR/CADR General Session & Exhibition 2015.03.12 Boston
4. Tonami K,Sano K,Iwasaki N,Takahashi H,Araki K. Change of dentin wettability by Xe excimer lamp irradiation. Spring Meeting of Japanese Society for Dental Materials and Devices 2015.04.12
5. Arakida T,Kanazawa M,Iwaki M,Yamamoto S,Nakamura T,Andou K,Minakuchi S,Handa K,Wakabayashi N. A case report of fabricating complete dentures applying optimal scanar. 2015.05.30
6. Tonami K, Yamada A, Umemori S, Noritake K, Iwaki M, Ohara S, Hideshima M, Nitta H, Oda S, Kinoshita A, Araki K, Mataka S. Change in dental students' awareness of comprehensive view of human during experiential learning of "Introduction of Behavioral Science. 34th JDEA annual meeting 2015.07.10
7. Ken-ichi Tonami, Chikako Nakamura, Azusa Yamada, Sachi Umemori, Kanako Noritake, Maiko Iwaki, Masayo Sunaga, Satoko Ohara, Masayuki Hideshima, Jun Tsuruta, Hiroshi Nitta, Shigeru Oda, Atsuhiko Kinoshita, Kouji Araki, Shiro Mataka. Development of professionalism during experiential learning at welfare facilities. 26th seaade Annual Scientific Meeting, Bali, Indonesia 2015.08.12 Bali, Indonesia
8. Tonami K, Kimura Y, Noritake K, Hobo K, Hayashi s, Mataka S, Araki K. Quantify of geometric feature of teeth crown using fractal dimension. The Japanese Society of Oral Diagnosis/Oral Medicine Annual Meeting 2015.09.04
9. Manabu Kanazawa, Maiko Iwaki, Daisuke Sato, Yuri Omura, Anna Miyayasu, Shohei Kasugai, Shunsuke Minakuchi. Immediate Loading of Two-Implant Mandibular Overdentures: 3-year Prospective Study. 16th meeting of the International College of Prosthodontists 2015.09.17 Seoul, Korea
10. Takahashi K, Tsuruta J, Tonami K, Araki K. Relation between finger dexterity and cutting precision. The Stomatological Society, Japan, Annual Meeting 2015.12.26

Psychosomatic Dentistry

Professor	Akira Toyofuku
Assistant Professor	Miho Takenoshita
	Tatsuya Yoshikawa
Hospital Staff	Takeru Kyuragi
	Motoko Watanabe
	Yojiro Umezaki
Graduate Student	Yukiko Shinohara
	Anna Suzuki
	Rou Mikuzuki
	Tomohisa Kitamura
Lecturer (part-time)	Haruhiko Motomura
	Ayano Katagiri
	Yuuichi Kato

(1) 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

(2) Lectures & Courses

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.

(3) 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.

(4) Publications

[Original Articles]

1. Motoko Watanabe, Yojiro Umezaki, Anna Miura, Yukiko Shinohara, Tatsuya Yoshikawa, Tomomi Sakuma, Chisa Shitano, Ayano Katagiri, Miho Takenoshita, Akira Toriihara, Akihito Uezato, Toru Nishikawa, Haruhiko Motomura, Akira Toyofuku. Comparison of cerebral blood flow in oral somatic delusion in patients with and without a history of depression: a comparative case series. *BMC Psychiatry*. 2015.03; 15(1); 422
2. Y Umezaki, B W Badran, T S Gonzales, M S George. Daily left prefrontal repetitive transcranial magnetic stimulation for medication-resistant burning mouth syndrome. *Int J Oral Maxillofac Surg*. 2015.08; 44(8); 1048-1051
3. 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*. 9(2); 234-242

[Conference Activities & Talks]

1. Chisa Shitano, Miho Takenoshita, Takashi Ono, Akira Toyofuku. FEATURES OF ORAL PSYCHOSOMATIC DISORDER IN ORTHODONTIC PATIENTS. 91th Congress of European Orthodontic Society 2015.06.18 Venice/Italy
2. Asymmetric brain perfusion SPECT in patients with Phantom bite Syndrome. 2015.06.26
3. Effectiveness of amitriptyline for atypical odontalgia. 2015.06.26
4. Knowledge about diagnosis criteria of major depression disorder. 2015.06.27
5. Motoko Watanabe, Yojiro Umezaki, Anna Miura, Yukiko Shinohara, Tatsuya Yoshikawa, Miho Takenoshita, Akira Toriihara, Akihito Uezato, Toru Nishikawa, Haruhiko Motomura, Akira Toyofuku. Comparison of

cerebral blood flow in oral somatic delusion in patients with and without a history of depression. 23rd World Congress on Psychosomatic Medicine 2015.08.21

6. Anna Miura, Motoko Watanabe, Yukiko Shinohara, Tatsuya Yoshikawa, Miho Takenoshita, Akira Toyofuku. Effectiveness of amitriptyline in atypical odontalgia. 23rd World Congress on Psychosomatic Medicine 2015.08.21 Glasgow
7. Ayano Katagiri , Hiroto Saito , Kinuyo Ohara , Masamichi Shinoda , Akira Toyofuku and Koichi Iwata. Satellite glial cell activation via extracellular signal-regulated kinase phosphorylation, associated with phenotypic change in trigeminal ganglion neurons, is involved in lingual neuropathic pain. SfN 2015 2015.10.17 McCormick Place, Chicago

Behavioral Dentistry

Professor Shiro Mataki
 Associate Professor Hiroshi Nitta
 Research Associate Azusa Yamada
 Research Associate Sachi Sakairi (child-care leave)

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. Ohara Y, Yoshida N, Kono Y, Hirano H, Yoshida H, Mataki S, Sugimoto K.. Effectiveness of an oral health educational program on community-dwelling older people with xerostomia. *Geriatr Gerontol Int.* 2015.04; 15(4); 481-489
2. Ohara Y, Hirano H, Watanabe Y, Obuchi S, Yoshida H, Fujiwara Y, Ihara K, Kawai H, and Mataki S.. Factors associated with self-rated oral health among community-dwelling older Japanese: A cross-sectional study. *Geriatr Gerontol Int.* 2015.06; 15(6); 755-761
3. Ito S, Mataki S, Yoshida N, Ito T. Changes in self-efficacy before and after clinical practice of dental hygiene students *The journal of Japan Society of Dental Hygiene Education* . 2015.10; 6(2); 128-136

[Books etc]

1. Urabe A, Shimada K, Kawai S et al.. Today's Drug Therapy in 2015. Nankodo, 2015.01 (ISBN : 978-4-524-26197)

[Conference Activities & Talks]

1. Tonami K, Yamada A, Umemori S, Noritake K, Iwaki M, Ohara S, Hideshima M, Nitta H, Oda S, Kinoshita A, Araki K, Mataka S. Change in dental students' awareness of comprehensive view of human during experiential learning of "Introduction of Behavioral Science. 34th JDEA annual meeting 2015.07.10
2. Ken-ichi Tonami, Chikako Nakamura, Azusa Yamada, Sachi Umemori, Kanako Noritake, Maiko Iwaki, Masayo Sunaga, Satoko Ohara, Masayuki Hideshima, Jun Tsuruta, Hiroshi Nitta, Shigeru Oda, Atsuhiro Kinoshita, Kouji Araki, Shiro Mataka.. Development of professionalism during experiential learning at welfare facilities.. 26th Annual Scientific Meeting South East Asia Association for Dental Education (SEAADE). 2015.08.13 Bali, Indonesia

[Others]

1. The 28th Annual general meeting of the Japanese Society of Oral Diagnosis/Oral Medicine , 2015.09
In the meeting, we had 21 oral and 23 poster presentations.
Two special lectures, "Expectation in education" by Mr. Tsunehiro Shimizu, and "The role of body fluid in individual identification" by Prof. Koichi Sakurada and "The risk management for medically compromised patients" by Dr. Tsuneto Ohwatari were also presented.

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. Etsuko Iio, Kentaro Matsuura, Nao Nishida, Shinya Maekawa, Nobuyuki Enomoto, Mina Nakagawa, Naoya Sakamoto, Hiroshi Yatsushashi, Masayuki Kurosaki, Namiki Izumi, Yoichi Hiasa, Naohiko Masaki, Tatsuya Ide, Keisuke Hino, Akihiro Tamori, Masao Honda, Shuichi Kaneko, Satoshi Mochida, Hideyuki Nomura, Shuhei Nishiguchi, Chiaki Okuse, Yoshito Itoh, Hitoshi Yoshiji, Isao Sakaida, Kazuhide Yamamoto, Hisayoshi Watanabe, Shuhei Hige, Akihiro Matsumoto, Eiji Tanaka, Katsushi Tokunaga, Yasuhito Tanaka. Genome-wide association study identifies a PSMD3 variant associated with neutropenia in interferon-based therapy for chronic hepatitis C. Hum Genet. 2015.03; 134(3); 279-289

2. Miyako Murakawa, Yasuhiro Asahina, Mina Nakagawa, Naoya Sakamoto, Sayuri Nitta, Akiko Kusano-Kitazume, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Miki Taniguchi, Fumio Goto, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. Impaired induction of interleukin 28B and expression of interferon λ 4 associated with nonresponse to interferon-based therapy in chronic hepatitis C. *J Gastroenterol Hepatol*. 2015.06; 30(6); 1075-1084
3. 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.[Epub ahead of print] *Hepatol Res*. 2015.07;
4. Atsushi Tasaki, Akimoto Nimura, Tomoyuki Mochizuki, Kumiko Yamaguchi, Ryuichi Kato, Hiroyuki Sugaya, Keiichi Akita. Anatomic observation of the running space of the suprascapular nerve at the suprascapular notch in the same direction as the nerve. *Knee Surg Sports Traumatol Arthrosc*. 2015.09; 23(9); 2667-2673
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.[Epub ahead of print] *J Gastroenterol*. 2015.11;

[Conference Activities & Talks]

1. Jun Tsuruta. Interprofessional Education at TMDU. International Scientific Forum, FORIL XI 2015 2015.04.11
2. Asahina Y, Kawai-Kitahata F, Kaneko S, Nagata H, Goto F, Otani S, Taniguchi M, Murakawa M, Nitta S, Watanabe T, Tasaka-Fujita M, Nishimura-Sakurai Y, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Tanaka S, Tanabe M, Enomoto N, Watanabe M. Gene alterations in tert promoter, CTNNB1, and TP53 are closely associated with development and prognosis of hepatocellular carcinoma: comprehensive analyses by next generation sequencing technology. 50th The International liver congress 2015, EASL 2015.04.22 Vienna
3. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Otani, Miki Taniguchi, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Shinji Tanaka, Minoru Tanabe, Nobuyuki Enomoto and Mamoru Watanabe. Gene alterations in TERT promoter, CTNNB1, and TP53 are closely associated with development and prognosis of hepatocellular carcinoma : Comprehensive analyses by next generation sequencing technology. The 3rd JSGE International Topic Conference 2015.04.24 Sendai
4. Jun Tsuruta. Session 6 : Challenges and Perspectives in Dental Education, Quality Assurance in Dental Education, “ Dentist & Shikaishi” . 6th Hiroshima Conference on Education and Science in Dentistry 2015.10.24 Hiroshima
5. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Hiroko Nagata, Syun Kaneko, Sayuri Nitta, Takako Watanabe, Yasuhiro Itsui, Mina Nakagawa, Sei Kakinuma, Sayuki Iijima, Yasuhito Tanaka, Mamoru Watanabe, Yujiro Tanaka. Expression of IFN λ 4 in liver is closely associated with non-response to antiviral therapy through the regulation of basal expression of ISGs in chronic hepatitis C patients but not in hepatitis B patients. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
6. Takako Watanabe, Yasuhiro Asahina, Mina Nakagawa, Sei Kakinuma, Yasuhiro Itsui, Hiroko Nagata, Miyako Murakawa, Fukiko Kawai-Kitahata, Mika Miura, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Serial change of resistant associated variants during early phase of NS3/4A triple therapy and the final virological outcome: analyses by ultra-deep sequencing technology. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
7. Hiroko Nagata, Yasuhiro Itsui, Fukiko Kawai-Kitahata, Shun Kaneko, Miyako Murakawa, Sayuri Nitta, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Yasuhiro Asahina. Variations of the host genome and

interaction of hepatitis B viral X protein associated with hepatocarcinogenesis. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA

8. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Watanabe T, Otani S, Goto F, Nagata H, Kaneko S, 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 with clinicopathological features. AASLD The Liver Meeting 2015 2015.11.14 San Francisco, CA
9. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Sayuri Nitta, Tomoyuki Tsunoda, Masato Miyoshi, Hiroko Nagata, Fumio Goto, Satoshi Otani, Miyako Murakawa, Fukiko Kawai-Kitahata, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Mamoru Watanabe. Human induced pluripotent stem cell-derived hepatic progenitor-like cells and hepatocyte-like cells as a model for interaction between hepatitis B virus and host cells. AASLD The Liver Meeting 2015 2015.11.16 San Francisco, CA

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

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. Keisuke Sato, Peristera Roboti, Alexander A Mironov, Martin Lowe. Coupling of vesicle tethering and Rab binding is required for in vivo functionality of the golgin GMAP-210. *Mol. Biol. Cell.* 2015.02; 26(3);

537-553

2. Peristera Roboti, Keisuke Sato, Martin Lowe. The golgin GMAP-210 is required for efficient membrane trafficking in the early secretory pathway. *Journal of Cell Science*. 2015.04; 128(8); 1595-1606
3. Akira Takai, Masahiro Nakano, Kenta Saito, Remi Haruno, Tomonobu M Watanabe, Tatsuya Ohyanagi, Takashi Jin, Yasushi Okada, Takeharu Nagai. Expanded palette of Nano-lanterns for real-time multicolor luminescence imaging. *Proc. Natl. Acad. Sci. U.S.A.*. 2015.04; 112(14); 4352-4356
4. Kawagishi Masahiko, Obara Yuki, Suzuki Takayuki, Hayashi Masumi, Misawa Kazuhiko, Terada Sumio. Direct label-free measurement of the distribution of small molecular weight compound inside thick biological tissue using coherent Raman microspectroscopy *Sci Rep*. 2015.09; 5; 13868

[Misc]

1. Kenta Saito, Takeharu Nagai. Recent progress in luminescent proteins development. *Curr Opin Chem Biol*. 2015.08; 27; 46-51
2. Masahito Yamanaka, Kenta Saito, Nicholas I Smith, Yoshiyuki Arai, Kumiko Uegaki, Yasuo Yonemaru, Kentaro Mochizuki, Satoshi Kawata, Takeharu Nagai, Katsumasa Fujita. Visible-wavelength two-photon excitation microscopy for fluorescent protein imaging. *J Biomed Opt*. 2015.10; 20(10); 101202

[Conference Activities & Talks]

1. Masahiko Kawagishi, Yuki Obara, Takayuki Suzuki, Masumi Hayashi, Kazuhiko Misawa, Sumio Terada. Measuring the Distribution of Taurine Molecule Inside Biological Tissue via Intrinsic Molecular Vibrations using Nonlinear Raman Spectroscopy. *Biophysical Society 59th Annual Meeting* 2015.02.11 Baltimore, Maryland, USA
2. Masahiko Kawagishi, Yuki Obara, Takayuki Suzuki, Masumi Hayashi, Kazuhiko Misawa, Sumio Terada . Measuring the distribution of small molecule compounds inside biological tissue via intrinsic molecular vibrations using nonlinear Raman spectroscopy . the 120th Annual Meeting of The Japanese Association of Anatomists / the 92nd Annual Meeting of The Physiological Society of Japan 2015.03.23 Kobe, Hyogo, Japan
3. Masahiko Kawagishi, Yuki Obara, Takayuki Suzuki, Masumi Hayashi, Kazuhiko Misawa, Sumio Terada. Measuring the distribution of small molecule compounds inside biological tissue via intrinsic molecular vibrations using nonlinear Raman spectroscopy. *The 38th Annual Meeting of the Japan Neuroscience Society* 2015.07.29 Kobe, Hyogo, Japan
4. 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. *The 2nd East-Asia Microscopy Conference* 2015.11.25 Himeji, Hyogo, Japan

Systems Neurophysiology

Professor Izumi Sugihara
Associate Professor Yuriko Sugiuchi
Lecturer Yoshiko Izawa
Assistant Professor Mayu Takahashi
JSPS Postdoctoral Research Fellow Hermina Nedelescu
Students (doctor) 4
Students (master) 1
JSPS Overseas Postdoctoral Fellow, 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 cellular through the organismic levels. For students to gain first-hand experience in basic matters such as generation and propagation of excitation in nerve cells, we have developed a computer simulation program for a part of the laboratory course. We have had a “project semester” student (4th year in the medical school).

(5) Publications

[Original Articles]

1. Vibulyaseck S, Luo Y, Fujita H, Oh-Nishi A, Ohki-Hamazaki H, Sugihara I. Compartmentalization of the chick cerebellar cortex based on the link between the striped expression pattern of aldolase C and the topographic olivocerebellar projection Journal of Comparative Neurology. 2015.09; 523(13); 1886-1912

[Misc]

1. Sugihara Izumi. Anatomy (lobular organization) and basic functional localization of the cerebellum Journal of Clinical and Experimental Medicine (IGAKU NO AYUMI). 2015.12; 255(10); 927-933

[Conference Activities & Talks]

1. Izumi Sugihara. Precise relationship among input-output connections, somatotopic representation and zebrin stripes in the cerebellum. The 92th Annual Meeting of the Physiological Society of Japan 2015.03.23 Kobe
2. M. Takahashi, Y. Sugiuchi, Y. Shinoda . Morphological substrates of tectal commissural inhibition and excitation in relation to saccade coordinates and "Listing's law".. the 92nd Annual Meeting of the Physiological Society of Japan 2015.03.23 Kobe
3. Izawa, Y., Suzuki, H.. Contribution of the activity of frontal eye field fixation neurons to the suppression of saccades and smooth pursuit eye movements in the monkey. The Joint Meeting of the 120th Annual Meeting of the Japanese Association of Anatomists, the 92nd Annual Meeting of the Physiological Society of Japan 2015.03.23 Kobe
4. Mayu Takahashi. Neural mechanisms for reducing degrees of freedom in voluntary and vestibular eye movement systems. International Symposium on Hand movement and Muscle synergy “New approaches to complex musculoskeletal systems” 2015.07
5. Yoshiko Izawa, Hisao Suzuki. Effects of microstimulation of the frontal eye field on eye and neck movements in the monkey. The Gordon Research Conference 2015 on Eye Movements 2015.07.26 Bentley University, Waltham, MA, U.S.A.
6. Izumi Sugihara, Mitsuhiro Ueda, Takahiro Ando, Yuanjun Luo. Single axon morphology of vestibulocerebellar mossy fibers indicates the phylogenetically old nature of the vestibulocerebellum. The 38th Annual Meeting of the Japan Neuroscience Society 2015.07.28 Yokohama

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.

(4) Publications

[Original Articles]

1. Fujikawa, M., Sugawara, K., Tanabe, T. and Yoshida, M. . Assembly of human mitochondrial ATP synthase through two separate intermediates, F1-c-ring and b-e-g complex. FEBS Letters . 2015.08;

Molecular Neuroscience

Professor Kohichi Tanaka
Associate Professor Hidenori Aizawa (2015/5/31)
Tomomi Aida (2015/7/1)
Assistant Professor Tomomi Aida (2015/6/30)
Project Assistant Professor Masashi Ohmachi(2015/6/15)
Graduate Student (doctor course)
Cui Wanpeng
Zhao Zhuoyang
Kaori Sugiyama
Graduate Student (master course)
Mina Kusunose
Moeko Tanaka
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. In the cerebellum, both GLAST, a glial glutamate transporter, and CDC42EP4 the small GTPase-effector protein, is exclusively expressed in Bergmann glia and localizes beneath specific membrane domains enwrapping dendritic spines of Purkinje cells. We show that CDC42EP4 forms complexes with septin hetero-oligomers, which interact with GLAST. In *Cdc42ep4* $-/-$ mice, GLAST is dissociated from septins and is delocalized away from the parallel fibre-Purkinje cell synapses. The excitatory postsynaptic current exhibits a protracted decay time constant, reduced sensitivity to a competitive inhibitor of the AMPA-type glutamate receptors (γ DGG) and excessive baseline inward current in response to a subthreshold dose of a nonselective inhibitor of the glutamate transporters/EAAT1–5 (DL-TBOA). We propose that the CDC42EP4/septin-based glial scaffold facilitates perisynaptic localization of GLAST and optimizes the efficiency of glutamate-buffering and clearance. Glutamate-mediated excitotoxicity that occurs due to a deficiency of the glial glutamate transport GLT is one of several potential pathogenic mechanisms of motor neuron death in amyotrophic lateral sclerosis (ALS). However, it remains unknown whether this deficiency is a primary cause or a secondary consequence of motor neuron degeneration. Here, we generated conditional knockout mice that lacked GLT1 specifically in the spinal cord

(GLT1-cKO mice) using the Cre/LoxP system. GLT1-cKO mice showed motor deficits, motor neuron loss and nuclear TDP-43 loss. Thus, dysfunction of glial glutamate transporters is sufficient to phenocopy ALS in mice.

2. Development of genome editing technologies

Genetically modified mice such as knockout and knockin mice have drastically improved our understanding of the functions of genes in vivo. However, the generation of genetically modified mice relies on homologous recombination in ES cells, which is a time-consuming, laborious, and expensive process. Recent development of genome editing technologies has enabled direct manipulation of the genome in mouse zygotes with out ES cells, thereby providing new avenues for simple, convenient, highly efficient, and ultra-rapid production of genetically modified mice. We developed highly efficient cloning-free CRISPR/Cas system for the production of genetically modified mice, especially for knockin mice carrying functional gene cassettes. Our novel method provides ultra convenient and highly efficient CRISPR/Cas-mediated genome editing and accelerates functional genomic research in vivo.

(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. Nakamori, T., Sato, K., Kinoshita, M., Kanamatsu, T., Sakagami, H., Tanaka, K., Ohki-Hamazaki, H. . Positive feedback of NR2B-containing NMDA receptor activity is the initial step toward visual imprinting: a model for juvenile learning. *J Neurochem.* 2015.01; 132(1); 110-123
2. Kimura, A., Guo, X., Noro, T., Harada, C., Tanaka, K., Namekata, K., Harada, T. Valproic acid prevents retinal degeneration in a murine model of normal tension glaucoma. *Neurosci Lett.* 2015.02; 588; 108-113
3. Yanagisawa, M., Aida, T., Takeda, T., Namekata, K., Harada, T., Shinagawa, R., Tanaka, K. . Arundic acid attenuates retinal ganglion cell death by increasing glutamate/aspartate transporter expression in a model of normal tension glaucoma. *Cell Death Dis.* 2015.03; 6; e1693
4. Aida T, Chiyo K, Usami T, Ishikubo H, Imahashi R, Wada Y, Tanaka KF, Sakuma T, Yamamoto T, Tanaka K.. Cloning-free CRISPR/Cas system facilitates functional cassette knock-in in mice. *Genome Biol.* 2015.04; 16; 87

5. Aida, T., Yoshida, J., Nomura, M., Tanimura, A., Iino, Y., Soma, M., Bai, N., Ito, Y., Cui, W., Aizawa, H., Yanagisawa, M., Nagai, T., Takata, N., Tanaka, K.F., Takayanagi, R., Kano, M., Gotz, M., Hirase, H., Tanaka, K.. Astroglial glutamate transporter deficiency increases synaptic excitability and leads to pathological repetitive behaviors in mice. *Neuropsychopharmacology*. 2015.06; 40(7); 1569-1579
6. Ishii, K., Kubo, K., Endo, T., Yoshida, K., Benner, S., Ito, Y., Aizawa, H., Aramaki, M., Yamanaka, A., Tanaka, K., Takata, N., Tanaka, K., Mimura, M., Tohyama, C., Kakeyama, M., Nakajima, K.. Neuronal heterotopias affect the activities of distant brain areas and lead to behavioral deficits. *J Neurosci*. 2015.09; 35(36); 12432-12445
7. Ageta-Ishihara, N., Yamazaki, M., Konno, K., Nakayama, H., Abe, M., Hashimoto, K., Nishioka, T., Kaibuchi, K., Hattori, S., Miyakawa, T., Tanaka, K., Huda, F., Hrai, H., Hashimoto, K., Watanabe, M., Sakimura, K., Kinoshita, M.. A CDC42EP4/septin-based perisynaptic glial scaffold facilitates glutamate clearance. *Nature Commun*. 2015.12; 6; 10090

Neuropathology

Professor: Hitoshi Okazawa

Practical professor: Kazuhiko Tagawa

Project Lecturer/Part-time Lecturer

: Nobuyuki Nukina, Haruhisa Inoue, Masaki Sone, Toshiki Uchihara

Assistant professor: Takuya Tamura

Project Assistant professor: Xigui Chen, Kyota Fujita, Hidenori Homma, Kazumi Motoki

Assistant: Shigemi Sato, Mikiyo Fujii, Xuemei Zhang

Secretary: Rumi Innami, Ayako Seki

Graduate Student: Juliana Bosso Taniguchi, Mao Ying, Eriko Hoshino

(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.

Starvation induced autophagy enhances accumulation of amyloid-beta ($A\beta$) in brain

We developed a new technique to observe macroautophagy in the brain in vivo, and examined whether fasting induced macroautophagy in neurons and how the induction was different between Alzheimer's disease (AD) model and control mice. Lentivirus for EGFP-LC3 injected into the brain successfully visualized autophagosome in living neurons by two-photon microscopy. The time-lapse imaging revealed that fasting increased the number, size and signal intensity of autophagosome in neurons. In AD model mice, these parameters of autophagosome were higher at the basal levels before starvation, and increased more rapidly by fasting than in control mice. However, metabolism of exogenous labeled $A\beta$ evaluated by the new technique suggested that the activated macroautophagy was insufficient to degrade the intracellular $A\beta$ increased by enhanced uptake from extracellular space after fasting. Ordinary immunohistochemistry also revealed that fasting increased intracellular

accumulation of endogenous A β , triggered cell dysfunction but did not mostly decrease extracellular A β accumulation. Moreover, we unexpectedly discovered a circadian rhythm of basal level of macroautophagy. These results revealed new aspects of neuronal autophagy in normal/AD states and indicated usefulness of our method for evaluating autophagy functions in vivo.

Neurodegenerative diseases, including AD, have a unique pathological feature which is abnormal protein accumulation inside or outside of cells. Two distinct abnormal proteins accumulate in AD brain. The senile plaques consist of abnormal protein called beta-amyloid (A β) outside cells, and the neurofibrillary tangles that tau protein aggregates inside the cell. On the other hand, two distinct protein degradation systems are well-studied as cellular mechanism to remove abnormal proteins, ubiquitin-proteasome and autophagy systems. Autophagy system is further classified to “basal autophagy” which works at a constant level and “induced autophagy (macroautophagy)” which is activated in calorie restriction.

Macroautophagy has been known to play a significant role in tissues other than the brain. While a report suggested that macroautophagy in brain tissue is not observed (Mizushima et al, Mol Biol Cell 2004; while there are, etc.), except for the aggregation of the abnormal protein-induced autophagy by calorie restriction, etc. in neurodegenerative disease, a result of improving the symptoms has been reported by many (Ravikumar et al, Nat Genet 2004 ; etc.) that the presence or absence of induced autophagy in nerve cells was not settled. Furthermore, our proof of the induced autophagy in higher animals was important, since the signaling pathway from the insulin receptor via mTOR (mammalian target of rapamycin) is considered important, and diabetes and high calorie are said risk factors of Alzheimer’s disease pathology. Therefore, in this study it was the first object of the present invention is to clarify the "presence or absence of induced autophagy in nerve cells".

(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. Chen, X., Kondo, K., Motoki, K., Homma, H., Okazawa, H.. Fasting activates macroautophagy in neurons of Alzheimer’s disease mouse model but is insufficient to degrade amyloid-beta. Scientific Reports. 2015.07; 5; 12115

[Misc]

1. Fujita K, Okazawa H. A functional deficiency of TERA/VCP/p97 contributes to impaired DNA damage repair in multiple polyglutamine diseases. Annual Review Shinkei 2015. 2015.01; 65-72
2. Shiwaku, H., Okazawa, H.. Impaired DNA damage repair as a common feature of neurodegenerative diseases and psychiatric disorders. Current Molecular Medicine. 2015.02; 15(2); 119-128

[Conference Activities & Talks]

1. Hitoshi Okazawa. In utero treatment for PQBP-1 gene mutations. The 10th International Meeting on Copy Number Variants and Genes in Intellectual Disability and Autism. 2015.04.16 La Cittadella dell’Oasi (Troina, Italy)

2. Ito H, Fujita K, Tagawa K, Chen X, Homma H, Sasabe T, Shimizu J, Shimizu S, Muramatsu S, Okazawa H. HMGB1 gene therapy ameliorates phenotype of mutant ataxin-1 knock-in mice. The 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21
3. Tagawa K, Homma H, Saito A, Murayama S, Iwatsubo T, Miyano S, Okazawa H. Comprehensive phosphoproteome analysis in preclinical Alzheimer's disease brain. The 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21
4. Tagawa K, Homma H, Saito A, Murayama S, Iwatsubo T, Miyano S, Okazawa H. Comprehensive phosphoproteome analysis in preclinical Alzheimer's disease brain . The 56th Annual Meeting of the Japanese Society of Neuropathology 2015.06.04
5. Tagawa K, Homma H, Saito A, Murayama S, Iwatsubo T, Miyano S, Okazawa H. Comprehensive phosphoproteome analysis in preclinical Alzheimer's disease brain. The 38th Annual Meeting of the Japan Neuroscience Society 2015.07.30

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, Noriaki Shimada, Kei Morohoshi, Tae Yokoi
Graduate student;Tomoka Ishida, Yuko Iwasaki, Kosei Shinohara,
Liu hongcling

(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. Kimura Y, Ohno-Matsui K. Association between the CDKN2B-AS1 gene and primary open angle glaucoma with high myopia in Japanese patients. *Ophthalmic genetics*. 2015;
2. Natsuko Nagaoka, Jost B Jonas, Kei Morohoshi, Muka Moriyama, Noriaki Shimada, Takeshi Yoshida, Kyoko Ohno-Matsui. Glaucomatous-Type Optic Discs in High Myopia. *PLoS ONE*. 2015; 10(10); e0138825
3. Noriko Koizumi, Tsutomu Inatomi, Takashi Suzuki, Atsushi Shiraishi, Yuichi Ohashi, Michiko Kandori, Dai Miyazaki, Yoshitsugu Inoue, Takeshi Soma, Kohji Nishida, Hiroshi Takase, Sunao Sugita, Manabu Mochizuki, Shigeru Kinoshita, . Clinical features and management of cytomegalovirus corneal endotheliitis: analysis of 106 cases from the Japan corneal endotheliitis study. *Br J Ophthalmol*. 2015.01; 99(1); 54-58
4. Hiroshi Takase, Annabelle A Okada, Hiroshi Goto, Nobuhisa Mizuki, Kenichi Namba, Nobuyuki Ohguro, Koh-Hei Sonoda, Makoto Tomita, Hiroshi Keino, Takeshi Kezuka, Reo Kubono, Kazuomi Mizuuchi, Etsuko Shibuya, Hiroyuki Takahashi, Ryoji Yanai, Manabu Mochizuki. Development and validation of new diagnostic criteria for acute retinal necrosis. *Jpn. J. Ophthalmol.*. 2015.01; 59(1); 14-20
5. Naonori Ohno, Hideki Murai, Yukihisa Suzuki, Motohiro Kiyosawa, Aya M Tokumaru, Kenji Ishii, Kyoko Ohno-Matsui. Alteration of the optic radiations using diffusion-tensor MRI in patients with retinitis pigmentosa. *Br J Ophthalmol*. 2015.01; 99((8)); 1051-1054
6. Ohno-Matsui Kyoko, Kawasaki Ryo, Jonas Jost B, Gemmy Cheung Chui Ming, Saw Seang-Mei, Verhoeven Virginie J M, Klaver Caroline C W, Moriyama Muka, Shinohara Kosei, Kawasaki Yumiko, Yamazaki Mai, Meuer Stacy, Ishibashi Tatsuro, Yasuda Miho, Yamashita Hidetoshi, Sugano Akira, Wang Jie Jin, Mitchell

- Paul, Wong Tien Yin, META-analysis for Pathologic Myopia (META-PM) Study Group. International Photographic Classification and Grading System for Myopic Maculopathy. *Am J Ophthalmol.* 2015.01;
7. Soma Ryoko, Moriyama Muka, Ohno-Matsui Kyoko. Hemodynamics of focal choroidal excavations. *Int Ophthalmol.* 2015.01;
8. Tanaka Yuichiro, Shimada Noriaki, Ohno-Matsui Kyoko. Extreme Thinning or Loss of Inner Neural Retina Along the Staphyloma Edge in Eyes With Pathologic Myopia. *Am J Ophthalmol.* 2015.01;
9. Ishida Tomoka, Moriyama Muka, Tanaka Yuichiro, Shinohara Kosei, Shimada Noriaki, Yoshida Takeshi, Ohno-Matsui Kyoko. Radial tracts emanating from staphyloma edge in eyes with pathologic myopia. *Ophthalmology.* 2015.01; 122(1); 215-216
10. Natural course and treatment of myopic traction maculopathy 2015.01; 7(11); 851-852
11. Yoshiyuki Kawashima, Yoshihiro Noguchi, Hiroshi Takase, Masatoki Takahashi, Shintaro Horie. Bilateral hearing impairment as the initial symptom of sympathetic ophthalmia. *Am J Otolaryngol.* 2015.02;
12. Masahiro Miyake, Kenji Yamashiro, Yasuharu Tabara, Kenji Suda, Satoshi Morooka, Hideo Nakanishi, Chiea-Chuen Khor, Peng Chen, Fan Qiao, Isao Nakata, Yumiko Akagi-Kurashige, Norimoto Gotoh, Akitaka Tsujikawa, Akira Meguro, Sentaro Kusahara, Ozen Polasek, Caroline Hayward, Alan F Wright, Harry Campbell, Andrea J Richardson, Maria Schache, Masaki Takeuchi, David A Mackey, Alex W Hewitt, Gabriel Cuellar, Yi Shi, Luling Huang, Zhenglin Yang, Kim Hung Leung, Patrick Y P Kao, Maurice K H Yap, Shea Ping Yip, Muka Moriyama, Kyoko Ohno-Matsui, Nobuhisa Mizuki, Stuart MacGregor, Veronique Vitart, Tin Aung, Seang-Mei Saw, E-Shyong Tai, Tien Yin Wong, Ching-Yu Cheng, Paul N Baird, Ryo Yamada, Fumihiko Matsuda, , Nagahisa Yoshimura. Identification of myopia-associated WNT7B polymorphisms provides insights into the mechanism underlying the development of myopia. *Nat Commun.* 2015.03; 6; 6689
13. Ikuno Yasushi, Ohno-Matsui Kyoko, Wong Tien Yin, Korobelnik Jean-Francois, Vitti Robert, Li Tummy, Stemper Brigitte, Asmus Friedrich, Zeitz Oliver, Ishibashi Tatsuro, MYRROR Investigators *. Intravitreal Aflibercept Injection in Patients with Myopic Choroidal Neovascularization: The MYRROR Study. *Ophthalmology.* 2015.03;
14. Yoshimasa Ando, Makoto Inoue, Kyoko Ohno-Matsui, Yumi Kusumi, Tomohiro Iida, Akito Hirakata. MACULAR DETACHMENT ASSOCIATED WITH INTRACHOROIDAL CAVITATION IN NONPATHOLOGICAL MYOPIC EYES. *Retina (Philadelphia, Pa.).* 2015.05;
15. I-Chia Liang, Noriaki Shimada, Yuichiro Tanaka, Natsuko Nagaoka, Muka Moriyama, Takeshi Yoshida, Kyoko Ohno-Matsui. Comparison of Clinical Features in Highly Myopic Eyes with and without a Dome-Shaped Macula. *Ophthalmology.* 2015.05;
16. Ishida Tomoka, Shinohara Kosei, Tanaka Yuichiro, Moriyama Muka, Morohoshi Kei, Shimada Noriaki, Yoshida Takeshi, Ohno-Matsui Kyoko. Choriorretinal folds in eyes with myopic staphyloma. *Am J Ophthalmol.* 2015.06;
17. Kei Morohoshi, Chuan-Hui Kuo, Masaharu Ohbayashi, Nishal Patel, Victor N. Chong, Alan C. Bird, Santa J. Ono. Anti-glutamine synthetase and other potential autoantibody biomarkers in the sera of patients with age-related macular degeneration 2015.07; 3;
18. Comparison of measurement of the eye position using an eye-tracking system and alternate prism cover test 2015.07; 8(7); 492-495
19. Yugo Kimura, Tadamichi Akagi, Masahiro Miyake, Kenji Yamashiro, Munemitsu Yoshikawa, Hiroshi Yamada, Tomoko Hasegawa, Kenji Suda, Hideo Nakanishi, Hanako Ohashi-Ikeda, Norimoto Gotoh, Masanori Hangai, Muka Moriyama, Kyoko Ohno-Matsui, Nagahisa Yoshimura. Association between the CDKN2B-AS1 Gene and Primary Open Angle Glaucoma with High Myopia in Japanese Patients. *Ophthalmic Genet..* 2015.09; 1-3
20. Pavan Kumar Verkicharla, Kyoko Ohno-Matsui, Seang Mei Saw. Current and predicted demographics of high myopia and an update of its associated pathological changes. *Ophthalmic Physiol Opt.* 2015.09; 35(5); 465-475

21. Ishida T, Shinohara K, Tanaka Y, Moriyama M, Morohoshi K, Shimada N, Yoshida T, Ohno-Matsui K. Chorioretinal folds in eyes with myopic staphyloma *Am J Ophthalmol.* 2015.09; 160(3);
22. Nagaoka N, Jonas JB, Morohoshi K, Moriyama M, Shimada N, Yoshida T, Ohno-Matsui K. Glaucomatous-Type Optic Discs in High Myopia *PLoS One.* 2015.10; 10(10);
23. 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.* 2015.11;
24. Kyoko Ohno-Matsui, Jost B Jonas, Richard F Spaide. Macular Bruch's Membrane Holes in Choroidal Neovascularization-Related Myopic Macular Atrophy by Swept-Source Optical Coherence Tomography. *Am. J. Ophthalmol.* 2015.11;
25. Side Effects of Low Dose Atropine 2015.11; 119(11); 812-816
26. Ohno-Matsui K. Glaucomatous-Type Optic Discs in High Myopia. *PLOS ONE.*

[Books etc]

1. Ohno-Matsui K.. *Myopic Optic Neuropathy. Myopia and Glaucoma.* Springer, 2015 (ISBN : 978-4431556718)
2. Toshio Modegi, Yoichi Takahashi, Tae Yokoi, Muka Moriyama, Noriaki Shimada, Ikuo Morita, Kyoko Ohno-Matsui. *Comparative Analysis of Retinal Fundus Images with the Distant Past Images Using a Vessel Extraction Technique.* 2015 (ISBN : 9783319230238)

[Misc]

1. Koju Kamoi. Pre-surround division technique devised for posterior polar cataract surgery. *Ocular Surgery News U.S. Edition.* 2015.02;
2. Koju Kamoi. New effective surgical technique for patients with posterior polar cataracts. *Cataract News Today.* 2015.03;
3. Koju Kamoi. Pre-surround division technique devised for posterior polar cataract surgery. *Ocular Surgery News APAO edition.* 2015.03; 40-45
4. Koju Kamoi. Pre-Surround Division. *Cataract & Refractive Surgery Today Europe.* 2015.06; 28-30
5. 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. Tae Yokoi, Muka Moriyama, Noriaki Shimada, Toshio Modegi, Youichi Takahashi, Junichi Kondo, Ikuo Morita, Kyoko Ohno-Matsui. Long-term alterations of retinal vascular patterns and optic disc shape in highly myopic eyes. 10th ochanomizu advanced medical seminar 2015.01.09 Tokyo
2. Kyoko Ohno-Matsui. Imaging of Pathologic Myopia. 2th Kyoto macular disease seminar 2015.01.23 Kyoto
3. Kyoko Ohno-Matsui. Current Management of Choroidal Neovascularization due to Pathologic Myopia. Asia-ARVO 2015 2015.02.16
4. Kosei Shinohara, Takeshi Yoshida, Tomoka Ishida, Liu Hongding, Ikuo Morita, Kyoko Ohno-Matsui. Form deprivation myopia in wistar rats. Asia-ARVO 2015 2015.02.16 Yokohama
5. Tomoka Ishida, Takeshi Yoshida, Kosei Shinohara, Liu Hongding, Kyoko Ohno-Matsui.. The role of sirt1 for regulating VEGF in human RPE. Asia—ARVO 2015 2015.02.17
6. Koju Kamoi, Yukiko Terada, Kazunori Miyata, Manabu Mochizuki, Kyoko Ohno-Matsui.. Analysis of complications in patients with HTLV-1 uveitis.. Asia-ARVO 2015.02.17

7. Kyoko Ohno-Matsui. Clinical practice of pathologic myopia-clinical study for myopic CNV and case conference.. Lunch time seminar 18.Asia-ARVO 2015 2015.02.19 Yokohama
8. Izabela P. Klaska, Lucia Kuffova, Koju Kamoi, Corina Bobu, Christina Martin-Granados, Ralph M. Steinman, John V. Forrester. Targeted delivery of self-antigen to dendritic cells attenuates uveoretinitis in mice. Keystone Symposia 2015.03
9. Kyoko Ohno-Matsui. Terminology and classification of pathologic myopia. . WHO-BHVI joint Global Scientific Meeting on Myopia 2015.03.06 Sydney, Australia
10. Kyoko Ohno-Matsui. Imaging of the Highly Myopic Optic Nerve Head. 30th APAO(Asia-Pacific Academy of Ophthalmology) 2015.03.31 Guangzhou, China
11. Kyoko Ohno-Matsui. Pathological Consequences of High Myopia. 30th APAO(Asia-Pacific Academy of Ophthalmology) 2015.04.01 Guangzhou, China
12. Hiroshi Takase. Experimental use of vitrectomy specimens in uveitis research. The 30th Asia-Pacific Academy of Ophthalmology Congress 2015.04.02 Guangzhou, China
13. Kyoko Ohno-Matsui. Wide-Field Fundus Imaging of Pathologic Myopia. 30th APAO(Asia-Pacific Academy of Ophthalmology) 2015.04.02 Guangzhou, China
14. Kyoko Ohno-Matsui. Visual Outcomes in Patients with Myopic Choroidal Neovascularisation Receiving Intravitreal Afibercept Injection. 30th APAO(Asia-Pacific Academy of Ophthalmology) 2015.04.02 Guangzhou, China
15. Kyoko Ohno-Matsui. Lamina Cribrosa Changes in Myopia: Implications in Glaucoma Diagnosis and Monitoring. 30th APAO(Asia-Pacific Academy of Ophthalmology) 2015.04.04
16. Koju Kamoi, Zhaorong Guo, Shintaro Horie, Kyoko Ohno-Matsui.. The role of HTLV-1 infected RPE cells in the pathogenesis of HTLV-1 uveitis. ARVO Annual Meeting 2015.05.05 Denver
17. Shintaro Horie, Koju Kamoi, Zhaorong Guo, Kyoko Ohno-Matsui. Character of PMA-Stimulated THP-1 Cells under Ocular Diabetic Condition. ARVO Annual Meeting 2015.05.05 Denver
18. Hiroshi Takase. ICG angiography of recurrent/chronic Vogt-Koyanagi-Harada disease. 9th International Workshop on VKH and Sympathetic Ophthalmia 2015.05.15 Cebu, Philippines
19. Hiroshi Takase. Novelties in imaging of ocular sarcoidosis. 5th International Workshop on Ocular Sarcoidosis 2015.05.16 Cebu, Philippines
20. Kyoko Ohno-Matsui. Updates on Myopic CNV. SNEC 25th ANNIVERSARY INTERNATIONAL MEETING 2015.05.22 SINGAPORE
21. Kyoko Ohno-Matsui. Imaging & Management Decisions in Complications Associated with Pathological Myopia. SNEC 25th ANNIVERSARY INTERNATIONAL MEETING 2015.05.22 SINGAPORE
22. Kyoko Ohno-Matsui. Optic Disc Shape and Visual Field Defects in Eyes with Pathologic Myopia.. World Glaucoma Congress 2015 2015.06.09 Hong Kong, China
23. Kyoko Ohno-Matsui. Myopic maculopathy-update on its understanding and management.. Update on high myopia and its associated disease. 2015.06.13 Taipei, Taiwan
24. Kyoko Ohno-Matsui. Key Note Speech - What is the fundamental nature of PM? – a short excursion into histology, morphology and 3D anatomy.. 2nd international conference of pathologic myopia (iPM) 2015.06.19 Kyoto, Japan
25. Kyoko Ohno-Matsui. Definition of PM – followed by consensus discussion.. 2nd international conference of pathologic myopia (iPM) 2015.06.20 Kyoto, Japan
26. Kyoko Ohno-Matsui. Scleral and Choroidal Imaging.. 2nd international conference of pathologic myopia (iPM) 2015.06.20 Kyoto, Japan
27. Hiroshi Takase. Choroidal thickness in acute and convalescent Vogt-Koyanagi-Harada disease. European Association for Vision and Eye Research 2015 2015.10.08 Nice, France

28. Ayako Arai, Hiroshi Takase, Kouhei Yamamoto, Hiroki Akiyama, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. The 77th Annual Meeting of the Japanese Society of Hematology 2015.10.17 Kanazawa
29. Tae Yokoi. Mystery case with pathologic myopia. Fluorescein Conference in Tokyo (FCIT) at Nagoya 2015.10.23 Nagoya
30. Kyoko Ohno-Matsui.. Swept-Source OCT.. American Academy of Ophthalmology 2015.11.14 Las Vegas, USA
31. Paulo Stanga, Madgy Mussa, Richard F. Spaide, Kyoko Ohno-Matsui.. Spectral domain and swept source OCT in the diagnosis and management of vitreoretinal and uveitic disorders.. American Academy of Ophthalmology 2015.11.16 Las Vegas, USA
32. Ayako Arai, Hiroshi Takase, Kouhei Yamamoto, Hiroki Akiyama, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. 57th ASH Annual Meeting and Exposition 2015.12.05 Orlando

Otorhinolaryngology

Professor: Takeshi Tsutsumi

Junior Associate Professor: Yasuhiro Suzuki

Junior Associate Professor: Yoshiyuki Kawashima

Assistant Professor: Tarou Fujikawa, Fuminori Nomura, Yuichiro Inaba

Hospital Staff: Akihisa Tasaki, Kouta Mizushima, Takanori Takeda, Ryuhei Okada, Yumiko Tateishi

Graduate Student: Yoshimi Tameguchi, Katsura Yamamoto, Keiko Ohno, Ayane Makabe

(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

(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. Yoshiyuki Kawashima, Yoshihiro Noguchi, Hiroshi Takase, Masatoki Takahashi, Shintaro Horie. Bilateral hearing impairment as the initial symptom of sympathetic ophthalmia. *Am J Otolaryngol.* 2015.02;
2. Taro Fujikawa, Satoru Shirakura, Akio Hatanaka, Wataru Okano, Takao Tokumaru, Masato Yamada, Yoshihiro Saito, Takeshi Beppu. A Case of Severe Hyponatremia Caused by Renal Salt Wasting Syndrome in Oropharyngeal Cancer. *Nippon Jibiinkoka Gakkai Kaiho.* 2015.08; 118(8); 1046-1052
3. Kiyoto Kurima, Seham Ebrahim, Bifeng Pan, Miloslav Sedlacek, Prabuddha Sengupta, Bryan A Millis, Runjia Cui, Hiroshi Nakanishi, Taro Fujikawa, Yoshiyuki Kawashima, Byung Yoon Choi, Kelly Monahan, Jeffrey R Holt, Andrew J Griffith, Bechara Kachar. TMC1 and TMC2 Localize at the Site of Mechanotransduction in Mammalian Inner Ear Hair Cell Stereocilia. *Cell Rep.* 2015.09; 12(10); 1606-1617
4. Midori Nagaoka, Yoshihiro Noguchi, Yoshiyuki Kawashima, Taku Ito, Hiroko Koda, Ken Kitamura. Long-term result of meatoplasty using inferiorly based retroauricular island pedicle flap for external auditory canal stenosis. *Auris Nasus Larynx.* 2015.10;
5. Atsumori Hamahata, Takeshi Beppu, Taro Fujikawa, Takashi Yamaki, Hiroyuki Sakurai. Usefulness of a Reconstructive Method for Oropharyngeal Defect Including the Larger Soft Palate with the Bent Anterolateral Thigh Flap. *Journal of Reconstructive Microsurgery.* 2015.11; 31(9); 688-691
6. 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

[Misc]

1. Yoshiyuki Kawashima, Kiyoto Kurima, Bifeng Pan, Andrew J Griffith, Jeffrey R Holt. Transmembrane channel-like (TMC) genes are required for auditory and vestibular mechanosensation. *Pflugers Arch..* 2015.01; 467(1); 85-94

[Conference Activities & Talks]

1. Suzuki Y, Inaba Y, Inoue-Nagaoka M. The relationship between eosinophils and non-specific/specific IgE responses in allergic rhinitis and chronic sinusitis patients.. *EAACI Congress 2015* 2015.06.13 Barcelona Spain
2. Takeshi Tsutsumi. Japanese Health System. Ground Round of Vanderbilt University, Bill Wilkerson Center 2015.08.28
3. Suzuki Y, Inaba Y, Tsutsumi T. The relationship between non-specific IgE and nasal diseases. *Annual Meeting of the Japanese Rhinology Society* 2015.10.03 Hiroshima Japan
4. Suzuki Y, Inaba Y, Tsutsumi T. The relationship between the relevance of allergic disease and the value of non-specific IgE.. *World Allergy Congress 2015* 2015.10.14 Seoul Korea
5. Suzuki Y, Kiyokawa Y, Inaba Y, Tasaki A, Nagaoka M, Tsutsumi T. Treatment result evaluation of Ryoikeijutsukanto in our department for five years. 2015.10.24 Tokyo Japan

Neurology and Neurological Science

Professor YOKOTA Takanori
Junior Associate Professor SANJO Nobuo
Junior Associate Professor ISHIBASHI Satoru
Assistant Professor OHKUBO Takuya
Assistant Professor NISHIDA Yoichiro
Assistant Professor SATO Nozomu
Assistant Professor OZAKI Kokoro
Project Junior Associate Professor NAGATA Tetsuya
Project Assistant Professor NISHINA Kazutaka
Project Assistant Professor ISHIGURO Taro
Project Assistant Professor KUWAHARA Hiroya
Project Assistant Professor YUI Daishi
Project Assistant Professor PIAO Wenying
Project Researcher ASADA Ken
Graduate Student HIGUMA Maya
Graduate Student SOGA Kazumasa
Graduate Student NUMASAWA Yoshiyuki
Graduate Student ABE Keisuke
Graduate Student YOSHIOKA Kotaro
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 ISHIDU 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 REYILA Mamuti
Graduate Student SU SU Lei Mon
Research Student FURUKAWA Fumiko
Graduate Student KUNIEDA Taiki
Graduate Student SHIMOURA Takahiro

(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. Yoichiro Nishida, Akihiko Ueda, Yukio Ando, Tadashi Ichikawa. Skin Biopsy-based Diagnosis of CADASIL with Atypical MRI Findings. *Intern. Med.* 2015; 54(5); 537-538
2. Nakamura Y, Ae R, Takumi I, Sanjo N, Kitamoto T, Yamada M, Mizusawa H. Descriptive epidemiology of prion disease in Japan: 1999-2012. *J Epidemiol.* 2015; 25(1); 8-14
3. Obayashi M, Stevanin G, Synofzik M, Monin ML, Duyckaerts C, Sato N, Streichenberger N, Vighetto A, Desestret V, Tesson C, Wichmann HE, Illig T, Huttenlocher J, Kita Y, Izumi Y, Mizusawa H, Schöls L, Klopstock T, Brice A, Ishikawa K, Dürr A. Spinocerebellar ataxia type 36 exists in diverse populations and can be caused by a short hexanucleotide GGCTG repeat expansion. *J Neurol Neurosurg Psychiatry.* 2015; 86(9); 986-995
4. Yabe I, Matsushima M, Yoshida K, Ishikawa K, Shirai S, Takahashi I, Sasaki H. Rare frequency of downbeat positioning nystagmus in spinocerebellar ataxia type 31. *J Neurol Sci.* 2015; 350(1-2); 90-92
5. Ishibashi K, Miura Y, Ishikawa K, Ishii K, Ishiwata K. Decreased metabotropic glutamate receptor type 1 availability in a patient with spinocerebellar ataxia type 6: A (11)C-ITMM PET study. *J Neurol Sci.* 2015; 355(1-2); 202-205

6. Ohyagi M, Nakamura K, Watanabe M, Fujigasaki H. Embolic stroke during apixaban therapy for left atrial appendage thrombus. *J Stroke Cerebrovasc Dis.* 2015; 24(4); e101-102
7. Ozaki K, Sanjo N, Ishikawa K, Higashi M, Hattori T, Tanuma N, Miyata R, Hayashi M, Yokota T, Okawa A, Mizusawa H. Elevation of 8-hydroxy-2'-deoxyguanosine in the cerebrospinal fluid of three patients with superficial siderosis. *Neurol Clin Neurosci.* 2015; 3(3); 108-110
8. Yagi Y, Yokote H, Watanabe Y, Amino T, Kamata T, Kusunoki S. Taste impairment in Miller Fisher syndrome. *Neurol Sci.* 2015; 36(5); 809-810
9. Colangelo CM, Iovsev G, Chung L, Abbott T, Shifman M, Sakaue F, Cox D, Kitchen RR, Burton L, Tate SA, Gulcicek E, Bonner R, Rinehart J, Nairn AC, Williams KR. Development of a highly automated and multiplexed targeted proteome pipeline and assay for 112 rat brain synaptic proteins. *Proteomics.* 2015; 15(7); 1202-1214
10. Masaki Y, Inde T, Nagata T, Tanihata J, Kanamori T, Seio K, Takeda S, Sekine M. Enhancement of exon skipping in mdx52 mice by 2'-O-methyl-2-thioribothymidine incorporation into phosphorothioate oligonucleotides. *Med Chem Commun.* 2015; 6; 630-633
11. Kimura K, Morita H, Daimon M, Kawata T, Nakao T, Lee SL, Hirokawa M, Ebihara A, Nakajima T, Ozawa T, Yonemochi Y, Aida I, Motoyoshi Y, Mikata T, Uchida I, Komori T, Kitao R, Nagata T, Takeda S, Komaki H, Segawa K, Takenaka K, Komuro I. Prognostic impact of venous thromboembolism in patients with Duchenne muscular dystrophy: Prospective multicenter 5-year cohort study. *Int J Cardiol.* 2015; 191; 178-180
12. Echigoya Y, Aoki Y, Miskew B, Panesar D, Touznik A, Nagata T, Tanihata J, Nakamura A, Nagaraju K, Yokota T. Long-term efficacy of systemic multiexon skipping targeting dystrophin exons 45-55 with a cocktail of vivo-morpholinos in mdx52 mice. *Mol Ther Nucleic Acids.* 2015; 4; e225
13. Takenouchi T, Ohyagi M, Torii C, Kosaki R, Takahashi T, Kosaki K. Porencephaly in a fetus and HANAC in her father: variable expression of COL4A1 mutation. *Am J Med Genet A.* 2015; 167A(1); 156-158
14. Nishida Y, Ueda A, Ando Y, Ichikawa T. Skin biopsy-based diagnosis of CADASIL with atypical MRI findings. *Intern Med.* 2015; 54(5); 537-538
15. Ozaki K, Irioka T, Ishikawa K, Mizusawa H. CADASIL with a novel NOTCH3 mutation (Cys478Tyr). *J Stroke Cerebrovasc Dis.* 2015; 24(3); e61-62
16. Mitsui J, Matsukawa T, Sasaki H, Yabe I, Matsushima M, Dürr A, Brice A, Takashima H, Kikuchi A, Aoki M, Ishiura H, Yasuda T, Date H, Ahsan B, Iwata A, Goto J, Ichikawa Y, Nakahara Y, Momose Y, Takahashi Y, Hara K, Kakita A, Yamada M, Takahashi H, Onodera O, Nishizawa M, Watanabe H, Ito M, Sobue G, Ishikawa K, Mizusawa H, Kanai K, Hattori T, Kuwabara S, Arai K, Koyano S, Kuroiwa Y, Hasegawa K, Yuasa T, Yasui K, Nakashima K, Ito H, Izumi Y, Kaji R, Kato T, Kusunoki S, Osaki Y, Horiuchi M, Kondo T, Murayama S, Hattori N, Yamamoto M, Murata M, Satake W, Toda T, Filla A, Klockgether T, Wüllner U, Nicholson G, Gilman S, Tanner CM, Kukull WA, Stern MB, Lee VM, Trojanowski JQ, Masliah E, Low PA, Sandroni P, Ozelius LJ, Foroud T, Tsuji S. Variants associated with Gaucher disease in multiple system atrophy. *Ann Clin Transl Neurol.* 2015; 2(4); 417-426
17. Ohmori H, Hara A, Ishikawa K, Mizusawa H, Ando Y. Clinical characteristics of combined cases of spinocerebellar ataxia types 6 and 31. *J Neurogenet.* 2015; 29(2-3); 80-4
18. Pedroso JL, Abrahao A, Ishikawa K, Raskin S, de Souza PV, de Rezende Pinto WB, Braga-Neto P, de Albuquerque MV, Mizusawa H, Barsottini OG. When should we test patients with familial ataxias for SCA31? A misdiagnosed condition outside Japan? *J Neurol Sci.* 2015; 355(1-2); 206-208
19. Aikawa T, Mogushi K, Iijima-Tsutsui K, Ishikawa K, Sakurai M, Tanaka H, Mizusawa H, Watase K. Loss of MyD88 alters neuroinflammatory response and attenuates early Purkinje cell loss in a spinocerebellar ataxia type 6 mouse model. *Hum Mol Genet.* 2015; 24(17); 4780-4791
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21. Yokote H, Nose Y, Ishibashi S, Tanaka K, Takahashi T, Fujihara K, Yokota T, Mizusawa H. Spinal cord ring enhancement in patients with neuromyelitis optica. *Acta Neurol Scand.* 2015; 132(1); 37-41
22. Hashimoto Y, Honda T, Matsumura K, Nakao M, Soga K, Katano K, Yokota T, Mizusawa H, Nagao S, Ishikawa K. Quantitative evaluation of human cerebellum-dependent motor learning through prism adaptation of hand-reaching movement. *PLoS One.* 2015; 10(3); e0119376
23. Mizutani S, Usui N, Yokota T, Mizusawa H, Taira M, Katsuyama N. Depth perception from moving cast shadow in macaque monkey. *Behav Brain Res.* 2015; 288; 63-70
24. Ozaki K, Doi H, Mitsui J, Sato N, Iikuni Y, Majima T, Yamane K, Irioka T, Ishiura H, Doi K, Morishita S, Higashi M, Sekiguchi T, Koyama K, Ueda N, Miura Y, Miyatake S, Matsumoto N, Yokota T, Tanaka F, Tsuji S, Mizusawa H, Ishikawa K. A Novel Mutation in ELOVL4 Leading to Spinocerebellar Ataxia (SCA) With the Hot Cross Bun Sign but Lacking Erythrokeratoderma: A Broadened Spectrum of SCA34. *JAMA Neurol.* 2015; 72(7); 797-805
25. Yoshioka K, Watanabe K, Zeniya S, Ito Y, Hizume M, Kanazawa T, Tomita M, Ishibashi S, Miake H, Tanaka H, Yokota T, Mizusawa H. A Score for Predicting Paroxysmal Atrial Fibrillation in Acute Stroke Patients: iPAB Score. *J Stroke Cerebrovasc Dis.* 2015; 24(10); 2263-2269
26. Hattori T, Arai A, Yokota T, Imadome K, Tomimitsu H, Miura O, Mizusawa H. Immune-mediated Neuropathy with Epstein-Barrvirus-positive T-cell Lymphoproliferative Disease. *Intern Med.* 2015; 54(1); 69-73
27. Iwata R, Nakayama F, Hirochi S, Sato K, Piao W, Nishina K, Yokota T, Wada T. Synthesis and properties of vitamin E analog-conjugated neomycin for delivery of RNAi drugs to liver cells. *Bioorg Med Chem Lett.* 2015; 25(4); 815-819
28. Nishina T, Numata J, Nishina K, Yoshida-Tanaka K, Nitta K, Piao W, Iwata R, Ito S, Kuwahara H, Wada T, Mizusawa H, Yokota T. Chimeric Antisense Oligonucleotide Conjugated to α -Tocopherol. *Mol Ther Nucleic Acids.* 2015; 4; e220
29. Nishina K, Piao W, Yoshida-Tanaka K, Sujino Y, Nishina T, Yamamoto T, Nitta K, Yoshioka K, Kuwahara H, Yasuhara H, Baba T, Ono F, Miyata K, Miyake K, Seth PP, Low A, Yoshida M, Bennett CF, Kataoka K, Mizusawa H, Obika S, Yokota T. DNA/RNA heteroduplex oligonucleotide for highly efficient gene silencing. *Nat Commun.* 2015; 6; 7969
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34. Ethan A Winkler, Yoichiro Nishida, Abhay P Sagare, Sanket V Rege, Robert D Bell, David Perlmutter, Jesse D Sengillo, Sara Hillman, Pan Kong, Amy R Nelson, John S Sullivan, Zhen Zhao, Herbert J Meiselman, Rosalinda B Wenby, Jamie Soto, E Dale Abel, Jacob Makshanoff, Edward Zuniga, Darryl C De Vivo, Berislav V Zlokovic. GLUT1 reductions exacerbate Alzheimer's disease vasculo-neuronal dysfunction and degeneration. *Nat. Neurosci.* 2015.04; 18(4); 521-530
35. Yoneyama M, Mitoma H, Higuma M, Sanjo N, Yokota T, Terashi H. Ambulatory Gait Behavior in Patients with Dementia: A Comparison with Parkinson's Disease. *IEEE Trans Neural Syst Rehabil Eng.* 2015.09;
36. Iwasawa E, Ichijo M, Ishibashi S, Yokota T. Acute development of collateral circulation and therapeutic prospects in ischemic stroke. *Neural Regen Res.*

37. Yamasaki R, Matsushita T, Fukazawa T, Yokoyama K, Fujihara K, Ogino M, Yokota T, Miyamoto K, Niino M, Nomura K, Tomioka R, Tanaka M, Kawachi I, Ohashi T, Kaida KI, Matsui M, Nakatsuji Y, Ochi H, Fukaura H, Kanda T, Nagaishi A, Togo K, Mizusawa H, Murai H, Kira JI. Efficacy of intravenous methylprednisolone pulse therapy in patients with multiple sclerosis and neuromyelitis optica. *Mult Scler*. 2015; pii: 1352458515617248. (Advanced Online Publication).
38. Ichijo M, Iwasawa E, Numasawa Y, Miki K, Ishibashi S, Tomita M, Tomimitsu H, Kamata T, Fujigasaki H, Shintani S, Mizusawa H. Significance of Development and Reversion of Collaterals on MRI in Early Neurologic Improvement and Long-Term Functional Outcome after Intravenous Thrombolysis for Ischemic Stroke. *AJNR Am J Neuroradiol*. 36(10); 1839-1845
39. Ichijo M, Ishibashi S, Li F, Yui D, Miki K, Mizusawa H, Yokota T. Sphingosine-1-Phosphate Receptor-1 Selective Agonist Enhances Collateral Growth and Protects against Subsequent Stroke. *PLoS One*. 10(9); e0138029

[Misc]

1. Masaki Ohyagi, Takanori Yokota. [Treatment and prognosis of multifocal motor neuropathy] . 2015.09; 73 Suppl 7; 434-439

[Conference Activities & Talks]

1. Nonami H, Kanouchi T, Ishibashi T, Yokota T. A case of multiple cranial nerve palsies with characteristic myoclonus-like involuntary movements of facial and cervical muscles (Japanese). 9th Tokyo metropolitan neuromuscular electrodiagnosis forum 2015.01.24 Tokyo
2. Hiroya Kuwahara, Kazutaka Nishina, Wenying Piao, Takanori Yokota. Development of nanomachine that delivers therapeutic oligonucleotide across the blood-brain barrier into brain. 1st COINS International Symposium 2015.02.27 Tokyo
3. Ishikawa K, Ishiguro T, Soga K, Higashi M, Sato N, Obayashi M, Niimi Y, Mizusawa H, Yokota T. Molecular pathogenesis of spinocerebellar ataxia type 31 (SCA31). 56th Annual Meeting of the Japanese Society of Neurology 2015.05.20 Niigata
4. Kuwahara H, Anraku Y, Fukusato Y, Nitta K, Mizoguchi A, Nishina K, Mizusawa H, Kataoka K, Yokota T. A new drug delivery system across the blood-brain barrier into brain. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.20 Niigata
5. Ishibashi S, Ichijo M, Li F, Mizusawa H, Yokota T. S1PR1 expression and endothelial cell proliferation after focal ischemia in mice. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.20 Niigata
6. Ichijo M, Li F, Miki K, Ishibashi S, Mizusawa H, Yokota T. S1PR1 agonist exert a neuroprotective effect via enhancing collateral growth. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.20 Niigata
7. Yoshioka K, Sujino Y, Kunieda T, Shimo T, Tanaka K, Piao W, Kuwahara H, Nishina K, Obika S, Yokota T. Development of exon-skipping therapy by hetero-chimera-duplex oligonucleotide. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.20 Niigata
8. Ishiguro T, Fujikake N, Sato N, Ueyama M, Yokota T, Wada K, Mizusawa H, Nagai Y, Ishikawa K. SCA31-linked UGGAexp RNA causes progressive neurodegeneration in Drosophila. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.20 Niigata
9. Li F, Ishibashi S, Ichijo M, Yokota T. Oligonucleotide reduced gene expression in focal ischemic brain in mice. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata
10. Ozaki K, Yui D, Wakabayashi T, Nishida Y, Iwatsubo T, Ishikawa K, Yokota T, Mizusawa H. Expression profile:mice cerebellum on high fat diet, oxidative stress, and aging. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata
11. Nishida Y, Yui D, Nishina T, Mogushi K, Ishibashi S, Ishikawa K, Mizusawa H, Yokota T. Pla2g3 is increased in Alzheimer disease cerebrum and causes reduction of IDE. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata

12. Hattori T, Horovitz S, Lungu C, Ishiai S, Yokota T, Wassermann E, Hallett M. Neural Correlates of impaired Working Memory in Parkinson Disease. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata
13. Ohkubo T, Tajiri M, Abe K, Sekiguchi T, Uchihara T, Mizusawa H, Yokota T. Propagation of TDP-43 and pTDP-43 in non-human primate model of ALS. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata
14. Abe K, Tajiri M, Yui D, Ohkubo T, Yokota T. Selective uptake of C-terminal fragments of TDP-43 into exosome. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata
15. Soga K, Sato N, Ozaki K, Higashi M, Hatsuya H, Takao M, Murayama S, Ishikawa K, Yokota T, Mizusawa H. Analysis of gene expressions in spinocerebellar ataxia (SCA) 31. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata
16. Ota K, Ohkita M, Ishikawa K, Mizusawa H, Yokota T. Analysis of TPPP function in mitochondria using cultured HeLa cell. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.21 Niigata
17. Ishizu N, Hebisawa A, Yui D, Aikawa T, Mizusawa H, Yokota T, Watase K. Genetical studies on knockin mice carrying a PARK17 mutation. 56th Annual Meeting of the Japanese Society of Neurology 2015.05.22 Niigata
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19. Kanouchi T, Sekiguchi T, Yokota T. Local progression at the onset lower limb and spread to the upper limb in ALS (Japanese). 56th Annual Meeting of The Japanese Society of Neurology 2015.05.23 Niigata
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21. Hiroaki Yokota, Tomoyuki Kamata, Nobuo Sanjo, Takanori Yokota. Serum retinol levels are associated with brain volume loss in patients with multiple sclerosis.. MS medical symposium 2015.05.23 Niigata
22. Fumiko Furukawa, Nobuo Sanjo, Maya Higuma, Tetsuyuki Kitamoto, Masaki Hizume, Yoshikazu Nakamura, Tadashi Tsukamoto, Shigeo Murayama, Kagari Koshi, Takashi Matsukawa, Shoji Tsuji, Jun Goto, Msahito Yamada, Hidehiro Mizusawa, Takanori Yokota. Clinical features in Gerstmann-Sträussler-Scheinker syndrome with P105L mutation.. Prion2015 2015.05.26 Fort Collins, USA
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24. Maya Higuma, Nobuo Sanjo, Hiroshi Mitoma, Takanori Yokota. Relationship between attention and gait cycle in the patients with Alzheimer's disease.. Alzheimer's Association International Conference 2015 2015.07.18 Washington DC, USA
25. Higuma M, Sanjo N, Mitoma H, Yokota T. Relationship between attention and gait cycle in the patients with Alzheimer's disease. Alzheimer's Association International Conference 2015 2015.07.18 Washington, DC
26. Yokota T. DNA/RNA heteroduplex oligonucleotide for highly efficient gene silencing. The 21st Annual Meeting of Japan Society of Gene Therapy 2015.07.26 Osaka
27. Taro Ishiguro. Expanded UGGAA repeat RNA associated with SCA31 causes progressive neurodegeneration in Drosophila.. Symposium : Non-coding repeat diseases - underlying pathogenesis in RNA and protein metabolism; The 38th Annual Meeting of the Japan Neuroscience Society 2015.07.29
28. Ishiguro T, Fujikake N, Sato N, Ueyama M, Yokota T, Wada K, Mizusawa H, Nagai Y, Ishikawa K.. Expanded UGGAA repeat RNA associated with SCA31 causes progressive neurodegeneration in Drosophila. The 38th Annual Meeting of the Japan Neuroscience Society, 2015.07.29 Kobe, Japan
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31. Kuwahara H, Shimoura T, Song J, Yoshida-Tanaka K, Nishina K, Nagata T, Yokota T. A new platform technology to regulate the blood-brain barrier for molecular targeted therapy of multiple sclerosis. Asia-Pacific School of Neuroimmunology 2015 2015.08.30 Tokyo, Japan
32. Nobuo Sanjo, Tsuyoshi Hamaguchi, Tadashi Tsukamoto, Yoshikazu Nakamura, Tetsuyuki Kitamoto, Masahito Yamada, Takanori Yokota, Hidehiro Mizusawa, Prion Disease Surveillance Committee (Japan). Surveillance of prion disease in Japan. Asian Pacific Prion Symposium 2015 2015.09.04 Kanazawa, JPN
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35. Furukawa F, Sanjo N, Kobayashi A, Hamaguchi T, Yamada M, Kitamoto T, Mizusawa H, Yokota T. Amyloid- β 42 deposition in the brain of the Gerstmann-Sträussler-Scheinker disease with the P105L mutation. Asian Pacific Prion Symposium 2015 2015.09.04 Kanazawa, Japan
36. Sanjo N, Hamaguchi T, Tsukamoto T, Nakamura Y, Kitamoto T, Yamada M, Yokota T, Mizusawa H. Surveillance of prion disease in Japan. Asian Pacific Prion Symposium 2015 2015.09.04 Kanazawa, Japan
37. Tsukamoto T, Sanjo N, Hamaguchi T, Nakamura Y, Kitamoto T, Yamada M, Mizusawa H. CJD with M232R: Its clinic-pathological features. Asian Pacific Prion Symposium 2015 2015.09.04 Kanazawa, Japan
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42. Kunieda T, Yoshioka K, Sujino Y, Yoshida-Tanaka K, Piao W, Kuwahara H, Nishina K, Nagata T, Yokota T. Enhancement of potency by gapmer type antisense oligonucleotides with Hetero-Chimera-Duplex-Oligonucleotide (HEDO). 11th Annual Meeting of the Oligonucleotide Therapeutics Society 2015.10.13 Leiden, Netherlands
43. Yoshioka K, Yoshida-Tanaka K, Piao W, Nishina T, Kuwahara H, Nishina K, Yokota T. Heteroduplex oligonucleotide (HDO): efficient drug delivery and processing mechanism. 11th Annual Meeting of the Oligonucleotide Therapeutics Society 2015.10.13 Leiden, Netherlands
44. Hiroya Kuwahara, Takahiro Shimoura, Jingdong Song, Kie Yoshida-Tanaka, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. A new therapeutic oligonucleotide to regulate the blood-brain barrier. 11th Annual Meeting of the Oligonucleotide Therapeutics Society 2015.10.14 Leiden
45. Kuwahara H, Shimoura T, Song J, Yoshida-Tanaka K, Nishina K, Nagata T, Yokota T. A new therapeutic oligonucleotide to regulate the blood-brain barrier. 11th Annual Meeting of the Oligonucleotide Therapeutics Society 2015.10.14 Leiden, Netherlands

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49. Kuwahara H, Shimoura T, Song J, Yoshida-Tanaka K, Nishina K, Nagata T, Yokota T. A new therapeutic oligonucleotide to regulate the blood-brain barrier in vivo. Barcelona BioMed Conference on "Blood Brain Barrier" 2015.11.02 Barcelona, Spain
50. Kanouchi T, Yokota T. Symposium 3. Electrophysiological approach to the pathomechanism of lesion spread in ALS (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.05 Osaka
51. Ono D, Kanouchi T, Sanjo N, Nishida Y, Ishikawa K, Yokota T. Somatosensory evoked potential in the patients with spinal cord atrophy in neuromyelitis optica and multiple sclerosis (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.05 Osaka
52. Narumi J, Kanouchi T, Akaza M, Aoyagi E, Yanagi N, Ohta N, Sumi Y, Yokota T, Hagihara M, Tohda S. Study for quality control in nerve conduction study (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.05 Osaka
53. Iida S, Suzuki M, Sanjo N, Nishida Y, Kanouchi T, Yokota T. Predictive factors in nerve conduction study for remission maintenance therapy in CIDP (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.06 Osaka
54. Kanouchi T, Sekiguchi T, Yokota T. Correlation between disease progression in the onset limb and symptom spread to the bulbar region in ALS (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.06 Osaka
55. Kuwahara H, Shimoura T, Song J, Yoshida-Tanaka K, Nishina K, Nagata T, Yokota T. Heteroduplex oligonucleotide to regulate the blood-brain barrier. 2nd COINS International Symposium 2015.11.24 Tokyo, Japan
56. Yokota T. 2'-DNA/RNA heteroduplex oligonucleotide for highly efficient gene silencing. 2015 International Chemical Congress of Pacific Basin Societies 2015.12.15 Honolulu, HI
57. Inagaki M, Uematsu R, Araki Y, Sakamoto S, Ishibashi S, Kashida H, Asanuma H, Yokota T, Wada T. Synthesis and antisense activities of new type of chimeric PRNA-DNA derivatives containing phosphoramidate linkage in PRNA-DNA junction. 2015 International Chemical Congress of Pacific Basin Societies 2015.12.17 Honolulu, HI
58. Asai M, Uematsu R, Araki Y, Sakamoto S, Ishibashi S, Yokota T, Wada T. Tuning and optimization of on-off switching pH of PRNA for hypoxia specificity. 2015 International Chemical Congress of Pacific Basin Societies 2015.12.17 Honolulu, HI

Psychiatry and Behavioral Sciences

Professor Toru NISHIKAWA, Takayuki OKADA (2015.9 ~)
Associate Professor Akeo KURUMAJI
Junior Associate Professor
Naoki YAMAMOTO, Takashi TAKEUCHI
Assistant Professor
Daisuke JITOKU, Akihito UEZATO, Hiroo MITSUSADA,
Yuichiro ABE, Kohei HINO,
Mizue HOB0 (Department of Sleep Modulatory Medicine)
Technical Specialist Asami UMINO
Medical Staff
Yuya TERASAWA (~ 2015.3), Yu TOMIOKA (~ 2015.9),
Hitoshi MUTO, Takehiro TAMURA, Shunsuke TAKAGI (2015.4 ~),
Ryotaro SAITO (2015.4 ~)
Medical Fellow
Sayuri ISHIWATA (~ 2015.3)
Technical Assistant
Yasuhiro OKA, Miyuki SAITO, Hisashi YAMADA, YUi NOZAKI (~ 2015.3)
Momoko KOBAYASHI (2015.4 ~),
Kazunori MURAKAMI (2015.4 ~), Yukari WAKAYAMA (2015.4 ~)
Research Assistant
Michio ITASAKA (~ 2015.3), Meri SASAKI (~ 2015.3), Ayano SOMEYA,
Sayaka SAITO (2015.2 ~), Sayuri ISHIWATA (2015.10 ~),
Momoko KOBAYASHI (~ 2015.3)
Graduate Students
Syunsuke TAKAGI (~ 2015.3), Masakazu UMINO, Kazuo TAKIGUCHI,
Megumi GOTO, Ko FURUTA, Tomoya SHIRAISHI (~ 2015.3),
Keiko ONO (~ 2015.3), Misa NONAKA (~ 2015.3), Mai Kato (2015.4 ~), Kanae Hayakawa (2015.4 ~)

(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

(ii) 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.

(iii) 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. Jitoku D, Yamamoto N, Iwayama Y, Toyota T, Miyagi M, Enokida T, Tasaka Y, Umino M, Umino A, Uezato A, Iwata Y, Suzuki K, Kikuchi M, Hashimoto T, Kanahara N, Kurumaji A, Yoshikawa T, Nishikawa T.. Association study of H2AFZ with schizophrenia in a Japanese case-control sample. *J Neural Transm.* 2015; 122(6); 915-923
2. Ishiwata S, Umino A, Balu D, Coyle JT, Nishikawa T.. Neuronal serine racemase regulates extracellular D-serine levels in the adult mouse hippocampus. *J Neural Transm.* 2015; 122(8); 1099-1103
3. Uezato A, Yamamoto N, Iwayama Y, Hiraoka S, Hiraaki E, Umino A, Haramo E, Umino M, Yoshikawa T, Nishikawa T. Reduced cortical expression of a newly identified splicing variant of the DLG1 gene in patients with early-onset schizophrenia. *Transl Psychiatry.* 2015; 5; e654
4. Soshi T, Noda T, Ando K, Nakazawa K, Tsumura H, Okada T. Neurophysiological modulation of rapid emotional face processing is associated with impulsivity traits. *BMC Neurosci.* 2015; 16(1); 87
5. Soshi T, Noda T, Ando K, Nakazawa K, Tsumura H, Okada T. Impulsivity is Associated with Early Sensory Inhibition in Neurophysiological Processing of Affective Sounds. *Front Psychiatry.* 2015; 6; 141
6. Yoshiike T, Nishida M, Yagishita K, Nariai T, Ishii K, Nishikawa T. . Altered sleep spindle in delayed encephalopathy after acute carbon monoxide poisoning *Journal of Clinical Sleep Medicine.* 2015;
7. Takagi S, Balu DT, Coyle JT. Subchronic pharmacological and chronic genetic NMDA receptor hypofunction differentially regulate the Akt signaling pathway and Arc expression in juvenile and adult mice. *Schizophr Res.* 2015.03; 162(1-3); 216-221
8. Watanabe M, Umezaki Y, Miura A, Shinohara Y, Yoshikawa T, Sakuma T, Shitano C, Katagiri A, Takenoshita M, Toriihara A, Uezato A, Nishikawa T, Motomura H, Toyofuku A.. Comparison of cerebral blood flow in oral somatic delusion in patients with and without a history of depression: a comparative case series. *BMC Psychiatry.* 2015.05; 15; 42
9. 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.* 2015.05;
10. 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. *Am J Geriatr Psychiatry.* 2015.09;

11. Suzuki S, Takeuchi T, Okano T, Kamiya N, Sugiyama T, Ebine M, Matsuda H, Suzuki T, Okai T, Takeda S, Ochiai K, Kinoshita K. Problems of Perinatal Mental Health Care in Tokyo, Japan. J Clin Med Res. 2015.12; 7(12); 1013

[Conference Activities & Talks]

1. Uezato A, Toyofuku A, Yamamoto N, Kurumaji A, Nishikawa T. Assessing patients with psychosomatic oral dysesthesia (oral cenesthopathy) by Oral DRS. WPA Rregional Congress Osaka Japan 2015 2015.06.05 Osaka
2. Nishikawa T. Calcium-Permeable AMPA Receptor and Asc-1 Transporter Regulate the Cortical Extracellular D-Serine Concentration:Potential Targets for Development of Novel Pharmacotherapy for NMDA Receptor Dysfunction in Schizophrenia. ACNP 54th Annual Meeting 2015.12.09 Florida

Neurosurgery

Professor: Taketoshi Maehara

Associate Professor: Tadashi Nariai

Assistant Professors: Yoji Tanaka and Motoki Inaji

Hospital stuffs:

Takashi Sugawara, Yoshihisa Kawano, Kaoru Tamura, Kazutaka Sumita, Maki Mukawa, Motoshige Yamashina, Shihori Hayashi, Juri Kiyokawa, Kazuhide Shimizu, Yusuke Ebiko, Asumi Orihara, Satoru Takahashi and Naoki Taira

Graduate Students: Shin Hirota, Tomoyuki Kino, Maki Mukawa, Masahumi Sasaki, Yoshiteru Obata, Yousuke Ishii, Sakyo Hirai, Yasuhiro Ueda, Jun Karakama, Takahiro Ogishima, Shihori Hayashi, Kazuhide Shimizu, Dong Xlao Shu, Kenji Yamada, Shouko Hara and Satoka Hashimoto

(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. Sung Hugh Choi, Kaoru Tamura, Rajiv Kumar Khajuria, Deepak Bhare, Irina Nesterenko, Jack Lawler, Khalid Shah. Antiangiogenic variant of TSP-1 targets tumor cells in glioblastomas. *Mol. Ther.* 2015.02; 23(2); 235-243
2. Moteki, Y. Onda, H. Kasuya, H. Yoneyama, T. Okada, Y. Hirota, K. Mukawa, M. Nariai, T. Mitani, S. Akagawa, H.. Systematic Validation of RNF213 Coding Variants in Japanese Patients With Moyamoya Disease *J Am Heart Assoc.* 2015.05; 4(5);
3. T Nakamura, K Tateishi, T Niwa, Y Matsushita, K Tamura, M Kinoshita, K Tanaka, S Fukushima, H Takami, H Arita, A Kubo, T Shuto, M Ohno, Y Miyakita, S Kocialkowski, T Sasayama, N Hashimoto, T Maehara, S Shibui, T Ushijima, N Kawahara, Y Narita, K Ichimura. Recurrent mutations of CD79B and MYD88 are the hallmark of primary central nervous system lymphomas. *Neuropathol. Appl. Neurobiol.* 2015.06;
4. Takashi Sugawara, Masaru Aoyagi, Takahiro Ogishima, Yoshihisa Kawano, Masashi Tamaki, Tomoyuki Yano, Atsunobu Tsunoda, Kikuo Ohno, Taketoshi Maehara, Seiji Kishimoto. Extended orbital exenteration for sinonasal malignancy with orbital apex extension: surgical technique and clinical analysis. *J. Neurosurg.* 2015.07; 123(1); 52-58
5. Hirokazu Takami, Shintaro Fukushima, Kohei Fukuoka, Tomonari Suzuki, Takaaki Yanagisawa, Yuko Matsushita, Taishi Nakamura, Hideyuki Arita, Akitake Mukasa, Nobuhito Saito, Masayuki Kanamori, Toshihiro Kumabe, Teiji Tominaga, Keiichi Kobayashi, Motoo Nagane, Toshihiko Iuchi, Kaoru Tamura, Taketoshi Maehara, Kazuhiko Sugiyama, Mitsutoshi Nakada, Yonehiro Kanemura, Masahiro Nonaka, Kiyotaka Yokogami, Hideo Takeshima, Yoshitaka Narita, Soichiro Shibui, Yoichi Nakazato, Ryo Nishikawa, Koichi Ichimura, Masao Matsutani. Human chorionic gonadotropin is expressed virtually in all intracranial germ cell tumors. *J. Neurooncol.* 2015.08; 124(1); 23-32
6. 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.* 2015.09;
7. 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.* 2015.12;

[Conference Activities & Talks]

1. Tadashi Nariai. Clinical benefit of PET metabolic image for the gamma knife radiosurgery against malignant brain tumor. The 4th Biennial Congress of the Asian Leksell Gamma Knife Society 2015.02.15

2. Tamura, K., Aoyagi, M., Ando, N., Ogishima, T., Nariai, T., Yamamoto, M., Ohno, K., Maehara, T.. Glioma stem-like cell expansion and tumor vascular damage in de novo glioblastomas after gamma knife surgery plus external beam radiation. 2015.02.21
3. Motoki Inaji, Masaaki Yamamoto, Tadashi Nariai, Yoji Tanaka, Yoichi Urakawa, Kiichi Ishiwata, Kenji Ishii, Taketoshi Maehara.. Validation of MRI T1/T2 mismatch method and Methionine PET for accurate differentiation between radiation injury and recurrence of metastatic brain tumor after gamma knife radiosurgery.. The 4th Biennial Congress of the Asian Leksell Gamma Knife Society. 2015.02.21 Yokohama
4. Kei Wagatsuma, Keiichi Oda, Kenta Miwa, Motoki Inaji Shihori Hayashi, Muneyuki Sakata, Kenji Ishibashi, Jun Toyohara Kenji Ishii, Kiichi Ishiwata. Effects of a novel additional neck-shield and time of flight on quality of cerebral imaging in 15O-labeled gas inhalation study. SNMMI 2015 2015.06.06 Baltimore
5. Tadashi Nariai. PET H215O Study in Moyamoya Disease and the Other Chronic Occlusive CVD. Neuroradiological Seminar at Stanford University 2015.06.12
6. Sato A, Kudo T, Inaji M, Tanaka Y, Ishiwata K, Ishii K, Maehara T, Nariai T. . Progressive occlusion of intracranial arteries and worsening of ischemic event among patients with adult moyamoya disease. 4th International Moyamoya Meeting, 2015.07.02
7. Taira N, Tanaka Y, Inaji M, Kudo T, Maehara T, Nariai T. Serial measurement of cerebral hemodynamics with ASL-MRI after indirect bypass surgery for patients with moyamoya disease. 4th International Conference on Moyamoya Disease 2015.07.02
8. Akihito Sato, Takumi Kudo, Motoki Inaji, Yoji Tanaka, Kiishi Ishiwata, Kenji Ishii, Taketoshi Maehara, Tadashi Nariai.. Progressive occlusion of intracranial arteries and worsening of ischemic event among patients with adult moyamoya disease.. 4th International Conference on Moyamoya Disease. 2015.07.03 Berlin, Germany
9. Naoki Taira, Yoji Tanaka, Motoki Inaji, Takumi Kudoh, Taketoshi Maehara, Tadashi Nariai. . Serial measurement of cerebral hemodynamics with ASL-MRI after indirect bypass surgery for patients with moyamoya disease.. 4th International Conference on Moyamoya Disease. 2015.07.04 Berlin, Germany
10. Takumi Kudo, Tadashi Nariai, Motoki Inaji, Chihiro Hosoda, Shihori Hayashi, Taketoshi Maehara, Kiichi Ishiwata, Kenji Ishii.. Amelioration of brain metabolism and higher brain function by surgical revascularization against adult moyamoya disease. –A positron emission tomography study-. 4th International Conference on Moyamoya Disease. 2015.07.04 Berlin, Germany
11. Maki Mukawa, Tadashi Nariai, Takumi Kudo, Kazutaka Sumita, Hideaki Onda, Hidetoshi Kasuya, Taketoshi Maehara, Hiroyuki Akagawa.. Analysis of genetic variant RNF213 (c. 14576G> A) in 5 pairs of Japanese identical twin with moyamoya disease of juvenile onset.. 4th International Conference on Moyamoya Disease. 2015.07.04 Berlin, Germany
12. Tadashi Nariai, Maki Mukawa, Takumi Kudo, Kazuki Sumita, Hideaki Onda, Hidetoshi Kasuya, Taketoshi Maehara, Hiroyuki Akagawa. Analysis of genetic variant RNF213 (c. 14576G> A) in 5 pairs of Japanese identical twins with moyamoya disease of juvenile onset.. 15th INTERIM MEETING OF THE WORLD FEDERATION OF NEUROSURGICAL SOCIETIES 2015.09.11 Rome, Italy
13. Taketoshi Maehara, Motoki Inaji, Shihori Hayashi, Asumi Orihara, Azusa Tabata, Keiko Hara. Usefulness of ictal HFO analysis and hippocampal transection for patients with MRI-negative neocortical epilepsy . The 8th AESC 2015.10.05
14. Taketoshi Maehara, Motoki Inaji, Shihori Hayashi, Asumi Orihara, Azusa Tabata, Keiko Hara. Our experiences of hippocampal transection for various types of TLE. The 8th AESC 2015.10.05
15. MAYU SASAKAWA. The clinical features of Carmustin wafers in the treatment of high grade glioma. The 74th Annual Meeting of the Japan Neurosurgical Society 2015.10.14
16. MAYU SASAKAWA. Correlation between high frequency oscillation and SEV of intraoperative ECoG among mesial temporal epilepsy patients. The 49th Congress of the Japan Epilepsy Society 2015.10.30

17. Hara, S, Tanaka Y, Ueda Y, Hayashi S, Inaji M, Ishiwata K, Ishii K, Maehara T, Nariai T. Non-invasive evaluation of cerebral blood flow and perfusion delay of moyamoya disease using arterial spin-labeling MRI with multiple post-labeling delay: comparison with ^{15}O gas -PET and with dynamic susceptibility contrast MRI.. The 10th Asian Oseanian Congress of Neuroradiology (AOCNR2015) 2015.11.05
18. Sakyo Hirai, Tadashi Nariai, Motoki Inaji, Yoji Tanaka, Taketoshi Maehara. Correlation between clinical presentation of patients with moyamoya disease and hemodynamic parameters measured with dynamic susceptibility contrast magnetic resonance imaging.. The 10th Asian Oseanian Congress of Neuroradiology (AOCNR2015) 2015.11.05
19. Tamura, K., Inaji, M., Nariai, T., Hayashi, S., Tanaka, Y., Tamaki, M., Hirai, S., Saigusa, K., Ishii, K., Ishiwata, K., Maehara, T.. Evaluation of the treatment response of malignant glioma on bevacizumab therapy using ^{11}C -methionine positron emission tomography. 20th Annual Scientific Meeting of the Society for Neuro-Oncology 2015.11.19
20. Nakano T, Tanaka Y, Tamura K, Inaji M, Hayashi S, Nariai T, Ishii K, Ishiwata K, Maehara T. Usefulness of ^{11}C -methionine positron emission tomography for the monitoring of treatment response and recurrence in a patient with malignant glioma on bevacizumab therapy. 20th Annual Scientific Meeting and Education Day of the Society for Neuro-Oncology 2015.11.19
21. Taketoshi Maehara, Motoki Inaji, Keiko Hara. Curative surgery after introduction of ictal HFO analysis for adult patients with MRI-negative neocortical epilepsy. 69th AES 2015.12.05

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**[Original Articles]**

1. Hayashi S, Maehara T, Mukawa M, Aoyagi M, Yoshino Y, Nemoto S, Ono T, Ohno K.. Successful coil embolization of a ruptured basilar artery aneurysm in a child with leukemia: a case report. *Neurol Med Chir (Tokyo)* . 2015; 54(2); 150-154
2. Masahiko Ichijo, Satoru Ishibashi, Fuying Li, Daishi Yui, Kazunori Miki, Hidehiro Mizusawa, Takanori Yokota. Sphingosine-1-Phosphate Receptor-1 Selective Agonist Enhances Collateral Growth and Protects against Subsequent Stroke. *PLoS ONE*. 2015; 10(9); e0138029
3. Katsunari Namba, Ayuho Higaki, Naoki Kaneko, Toshihiro Mashiko, Shigeru Nemoto, Eiju Watanabe. Microcatheter Shaping for Intracranial Aneurysm Coiling Using the 3-Dimensional Printing Rapid Prototyping Technology: Preliminary Result in the First 10 Consecutive Cases. *World Neurosurg*. 2015.07; 84(1); 178-186
4. M Ichijo, E Iwasawa, Y Numasawa, K Miki, S Ishibashi, M Tomita, H Tomimitsu, T Kamata, H Fujigasaki, S Shintani, H Mizusawa. Significance of Development and Reversion of Collaterals on MRI in Early Neurologic Improvement and Long-Term Functional Outcome after Intravenous Thrombolysis for Ischemic Stroke. *AJNR Am J Neuroradiol*. 2015.10; 36(10); 1839-1845

[Misc]

1. Kazunori Miki. Vascular anatomy of cerebellar 2015.12; 255(10); 935-939

[Conference Activities & Talks]

1. Aoyama,J., Nemoto,S. The simulation of removing blood clots by using the artificial clot. . ABCWIN Seminar 2015 Anatomy- Biology-Clinical Correlations (ABC) / Working Group of Interventional Neuroradiology (WIN) 2015.01.18
2. Shigeru Nemoto. 3D vascular model is valuable in neurointervention.. ABCWIN Seminar 2015 Anatomy-Biology-Clinical Correlations (ABC) / Working Group of Interventional Neuroradiology (WIN) 2015.01.21
3. Shigeru Nemoto. ENDOVASCULAR SIMULATION SYSTEM OF ACUTE CLOT RETRIEVING WITH THE SILICONE VASCULAR MODEL AND ARTIFICIAL CLOT. 38th European Society of Neuroradiology 2015.09.21 Naples, Italy
4. Shigeru Nemoto. 3D DSA and 3D vascular model. Siemens Users' meeting 2015.10.26
5. Shigeru Nemoto. Artificial clot and endovascular training model of clot removal for acute embolic stroke. . The 13th congress of WFITN 2015.11.09
6. Yoshino Y, Nemoto S, Miki K, Karakama J, Tsunoda A, Sugimoto T, Kishimoto S. Multidirectional tumor embolization for Juvenile nasopharyngeal angiofibroma.. The 31th Annual Meeting of The Japanese Society for Neuroendovascular Therapy 2015.11.19
7. Yoshino Y, Nemoto S, Miki K, Karakama J, Sasagawa M, Maehara T. The role and controversy of adjunctive technique for cerebral aneurysm coil embolization.. The 31th Annual Meeting of The Japanese Society for Neuroendovascular Therapy 2015.11.19
8. Evaluating the effect of intra arterial fasudil injection for vasospasm of subarachnoid hemorrhage using the novel angiographic analysis.. 2015.11.21
9. Nakano T, Karakama J, Miki K, Yoshino Y, Maehara T, Nemoto S. A case of Extracranial internal carotid artery giant aneurysm treated with a covered stent.. 2015.12.05

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 Yoshitaka NAGAI

(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, giving an insight into the understanding the pathology of psychiatric diseases caused by mutations in this gene (Hori et al, PLoS One, 2015). We identified origins of cerebellar oligodendrocytes and showed their development is controlled by the transcription factor, Sox9 (Hashimoto et al., Mech Dev in press).

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 MR. 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 blocking effect against reprogramming by high heteroplasmic state of pathogenic mitochondrial DNA mutation (Yokota M, et al. Hum Mol Genet 2015) and we studied variability in clinical features on SOX10 knocked-in mice (Itoh Y, et al. Neurobiol Dis 2015).

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. In this year, we obtained evidence suggesting that cerebrospinal fluid fibrinogen concentration is a useful biomarker subtyping depression (Sci Rep, 2015). We found the effect of glucocorticoid, a stress hormone, on the trafficking of BDNF in dendrite of neurons (Sci Rep, 2015). In a brain imaging study, we found that electro-convulsive therapy has a neurotrophic effects on the gray matter volume (J Affect Disord, 2015).

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 2014, as basic researches, we examined the safety of long-term exploration to the high-frequency sounds using mice and the effect on dopamine release induced by the exploration of 50kHz ultrasonic vocalization of rats. 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.

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 the molecular mechanisms of dendritic spines during developmental in emotion related-mid-frontal cortex (Sasaki et al., Brain, Structure, and Function, 2015)

6) Molecular pathogenesis and therapies of neurodegenerative diseases

(Yoshitaka Nagai, Department of Degenerative Neurological Diseases, National Institute of Neuroscience, NCNP)

As we face global aging of the population, a challenging theme has emerged, namely, to overcome late-onset incurable neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and polyglutamine diseases. Recent great progress of molecular genetics and biomedical research revealed that these diseases share a common molecular pathogenesis; protein misfolding and aggregation plays a central role in neurodegeneration. In our department, researchers with various backgrounds such as medicine, pharmacy, biology, and chemistry, are taking advantage of a variety of techniques including molecular genetics, molecular & structural biology, chemical biology, and various animal models (flies, mice, marmosets), to understand the molecular pathogenesis of and to develop therapies for these neurodegenerative diseases.

In this year, we discovered a novel mechanism of non-cell autonomous regulation of proteostasis by exosome-mediated intercellular transmission (Takeuchi et al., PNAS 2015). We also revealed an accelerated prion-like conversion of α -synuclein by glucocerebrosidase deficiency implicated in Parkinson's disease (Suzuki et al., Hum. Mol. Genet. 2015), and a protective role of the p62-mediated autophagy in degrading polyglutamine protein oligomers (Saitoh et al., J. Biol. Chem. 2015). We also reported delayed synaptic maturation underlying in neuronal dysfunction in spinocerebellar ataxia type 1 (Hatanaka et al., Sci. Rep. 2015).

(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) Hori K, Nagai T, Shan W, Sakamoto A, Abe M, Yamazaki M, Sakimura K, Yamada K, Hoshino M. Heterozygous disruption of Autism susceptibility candidate 2 causes impaired emotional control and cognitive memory. PLoS One, 10 (12): e0145979, 2015
- 2) Hashimoto R, Hori K, Owa T, Miyashita S, Dewa K, Masuyama N, Sakai K, Hayase Y, Seto Y, Inoue YU, Inoue T, Ichinohe N, Kawaguchi Y, Akiyama H, Koizumi S, Hoshino M. Origins of oligodendrocytes in the cerebellum, whose development is controlled by the transcription factor, Sox9. Mech Dev, 2016, in press
- 3) Egusa SF, Inoue YU, Asami J, Terakawa YW, Hoshino M, Inoue T. Classic cadherin expressions

- balance postnatal neuronal positioning and dendrite dynamics to elaborate the specific cytoarchitecture of the mouse cortical area. *Neurosci Res*, 2015, in press
- 4) Ruffault P-L, D'Autreaux F, Hayes JA, Nomaksteinsky M, Autran S, Fujiyama T, Hoshino M, Hagglund M, Kiehn O, Brunet J-F, Fortin G, Goridis C. The retrotrapezoid nucleus neurons expressing *Atoh1* and *Phox2b* are essential for the respiratory response to CO₂. *eLife*, 10.7554, 2015
 - 5) De Luca A, Parmigiani E, Tosatto G, Martire S, Hoshino M, Buffo A, Leto K, Rossi F. Exogenous Sonic Hedgehog modulates the pool of GABAergic interneurons during cerebellar development. *Cerebellum*, 14 (2): 72-85, 2015
 - 6) Watanabe T, Kakeno M, Matsui T, Sugiyama I, Arimura N, Matsuzawa K, Shirahige A, Ishidate F, Nishioka T, Taya S, Hoshino M, Kaibuchi K. TTBK2 with EB1/3 regulates microtubule dynamics in migrating cells through KIF2A phosphorylation. *J Cell Biol*, 210 (5): 737-751, 2015
 - 7) Yamaguchi M, Watanabe Y, Ohtani T, Uezumi A, Mikami N, Nakamura M, Sato T, Ikawa M, Hoshino M, Tsuchida K, Miyagoe-Suzuki Y, Tsujikawa K, Takeda S, Yamamoto H, Fukada S. Calcitonin Receptor Signaling Inhibits Muscle Stem Cells from Escaping the Quiescent State and the Niche. *Cell Rep*, 13 (2): 302-301, 2015
 - 8) Yokota M, Hatakeyama H, Okabe S, Ono Y, Goto Y. Mitochondrial respiratory dysfunction caused by a heteroplasmic mitochondrial DNA mutation blocks cellular reprogramming. *Hum Mol Genet* 24(16): 4698-4709, 2015
 - 9) Itoh Y, Inoue N, Inoue Y-U, Nakamura S, Matsuda Y, Inagaki M, Ohkubo T, Asami J, Terakawa Y-W, Kohsaka S, Goto Y, Akazawa C, Inoue T, Inoue K. Additive dominant effect of a SOX10 mutation underlies a complex phenotype of PCWH. *Neurobiol Dis* 80: 1-14, 2015
 - 10) Nakajima S, Numakawa T, Adachi N, Yoon HS, Odaka H, Ooshima Y, Kunugi H. The inactivation of extracellular signal-regulated kinase by glucagon-like peptide-1 contributes to neuroprotection against oxidative stress. *Neurosci Lett*. 2016 Jan 28;616:105-110.
 - 11) Hori H, Sasayama D, Teraishi T, Yamamoto N, Nakamura S, Ota M, Hattori K, Kim Y, Higuchi T, Kunugi H. Blood-based gene expression signatures of medication-free outpatients with major depressive disorder: integrative genome-wide and candidate gene analyses. *Sci Rep*. 2016 Jan 5;6:18776.
 - 12) Ogawa S, Kunugi H. Inhibitors of Fatty Acid Amide Hydrolase and Monoacylglycerol Lipase: New Targets for Future Antidepressants. *Curr Neuropharmacol*. 2015 Nov 26;13(6):760-75. PubMed PMID: 26630956.
 - 13) Nakajima S, Numakawa T, Adachi N, Ooshima Y, Odaka H, Yoshimura A, Kunugi H Self-amplified BDNF transcription is a regulatory system for synaptic maturation in cultured cortical neurons. *Neurochem Int*. 2015 Dec;91:55-61.
 - 14) Ota M, Sato N, Okamoto T, Noda T, Araki M, Yamamura T, Kunugi H. Neuromyelitis optica spectrum disorder and multiple sclerosis: Differentiation by a multimodal approach. *Mult Scler Relat Disord*. 2015 Nov;4(6):515-20.
 - 15) Teraishi T, Hori H, Sasayama D, Matsuo J, Ogawa S, Ota M, Hattori K, Kajiwarra M, Higuchi T, Kunugi H. (13)C-tryptophan breath test detects increased catabolic turnover of tryptophan along the kynurenine pathway in patients with major depressive disorder. *Sci Rep*. 2015 Nov 3;5:15994.
 - 16) Wakabayashi C, Numakawa T, Ooshima Y, Hattori K, Kunugi H. Possible role of the dopamine D1 receptor in the sensorimotor gating deficits induced by high-fat diet. *Psychopharmacology (Berl)*. 2015 Dec;232(24):4393-400.
 - 17) Ota M, Noda T, Sato N, Okazaki M, Ishikawa M, Hattori K, Hori H, Sasayama D, Teraishi T, Sone D, Kunugi H. Effect of electroconvulsive therapy on gray matter volume in major depressive disorder. *J Affect Disord*. 2015 Nov 1;186:186-91.
 - 18) Adachi N, Numakawa T, Nakajima S, Fukuoka M, Odaka H, Katanuma Y, Ooshima Y, Hohjoh H, Kunugi H. Glucocorticoid affects dendritic transport of BDNF-containing vesicles. *Sci Rep*. 2015 Aug 4;5:12684.
 - 19) Ota M, Ogawa S, Kato K, Masuda C, Kunugi H. Striatal and extrastriatal dopamine release in the common marmoset brain measured by positron emission tomography and [(18)F]fallypride. *Neurosci Res*. 2015 Dec;101:1-5.
 - 20) Hattori K, Ota M, Sasayama D, Yoshida S, Matsumura R, Miyakawa T, Yokota Y, Yamaguchi S, Noda T, Teraishi T, Hori H, Higuchi T, Kohsaka S, Goto Y, Kunugi H. Increased cerebrospinal fluid fibrinogen in major depressive disorder. *Sci Rep*. 2015 Jun 17;5:11412.
 - 21) Wakabayashi C, Numakawa T, Odaka H, Ooshima Y, Kiyama Y, Manabe T, Kunugi H, Iwakura Y. IL-1 receptor-antagonist (IL-1Ra) knockout mice show anxiety-like behavior by aging. *Neurosci Lett*.

- 2015 Jul 10;599:20-5.
- 22) Ota M, Wakabayashi C, Sato N, Hori H, Hattori K, Teraishi T, Ozawa H, Okubo T, Kunugi H. Effect of L-theanine on glutamatergic function in patients with schizophrenia. *Acta Neuropsychiatr*. 2015 Oct;27(5):291-6.
 - 23) Matsuo J, Kamio Y, Takahashi H, Ota M, Teraishi T, Hori H, Nagashima A, Takei R, Higuchi T, Motohashi N, Kunugi H. Autistic-like traits in adult patients with mood disorders and schizophrenia. *PLoS One*. 2015 Apr 2;10(4):e0122711.
 - 24) Kunugi H, Hori H, Ogawa S. Biochemical markers subtyping major depressive disorder. *Psychiatry Clin Neurosci*. 2015 Oct;69(10):597-608.
 - 25) Kasahara K, DaSalla CS, Honda M, Hanakawa T: Neuroanatomical correlates of brain-computer interface performance. *Neuroimage*, 110 (15): 95-100, 2015.
 - 26) Sasaki T, Aoi H, Oga T, Fujita I, Ichinohe N. Postnatal development of dendritic structure of layer III pyramidal neurons in the medial prefrontal cortex of marmoset. *Brain Struct Funct*. (2015) 220(6):3245-58.
 - 27) Ichinohe N. On-going elucidation of mechanisms of primate specific synaptic spine development using the common marmoset (*Callithrix jacchus*). *Neurosci Res*. 2015 93:176-8.
 - 28) Eradath MK, Abe H, Matsumoto M, Matsumoto K, Tanaka K, Ichinohe N. Anatomical inputs to sulcal portions of areas 9m and 8Bm in the macaque monkey. *Front Neuroanat*. (2015) 12:9:30.
 - 29) Yasue M, Nakagami A, Banno T, Nakagaki K, Ichinohe N, Kawai N. Indifference of marmosets with prenatal valproate exposure to third-party non-reciprocal interactions with otherwise avoided non-reciprocal individuals. *Behav Brain Res*. 2015 292:323-6.
 - 30) Suzuki W, Tani T, Banno T, Miyakawa N, Abe H, Ichinohe N. Functional columns in superior temporal sulcus areas of the common marmoset. *Neuroreport*. 2015 26(18):1133-9
 - 31) Suzuki W, Banno T, Miyakawa N, Abe H, Goda N, Ichinohe N. Mirror Neurons in a New World Monkey, Common Marmoset. *Front Neurosci*. 2015 10:9:459..
 - 32) Saitoh Y, Fujikake N, Okamoto Y, Popiel HA, Hatanaka Y, Ueyama M, Suzuki M, Gaumer S, Murata M, Wada K, Nagai Y. p62 plays a protective role in the autophagic degradation of polyglutamine protein oligomers in polyglutamine disease model flies. *J Biol Chem* 290(3): 1442-1453, 2015
 - 33) Takeuchi T, Suzuki M, Fujikake N, Popiel HA, Kikuchi H, Futaki S, Wada K, Nagai Y. Intercellular chaperone transmission via exosomes contributes to maintenance of protein homeostasis at the multicellular organismal level. *Proc. Natl. Acad. Sci. USA* 112(19): E2497-2506, 2015
 - 34) Takahashi M, Suzuki M, Fukuoka M, Fujikake N, Watanabe S, Murata M, Wada K, Nagai Y, Hohjoh H. Normalization of overexpressed α -synuclein causing Parkinson's disease by a moderate gene silencing with RNA interference. *Mol. Ther. Nucleic Acids* 4: e241, 2015
 - 35) Suzuki M, Fujikake N, Takeuchi T, Kohyama-Koganeya A, Nakajima K, Hirabayashi Y, Wada K, Nagai Y. Glucocerebrosidase deficiency accelerates an accumulation of proteinase K-resistant α -synuclein and aggravates neurodegeneration in a *Drosophila* model of Parkinson's disease. *Hum. Mol. Genet*. 24(23): 6675-6686, 2015
 - 36) Hatanaka Y, Watase K, Wada K, Nagai Y. Abnormalities in synaptic dynamics during development in a mouse model of spinocerebellar ataxia type 1. *Sci. Rep*. 5: 16102, 2015
 - 37) Araki K, Yagi N, Ikemoto Y, Yagi H, Choong C-J, Hayakawa H, Beck G, Sumi H, Fujimura H, Moriwaki T, Nagai Y, Goto Y, Mochizuki H. Synchrotron FTIR micro-spectroscopy for structural analysis of Lewy bodies in the brain of Parkinson's disease patients. *Sci. Rep*. 5: 17625, 2015

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. Tsai, S.H., Kinoshita, M., Kusu, T., Kayama, H., Okumura, R., Ikeda, K., Shimada Y., Takeda A., Yoshikawa, S., Obata-Ninomiya, K., Kurashima, Y., Sato, S., Umemoto, E., Kiyono, H., Karasuyama, H., and Takeda, K.. The Ectoenzyme E-NPP3 Negatively Regulates ATP-Dependent Chronic Allergic Responses by Basophils and Mast Cells. *Immunity*. 2015.02; 42(2); 279-293
2. 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*. 2015.02; Epub ahead of print;
3. Poliani, P.L., Wang, Y., Fontana, E., Robinette, M.L., Yamanishi, Y., Gilfillan, S., Colonna, M.. TREM2 sustains microglial expansion during aging and response to demyelination. *J. Clin. Invest.*. 2015.05; 125(5); 2161-2170
4. Morita, H., Arae, K., Unno, H., Nambu, A., Oboki, K., Ohno, T., Matsuda, A., Toyama, S., Miyauchi, K., Yamaguchi, S., Narushima, S., Kajiwar, N., Iikura, M., Suto, H., McKenzie, A., Takahashi, T., Karasuyama, H., Okumura, K., Azuma, M., Galli, S.J., Moro, K., Akdis, C., Koyasu, S., Kubo, M., Sudo, K., Saito, H., Matsumoto, K., and Nakae, S.. An Interleukin-33-Mast Cell-Interleukin-2 Axis Suppresses Papain-Induced Allergic Inflammation by Promoting Regulatory T Cell Numbers. *Immunity*. 2015.07; 43(1); 175-186

5. LiHua, L., Yoshikawa, S., Ohta, T., Horiguchi, K., Kawano, Y., Ohtsu, H., Yamanishi, Y., and Karasuyama, H.. Large particulate allergens can elicit mast cell-mediated anaphylaxis without exit from blood vessels as efficiently as do small soluble allergens. *Biochem. Biophys. Res. Commun.* . 2015.11; 467(6 (1)); 70-75

[Misc]

1. Miyake K, Karasuyama H.. Non-redundant roles of basophils in the skin and mucosa *Igaku no Ayumi.* 2015.05; 253(5); 410-417

[Conference Activities & Talks]

1. Miyake K, Nagao T, Yahagi Y, Yoshikawa S, Yamanishi Y, Karasuyama H. GM-CSF can promote MHC class II expression and ability of antigen presentation in basophils.. The 64th Meeting of Japanese Society of Allergology 2015.05.26 Tokyo, Japan
2. Soichiro Yoshikawa. STIM1 plays an essential role in the development of basophil-mediated chronic allergic inflammation.. NIPS International workshop TRPs and SOCs unconventional Ca²⁺ physiology 2015.06.05 Okazaki, Japan
3. Hajime Karasuyama. Basophil: A Key Player in Immunity and Inflammation. XXIV World Allergy Congress (WAC 2015) 2015.10.17 Seoul, Korea
4. Hajime Karasuyama. Basophils have emerged as a key player in immunity.. RIKEN-IMS Seminar 2015.10.29 Yokohama, Japan
5. Hajime Karasuyama. Basophils play critical roles in allergy and protective immunity in the skin.. 14th International Workshop on Langerhans Cells 2015.11.07 Kyoto, Japan
6. Tsutsui H, Yamanishi Y, Tatebayashi S, Yoshikawa S, Sato S, Karasuyama H. Basophil-specific protease mMCP-8 triggers skin inflammation through activation of dermal fibroblasts.. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo, Japan
7. Miyake K, Shiozawa N, Nagao T, Yahagi Y, Yoshikawa S, Yamanishi Y, Karasuyama H. Basophils acquire MHC class II molecules from DCs and exert antigen presenting capacity.. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo, Japan
8. 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-mediated chronic allergic inflammation in the skin: what makes a foreign material to be an allergen?. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo, Japan
9. Toyama S, Matsuda A, Saito H, Nakae S, Karasuyama H, Matsumoto K. A novel protease, PRSS33 (serine protease 33) is specifically and constitutively expressed in Eosinophils.. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo, Japan
10. Hajime Karasuyama. Emerging roles of basophils in acquired protective immunity to parasitic infections.. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo, Japan

[Awards & Honors]

1. Best presentation award (English Session-Oral 2 Pathophysiology allergy and immune responses (2) session, The 64th Meeting of Japanese Society of Allergology) (Kensuke Miyake), Japanese Society of Allergology, 2015.05

Molecular Virology

Professor : Shoji YAMAOKA
Project Professor : Eiji IDO
Assistant Professor: Hiroaki TAKEUCHI, Takeshi Yoshida
Medical Technologist : Yoshio INAGAKI
Secretary : Kumiko THORPE-MATSUI
Research Assitant : Akiko HAMANO

-Students-
Ph.D. course: Miho OHSAKO
Ensho CHO
Hideki SAITO
Hirona ICHIKAWA
Naoto SUZUKI
NDZINU JERRY KWAME
AZIATI ISHMAEL DZIGBDRDI KWASI
MXWELL MAMFE SAKYIAMAH
Master course: Yurika KOMATSUDA
Takuma NATSUI
Yuta IYODA
Kenjiro MAEDA
Maiko Takagi
Tsuyoshi Horikawa
Kensuke Wada

(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. Kinpara S, Ito S, Takahata T, Saitoh Y, Hasegawa A, Kijiyama M, Utsunomiya A, Masuda M, Miyazaki Y, Matsuoka M, Nakamura M, Yamaoka S, Masuda T, Kannagi M.. Involvement of double-stranded RNA-dependent protein kinase and antisense viral RNA in the constitutive NF κ B activation in adult T-cell leukemia/lymphoma cells. *Leukemia*. 2015; 29; 1425-1444
2. Suzuki M, Tung NH, Kwofie KD, Adegle R, Amoa-Bosompem M, Sakyamah M, 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, Yamaoka S, Yamaguchi Y, Edoh D, Koram K, Ohta N, Boakye DA, Ayi I, Shoyama Y. . New anti-trypanosomal active tetracyclic iridoid isolated from *Morinda lucida* Benth. *Bioorg Med Chem Lett*.. 2015; 25; 3030-3033
3. Hori T, Barnor J, Nguyen Huu T, Morinaga O, Hamano A, Ndzinu J, Frimpong A, Minta-Asare K, Amoa-Bosompem M, Brandful J, Odoo J, Bonney J, Tuffour I, Owusu BA, Ofosuhene M, Atchoglo P, Sakyamah M, Adegle R, Appiah-Opong R, Ampofo W, Koram K, Nyarko A, Okine L, Edoh D, Appiah A, Uto T, Yoshinaka Y, Uota S, Shoyama Y, Yamaoka S.. Procyanidin trimer C1 derived from *Theobroma cacao* reactivates latent human immunodeficiency virus type 1 provirus. *Biochem Biophys Res Commun*. . 2015; 459; 288-293
4. Kinpara S, Ito S, Takahata T, Saitoh Y, Hasegawa A, Kijiyama M, Utsunomiya A, Masuda M, Miyazaki Y, Matsuoka M, Nakamura M, Yamaoka S, Masuda T, Kannagi M. Involvement of double-stranded RNA-dependent protein kinase and antisense viral RNA in the constitutive NF κ B activation in adult T-cell leukemia/lymphoma cells. *Leukemia*. 2015; 29; 1425-1444
5. Hori T, Barnor J, Nguyen Huu T, Morinaga O, Hamano A, Ndzinu J, Frimpong A, Minta-Asare K, Amoa-Bosompem M, Brandful J, Odoo J, Bonney J, Tuffour I, Owusu BA, Ofosuhene M, Atchoglo P, Sakyamah M, Adegle R, Appiah-Opong R, Ampofo W, Koram K, Nyarko A, Okine L, Edoh D, Appiah A, Uto T, Yoshinaka Y, Uota S, Shoyama Y, Yamaoka S.. Procyanidin trimer C1 derived from *Theobroma cacao* reactivates latent human immunodeficiency virus type 1 provirus. *Biochem Biophys Res Commun*. *Biochem Biophys Res Commun*. . 2015; 459; 288-293
6. Suzuki M, Tung NH, Kwofie KD, Adegle R, Amoa-Bosompem M, Sakyamah M, 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, Yamaoka S, Yamaguchi Y, Edoh D, Koram K, Ohta N, Boakye DA,

Ayi I, Shoyama Y.. New anti-trypanosomal active tetracyclic iridoid isolated from *Morinda lucida* Benth. *Bioorg Med Chem Lett*.. 2015; 25; 3030-3033

7. Karasawa S, Yoza K, Tung N.H., Uto T, Morinaga O, Suzuki M, Kwofie K.D. , Amoa-Bosompem M, Boakye Daniel A, Ayi I, Adegle R, Sakyiamah M, Ayertey F, Aboagye F, Appiah Alfred A, Owusu Kofi B-A, Tuffour I , Atchoglo P, Frempong Kwadwo K, Anyan William K, Appiah-Opong R, Nyarko Alexander K, Yamashita T, Yamaguchi Y, Edoh D, Koram K, Yamaoka S, Ohta N, Shoyama Y. . Determination of the absolute configuration of the novel anti-trypanosomal iridoid molucidin isolated from *Morinda lucida* by X-ray analysis. *Tetrahedron Letters*.. 2015; 56(52); 7158-7160
8. Saitoh Y, Hamano A, Mochida K, Kakeya A, Uno M, Tsuruyama E, Ichikawa H, Tokunaga F, Utsumomiya A, Watanabe T, Yamaoka S.. A20 targets caspase-8 and FADD to protect HTLV-I-infected cells. *Leukemia*. . 2015; 10(1038); 267

[Books etc]

1. Shoji Yamaoka. *Protein Modifications in Pathogenic Dysregulation of Signaling*. Springer, 2015

[Misc]

1. Takeshi Yoshida, Hirofumi Akari. Role of accessory proteins in primate lentiviral immunopathogenesis 2015.02; 17(1); 7-13

[Conference Activities & Talks]

1. Shoji YAMAOKA. A20 interacts with Caspase-8 and FADD to protect adult T-cell leukemia cells.. 2and International Symposium on Protein Modefication in Pathogenic Dysregulation of Signaling. 2015.01.23 Tokyo
2. Hirona Ichikawa, Yasunori Saitoh, Eri Tsuruyama, Fuminori Tokunaga and Shoji Yamaoka. Ubiquitin-editing enzyme A20 inhibits TNF α -induced apoptosis of cancer cells through the C-terminal zinc finger domain. 2and International Symposium on Protein Modefication in Pathogenic Dysregulation of Signaling. 2015.01.23 Tokyo
3. Hideki Saito. N-terminally truncated POM121C, a component of nuclear pore complexes, inhibits HIV-1 replication. 2015.05.19 Cold Spring Harbor Laboratory
4. Yohei Seki, Akatsuki Saito, Takeshi Yoshida, Yorifumi Sato, Shigeyoshi Harada, Kazuhisa Yoshimura, Yuji Watanabe, Yasumasa Iwatani, Yasuhiro Yasutomi, Tetsuro Matano, Tomoyuki Miura, Hirofumi Akari. Novel elite controller model by HIV-1mt-infected cynomolgus macaques. 33rd Annual Symposium on Nonhuman Primate Models for AIDS 2015.10.13 California
5. Hiroaki Takeuchi. MELK regulates multiple steps of HIV-1 replication in human cells. The 63rd Annual Meeting of the Japanese Society for Virology 2015.11.23 Fukuoka International Congress Center
6. Is HIV-1 Vpu Oligomerization Required for Its Functions?. 2015.12.01

Immunotherapeutics

Professor: Mari KANNAGI
 Associate Professor: Takao MASUDA
 Assistant Professor: Atsuhiko HASEGAWA (Lecturer)
 Assistant Professor: Yoshiko NAGANO
 Postdoctoral Fellow: Shuichi KINPARA, Sayaka ITO, Natsuko TAKATSUKA
 Graduate Student: Yoko SATO, Satomi ANDO, Tatsuro TAKAHATA, Yuji MURAKAMI, Leila SAWADA, Kazuki MIURA

(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 κ 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 κ B, ATL cells exhibit NF κ 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 κ B activation in Tax-negative ATL cells. Our findings elucidate a novel Tax-independent mechanism of NF κ 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 stuffs 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. Takao Masuda, Yoko Sato, Yu-Lun Huang, Satoshi Koi, Tatsuro Takahata, Atsuhiko Hasegawa, Gota Kawai, Mari Kannagi. Fate of HIV-1 cDNA intermediates during reverse transcription is dictated by transcription initiation site of virus genomic RNA. *Sci Rep.* 2015; 5; 17680
2. Youko Suehiro, Atsuhiko Hasegawa, Tadafumi Iino, Amane Sasada, Nobukazu Watanabe, Masao Matsuoka, Ayako Takamori, Ryuji Tanosaki, Atae Utsunomiya, Ilseung Choi, Tetsuya Fukuda, Osamu Miura, Shigeo Takaishi, Takanori Teshima, Koichi Akashi, Mari Kannagi, Naokuni Uike, Jun Okamura. Clinical outcomes of a novel therapeutic vaccine with Tax peptide-pulsed dendritic cells for adult T cell leukaemia/lymphoma in a pilot study. *Br. J. Haematol.* 2015.01;
3. S Kinpara, S Ito, T Takahata, Y Saitoh, A Hasegawa, M Kijiyama, A Utsunomiya, M Masuda, Y Miyazaki, M Matsuoka, M Nakamura, S Yamaoka, T Masuda, M Kannagi. Involvement of double-stranded RNA-dependent protein kinase and antisense viral RNA in the constitutive NF κ B activation in adult T-cell leukemia/lymphoma cells. *Leukemia.* 2015.05; 29; 1425-1444

[Conference Activities & Talks]

1. Atsuhiko Hasegawa. Tax-specific T-cell responses in allo-HSCT for ATL. Seventh Annual T-cell Lymphoma Forum 2015.01

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. Satoru Miyakura and Masayuki Hara. Molecular Characterization of UKp83/68, a Widespread Nuclear Proteins that Bind Poly(A) and Colocalize with a Nuclear Speckle's Component J Med Dent Sci. 2015.06; 62(2); 43-56

[Conference Activities & Talks]

1. Masayuki Hara, Akio Noto, Ken Egawa, Hiratsugu Yokota. About a reducing method of the radiation dose derived from cesium-137 on the surface of polluted soil. 15th International Congress of Radiation Research 2015.05.25 Kyoto International Conference Center, Kyoto

Biodefense Research

Professor Toshiaki Ohteki
 Junior Associate Professor Nobuyuki Onai
 Assistant Professor Hiroyuki Tezuka
 Assistant Professor Yusuke Nakanishi
 Adjunct Lecturer Taku Sato
 Project Junior Assistant Professor Junpei Asano
 Project Junior Assistant Professor Mihoko Kajita
 Graduate Student Shunsuke Kawamura
 Graduate Student Minako Inazawa
 Graduate Student Kana Minamide
 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 dendritic cells, the control tower of the immune system

Dendritic cells (DCs) maintain immune tolerance under steady-state conditions, and activate immune cells upon infection. In this context, it is important to identify the progeny cells committed solely to DC differentiation, i.e. DC progenitors from the points of view of DC development and clinical applications.

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 highly express E2-2, an essential transcription factor for pDC development, and produce a large number of pDCs. Together with the common monocyte/macrophage progenitors, cMoP, identified by other group, we proposed a current model for mononuclear phagocyte differentiation pathway (Immunity 2014).

Based on these achievements, we are currently trying to identify human progenitors of mononuclear phagocytes. The discovery of human mononuclear phagocyte progenitors producing fresh DCs or monocytes/macrophages will be a milestone, leading to the development of prophylactic and therapeutic applications for infectious dis-

eases, cancers, and autoimmune diseases.

2) Discovery of a new function of microbiota to attract monocyte/macrophage migration

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. The microbiota in the large intestine is denser and more diverse than that in the small intestine, and mostly consists of Gram-positive Firmicutes or Gram-negative Bacteroidetes; which are conserved in humans and mice. Although the presence of Gram-negative bacteria, *Bacteroides/Prevotella* or *Enterobacteriaceae* in the colon is a risk factor for developing IBD, the role of Gram-positive bacteria in colitis is unknown.

Using a mouse dextran sodium sulfate (DSS)-induced colitis model, we show here that commensal Gram-positive bacteria trigger the mobilization of inflammatory monocytes and macrophages into the colon (Mucosal Immunol 2015). $\text{TNF-}\alpha$ is a representative cytokine that aggravates colitis, and predominantly produced by monocytes/macrophages. Interestingly, pretreating mice with vancomycin, which eliminated Gram-positive bacteria, particularly the *Lachnospiraceae* family, significantly reduced the severity of the colitis, evaluated by the body weight loss, colon length, pro-inflammatory cytokine level, massive leukocytic infiltration etc. Importantly, vancomycin treatment specifically downregulated the colonic epithelial cell (cEC) expression of CCR2 ligands, which are critical chemokines for monocyte/macrophage mobilization into the inflamed colon. In addition, 16S rRNA analysis showed that vancomycin treatment dramatically reduced *Lachnospiraceae*, the most abundant order of Clostridiales in untreated control mice. As the sera from Crohn's disease patients and colitic mice react with *Lachnospiraceae* bacterium A4 flagella, our findings provide a new environmental risk factor and new therapeutic approaches for IBD.

This paper has been selected by the Society for Mucosal Immunology as a Featured Paper of the Month (February, 2015).

2. Research on tissue stem cells

1) Understanding of tissue homeostasis on the basis of immune cell-tissue stem cell interplay

We recently 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, which was applicable to the treatment of Sly syndrome, a congenital storage disorder with β -glucuronidase deficiency, in which it restored enzyme expression at the HSC level. Our findings suggest type I IFN-based preconditioning, combined with HSC transplantation, as a novel non-genotoxic treatment for some congenital diseases (Blood 2013).

2) Maintenance machinery of intestinal stem cells

Intestinal stem cells (ISCs) are an exclusive source of intestinal epithelial cell regeneration. We have identified 2 genes that are essential for the maintenance of ISCs, and are currently studying the molecular basis of how these genes control ISC homeostasis.

(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. Nakanishi Y, Taku Sato, and Toshiaki Ohteki. Commensal gram-positive bacteria initiate colitis by inducing monocyte/macrophage mobilization Mucosal Immunology. 2015; 8; 152-160
2. Kobayashi H, Kobayashi CI, Nakamura-Ishizu A, Karigane D, Haeno H, Yamamoto KN, Sato T, Ohteki T, Hayakawa Y, Barber GN, Kurokawa M, Suda T, and Takubo K. Bacterial c-di-GMP affects hematopoietic stem/progenitors and their niches through STING. Cell Reports. 2015; 111; 71-84

3. Liu J, Guo YM, Onai N, Ohyagi H, Hirokawa M, Takahashi N, Tagawa H, Ubukawa K, Kobayahi I, Tezuka H, Minamiya Y, Ohteki T, and Sawada K . Cytosine-phosphorothionate- guanine oligodeoxynucleotides exacerbates hemophagocytosis by inducing tumor necrosis factor- α production in mice after bone marrow transplanation. Biol Blood Marrow Transplant 2015 Epub ahead of print. 2015;

[Conference Activities & Talks]

1. Ohteki T. Identification of mononuclear phagocyte progenitors. The 44th Annual Meeting of the Japanese Society for Immunology 2015.11.18 Sapporo

Pathological Cell Biology

Professor : Shigeomi SHIMIZU
Associate Professor : Norio SHIMIZU
Junior Associate Professor : Satoko ARAKAWA
Tokunin Junior Associate Professor : Masatsune TSUJIOKA, Satoshi TORII
Assistant Professor : Shinya HONDA, Hirofumi YAMAGUCHI
Tokunin Assistant Professor : Michiko MUROHASHI, Minkyon SHIN,
Nobuhiro Fujikake, Ken WATANABE
Postdoctoral fellow (PD1) : Go Yoshida
Secretary : Hitomi Fukabori, Mari NOGUCHI, Kayo HATTANDA
Research Assistant : Ikuyo YOSHINO, Kyoko TSUJIMURA,
Mariko SUNADA, Hajime SAKURAI
Graduate Student : Yuna SUGIMOTO, Toyokazu SEKI, Saori NOGUCHI,
Yuta GOTO, Miyuki NAKAI, Hatuki ENDO,
Hajime MOCHIDUKI, Masahiro KAWATA ,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. S. Yoshida, Y. Sugimura, Y. Hazama, Y. Nishiyama, T. Yano, S. Shimizu, T. Hosoya. . A mild and facile synthesis of aryl and alkenyl sulfides via copper-catalyzed deborylthiolation of organoborons with thiosulfonates. *Chemical Commun.* 2015; 51; 16613-16616
2. S. Arakawa, I. Nakanomyo, Y. Kudo-Sakamoto, H. Akazawa, I. Komuro, S. Shimizu.. Identification of a novel compound that inhibits both mitochondria-mediated necrosis and apoptosis. *Biochem. Biophys. Res. Commun.* 2015; 467; 1006-1011
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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 provides general care for common pediatric diseases. On the other hand, we also provides advanced therapeutic intervention for hematology-Oncology, immunology, cardiology, neurology, endocrinology, nephrology, neonatology, allergy and rheumatology. Our mission is not only providing clinical care for children, to save the children who suffered an intractable diseases through development of novel therapeutic approach based on basic research for global life sciences.

(2) Research

We are interested in a broad spectrum of subjects in life science field as shown below.

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. Elucidation of pathogenesis in glomerulosclerosis formation and mechanism in podocyte
8. Research of infectivity in patients with refractory nephrotic syndrome
9. Identification of responsible genes for Galloway-Mowat syndrome
10. Molecular mechanisms of primary pulmonary hypertension
11. Lung injury induced by cytokines/monocytes/granulocytes
12. Pathogenesis of periventricular leukomalacia and bronchopulmonary dysplasia
13. Elucidating the molecular mechanisms of gonadal development
14. Molecular pathology of congenital adrenal diseases and disorder of sex development

15. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
16. ATM dependent cellular differentiation
17. Neural diseases based on defective DNA damage response
18. Investigation of molecule marker determine the prognosis of infant leukemia
19. Development of therapeutic strategy targeting homologous recombination repair
20. Genetic background of leukemia development

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Science, Hiroshima University, Istitute 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 leadership 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. Hierarchy of leukemic stem cell from infantile leukemia mice has been analyzing using NOG SCID mice collaborated with RIKEN. In addition to leukemic stem cell research, comprehensive genome research has been conducted. These research will be lead to identification of novel therapeutic approach for pediatric leukemia.

● Cardiology Group

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. We are currently researching for these themes as follows.

One theme was “The effect of Dexmedetomidine for PH” Dr. Yusuke Kajikawa, a 2nd grader of postgraduate course, has continued this research since 2014 by using Dexmedetomidine (DEX) administration for monocrotaline (MCT)-induced PH rat model under Dr. Doi, Hosokawa and another cardiologist. DEX which was started to subcutaneously drip infused on 14th day after MCT injection at the rate of 2 μ g/kg/hr by the osmotic pump apparently improved the survival curve, RV pressure overload, and medial hypertrophy of pulmonary arterioles. We speculate that β arrestin 1, which binds to G protein coupled receptors, regulates NF- κ B expression, that is inhibition of inflammatory signal transduction, that leads to improvement of pulmonary arterial smooth muscle cell proliferation (PASMC). We are now under investigation for this hypothesis. This year, he gave presentations about these results at some conferences of the 21th Japanese Society of Pediatric Pulmonary Circulation, the 79th Japanese Circulation Society, and American Heart Association Scientific Sessions 2015.

Another theme was “The synergistic effects of Incretin-related drugs (DPP-4 inhibitor and GLP-1 receptor

agonist)” Dr. Hosokawa, an assistant professor, is now focusing on that alogliptin (DPP-4 inhibitor) and liraglutide (GLP-1 receptor agonist), both of which are for diabetes mellitus type 2, have the various kinds of positive effects on cardiovascular system. When we administered these agents to MCT-induced PH rat model, the survival rate, hemodynamic results, and histological findings were the best in both of agents group compared to those of each agent group. We speculate two mechanisms of action. One is that DPP-4 (CD26) acts as a co-stimulator of T lymphocyte, that involves PASMC proliferation, and another is that GLP-1 receptor stimulation has an action of pulmonary vasodilation. So we are also now investigation for this hypothesis. In addition, he gave a presentation at a symposium of conference of 79th Japanese Circulation Society. As the clinical research, we were engaged in four multi-center-associated clinical studies. All of them were related to The Japanese Society of Pediatric Cardiology and Cardiac Surgery. These themes were “Clinical backgrounds of Eisenmenger syndrome”, “Research of screening and management strategy for Long QT syndrome”, “Efficacy of school-based heart examination in early detection of idiopathic pulmonary arterial hypertension” and “Research for protection of RSV infection in patients with congenital heart disease by palivizumab (Genetical Recombination) in Japan”. We were also engaged in “Research for social background of heart transplantation in children” and “Research for establishment of guideline on clinical diagnosis of pediatric cardiomyopathy” in Grants-in Aid for Scientific Research of Ministry of Health, Labour and Welfare

● Neurology Group

- 1) Genetic background of epileptic encephalopathy and intractable epilepsy
- 2) Efficacy and safety of very-low-dose betamethasone therapy in ataxia telangiectasia

● Endocrinology Group

Currently, our research is focused on elucidating the molecular mechanisms of congenital diseases of endocrine organs, especially adrenal glands and gonads. Our ultimate goal is developing the radical treatment systems for the congenital endocrine diseases by using regenerative medicine.

Our current projects are bellows

#1: Molecular mechanisms of gonadal development

We are trying to elucidate molecular mechanisms of gonadal development. Especially, we are focusing on elucidating epigenetic network of gonadal development and gonadal cell differentiation. We are also trying to clarify the precise function of transcription factors, such as Sfl, Foxl2 and Sox9.

In collaborating with M. Kanai (Department of Experimental Animal Model for Human Disease), Syuji 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, including making genetic modified mice.

#2: Molecular pathological mechanisms in congenital adrenal hyperplasia.

Congenital adrenal hyperplasia is one of the disorder of sex development (DSD), and now we are treating more than 40 patients.

Including the relationships between genotype and phenotype, the molecular mechanisms of the disease has not been clarified yet. Including functional analysis of novel mutations of the steroidogenic enzymes, we are trying to elucidate the pathology of the disease.

#3: Elucidating the mechanisms of congenital disorder of endocrine organs

We also try to elucidate the molecular mechanisms of congenital disorder of endocrine organs. Understanding the molecular pathology of the diseases will be beneficial to develop innovative treatment of the diseases.

Current ongoing projects will be integrated systematically further, and will be applicable to develop innovative treatment of congenital endocrine disorder, including regenerative medicine.

● Nephrology Group

We are conducting research to elucidate the pathogenesis of glomerulosclerosis formation and function of podocyte, and we are focusing on research about infectivity in patients with refractory nephrotic syndrome. Another aim of our research is to identify responsible genes of Galloway-Mowat syndrome and congenital arterial hypoplasia.

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

To elucidate molecular mechanisms for food allergy such as against milk and egg is one of the main projects of our group. In the light of recent progress of immunology, we analyze the function of regulatory T cells which inhibit Th2 type immune response. We also define the roles of innate immune responses in host defense against foreign antigens entering skin and mucosal tissues. Clinical and epidemiological study on food allergy is another major field in our study. We conduct clinical studies of specific oral tolerance induction in food allergy in which the offending food is administered orally in order to achieve tolerance. In collaboration with the Japanese Society of Pediatric Allergy and Clinical Immunology, we conduct several clinical studies to refine pharmacologic therapy listed in the Japanese pediatric guideline for the treatment and management of asthma.

(3) Education

New curriculum which has been introduced since 2011 was expanded up to the 5th graders in 2015. Systematic lectures for the 3rd and the first 2 months of the 4th graders of medical students was called “Bloc Lecture” and performed together with pediatrics, obstetrics and gynecology as “Reproduction and Development” bloc. The “Bloc 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, two cases including congenital heart disease and hybrid with delivery and neonatology, and two team based learning (TBL). Moreover, we also took charge of several lectures in the another blocs, for example six lectures related to pediatric cardiology in “Cardiology” bloc, four lectures related to pediatric oncology in “Oncology and Malignancy” bloc, one lecture related to pediatric pulmonology in “Pulmonology” bloc, and three lectures related to pediatric infection in “Infection and Clinics” bloc. Total 46 systematic lectures were almost produced by the staffs of Department of Pediatrics and Developmental Biology, and Department of Pediatrics, Perinatal and Maternal Medicine except a couple of lectures by the part-time lecturers.

Opportunity of training in scientific research, so-called project semester, was provided for the 4th graders during June to November. No student was engaged in the pediatric research in 2015. 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. 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 the last year.

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 4 staffs, including 4 senior with diplomate of board of pediatrics, hematology, and/or pediatric hematology/oncology and 3 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 Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG), 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. Hematopoietic stem cell transplantation (HSCT): In 2015, we performed HSCT for 9 cases; related bone marrow transplantation (BMT) (n=3) (including 2 haploid identical or non sibling donor source), unrelated BMT (n=1), unrelated cord blood transplantation (n=4). All 9cases were for PID patients. Our experience of HSCT exceeds 162 cases including more than 59 cases with primary immunodeficiency diseases, so far. We are also working on novel HSCT 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. Efficacy of betamethasone for ataxia telangiectasia (A-T). HSCT 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 our University affiliated hospitals, there were 16 Board Certified Pediatric Cardiologists. Last year there were four full-time doctors, one Board Certified Pediatric Cardiologist (Doi S, MD, PhD) and four pre-Board Certified Pediatric Cardiologists (Hosokawa S, MD, PhD, Yamaguchi Y, MD, Takei A, MD and Nagashima A, MD) in The University Hospital, who were engaged in the diagnosis and treatment for every kinds 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. Takei actually worked as a staff of pediatric cardiovascular surgery.

The hospitalization number of patients was 134, an increase of 40% compared to the year before the last and the average length of hospital stay was 8.2 days, which was excluded only two end stage patients. Admitted

patients were increased chiefly because patients with congenital heart disease (CHD) were regularly admitted in for operation (18 patients were performed surgery) and patients with pulmonary hypertension (PH) were gradually increased to be admitted. The diseases of admitted patients were 78 CHD, acquired heart diseases such as 20 PH, 18 cardiac arrhythmias, 17 Kawasaki diseases (KD), and several another diseases. 59 cardiac catheterizations were performed, which contained 42 CHD, 9 PH, 6 KD and 2 cardiac arrhythmias. Catheter interventions were performed on two patients, one was pulmonary valve stenosis and another was WPW syndrome.

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 9-year-old boy who was the first child patient 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, 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 acute and chronic glomerular diseases, nephrotic syndrome, chronic kidney disease, congenital abnormality of kidney and urinary tract, and acute kidney injury that requires acute blood purification. We perform kidney biopsy and imaging examination for diagnosis. 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, etc., and 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 in Tokyo Medical and Dental University Hospital Faculty of Medicine. Group conference is held on 4th Thursday every month to discuss 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, which provide us 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 and Development and Tokyo Women's Medical Hospital 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 standard medical service following clinical guidelines for allergic diseases but highly advanced treatment is provided.

We conduct public educational activities about allergic diseases, organizing specific lecture meetings in cooperation with local public health center 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.

We have started treatment for children with pediatric rheumatic diseases with cooperation of Department of Rheumatology.

● 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 inducing 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. Kentaro Miyai, Toshikazu Onishi, Kenichi Kashimada, Yukihiro Hasegawa. Urinary calcium to creatinine ratio: a potential marker of secondary hyperparathyroidism in patients with vitamin D-dependent rickets type 1A. *Endocr. J.* 2015; 62(1); 61-68
2. Tomohito Takimoto, Hidetoshi Takada, Masataka Ishimura, Makiko Kirino, Kenichiro Hata, Osamu Ohara, Tomohiro Morio, Toshiro Hara. Wiskott-Aldrich Syndrome in a Girl Caused by Heterozygous WASP Mutation and Extremely Skewed X-Chromosome Inactivation: A Novel Association with Maternal Uniparental Isodisomy 6. *Neonatology*. 2015; 107(3); 185-190
3. Kenichi Kashimada, Tomohiro Ishii, Keisuke Nagasaki, Makoto Ono, Toshihiro Tajima, Ichiro Yokota, Yukihiro Hasegawa. Clinical, biochemical, and genetic features of non-classical 21-hydroxylase deficiency in Japanese children. *Endocr. J.* 2015; 62(3); 277-282
4. Nishida N, Yang X, Takasaki I, Imai K, Kato K, Inoue Y, Imamura T, Miyashita R, Kato F, Yamaide A, Mori M, Saito S, Hara J, Adachi Y, Miyawaki T, Kanegane H.. Dysgammaglobulinemia Associated With Glu349del, a Hypomorphic XIAP Mutation. *J Investig Allergol Clin Immunol*. 2015; 25(3); 205-213
5. Rebound Thymic Hyperplasia after chemotherapy in a patient with Hodgkin's lymphoma.- Case report and a literature review of PET/CT - 2015.01; 68(1); 131-136
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[Conference Activities & Talks]

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5. epilepsy in acute lymphoblastic leukemia. The 118th Annual Meeting of the Japan Pediatric Society 2015.04.18 Osaka
6. Ataxia Telangiectasia patient with intractable Cytomegalovirus encephalitis. The 118th Annual Meeting of the Japan Pediatric Society 2015.04.19 Osaka
7. Hirokazu Kanegane. XLP (X-linked lympho proliferative syndrome) and Epstein-Barr virus infection.. V Simpósio Internacional de Immunodeficiências Primárias—SIDEP, 5 2015.05.20
8. Yuji Sugawara. Child neurology training in Italy. The 59th Annual Meeting of the Japanese Society of Child Neurology 2015.05.29 Osaka
9. Kenichi Kashimada, Yohei Matsubara, Tomoko Kato, Takashi Nakasuji, Hiromitsu Tanaka, Zhou Zhi, Shizuko Ichinose, Tomoki Chiba, Yoshiaki Ito, Yumiko Saga, Tomohiro Morio, Shuji Takada, Hiroshi Asahara. TALEN-Mediated Gene Disruption on Y Chromosome Reveals Critical Role of EIF2S3Y in Mouse Spermatogenesis. Germinal Stem Cell Biology, Gordon Research Conference 2015.05.31
10. Ryuichi Nakagawa, Atsumi Tsuji, Yuki Aoki, Keisuke Nakajima, Akito Sutani, Yuichi Miyakawa, Kei Takazawa, Daisuke Tomizawa, Masatoshi Takagi, Kenichi Kashimada, Tomohiro Morio. Total-Body Irradiation is a major risk factor for young adult onset diabetes mellitus and hyperlipidemia i childhood cancer survivors after hematopoietic stem cell transplantation. ESPE 2015.10.01 Barcelona

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12. Masatoshi Takagi. ATM regulates adipocyte differentiation and contributes to glucose homeostasis. 16th Ataxia Teleangiectasia Workshop 2015.10.12 Beijing
13. Taki Atsuko. Symposium 1. Contribution of university hospitals and laboratory for neonatal medicine. "Academic women working while caring for children" . The 60th Meeting of Japan Society for Neonatal Health and Development 2015.10.23 Morioka
14. Masatoshi Takagi. Cancer in Maffuci and Ollier disease. I-BFM Genetic Variation Working Group Meeting Lodz 2015 2015.10.30 Poland
15. Kajikawa Y, Hosokawa S, Wakabayashi K, Maejima Y, Isobe M, Doi S. Dexmedetomidine Ameliorates Monocrotaline Induced Pulmonary Arterial Hypertension in Rats. American Heart Association Scientific Sessions 2015 2015.11.10 Orland, USA
16. Masatoshi Takagi. Natural history of RALD or RAS mutated JMML with autoimmunity. JMML Working Group 2015.12.04 Orlando
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Rheumatology

Professor emeritus	Nobuyuki MIYASAKA
Professor	Hitoshi KOHSAKA Masayoshi HARIGAI(1) Masaaki MORI(1) Tetsuo KUBOTA(2) Kazuki TAKADA(3) Ryuji KOIKE(2)
Associate Professor	Kimito KAWAHATA Kenji NAGASAKA(1)
Junior Associate Professor	Michi Tanaka(1) Hideyuki IWAI(5)
Assistant Professor	Tetsuya SAITO, Naoki KIMURA, Tadashi HOSOYA, Yusuke MATSUO, Waka YOKOYAMA, Ryoko SAKAI(1), Shoko KASAI(4), Yoko YOSHIHASHI(3)
Visiting Lecturer	Hiroyuki HAGIYAMA, Makoto SOEJIMA, Tatsuhiko SUGIHARA, Fumihiko SUZUKI, Akito TAKAMURA, Kaori IMAI, Nobuyuki MIYASAKA, Reiko TSUBATA, Jyunko NISHIO, Toshihiro MATSUO
Graduate Student	Hisanori HASEGAWA, Fumio HIRANO, Mari KIHARA, Natsuka UMEZAWA, Masako UTSUNOMIYA, Hirokazu SASAKI, Akio YAMAMOTO, Akiko MINAMI, SHINOHARA, Yasuhiro TAGAWA, Mari KAMIYA
Resident Physician	Takeshi KUSUDA, Tatsuya KAWASAKI, Masami TOKURA, Marina TSUCHIDA, Ayaka MAEDA
Office Administrator	Rie FUJIME, Kaori KONNO, Kanako KURIMORI, Tomoko TAKAHASHI(1)
Technical Staff	Hidemi KASAHARA, Ayako SHIMADA

(1) Department of Pharmacovigilance, (2) Medical Innovation Promotion Center, (3) 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) Development of new therapeutics for the treatment of rheumatoid arthritis targeting cell cycle regulators, inflammatory molecules and synovial fibroblasts.
- 2) Investigation of mechanism and development of new therapeutics for the treatment of polymyositis.
- 3) Analysis of the roles of chemokine and bioactive lipid on the pathogenesis of rheumatic diseases.
- 4) Establishment of evidence-based treatment of rheumatic diseases by implementing several cohort studies.

(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 a large number of patients with diverse rheumatic diseases with 29,383 clinic visits and 329 hospital admissions in 2015. 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.

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

1. N Nishida, X Yang, I Takasaki, K Imai, K Kato, Y Inoue, T Imamura, R Miyashita, F Kato, A Yamaide, M Mori, S Saito, J Hara, Y Adachi, T Miyawaki, H Kanegane. Dysgammaglobulinemia Associated With Glu349del, a Hypomorphic XIAP Mutation. *J Invest Allergol Clin Immunol.* 2015; 25(3); 205-213
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37. Kimura N, Hirata S, Miyasaka N, Kawahata K, Kohsaka H. Injury and subsequent regeneration of muscles activate local innate immunity to facilitate development and relapse of autoimmune myositis *Arthritis Rheumatol.*
38. Okiyama N, Hasegawa H, Oida T, Hirata S, Yokozeiki H, Fujimoto M, Miyasaka M, Kohsaka H. Experimental myositis inducible with transfer of dendritic cells presenting a skeletal muscle C protein-derived CD8 epitope peptide *Int Immunol.*

[Misc]

1. Kenji Nagasaka. Efficacy of tocilizumab for giant cell arteritis and Takayasu arteritis *Rheumatology.* 2015.04; 53(4); 355-362
2. A novel therapeutic concept for arthritis: Cell cycle regulation therapy combined with cytokine blockade 2015.07; 33(12); 140-146
3. Naoki Kimura. Safety and effectiveness of partial blood flow restriction training in polymyositis and dermatomyositis *Rheumatology.* 2015.09; 54(3); 323-328
4. Kenji Nagasaka. Primary small and medium vessel vasculitis *Rheumatology.* 2015.09; 54(3); 287-295

[Conference Activities & Talks]

1. - Hitoshi Kohsaka.. Muscle atrophy and its prevention during treatment of myositis.. 3rd Chinese Myositis Workshop 2015.03.05 Beijing, China
2. - Hitoshi Kohsaka.. Translational medicine for complete suppression of arthritis - Combination of two distinct approaches -. Medlab Asia pacific 2015.03.22 Singapore
3. Naoki Kimura, Shinya Hirata, Nobuyuki Miyasaka, Kimito Kawahata, Hitoshi Kohsaka. Injury and subsequent regeneration of muscles activate local innate immunity to facilitate development and relapse of autoimmune myositis. The 59th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2015.04.24 Nagoya, Japan
4. Naoki Kimura, Shinya Hirata, Nobuyuki Miyasaka, Kimito Kawahata, Hitoshi Kohsaka. Injury and Subsequent Regeneration of Muscles Activate Local Innate Immunity to Facilitate Development and Relapse of Autoimmune Myositis. First International Conference on MYOSITIS 2015.05.08
5. - Hitoshi Kohsaka.. Seed and soil model for autoimmunity in myositis.. 1st International Conference on Myositis 2015.05.08 Stockholm, Sweden
6. Hitoshi Kohsaka. Seed and soil model for autoimmunity in myositis.. 1st International Conference on Myositis 2015.05.08 Stockholm, Sweden
7. Naoko Okiyama, Hisanori Hasegawa, Takamori Oida, Shinya Hirata, Hiroo Yokozeiki, Manabu Fujimoto, Nobuyuki Miyasaka, Hitoshi Kohsaka.. Experimental Myositis Inducible with Transfer of Dendritic Cells Presenting a Skeletal Muscle C protein-derived CD8 Epitope Peptide.. 1st International Conference on Myositis 2015.05.08 Stockholm, Sweden

8. Naoki Kimura, Shinya Hirata, Nobuyuki Miyasaka, Kimito Kawahata, Hitoshi Kohsaka.. Injury And Subsequent Regeneration Of Muscles Activate Local Innate Immunity To Facilitate Development And Relapse Of Autoimmune Myositis.. 1st International Conference on Myositis 2015.05.08 Stockholm, Sweden
9. Yoko Yoshihashi-Nakazato, Kimito Kawahata, Naoki Kimura, Hitoshi Kohsaka.. Interferon-gamma but not interleukin-4 restrains experimental myositis. . 1st International Conference on Myositis 2015.05.08 Stockholm, Sweden
10. F. Hirano, W. Yokoyama, H. Yamazaki, K. Amano, Y. Kaneko, A. Kawakami, T. Matsui, R. Sakai, R. Koike, N. Miyasaka, M. Harigai. SDAI REMISSION AT WEEK 24 IS A PREDICTOR OF GOOD FUNCTIONAL AND STRUCTURAL OUTCOMES AT WEEK 72 IN A T2T IMPLEMENTING COHORT. EULAR2015 2015.06.11 Rome
11. Fumitaka Mizoguchi, Kamil Slowikowski, Chamith Fonseka, Soumya Raychaudhuri and Michael B. Brenner. Understanding fibroblast heterogeneity and fibroblast-mediated pathology. Cell Circuits and Epigenomics Program Seminar. Broad Institute 2015.06.22 Cambridge, USA
12. Fumitaka Mizoguchi. Identification of Synovial Fibroblast Subsets That Define Pathology in Rheumatoid Arthritis. International RA Genetics Meeting 2015.11.07
13. Fumitaka Mizoguchi, Kamil Slowikowski, Sook Kyung Chang, Deepak A. Rao, Hung Nguyen, Erika H. Noss, Brandon E. Earp, Philip E. Blazar, John Wright, Barry P. Simmons, Nir Hacohen, Peter A. Nigrovic, Soumya Raychaudhuri and Michael B. Brenner. Identification of Synovial Fibroblast Subsets That Define Pathology in Rheumatoid Arthritis. 2015 American College of Rheumatology/ Association of Rheumatology Health Professionals Annual Meeting 2015.11.09 San Francisco, USA
14. Naoki Kimura, Kimito Kawahata, Hitoshi Kohsaka. Peripheral license for autoimmune-mediated tissue injury revealed from a murine model of polymyositis. The 44th Annual Meeting of the Japanese Society for Immunology 2015.11.20 Sapporo, Japan
15. - Hitoshi Kohsaka. Complete supression of arthritis with two distinct therapeutic approaches.. Korean Society of Synovits Research 2015 Symposium 2015.12.19 Seoul

Dermatology

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Associate Professor:Ken IGAWA

Junior Associate Professor:Takeshi NAMIKI,Takaaki HANAFUSA

Project Junior Associate Professor:Kaoru TAKAYAMA

Assistant Professor:Shoun TOKORO,Makiko UENO,Kohei NOJIMA

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(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. Kondo T, Namiki T, Coelho SG, Valencia JC, Hearing VJ.. Oculocutaneous albinism: developing novel antibodies targeting the proteins associated with OCA2 and OCA4. *J Dermatol Sci.* . 2015.01; 77(1); 21-27
2. Yamamoto T, Yokozeki H.. Scalp sarcoidosis mimicking organoid nevus. *Eur J Dermatol.* 2015.02; 25(1); 78-79
3. Yamamoto T, Yokozeki H.. Subcutaneous sarcoidal granuloma underlying porokeratosis in a patient with sarcoid-lymphoma syndrome. *Eur J Dermatol.* 2015.02; 25(1); 84-85
4. 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.* . 2015.03;
5. Igawa K, Konishi M, Moriyama Y, Fukuyama K, Yokozeki H.. Erythroderma as drug eruption induced by intravesical mitomycin C therapy. *J Eur Acad Dermatol Venereol.* . 2015.03; 29(3); 613-614
6. Tsuji G, Okiyama N, Villarroel VA, Katz SI.. Histone deacetylase 6 inhibition impairs effector CD8 T-cell functions during skin inflammation. *J Allergy Clin Immunol.* . 2015.03; 135(5); 1228-1239
7. Takayama N, Nakazono S, Kumagai J, Chiorean R, Sitaru C, Ishii N, Hashimoto T, Namiki T.. Pemphigoid gestationis with IgG autoantibodies to both the 120 kDa LAD-1 and the BP180 NC16a domain. *Eur J Dermatol.* . 2015.04; 25(2); 190-192
8. Yamamoto T, Yokozeki H.. Discoid lupus erythematosus in a patient with myasthenia gravis. *Int J Rheum Dis.* 2015.05;
9. Hashimoto T, Satoh T, Yokozeki H.. Protective Role of STAT6 in Basophil-Dependent Prurigo-like Allergic Skin Inflammation. *J Immunol.* . 2015.05; 194(10); 4631-4640
10. Namiki T, Yaguchi T, Nakamura K, Valencia JC, Coelho SG, Yin L, Kawaguchi M, Vieira WD, Kaneko Y, Tanemura A, Katayama I, Yokozeki H, Kawakami Y, Hearing VJ.. NUAKE2 Amplification Coupled with PTEN Deficiency Promotes Melanoma Development via CDK Activation. *Cancer Res.* 2015.06; 75(13); 2708-2715
11. Okiyama N, Hasegawa H, Oida T, Hirata S, Yokozeki H, Fujimoto M, Miyasaka N, Kohsaka H. . Experimental myositis inducible with transfer of dendritic cells presenting a skeletal muscle C protein-derived CD8 epitope peptide. *Int Immunol.* . 2015.07; 27(7); 327-332
12. Ugajin T, Nishida K, Yamasaki S, Suzuki J, Mita M, Kubo M, Yokozeki H, Hirano T.. Zinc-binding metallothioneins are key modulators of IL-4 production by basophils. *Mol Immunol.* . 2015.08; 66(2); 180-188
13. Arima Y, Namiki T, Kato K, Ueno M, Iikawa M, Tokoro S, Takayama K, Miura K, Yokozeki H.. Pigmented squamous cell carcinoma of the cheek and its dermoscopic features. *J Dermatol.* . 2015.09; 42(9); 918-920
14. Arima Y, Namiki T, Kato K, Tokoro S, Takayama K, Yokozeki H.. Case of extensive pyoderma gangrenosum with a neutrophilic leukemoid reaction. *J Dermatol.* 2015.10;
15. Arima Y, Namiki T, Ueno M, Kato K, Tokoro S, Takayama K, Miura K, Yokozeki H.. Histiocytoid sweet syndrome: a novel association with relapsing polychondritis. *Br J Dermatol.* . 2015.10;
16. Inoue-Nishimoto T, Hanafusa T, Igawa K, Azukizawa H, Yokomi A, Yokozeki H, Katayama I.. Possible association of anti-tumor necrosis factor- α antibody therapy with the development of scleroderma-like changes with lichen planus. *Eur J Dermatol.* . 2015.10; 25(5); 513-515
17. Ugajin T, Takahashi M, Miyagishi C, Takayama K, Yokozeki H.. A case of bullous pemphigoid associated with infiltration and activation of basophils. *Br J Dermatol.* . 2015.10; 173(4); 1095-1098
18. Kato K, Igawa K, Nishizawa A, Takayama K, Yokozeki H.. Allergic contact dermatitis induced by the anionic surfactant, sodium N-methyl-N-(1-oxododecyl)-beta-alaninate, contained in a daily-use shampoo. *J Eur Acad Dermatol Venereol.* . 2015.11;

19. Namiki T, Miura K, Yokozeki H.. Multiple CD163(+) adult xanthogranuloma associated with myelodysplastic syndrome. *J Dermatol.* 2015.11; 42(11); 1106-1107
20. Iikawa M, Namiki T, Arima Y, Kato K, Arai M, Ueno M, Tokoro S, Miura K, Yokozeki H.. Extraocular sebaceous carcinoma in association with a clonal seborrheic keratosis: Dermoscopic features. *J Dermatol.* . 2015.11; 42(11); 1105-1106
21. 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.* 2015.12;
22. Tokoro S, Igawa K, Yokozeki H.. Herpes zoster ophthalmicus with severe ocular complications. *J Dermatol.* . 2015.12; 42(12); 1207-1208
23. Tokoro S, Namiki T, Ueno M, Sone Y, Kato K, Miura K, Yokozeki H.. Angiolymphoid hyperplasia with eosinophilia of the head arising within the aponeurosis. *J Dermatol.* . 2015.12; 42(12); 1190-1191

NCCHD Child Health and Development

Collaborative Professor	Akutsu, Hidenori
Collaborative Professor	Onodera, Masashi
Collaborative Professor	Fukami, Maki
Collaborative Professor	Hata, Kenichiro
Collaborative Professor	Takada, Shuji
Collaborative Professor	Yamauchi, Junji

(1) Research

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 neurological disease mechanism and target molecules using molecular biology and tissue engineering

(Yamauchi, Junji; Dept. of Pharmacology, National Institute for Child Health and Development)

We focus on middle embryonic-to-neonatal neuronal developmental stages and specially study glial development. Many genetic neuropathies are known to be glial dystrophies, which involve dysmyelinating/demyelinating diseases. We believe that knowing how glial cells develop is tightly related to clarifying how

glial neuropathies occur. These studies will allow us to present novel drug-target-molecules for neuropathies, as well as to provide paradigm of neuronal regeneration.

(2) 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) Publications

[Original Articles]

1. Akutsua H, Machida M, Kanzaki S, Sugawara T, Ohkura T, Nakamura N, Yamazaki-Inoue M, Miura T, Vemurib MC, Rao MS, Miyado K, Umezawa A. Xenogeneic-free defined conditions for derivation and expansion of human embryonic stem cells with mesenchymal stem cells. *Regenerative Therapy*. 1:18-29, 2015.
2. Fukuda A, Tanino M, Matoba R, Umezawa A, Akutsu H*. Imbalance between the expression dosages of X-chromosome and autosomal genes in mammalian oocytes. *Sci Rep*. 5:14101, 2015.
3. Miura T, Sugawara T, Fukuda A, Tamoto R, Kawasaki T, Umezawa A, Akutsu H*. Generation of primitive neural stem cells from human fibroblasts using a defined set of factors. *Biol Open*. 4(11):1595-607, 2015.
4. Mizuno H, Akutsu H, Kato K. Ethical acceptability of research on human-animal chimeric embryos: summary of opinions by the Japanese Expert Panel on Bioethics. *Life Sci Soc Policy*. 11(1):15, 2015.
5. Fukuda A, Mitani A, Miyashita T, Umezawa A, Akutsu H*. Chromatin condensation of Xist genomic loci during oogenesis in mice. *Development*. 142(23):4049-55, 2015.
6. Kagami M, Mizuno S, Matsubara K, Nakabayashi K, Sano S , Fuke T, Fukami M , Ogata T. Epimutations of the IG-DMR and the MEG3-DMR at the 14q32.2 imprinted region in two patients with Silver-Russell syndrome-compatible phenotype. *Eur J Hum Genet* 23(8):1062-1067, 2015
7. Izumi Y, Musha I, Suzuki E, Iso M, Jinno T, Horikawa R, Amemiya S, Ogata T, Fukami M, Ohtake A. Hypogonadotropic hypogonadism in a female patient previously diagnosed as having Waardenburg syndrome due to a SOX10 mutation. *Endocrine*. 49(2): 553–556, 2015
8. Nakashima S, Kato F, Kosho T, Nagasaki K, Kikuchi T, Kagami M, Fukami M, Ogata T. Silver-Russell syndrome without body asymmetry in three patients with duplications of maternally derived chromosome 11p15 involving CDKN1C. *J Hum Genet*. 60(2): 91–95, 2015
9. Saito K, Miyado M, Kobori Y, Tanaka Y, Ishikawa H, Yoshida A, Katsumi M, Saito H, Kubota T, Okada H, Ogata T, Fukami M. Copy-Number Variations in Y Chromosomal Azoospermia Factor Regions Identified by Multiplex Ligation-Dependent Probe Amplification. *J Hum Genet*. 60(3): 127–131, 2015
10. Igarashi M, Wada Y, Kojima Y, Miyado M, Nakamura M, Muroya K, Mizuno K, Hayashi Y, Nonomura K, Kohri K, Ogata T, Fukami M. Novel Splice Site Mutation in MAMLD1 in a Patient with Hypospadias. *Sex Dev*. 9(3): 130-135 2015
11. Kon M, Suzuki E, Dung VC, Hasegawa Y, Mitsui T, Muroya K, Ueoka K, Igarashi N, Nagasaki K, Oto Y, Hamajima T, Yoshino K, Igarashi M, Kato-Fukui Y, Nakabayashi K, Hayashi K, Hata K, Matsubara Y, Moriya K, Ogata T, Nonomura K, Fukami M. Molecular basis of non-syndromic hypospadias: Systematic mutation screening and genome-wide copy-number analysis of 62 patients. *Hum Reprod*. 30(3): 499–506, 2015
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[Review Articles]

1. Kon M, Fukami M. Submicroscopic copy-number variations associated with 46,XY disorders of sex development *Mol Cell Pediatr*. 2(1):7, 2015
2. Tomohiro Torii, and Junji Yamauchi*. A new signalsome containing cytohesin-2 and CCDC120 controls neurite outgrowth. *Med. Res. Arch*. 2(11): 19, 2015

Human Pathology

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(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. 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.* 2015; (in press);
2. Kana Minegishi, Takayasu Watanabe, Asuka Furukawa, Keisuke Uchida, Yoshimi Suzuki, Takumi Akashi, Fumito Maruyama, Ichiro Nakagawa, Yoshinobu Eishi. Genetic profiles of *Propionibacterium acnes* and identification of a unique transposon with novel insertion sequences in sarcoid and non-sarcoid isolates. *Sci Rep.* 2015; 5; 9832
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8. Ichiro Yamada, Naoyuki Miyasaka, Keigo Hikishima, Keiji Kato, Kazuyuki Kojima, Tatsuyuki Kawano, Eisaku Ito, Daisuke Kobayashi, Yoshinobu Eishi, Hideyuki Okano. Gastric Carcinoma: Ex Vivo MR Imaging at 7.0 T-Correlation with Histopathologic Findings. *Radiology*. 2015.06; 275(3); 841-848
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10. Pariko Yoroazu, Asuka Furukawa, Keisuke Uchida, Takumi Akashi, Tomoya Kakegawa, Tomohisa Ogawa, Junko Minami, Yoshimi Suzuki, Nobuyasu Awano, Haruhiko Furusawa, Yasunari Miyazaki, Naohiko Inase, Yoshinobu Eishi. Propionibacterium acnes catalase induces increased Th1 immune response in sarcoidosis patients. *Respir Investig*. 2015.07; 53(4); 161-169
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13. Yoshimitsu Akiyama, Yuki Koda, Sun-Ju Byeon, Shu Shimada, Taketo Nishikawaji, Ayuna Sakamoto, Yingxuan Chen, Kazuyuki Kojima, Tatsuyuki Kawano, Yoshinobu Eishi, Dajun Deng, Woo Ho Kim, Wei-Guo Zhu, Yasuhito Yuasa, Shinji Tanaka. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. *Oncotarget*. 2015.12;

[Conference Activities & Talks]

1. Yoshinobu Eishi. Screening for early gastric cancer. 46th World Congress of Surgery 2015.08.25 Bangkok, Thailand

Physiology and Cell Biology

Professor: Shu Takeda

Assistant professor: Toru Fukuda

Assistant professor: Shingo Sato

Assistant professor: Hiroki Ochi

(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.

(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. Wataru Suzuki, Atsushi Yamada, Ryo Aizawa, Dai Suzuki, Hidetoshi Kassai, Takeshi Harada, Mutsuko Nakayama, Ryo Nagahama, Koutaro Maki, Shu Takeda, Matsuo Yamamoto, Atsu Aiba, Kazuyoshi Baba, Ryutaro Kamijo. Cdc42 is critical for cartilage development during endochondral ossification. *Endocrinology*. 2015.01; 156(1); 314-322
2. Makoto Hirata, Shingo Sato, Jay S Wunder, Tak W. Mak, Benjamin A. Alman, etc.. Mutant IDH1 is sufficient to initiate enchondromatosis in mice *Proc Natl Acad Sci USA*. 2015.03; 112(9); 2829-2834
3. Chengshan Ma, Toru Fukuda, Hiroki Ochi, Satoko Sunamura, Cheng Xu, Ren Xu, Atsushi Okawa, Shu Takeda. Genetic determination of the cellular basis of the ghrelin-dependent bone remodeling. *Mol Metab*. 2015.03; 4(3); 175-185
4. Omri Bauer, Amnon Sharir, Ayako Kimura, Shay Hantisteanu, Shu Takeda, Yoram Groner. Loss of osteoblast runx3 produces severe congenital osteopenia. *Mol. Cell. Biol.*. 2015.04; 35(7); 1097-1109
5. A Sato, H Ochi, Y Harada, T Yogo, N Kanno, Y Hara. Bone morphogenetic protein 4 and bone morphogenetic protein receptor expression in the pituitary gland of adult dogs in healthy condition and with ACTH-secreting pituitary adenoma. *Domest. Anim. Endocrinol.*. 2015.09;
6. Toru Fukuda, Hiroki Ochi, Satoko Sunamura, Akina Haiden, Waka Bando, Hiroyuki Inose, Atsushi Okawa, Yoshinori Asou, Shu Takeda. MicroRNA-145 regulates osteoblastic differentiation by targeting the transcription factor Cbfb. *FEBS Lett.*. 2015.10; 589(21); 3302-3308
7. Hiroyuki Akagi, Hiroki Ochi, Satoshi Soeta, Nobuo Kanno, Megumi Yoshihara, Kenshi Okazaki, Takuya Yogo, Yasuji Harada, Hajime Amasaki, Yasushi Hara. A Comparison of the Process of Remodeling of Hydroxyapatite/Poly-D/L-Lactide and Beta-Tricalcium Phosphate in a Loading Site. *Biomed Res Int*. 2015.10; 2015; 730105
8. Qingxia Wei, Yuning J Tang, Veronique Voisin, Shingo Sato, Makoto Hirata, Heather Whetstone, Ilkyu Han, Laurie Ailles, Gary D Bader, Jay Wunder, Benjamin A Alman. Identification of CD146 as a marker enriched for tumor-propagating capacity reveals targetable pathways in primary human sarcoma *Oncotarget*. 2015.11; 6(37); 40283-40294

[Misc]

1. Ochi H, Takeda S.. The Two Sides of Vitamin E Supplementation. *Gerontology*. 2015; 61(4); 319-26
2. Leptin 2015.05; 98-99

[Conference Activities & Talks]

1. Shingo Sato, Qingxia Wei, Makoto Hirata, Yuning Tang, Shu Takeda, Jay S. Wunder, Benjamin Alman. Microarray and RNA sequencing analysis of pericyte-derived sarcomas in a novel sarcoma mouse model. Orthopaedic Research Society Annual Meeting 2015 2015.03.28 Las Vegas, USA
2. Shu Takeda. Regulation of bone remodelling by semaphorins and sensory innervations. 4th Joint Meeting of ECTS and IBMS 2015.04.27 Rotterdam, The Netherlands
3. Shu Takeda. Vitamin E and bone. 2015 SICEM 2015.05.01 Seoul, Korea
4. Sato S, Sawamura C, Matsumoto S, Takeda S, Okawa A. Establishment of medical and dental combined treatment system for cancer patients with bone metastasis. The 48th Annual Musculoskeletal Tumor Meeting of the Japanese Orthopaedic Association 2015.07.10 Takamatsu

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
D3	Peng Zhang
D3	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. Gender-specific medicine (GSM) for cardiovascular diseases

In the past few years, we have shown that non-genomic regulation of cardiac ion channels by sex hormones underlies, at least in part, gender difference in cardiac electrophysiology, and thus susceptibility to arrhythmias. This year, we used FRET imaging and LC/MS technology to show that non-genomic regulation of cardiac ion channels by sex hormones cross-talks with β -adrenergic receptor signaling specifically in the raft micro-domain.

2. Pathogenesis of atrial fibrillation (AF)

Atrial fibrillation (AF) is the most frequent arrhythmias, reaching more than 1 million patients in Japan. Associated cerebral infarction due to cardiogenic thrombosis (250,000 patients /year in Japan) and higher incidence of cognitive impairment cause reduced QOL and are main causes of bedridden old people. Thus, establishment of therapeutic strategy for AF is an urgent requirement.

(1) GWAS for AF

We had carried out most extensive GWAS (genome-wide association study) in Japan to determine gene polymorphisms associated with AF. Since 2011, we have participated in the international Meta-analysis called as CHARGE study. CHARGE study found 10 SNPs associated with AF: among them, 6 SNPs were associated with both European/American and Japanese, and 4 with European/American but not with Japanese.

(2) Functional analysis of AF associated genes

One of the sales-points of GWAS is the identification of novel pathogenic pathways and therapeutic targets due

to its comprehensibility. We carried out functional analysis for 6 genes associated with Japanese AF patients, and found a novel pathway generating abnormal automaticity in the pulmonary vein myocardium, which is the main triggering factor of atrial fibrillation.

(3) Risk stratification

Another sales-point of GWAS is the risk stratification of the diseases and its use for future personalized medicine. Based on GWAS data, we calculated AF risk score and classified them into 4 quartile groups. The highest risk group has 5.5 higher risk of AF development relative to the lowest risk group (left panel in Figure 1). The risk stratification yielded around 60% sensitivity and specificity (right panel in Figure 1), which are not enough for personalized medicine, and further studies to increase odds ratio are needed.

(4) Micro-RNAs in AF pathogenesis

Micro-RNAs have been implicated for pathogenesis of various diseases, including AF. We have been searching micro-RNAs involved in AF pathogenesis in AF mouse model and those acting as a bio-marker for AF development and progress in human circulating micro-RNAs. We found in mouse model that mir-27b was induced by dyslipidemia, one of the AF risk factor, and caused electrical remodeling in atrial muscle.

3. Pathogenesis of ventricular fibrillation (VF) and sudden cardiac death

Despite extensive effort by many researchers for years, VF remains the main cause of sudden death, and the biggest challenge in arrhythmia research. Last year, we showed that genetic deletion of the His-Purkinje system-specific transcription factor in mice exhibited exercise-related ventricular tachyarrhythmias. This year, we searched for genetic disturbance of this transcription factor in patients with idiopathic VF, and found that the mutations of this factor are responsible for idiopathic VF, and a common variant is a modifier of causative gene mutations for idiopathic VF.

4. Pannexin as a mechano-sensor of the heart

Heart is unique in the way that it is under mechano-stimuli for 24 hours and for 365 days. Inappropriate response to mechano-stimuli results in cardiovascular diseases, such as heart failure and cardiac hypertrophy. Thus, it is important to understand the mechano-sensor of the heart, yet it was not been well-described until recently. It has been proposed that pannexin, a type of gap-junction channel, is one of the mechano-sensor in the heart. Thus, we have been studying the role of pannexin as a mechano-sensor of the heart and its relation to cardiac pathology. Our data suggest that pannexin-1 provides a protective mechanism against acute pressure overload.

5. Use of iPS cells for arrhythmia research

In the past few years, we have aimed to use human iPS-derived cardiomyocytes (hiPS-CMs) for drug screening. hiPS-CMs include various types of cardiomyocytes, such as atrial, ventricular, and nodal types of cardiomyocytes, and exhibit relatively immature electrophysiological properties of cardiac cells, hindering high-quality drug screening. In order to generate mature ventricular-like hiPS-CMs, we over-expressed a gene into hiPS-CMs. The genetically-altered hiPS-CMs exhibited mature forms of action potentials and drug sensitivity. Our novel technique would be useful for evaluation of drug-induced alternation of repolarization processes in the human cardiomyocytes.

6. Use of state-of-art technology for cardiovascular research

(1) Use of motion vector technology for in vitro analysis of cardiac contraction

Motion vector technology created by Sony Co. (Dr. Matsui E. et al.) is the in vitro system to assay non-invasively contraction and relaxation speed of cardiac myocytes. We have tried to broaden its application to screening of cardiac toxicity of drugs. This year, we applied to examine cardiac toxicity of anti-cancer drugs.

(2) Use of 3-D cardiac simulator (UT-heart) for screening of cardiac toxicity of drugs

Prof. Hisada T. et al. in the University of Tokyo have developed 3-D cardiac simulator (UT-heart). We have tried to broaden its application to screening of cardiac toxicity of drugs. This year, we examined 10 standard drugs (high risk, intermediate risk, and no risk).

(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. Junko Kurokawa, Tetsuo Sasano, Masami Kodama, Min Li, Yusuke Ebana, Nobuhiro Harada, Shin-ichiro Honda, Haruaki Nakaya, Tetsushi Furukawa. Aromatase knockout mice reveal an impact of estrogen on drug-induced alternation of murine electrocardiography parameters. *J Toxicol Sci.* 2015; 40(3); 339-348
2. Mihoko Kawabata, Yasuhiro Yokoyama, Takeshi Sasaki, Susumu Tao, Kensuke Ihara, Yasuhiro Shirai, Tetsuo Sasano, Masahiko Goya, Tetsushi Furukawa, Mitsuaki Isobe, Kenzo Hirao. Severe iatrogenic bradycardia related to the combined use of beta-blocking agents and sodium channel blockers. *Clin Pharmacol.* 2015; 7; 29-36
3. Yusuke Ebana, Tetsushi Furukawa. Atrial fibrillation associated genes identified through genome-wide screening analysis - A review from viewpoints of bioinformatics, basic science, and clinical study - *CARDIOANGIOLOGY.* 2015.04; 77(4); 371-378
4. 2. Okada J, Yoshinaga T, Kurokawa J, Washio T, Furukawa T, Sawada K, Sugiura S, Hisada T. Screening system for drug-induced arrhythmogenic risk combining a patch clamp and heart simulator *Science Advance.* 2015.05; 1; e1400142
5. Saito Y, Nakamura K, Yoshida M, Sugiyama H, Ohe T, Kurokawa J, Furukawa T, Takano M, Nagase S, Morita H, Kusano KF, Ito H. Enhancement of spontaneous activity by HCN4 overexpression in mouse embryonic stem cell-derived cardiomyocytes – A possible biological pacemaker. *PLoS ONE.* 2015.09; 10(9); e0138193
6. Akiko Koizumi, Tetsuo Sasano, Wataru Kimura, Yoshihiro Miyamoto, Takeshi Aiba, Taisuke Ishikawa, Akihiko Nogami, Seiji Fukamizu, Harumizu Sakurada, Yoshihide Takahashi, Hiroaki Nakamura, Tomoyuki Ishikura, Haruhiko Koseki, Takuro Arimura, Akinori Kimura, Kenzo Hirao, Mitsuaki Isobe, Wataru Shimizu, Naoyuki Miura, Tetsushi Furukawa. Genetic defects in a His-Purkinje system transcription factor, *IRX3*, cause lethal cardiac arrhythmias. *Eur. Heart J..* 2015.10;
7. Yamakawa H, Muraoka N, Miyamoto K, Sadahiro T, Isomi M, Haginiwa S, Kojima H, Umei T, Akiyama M, Kuishi Y, Kurokawa J, Furukawa T, Fukuda K, Ieda M. Fibroblast growth factors and vascular endothelial growth factor promote cardiac reprogramming under defined conditions *Stem Cell Reports.* 2015.12; 5(6); 1128-1142

[Misc]

1. Tetsushi Furukawa. Type 3 long QT syndrome 2015.02; 27; 91-96

[Conference Activities & Talks]

1. Kurokawa J, Okada J, Hayashi E, Ashihara T, Yoshinaga T, Sugiura S, Li M, Kanda Y, Sekino Y, Sawada K, Hisada T, Furukawa T. A multidisciplinary approach for evaluation of drug-induced QT prolongation using human induced pluripotent stem cell-derived cardiomyocytes. 59th Biophysical Society Annual Meeting 2015.02.07 Baltimore
2. Sugiyama K, Sasano T, Furukawa T. Oxidative stress induced ventricular arrhythmia and impairment cardiac function in *Nos1ap* deleted mice. 2015 8th APHRS 2015.11.19
3. Furukawa T. iPS cells and arrhythmia mechanism. 2015 8th APHRS 2015.11.22 Melbourne

4. 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
5. 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
6. 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 Tetsushi KAGAWA (-March)
Associate Professor Ikuo NOBUHISA
Assistant Professor Kouichi TABU (June-)
Administrative Assistant Mako FUSHIMI (-February)
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 chromatin 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 aim to improve student's understanding of stem cells from multiple viewpoints.

(5) Publications

[Original Articles]

1. 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 to Cells*. 2015; in press;
2. Kokubu Y, Tabu K, Wang W, Muramatsu N, Murota Y, Nobuhisa I, Jinushi M, and Taga T. Induction of protumoral CD11c^{high} macrophages by glioma cancer stem cells through GM-CSF. *Genes to Cells*. 2015; in press;
3. 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*. 2015; in press;
4. 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. 2015; in press;

[Conference Activities & Talks]

1. Taga T and Tabu K. Characterization of C6 glioma cancer stem cells and their niche. Seoul National University, Cancer Research Institute (SNU CRI) Annual Symposium 2015 'Innovative Approaches to Explore Novel Druggable Targets' 2015.04.02 Hwasun, Korea
2. Saito K, Nobuhisa I, Anani M, Harada K, Takahashi S, and Taga T. Maintenance of intra-aortic hematopoietic cell clusters in the AGM region through the Sox17-Notch1-Hes1 axis. The 13th Stem Cell Symposium 2015.05.29 Ito International Research Center, Tokyo, Japan
3. Nobuhisa I and Taga T. Sox17 maintains the stem cell population of intra-aortic hematopoietic cell clusters in the aorta-gonad-mesonephros region. The 10th International Symposium of the Institute Network 2015.07.23 Furate Hall, Sapporo, Japan
4. Nobuhisa I, Osawa M, Uemura M, Harada K, Anani M, Saito K, Takagi H, Takahashi S, Kanai-Azuma M, Kanai Y, Iwama A, and Taga T. Sox17 is critical for the maintenance of stem cell phenotype of intra-aortic hematopoietic clusters of cells in the aorta-gonad-mesonephros region. International Society for Experimental Hematology 44th Annual Scientific Meeting 2015.09.17 The Kyoto International Conference, Kyoto, Japan
5. Saito K, Nobuhisa I, Anani M, Harada K, Takahashi S, 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. International Society for Experimental Hematology 44th Annual Scientific Meeting 2015.09.18 The Kyoto International Conference, Kyoto, Japan
6. Wang W, Tabu K, Kokubu Y, Hagiya Y, Ogura S, and Taga T. Splenic abnormal erythropoiesis in C6 glioma-bearing mice: an implication for their environment of cancer stem cells. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08 Nagoya Congress Center, Nagoya, Japan
7. Nobuhisa I, Saito K, Takahashi S, Harada K, Anani M, and Taga T. Sox17 maintains the stem cell population of intra-aortic hematopoietic cell clusters in the aorta-gonad-mesonephros region through Notch signaling. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.19 Sapporo Convention Center, Sapporo, Japan
8. Saito K, Nobuhisa I, Anani M, Harada K, Takahashi S, and Taga T. Maintenance of hematopoietic stem and progenitor cell phenotype of intra-aortic cell clusters in the AGM region as a site of definitive hematopoiesis through the Sox17-Notch1-Hes1 axis. The 38th Annual Meeting of the Molecular Biology Society of Japan 2015.12.01 Kobe International Conference Center, Kobe, Japan

9. Tabu K, Muramatsu N, and Taga T. Synthetic polymer-based approach revealed an adaptive capacity of glioma stem cells by inducing tumor-infiltrating and iron-accumulating macrophages. The 38th Annual Meeting of the Molecular Biology Society of Japan 2015.12.01 Kobe International Conference Center, Kobe, Japan

Molecular Pharmacology

Professor NODA Masaki
 Associate Professor
 EZURA Yoichi
 Assistant Professor
 IZU Yayoi

(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. Shuichi Moriya, Tadayoshi Hayata, Takuya Notomi, Smriti Aryal, Testuya Nakamaoto, Yayoi Izu, Makiri Kawasaki, Takayuki Yamada, Jumpei Shirakawa, Kazuo Kaneko, Yoichi Ezura, Masaki Noda. PTH regulates β 2-adrenergic receptor expression in osteoblast-like MC3T3-E1 cells. J. Cell. Biochem.. 2015.01; 116(1); 142-148
2. Yoichi Ezura, Junji Nagata, Masashi Nagao, Hiroaki Hemmi, Tadayoshi Hayata, Susan Rittling, David T Denhardt, Masaki Noda. Hindlimb-unloading suppresses B cell population in the bone marrow and peripheral circulation associated with OPN expression in circulating blood cells. J. Bone Miner. Metab.. 2015.01; 33(1); 48-54

3. Tadayoshi Hayata, Yoichi Ezura, Makoto Asashima, Ryuichi Nishinakamura, Masaki Noda. Dllard/Ctdnep1 Regulates Endochondral Ossification via Suppression of TGF- β Signaling. *J. Bone Miner. Res.* 2015.02; 30(2); 318-329
4. Wanting Lin, Yoichi Ezura, Yayoi Izu, Arayal Smriti, Makiri Kawasaki, Chantida Pawaputanon, Keiji Moriyama, Masaki Noda. Profilin Expression Is Regulated by Bone Morphogenetic Protein (BMP) in Osteoblastic Cells. *J. Cell. Biochem.* 2015.08;
5. Tetsuya Nakamoto, Yayoi Izu, Makiri Kawasaki, Takuya Notomi, Tadayoshi Hayata, Masaki Noda, Yoichi Ezura. Mice Deficient in CIZ/NMP4 Develop an Attenuated Form of K/BxN-Serum Induced Arthritis. *J. Cell. Biochem.* 2015.09;
6. Chantida Pawaputanon Na Mahasarakham, Yoichi Ezura, Makiri Kawasaki, Arayal Smriti, Shuichi Moriya, Takayuki Yamada, Yayoi Izu, Katsuhiko Nishimori, Yuichi Izumi, Masaki Noda. BMP-2 Enhances Lgr4 Gene Expression in Osteoblastic Cells. *J. Cell. Physiol.* 2015.09;
7. Shuichi Moriya, Yayoi Izu, Smriti Arayal, Makiri Kawasaki, Koki Hata, Chantida Pawaputanon Na Mahasarakham, Yuichi Izumi, Paul Saftig, Kazuo Kaneko, Masaki Noda, Yoichi Ezura. Cathepsin K Deficiency Suppresses Disuse-Induced Bone Loss. *J. Cell. Physiol.* 2015.10;
8. Makiri Kawasaki, Yoichi Ezura, Tadayoshi Hayata, Takuya Notomi, Yayoi Izu, Masaki Noda. TGF- β Suppresses Ift88 Expression in Chondrocytic ATDC5 Cells. *J. Cell. Physiol.* 2015.11; 230(11); 2788-2795
9. Jumpei Shirakawa, Hiroyuki Harada, Masaki Noda, Yoichi Ezura. PTH-Induced Osteoblast Proliferation Requires Upregulation of the Ubiquitin-Specific Peptidase 2 (Usp2) Expression. *Calcif. Tissue Int.* 2015.12;
10. Smriti Aryal A C, Kentaro Miyai, Yayoi Izu, Tadayoshi Hayata, Takuya Notomi, Masaki Noda, Yoichi Ezura. Nck influences preosteoblastic/osteoblastic migration and bone mass. *Proc. Natl. Acad. Sci. U.S.A.* 2015.12; 112(50); 15432-15437
11. Takuya Notomi, Miyuki Kuno, Akiko Hiyama, Yoichi Ezura, Masashi Honma, Toru Ishizuka, Kiyoshi Ohura, Hiromu Yawo, Masaki Noda. Membrane depolarization regulates intracellular RANKL transport in non-excitable osteoblasts. *Bone*. 2015.12; 81; 306-314

Stem Cell Biology

Professor : Emi Nishimura, M.D., Ph.D.
 Associate Professor: Daisuke Nanba, Ph.D.
 Assistant Professor : Hiroyuki Matsumura, Ph.D.
 Assistant Professor : Yasuaki Mohri, Ph.D.
 JSPS Research Fellow : Hironobu Morinaga, Ph.D.
 Project Assistant Professor : Makoto Fukuda, 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 β (TGF- β) (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. Sota Tate, Matome Imai, Natsuki Matsushita, Emi K. Nishimura, Shigeki Higashiyama, Daisuke Nanba. Rotation is the primary motion of paired human epidermal keratinocytes Journal of Dermatological Science. 2015.09; 79(3); 194-202

[Conference Activities & Talks]

1. Emi K. Nishimura. Melanocyte Stem Cells: a Key for Hair Graying and Melanoma. The 25th Annual Meeting of Korean Society for Investigative Dermatology 2015.03.27 Seoul, Korea
2. Emi K. Nishimura. Stem cells in skin appendages and their fate change by aging. 23rd World Congress of Dermatology 2015.06.08 Vancouver, Canada
3. Emi K. Nishimura. Hair follicle aging program in hair follicle stem cells orchestrates dynamic tissue aging and associated hair loss. Gordon Research Conferences-Epithelial Differentiation & keratinization 2015.07.12 Boston, USA

Respiratory Medicine

Professor: Naohiko INASE

Junior Associate Professor: Kimitake TSUCHIYA

Assistant Professor: Toshihide FUJIE, Tomoya TATEISHI, Haruhiko FURUSAWA, Masahiro ISHIZUKA,

Graduate Students: Mayuko TAO, Sahoko CHIBA, Yumi SAKAKIBARA,

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, Uchibori K, Fujiwara T, Ogata T, Yamauchi S, Shirai T, Masuo M, Okamoto T, Tateishi T, Furusawa H, Fujie T, Sakashita H, Tsuchiya K, Tamaoka M, Miyazaki Y, Inase N, Sumi Y. Dielectric blood coagulometry as a novel coagulation test. *J sci Res Rep.* 2015; 4(3); 180-188
2. Okamoto T, Tsutsui T, Suhara K, Furusawa H, Miyazaki Y, Inase N. Seasonal variation of serum KL-6 and SP-D levels in bird-related hypersensitivity pneumonitis. *Sarcoidosis Vasc Diffuse Lung Dis.* 2015; 31; 364-367
3. Suhara K, Miyazaki Y, Okamoto T, Yasui M, Tsuchiya K, Inase N. Utility of immunological tests for bird-related hypersensitivity pneumonitis. *Respir Investig.* 2015; 53; 13-21
4. Yorozu P, Furukawa A, Uchida K, Akashi T, Kakegawa T, Ogawa T, Minami J, Suzuki Y, Awano N, Furusawa H, Miyazaki Y, Inase N, Eishi Y. Propionibacterium acnes catalase induces increased Th1 immune response in sarcoidosis patients. *Respir Investig.* 2015; 53; 161-169
5. Tsutsui T, Miyazaki Y, Kuramochi J, Uchida K, Eishi Y, Inase N. The amount of avian antigen in chronic bird-related hypersensitivity pneumonitis *Ann Am Thorac Soc.* 2015; 12; 1013-1021
6. Ishizuka M, Miyazaki Y, Masuo M, Suhara K, Tateishi T, Yasui M, Inase N. Interleukin-17A and neutrophils in a murine model of bird-related hypersensitivity pneumonitis. *PLoS One.* 2015; 10(9); e0137978
7. Okamoto T, Fujii M, Furusawa H, Tsuchiya K, Miyazaki Y, Inase N. Usefulness of KL-6 and SP-D for the diagnosis and management of chronic hypersensitivity pneumonitis. *Respir Med.* 2015; 109; 1576-1581
8. Tsutsui T, Miyazaki Y, Okamoto T, Tateishi T, Furusawa H, Tsuchiya K, Fujie T, Tamaoka M, Sakashita H, Sumi Y, Inase N. Antigen avoidance tests for diagnosis of chronic hypersensitivity pneumonitis. *Respir Investig.* 2015; 53; 217-224
9. Miyazaki Y, Azuma A, Inase N, Taniguchi H, Ogura T, Inoue E, Takeuchi M, Yoshizawa Y, Sugiyama Y, Kudoh S, the IPF trial group in Japan. Cyclosporin A combined with low-dose corticosteroid treatment in patients with idiopathic pulmonary fibrosis. *Respir Investig.* 2015; 53; 288-295
10. Ishizuka M, Miyazaki Y, Tateishi T, Tsutsui T, Tsuchiya K, Inase N. Validation of inhalation provocation test in chronic bird-related hypersensitivity pneumonitis and new prediction score. *Ann Am Thorac Soc.* 2015.02; 12(2); 167-173
11. Sugiura M, Mitaka C, Haraguchi G, Tomita M, Inase N. Polymyxin b-immobilized fiber column hemoperfusion mainly helps to constrict peripheral blood vessels in treatment for septic shock. *J Intens Care.* 2015.03; 3(14); 1-7
12. Yamazaki H, Sakai R, Koike R, Miyazaki Y, Tanaka M, Nanki T, Watanabe K, Yasuda S, Kurita T, Kaneko Y, Tanaka Y, Nishioka Y, Takasaki Y, Nagasaka K, Nagasawa H, Tohma S, Dohi M, Sugihara T, Sugiyama H, Kawaguchi Y, Inase N, Ochi S, Hagiyaama H, Kohsaka H, Miyasaka N, Harigai M. Assessment of risks of pulmonary infection during 12 months following immunosuppressive treatment for active connective tissue diseases: a large-scale prospective cohort study. *J Rheumatol.* 2015.04; 42(4); 614-622

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)
- Project Associate Professor
 Masakazu NAGAHORI
- Junior Associate Professor
 Cheng-Hsin AZUMA
 Sei KAKINUMA (Department for Hepatitis Control),
 Yasuhiro ITSUI (Department of General Medicine)
 Eriko OKADA (Department of Endoscopic Diagnosis and Therapeutics)
 Katsuyoshi MATSUOKA
 (Department of Advanced Therapeutics in Gastrointestinal Diseases)
- Assistant Professor
 Shigeru OSHIMA, Takashi NAGAISHI, Toshimitu FUJII, Yasuhiro NEMOTO
 Tomohiro MIZUTANI
 (Department of Advanced Therapeutics in Gastrointestinal Diseases)
- Project Assistant Professor
 Sayuri NITTA
- Hospital Staff
 Yuki SAKURAI, Miyako MURAKAWA, Masayoshi FUKUDA, Maiko KIMURA,
 Hukiko KITAHATA, Kenji OOTANI, Kengo, NOZAKI, Kennichiro KOHASHI
 Isamu Shibata, Yuria TAKEI, Tomoaki AHIRASAKI
- AMED Fellow
 Keita FUKUSHIMA,
- Graduate Student
 Fumio GOTO, Taichi MATSUMOTO, Masanori KOBAYASHI, Toru NAKATA
 Yoichi NIBE, Hideji HIBIYA, Satoru FUJII, Hiroko NAGATA, Syun KANEKO,
 Chiaki MAEYASHIKI, Taro WATABE, Yuka MATSUMOTO, Kohei SUZUKI,
 Yuu ASANO, Kento TAKENAKA, Emi INOUE, Shintaro AKIYAMA
 Fumiaki ISHIBASHI, Ami KAWAMOTO, Masato MIYOSHI, Nisha JOSE
 Tomoyuki KAKUTA, Arisa TOKAI
- lecturer (part-time)
 Tadamitsu IWAMOTO

(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. Hiroki Kiyohara, Tadakazu Hisamatsu, Katsuyoshi Matsuoka, Makoto Naganuma, Hideto Kameda, Noriyuki Seta, Tsutomu Takeuchi, Takanori Kanai. Crohn's Disease in which the Patient Developed Aortitis during Treatment with Adalimumab. *Intern Med.* 2015; 54(14); 1725-1732
2. Hayashi R, Tsuchiya K, Fukushima K, Horita N, Hibiya S, Kitagaki K, Negi M, Itoh E, Akashi T, Eishi Y, Okada E, Araki A, Ohtsuka K, Fukuda S, Ohno H, Okamoto R, Nakamura T, Tanaka S, Chayama K, Watanabe M. Reduced human α -defensin 6 in non-inflamed jejunal tissue of Crohn's disease patients. (in press) *Inflamm Bowel Dis.* 2015;
3. Takashi Nagaishi, Mamoru Watanabe . Paradigm of T cell differentiation in IBD: Crohn's disease and ulcerative colitis. (in press) *Crohn's Disease and Ulcerative Colitis.* 2015;
4. Taniguchi M, Tasaka-Fujita M, Nakagawa M, Watanabe T, Kawai-Kitahata F, Otani S, Goto F, Nagata H, Kaneko S, Nitta S, Murakawa M, Nishimura-Sakurai Y, Azuma S, Itsui Y, Mori K, Yagi S, Kakinuma S, Asahina Y, Watanabe M. Evaluation of IFN resistance in newly established genotype 1b HCV cell culture system.(in press) *Journal of Clinical and Translational Hepatology.* 2015;
5. Calabrese E, Maaser C, Zorzi F, Kannengiesser K, Hanauer SB, Bruining DH, Iacucci M, Maconi G, Novak KL, Panaccione R, Strobel D, Wilson SR, Watanabe M, Pallone F, Ghosh S. Bowel Ultrasonography in the management of Crohn's disease. A review with recommendations of an international panel of experts. (in press) *Inflamm Bowel Dis.* 2015;
6. Yu Matsuzawa, Shigeru Oshima, Yoichi Nibe, Masanori Kobayashi, Chiaki Maeyashiki, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. RIPK3 regulates p62-LC3 complex formation via the caspase-8-dependent cleavage of p62. *Biochem Biophys Res Commun.* 2015.01; 456(1); 298-304
7. Masahiro Yoshida, Yoshikazu Kinoshita, Mamoru Watanabe, Kentaro Sugano. JSGE Clinical Practice Guidelines 2014: standards, methods, and process of developing the guidelines. *J Gastroenterol.* 2015.01; 50(1); 4-10
8. Bao H Duong, Michio Onizawa, Juan A Osés-Prieto, Rommel Advincula, Alma Burlingame, Barbara A Malynn, Averil Ma. A20 restricts ubiquitination of pro-interleukin-1 β protein complexes and suppresses NLRP3 inflammasome activity. *Immunity.* 2015.01; 42(1); 55-67
9. Katsuyoshi Matsuoka, Takanori Kanai. The gut microbiota and inflammatory bowel disease. *Semin Immunopathol.* 2015.01; 37(1); 47-55
10. Shintaro Akiyama, Daisuke Kikuchi, Toshifumi Mitani, Takeshi Fujii, Akihiro Yamada, Akira Matsui, Osamu Ogawa, Toshiro Iizuka, Shu Hoteya, Mitsuru Kaise. A case of mucinous adenocarcinoma in the setting of chronic colitis associated with intestinal spirochetosis and intestinal stricture. *Medicine (Baltimore).* 2015.01; 94(4); e493

11. Ulrike W Denzer, Thomas Rösch, Bilal Hoytat, Mohammed Abdel-Hamid, Xavier Hebutterne, Geoffroy Vanbiervelt, Jérôme Filippi, Haruiko Ogata, Naoki Hosoe, Kazuo Ohtsuka, Noriyuki Ogata, Keiichi Ikeda, Hiroyuki Aihara, Shin-Ei Kudo, Hisao Tajiri, Andras Treszl, Karl Wegscheider, Michel Greff, Jean-Francois Rey. Magnetically guided capsule versus conventional gastroscopy for upper abdominal complaints: a prospective blinded study. *J Clin Gastroenterol.* 2015.02; 49(2); 101-107
12. Yasuharu Maeda, Kazuo Ohtsuka, Shin-ei Kudo, Kunihiko Wakamura, Yuichi Mori, Noriyuki Ogata, Yoshiki Wada, Masashi Misawa, Akihiro Yamauchi, Seiko Hayashi, Toyoki Kudo, Takemasa Hayashi, Hideyuki Miyachi, Fuyuhiko Yamamura, Fumio Ishida, Haruhiro Inoue, Shigeharu Hamatani. Endoscopic narrow-band imaging efficiency for evaluation of inflammatory activity in ulcerative colitis. *World J Gastroenterol.* 2015.02; 21(7); 2108-2115
13. Hiroko Oshima, Mizuho Nakayama, Tae-Su Han, Kuniko Naoi, Xiaoli Ju, Yusuke Maeda, Sylvie Robine, Kiichiro Tsuchiya, Toshiro Sato, Hiroshi Sato, Makoto Mark Taketo, Masanobu Oshima. Suppressing TGF β signaling in regenerating epithelia in an inflammatory microenvironment is sufficient to cause invasive intestinal cancer. *Cancer Res.* 2015.02; 75(4); 766-776
14. Mamoru Watanabe. Recent dramatic evolution of the Journal of Gastroenterology (JG): a note from current Editorial Director and former Editor-in-Chief of JG. *J Gastroenterol.* 2015.03; 50(3); 249-251
15. Anil Kumar Asthana, Antony B Friedman, Giovanni Maconi, Christian Maaser, Torsten Kucharzik, Mamoru Watanabe, Peter R Gibson. The failure of gastroenterologists to apply intestinal ultrasound in inflammatory bowel disease in the Asia-Pacific: a need for action. *J Gastroenterol Hepatol.* 2015.03; 30(3); 446-452
16. Shinji Tanaka, Yusuke Saitoh, Takahisa Matsuda, Masahiro Igarashi, Takayuki Matsumoto, Yasushi Iwao, Yasumoto Suzuki, Hiroshi Nishida, Toshiaki Watanabe, Tamotsu Sugai, Ken-Ichi Sugihara, Osamu Tsuruta, Ichiro Hirata, Nobuo Hiwatashi, Hiroshi Saito, Mamoru Watanabe, Kentaro Sugano, Tooru Shimosegawa. Evidence-based clinical practice guidelines for management of colorectal polyps. *J Gastroenterol.* 2015.03; 50(3); 252-260
17. Etsuko Iio, Kentaro Matsuura, Nao Nishida, Shinya Maekawa, Nobuyuki Enomoto, Mina Nakagawa, Naoya Sakamoto, Hiroshi Yatsushashi, Masayuki Kurosaki, Namiki Izumi, Yoichi Hiasa, Naohiko Masaki, Tatsuya Ide, Keisuke Hino, Akihiro Tamori, Masao Honda, Shuichi Kaneko, Satoshi Mochida, Hideyuki Nomura, Shuhei Nishiguchi, Chiaki Okuse, Yoshito Itoh, Hitoshi Yoshiji, Isao Sakaida, Kazuhide Yamamoto, Hisayoshi Watanabe, Shuhei Hige, Akihiro Matsumoto, Eiji Tanaka, Katsushi Tokunaga, Yasuhito Tanaka. Genome-wide association study identifies a PSMD3 variant associated with neutropenia in interferon-based therapy for chronic hepatitis C. *Hum Genet.* 2015.03; 134(3); 279-289
18. Atsushi Sakuraba, Susumu Okamoto, Katsuyoshi Matsuoka, Toshiro Sato, Makoto Naganuma, Tadakazu Hisamatsu, Yasushi Iwao, Haruhiko Ogata, Takanori Kanai, Toshifumi Hibi. Combination therapy with infliximab and thiopurine compared to infliximab monotherapy in maintaining remission of postoperative Crohn's disease. *Digestion.* 2015.04; 91(3); 233-238
19. Keita Fukushima, Kiichiro Tsuchiya, Yoshihito Kano, Nobukatsu Horita, Shuji Hibiya, Ryohei Hayashi, Keisuke Kitagaki, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Shigeru Oshima, Takashi Nagaishi, Okamoto Ryuichi, Tetsuya Nakamura, Mamoru Watanabe. Atonal homolog 1 protein stabilized by tumor necrosis factor α induces high malignant potential in colon cancer cell line. *Cancer Sci.* 2015.05; 106(8); 1000-1007
20. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Masakazu Nagahori, Toshimitsu Fujii, Eiko Saito, Tomoyuki Fujioka, Katsuyoshi Matsuoka, Makoto Naganuma, Mamoru Watanabe. Correlation of the Endoscopic and Magnetic Resonance Scoring Systems in the Deep Small Intestine in Crohn's Disease. *Inflamm Bowel Dis.* 2015.05; 21(8); 1832-1838
21. Miyako Murakawa, Yasuhiro Asahina, Mina Nakagawa, Naoya Sakamoto, Sayuri Nitta, Akiko Kusano-Kitazume, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Miki Taniguchi, Fumio Goto, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. Impaired induction of interleukin 28B and expression of interferon λ 4 associated with nonresponse to interferon-based therapy in chronic hepatitis C. *J Gastroenterol Hepatol.* 2015.06; 30(6); 1075-1084

22. Yu Matsuzawa, Shigeru Oshima, Masahiro Takahara, Chiaki Maeyashiki, Yasuhiro Nemoto, Masanori Kobayashi, Yoichi Nibe, Kengo Nozaki, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Averil Ma, Mamoru Watanabe. TNFAIP3 promotes survival of CD4 T cells by restricting MTOR and promoting autophagy. *Autophagy*. 2015.06; 11(7); 1052-1062
23. Michio Onizawa, Shigeru Oshima, Ulf Schulze-Topphoff, Juan A Osés-Prieto, Timothy Lu, Rita Tavares, Thomas Prodhomme, Bao Duong, Michael I Whang, Rommel Advincula, Alex Agelidis, Julio Barrera, Hao Wu, Alma Burlingame, Barbara A Malynn, Scott S Zamvil, Averil Ma. The ubiquitin-modifying enzyme A20 restricts ubiquitination of the kinase RIPK3 and protects cells from necroptosis *Nat Immunol*. 2015.06; 16(6); 618-627
24. Tetsuro Takayama, Susumu Okamoto, Tadakazu Hisamatsu, Makoto Naganuma, Katsuyoshi Matsuoka, Shinta Mizuno, Rieko Bessho, Toshifumi Hibi, Takanori Kanai. Computer-Aided Prediction of Long-Term Prognosis of Patients with Ulcerative Colitis after Cytoapheresis Therapy. *PLoS ONE*. 2015.06; 10(6); e0131197
25. Shintaro Akiyama, Tsunao Imamura, Rikako Koyama, Tetsuo Tamura, Yuko Koizumi, Kazuo Takeuchi. Adrenal Metastasis and Hemorrhage Secondary to Hepatocellular Carcinoma. *Intern Med*. 2015.06; 54(12); 1513-1517
26. Katsuyoshi Matsuoka, Eiko Saito, Toshimitsu Fujii, Kento Takenaka, Maiko Kimura, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Tacrolimus for the Treatment of Ulcerative Colitis. *Intest Res*. 2015.07; 13(3); 219-226
27. 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.[Epub ahead of print] *Hepatol Res*. 2015.07;
28. Shin Fukudo, Hiroshi Kaneko, Hirotada Akiho, Masahiko Inamori, Yuka Endo, Toshikatsu Okumura, Motoyori Kanazawa, Takeshi Kamiya, Ken Sato, Toshimi Chiba, Kenji Furuta, Shigeru Yamato, Tetsuo Arakawa, Yoshihide Fujiyama, Takeshi Azuma, Kazuma Fujimoto, Tetsuya Mine, Soichiro Miura, Yoshikazu Kinoshita, Mamoru Watanabe, Kentaro Sugano, Tooru Shimosegawa. Evaluation of Kampo medicine in the clinical practice guideline for irritable bowel syndrome. *J Gastroenterol*. 2015.07; 50(7); 817-818
29. Taku Kobayashi, Yasuo Suzuki, Satoshi Motoya, Fumihito Hirai, Haruhiko Ogata, Hiroaki Ito, Noriko Sato, Kunihiro 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.[Epub ahead of print] *J Gastroenterol*. 2015.07;
30. Shin Matsui, Satoe Kasahara, Gen Morimoto, Osamu K Mikami, Mamoru Watanabe, Keisuke Ueda. Radioactive contamination of nest materials of the Eurasian Tree Sparrow *Passer montanus* due to the Fukushima nuclear accident: The significance in the first year. *Environ Pollut*. 2015.07; 206; 159-162
31. Shigeyuki Kawa, Kazuichi Okazaki, Kenji Notohara, Mamoru Watanabe, Tooru Shimosegawa. Autoimmune pancreatitis complicated with inflammatory bowel disease and comparative study of type 1 and type 2 autoimmune pancreatitis. *J Gastroenterol*. 2015.07; 50(7); 805-815
32. Naoki Yoshimura, Mamoru Watanabe, Satoshi Motoya, Keiichi Tominaga, Katsuyoshi Matsuoka, Ryuichi Iwakiri, Kenji Watanabe, Toshifumi Hibi. Safety and Efficacy of AJM300, an Oral Antagonist of α 4 Integrin, in Induction Therapy for Patients with Active Ulcerative Colitis.[Epub ahead of print] *Gastroenterology*. 2015.08;
33. Yasuo Suzuki, Toshiyuki Matsui, Hiroaki Ito, Toshifumi Ashida, Shiro Nakamura, Satoshi Motoya, Takayuki Matsumoto, Noriko Sato, Kunihiro Ozaki, Mamoru Watanabe, Toshifumi Hibi. Circulating Interleukin 6 and Albumin, and Infliximab Levels Are Good Predictors of Recovering Efficacy After Dose Escalation Infliximab Therapy in Patients with Loss of Response to Treatment for Crohn's Disease: A Prospective Clinical Trial. *Inflamm Bowel Dis*. 2015.09; 21(9); 2114-2122

34. Megumi Tasaka-Fujita, Nao Sugiyama, Wonseok Kang, Takahiro Masaski, Asako Murayama, Norie Yamada, Ryuichi Sugiyama, Senko Tsukuda, Koichi Watashi, Yasuhiro Asahina, Naoya Sakamoto, Takaji Wakita, Eui-Cheol Shin, Takanobu Kato. Amino acid polymorphisms in hepatitis C virus core affect infectious virus production and major histocompatibility complex class I molecule expression. *Sci Rep*. 2015.09; 5; 13994
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[Conference Activities & Talks]

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5. Matsuoka K, Saito E, Fujii T, Takenaka K, Nagahori M, Ohtsuka K, Watanabe M. The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) is useful to evaluate endoscopic improvement and to predict medium-term prognosis in Ulcerative Colitis patients treated with tacrolimus. 10th Congress of ECCO - Inflammatory Bowel Diseases 2015 2015.02.20 Barcelona
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7. Kiichiro Tsuchiya, Keita Fukushima, Mamoru Watanabe. The acquisition of cancer stemness by Atoh1 in colitis associated cancer. 8th Annual World Congress of Regenerative Medicine & Stem Cells 2015.03.21 Korea
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12. Katsuyoshi Matsuoka, Makoto Naganuma, Takanori Kanai. New drug development for inflammatory bowel disease in Japan : an example of collaboration between academia, industry, and government. The 101st General Meeting of the Japanese Society of Gastroenterology 2015.04.25 Sendai
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24. Watanabe M. Stem Cell Transplantation in Inflammatory Bowel Disease (IBD). Guangzhou International GI Summit (GIGIS2015) 2015.06.06 Guangzhou
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29. Kiichiro Tsuchiya. Mapping biopsy of entire small intestine is useful to assess the pathogenesis of Crohn's disease. AOCC2015 2015.06.19 Beijing
30. Katsuyoshi Matsuoka. Poster Round Group 6 (Chair) . AOCC2015 2015.06.19 Beijing
31. Katsuyoshi Matsuoka. Novel Diagnostic Criteria for Intestinal Behcet's Disease: The Reality. AOCC2015 2015.06.19 Beijing

32. Toshimitsu Fujii, Kento Takenaka, Yoshio Kitazume, Eriko Saito, Katsuyoshi Matsuoka, Masakazu Naga-hori, Kazuo Ohtsuka, Mamoru Watanabe. Modifying and validating endoscopic and magnetic resonance scoring systems for the deep small intestine in Crohn' s disease. AOCC2015 2015.06.19 Beijing
33. Mamoru Watanabe. 【Luncheon Symposium】 Chair. AOCC2015 2015.06.20 Beijing
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38. Mamoru Watanabe. Adult Tissue Stem Cell Therapy in Inflammatory Bowel Disease. IBD Advisory Board Meeting 2015.10.03 Tokyo
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49. Sayuri Nitta, Yasuhiro Asahina, Takaji Wakita, Takanobu Kato. Effects of Resistance Mutations of NS5A Inhibitor on Viral Production and Susceptibility to Anti-HCV Reagents in Recombinant Hepatitis C Viruses with NS5A of Genotype 1b. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA

50. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Hiroko Nagata, Syun Kaneko, Sayuri Nitta, Takako Watanabe, Yasuhiro Itsui, Mina Nakagawa, Sei Kakinuma, Sayuki Iijima, Yasuhito Tanaka, Mamoru Watanabe, Yujiro Tanaka. Expression of IFN λ 4 in liver is closely associated with non-response to antiviral therapy through the regulation of basal expression of ISGs in chronic hepatitis C patients but not in hepatitis B patients. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
51. Takako Watanabe, Yasuhiro Asahina, Mina Nakagawa, Sei Kakinuma, Yasuhiro Itsui, Hiroko Nagata, Miyako Murakawa, Fukiko Kawai-Kitahata, Mika Miura, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Serial change of resistant associated variants during early phase of NS3/4A triple therapy and the final virological outcome: analyses by ultra-deep sequencing technology. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
52. Hiroko Nagata, Yasuhiro Itsui, Fukiko Kawai-Kitahata, Shun Kaneko, Miyako Murakawa, Sayuri Nitta, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Yasuhiro Asahina. Variations of the host genome and interaction of hepatitis B viral X protein associated with hepatocarcinogenesis. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
53. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Watanabe T, Otani S, Goto F, Nagata H, Kaneko S, 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 with clinicopathological features. AASLD The Liver Meeting 2015 2015.11.14 San Francisco, CA
54. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Sayuri Nitta, Tomoyuki Tsunoda, Masato Miyoshi, Hiroko Nagata, Fumio Goto, Satoshi Otani, Miyako Murakawa, Fukiko Kawai-Kitahata, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Mamoru Watanabe. Human induced pluripotent stem cell-derived hepatic progenitor-like cells and hepatocyte-like cells as a model for interaction between hepatitis B virus and host cells. AASLD The Liver Meeting 2015 2015.11.16 San Francisco, CA
55. Tokai A, Nagaishi T, Watabe T, Jose N, Yamazaki M, Onizawa M, Suzuki M, Hosoya A, Kawai Risa, Adachi T, Watanabe M. CD66a may regulate BCR signaling in the activated B cells. The 44th Annual Meeting of the Japanese Society for Immunology 2015.11.20 Sapporo
56. Eriko Okada , Akihiro Araki, Sayuri Nitta , Mamoru Watanabe. The utilities and problems of the patency capsule for patients with non-suspected intestinal stenosis. Asian Pacific Digestive Week (APDW) 2015 2015.12.06 Taiwan
57. Satoru Fujii, Ryuichi Okamoto, Toru Nakata, Kohei Suzuki, Fumiaki Ishibashi, Ami Kawamoto, Sayaka Ohashi Segawa, Tomohiro Mizutani, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. Establishment of a 3D cell culture-based screening platform to identify natural products that can regulate transepithelial water transport of the human gastrointestinal tract. Pacificchem2015 2015.12.17 Hawaii

Specialized Surgeries

< Division of Specialized Surgeries >

Professor: Hiroyuki UETAKE

Associate Professor: Yoshinori INOUE

Junior Associate Professor: Toshiaki ISHIKAWA, Tsuyoshi NAKAGAWA

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 >

Tokuko HOSOYA, Kimihiro IGARI, Masato NISHIZAWA

Masahiro NAKAMURA, Yohei YAMAMOTO, Tsuyosi ICHINOSE

Sotaro KATSUI, 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

(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. Shinto E, Takahashi K, Yamaguchi T, Hashiguchi Y, Kotake K, Itabashi M, Yasuno M, Kanemitsu Y, Nishimura G, Akagi Y, Sato T, Kato T, Matsumoto H, Hase K, Sugihara K.. Validation and Modification of the Japanese Classification System for Liver Metastases from Colorectal Cancer:A Multi-institutional Study. *Ann Surg Oncol*. 2015; 22; 3888-3895
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5. Yasui H, Muro K, Shimada Y, Tsuji A, Sameshima S, Baba H, Satoh T, Denda T, Ina K, Nishina T, Yamaguchi K, Esaki T, Tokunaga S, Kuwano H, Boku N, Komatsu Y, Watanabe M, Hyodo I, Morita S, Sugihara K.. A phase 3 non-inferiority study of 5-FU/l-leucovorin/irinotecan (FOLFIRI) versus irinotecan/S-1 (IRIS) as second-line chemotherapy for metastatic colorectal cancer: updated results of the FIRIS study. *J Cancer Res Clin Oncol* . 2015.01; 141(1); 153-160
6. Sugihara K, Yoshida M, Ishiguro M.. Reply to the Letter to the Editor 'Is fluoropyrimidines without oxaliplatin optimal for the adjuvant treatment of mainstream stage III colon cancer ?' by Abali et al. *Ann Oncol*. 2015.01; 26; 245-246
7. Sunakawa Y, Stremtizer S, Cao S, Zhang W, Yang D, Wakatsuki T, Ning Y, Yamauchi S, Stintzing S, Sebio A, El-Khoueiry R, Matsusaka S, Parekh A, Barzi A, Azuma M, Watanabe M, Koizumi W, Lenz HJ. Association of variants in genes encoding for macrophage-related functions with clinical outcome in patients with locoregional gastric cancer. *Ann. Oncol.*. 2015.02; 26(2); 332-339
8. Igari K, Kudo T, Uchiyama H, Toyofuku T, Inoue Y.. Progression of perianeurysmal inflammation after endovascular aneurysm repair for inflammatory abdominal aortic and bilateral common iliac artery aneurysms. *Ann Vasc Surg*. 2015.02; 29(364); e1-e4
9. Takahashi H, Ishikawa T, Ishiguro M, Okazaki S, Mogushi K, Kobayashi H, Iida S, Mizushima H, Tanaka H, Uetake H, Sugihara K.. Prognostic significance of Traf2-and Nck-interacting kinase (TNK) in colorectal cancer. *BMC Cancer*. 2015.02; 15; 794
10. Uetake H, Yasuno M, Ishiguro M, Kameoka S, Shimada Y, Takahashi K, Watanabe T, Muro K, Baba H, Yamamoto J, Mizunuma N, Tamagawa H, Mochizuki I, Kinugasa Y, Kikuchi T, Sugihara K. A Multicenter Phase II Trial of mFOLFOX6 Plus Bevacizumab to Treat Liver-Only Metastases of Colorectal Cancer that are Unsuitable for Upfront Resection (TRICC0808). *Ann Surg Oncol*. 2015.03; 22(3); 908-915
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16. Igari K, Kudo T, Toyofuku T, Inoue Y.. Surgical Treatment of Cystic Adventitial Disease of the Popliteal Artery: Five Case Reports. *Case Rep Vasc Med.* 2015.08; 984681
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[Conference Activities & Talks]

1. Igari K, Kudo T, Toyofuku T, Inoue Y.. Crossing of infrapopliteal arterial chronic total occlusions with the Crosser™system.. 64th International congress of the European Society for Cardiovascular and Endovascular Surgery. 2015.03.26 Turkey (Istanbul)
2. Ishikawa T, Uetake H, Ishiguro M, Murotani K, Ueno H, Matsui S, Sugihara K, Tomita N.. MSI, 18qLOH, and clinicopathological features in stage II sporadic colon cancers: Biomarker study in a Phase III study of postoperative adjuvant chemotherapy for stage II colon cancer (SACURA trial). *ACCR 2015* 2015.04.22 Philadelphia (USA)
3. Igari K, Kudo T, Nakamura M, Nishizawa M, Uchiyama H, Koizumi S, Toyofuku T, Inoue Y.. The snorkel technique for endovascular aneurysm repair with challenging neck anatomy . *Cardiovascular Summit TCTAP 2015* 2015.04.28 Seoul (Republic of Korea)
4. Kinugasa Y, Ishiguro M, Nakatani E, Endo T, Shinozaki H, Takii Y, Takahashi Y, Mochizuki H, Kotake K, Kameoka S, Takahashi K, Watanabe M, Boku N, Tomita N, Sugihara K.. S-1 as adjuvant chemotherapy for stage III colon cancer: Updated outcomes of ACTS-CC trial.. *2015 ASCO Annual Meeting* 2015.06.01 Chicago (USA)
5. Kudo T.. The Current Situation of the Treatment for Peripheral Arterial Disease in Japan. . *The 9th Japan-Korea Joint Meeting for Vascular Surgery.* 2015.06.05 Yokohama (Japan)
6. Ichinose T, Sugano N.. A Case of Successful Inflow Reduction of a High-Inflow Vascular Access by RUDI (Revision Using Distal Inflow) Using Autologous Vein Graft.. *The 9th Japan-Korea Joint Meeting for Vascular Surgery.* 2015.06.05 Yokohama (Japan)
7. Katsui S, Igari K, Yamamoto Y, Nakamura M, Nishizawa M, Koizumi S, Toyofuku T, Kudo T, Inoue Y. . Crossing of infrapopliteal arterial chronic total occlusions with the Crosser™system.. *The 9th Japan-Korea Joint Meeting for Vascular Surgery* 2015.06.05 Yokohama (Japan)
8. Igari K, Kudo T, Toyofuku T, Inoue Y.. The assessment of peripheral perfusion for the patients with isolated infrapopliteal arterial lesions by indocyanine green angiography.. *46th World Congress of Surgery WCS 2015.* 2015.08.23 Bangkok (Thailand)
9. Nishizawa M, Igari K, Toyofuku T, Kudo T, Inoue Y. . A novel technique to infrainguinal arterial occlusions using the Crosser™system. . *46th World Congress of Surgery WCS 2015.* 2015.08.23 Bangkok (Thailand)
10. Igari K, Kudo T, Toyofuku T, Inoue Y.. A case of arteriovenous fistula after endovenous laser ablation for varicose vein. . *UIP Capter Meeting: Seoul UIP 2015* 2015.08.27 Seoul (Republic of Korea)
11. Uetake H. 【Chair】 Importance of 1st line treatment for extend survival of mCRC patients (Speaker: Stintzing S (University of Munich, Germany)) . *Meet the Expert Meeting with Dr.Stintzing* 2015.10.17 Tokyo
12. Ichinose T, Sugano N.. A case of infrarenal saccular abdominal aortic aneurysm with severe mural thrombus required supraceliac cross clamp.. *12th Tokyo-Shanghai International Symposium for Vascular Diseases.* 2015.11.14 Shanghai (China)

13. Ichinose T, Kudo T, Yamamoto Y, Nakamura M, Katsui S, Nishizawa M, Igari K, Toyofuku T, Inoue Y.. A case of deep vein thrombosis due to iliac vein compression treated by catheter directed thrombolysis and iliac vein stenting.. 12th Tokyo-Shanghai International Symposium for Vascular Diseases. 2015.11.14 Shanghai (China)
14. Yamamoto Y, Kudo T, Ichinose T, Nakamura M, Katsui S, Nishizawa M, Igari K, Koizumi S, Toyofuku T, Inoue Y. . A case of surgically rescued in-stent occlusion of the SFA with jailed profunda orifice.. 12th Tokyo-Shanghai International Symposium for Vascular Diseases. 2015.11.14 Shanghai (China)
15. Uetake H.. Maximize treatment outcome of mCRC from the first line treatment choice and beyond.. 2015 Avastin Colon Cancer Beyond Treatment Forum 2015.11.28 Taipei (Taiwan)
16. Uetake H.. Optimize mCRC Management from First Line Treatment Choice and Beyond.. International Colorectal Surgery Forum 2015.11.29 Taichung (Taiwan)
17. Uetake H.. Optimal management of mCRC on unresectable and boardline resectable patients.. 2015 Avastin Colon Cancer Expert visit in VGHTC 2015.11.30 Taichung (Taiwan)
18. Uetake H.. Maximize treatment outcome of Bevacizumab in first line therapy.. 2015 Avastin Colon Cancer Expert Meeting 2015.12.01 Kaohsiung (Taiwan)

Cardiovascular Medicine

Professor	Mitsuaki Isobe
Clinical Professor	Kenzo Hirao
Associate Professor	Takashi Ashikaga, Tetsuo Sasano (Graduate School of Health Care Sciences, Biofunctional Informatics)
Junior Associate Professor	Masahiko Goya
Assistant Professor	Mihoko Kawabata, Yasuhiro Maejima, Ryoko Azuma, Yusuke Ebana (Medical Research Institute, Bio-informational Pharmacology), Shunji Yoshikawa, Takeshi Sasaki, Taro Sasaoka, Yu Hatano, Daisuke Tezuka, Susumu Tao
Graduate Student	Yusuke Ito, Koji Sugiyama, Kentaro Takahashi, Natsuko Tamura, Ryo Watabe, Tetsuo Ohmi, Masahiko Setoguchi, Tomoko Manno, Daisuke Ueshima, Tomoyo Sugiyama, Kei Takayama, Chisato Takamura, Ryota Iwatsuka, Yuji Konishi, Toru Miyazaki, Yoko Kato, Yoichi Otaki, Masaaki Takigawa, Atsuhiko Yagishita, Tatsuya Fujinami, Osamu Inaba, Masahito Suzuki, Naoyuki Miwa, Rena Nakamura, Riri Watanabe, Masahiro Yamazoe, Tomoyuki Umemoto, Norifumi Murai, Shunsuke Hirose, Tetsuo Yamaguchi, Hironori Sato, Maki Ohno, Keiichi Hishikari, Takashi Nakagawa, Hidetsugu Nomoto, Yasuaki Tanaka, Tetsumin Lee, Yukihiro Inamura, Mie Seya, Tomomasa Takamiya, Kensuke Hirasawa

(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 research 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. Yoshiyuki Ikeda, Akihiro Shirakabe, Yasuhiro Maejima, Peiyong Zhai, Sebastiano Sciarretta, Jessica Toli, Masatoshi Nomura, Katsuyoshi Mihara, Kensuke Egashira, Mitsuru Ohishi, Maha Abdellatif, Junichi Sadoshima. Endogenous Drp1 mediates mitochondrial autophagy and protects the heart against energy stress. *Circ. Res.* 2015.01; 116(2); 264-278

2. Takayoshi Matsumura, Eisuke Amiya, Natsuko Tamura, Yasuhiro Maejima, Issei Komuro, Mitsuaki Isobe. A novel susceptibility locus for Takayasu arteritis in the IL12B region can be a genetic marker of disease severity. *Heart Vessels*. 2015.03;
3. Daisuke Tezuka, Masahiro Terashima, Yoko Kato, Akira Toriihara, Kensuke Hirasawa, Taro Sasaoka, Shunji Yoshikawa, Yasuhiro Maejima, Takashi Ashikaga, Jun-Ichi Suzuki, Kenzo Hirao, Mitsuaki Isobe. Clinical Characteristics of Definite or Suspected Isolated Cardiac Sarcoidosis: Application of Cardiac Magnetic Resonance Imaging and (18)F-Fluoro-2-deoxyglucose Positron-Emission Tomography/Computerized Tomography. *J. Card. Fail.*. 2015.04; 21(4); 313-322
4. Sebastiano Sciarretta, Peiyong Zhai, Yasuhiro Maejima, Dominic P Del Re, Narayani Nagarajan, Derek Yee, Tong Liu, Mark A Magnuson, Massimo Volpe, Giacomo Frati, Hong Li, Junichi Sadoshima. mTORC2 Regulates Cardiac Response to Stress by Inhibiting MST1. *Cell Rep*. 2015.04; 11(1); 125-136
5. Tezuka D, Terashima M, Kato Y, Toriihara A, Hirasawa K, Sasaoka T, Yoshikawa S, Maejima Y, Ashikaga T, Suzuki J, Hirao K, Isobe M.. Clinical characteristics of definite or suspected isolated cardiac sarcoidosis: Application of cardiac magnetic resonance imaging and (18)F-fluoro-2-deoxyglucose positron-emission tomography/computerized tomography. *Journal of Cardiac Failure*. 2015.04; 21(4); 313-322
6. Chikashi Terao, Takayoshi Matsumura, Hajime Yoshifuji, Yohei Kirino, Yasuhiro Maejima, Yoshikazu Nakaoka, Meiko Takahashi, Eisuke Amiya, Natsuko Tamura, Toshiki Nakajima, Tomoki Origuchi, Tetsuya Horita, Mitsuru Matsukura, Yuta Kochi, Akiyoshi Ogimoto, Motohisa Yamamoto, Hiroki Takahashi, Shingo Nakayamada, Kazuyoshi Saito, Yoko Wada, Ichiei Narita, Yasushi Kawaguchi, Hisashi Yamanaka, Koichiro Ohmura, Tatsuya Atsumi, Kazuo Tanemoto, Tetsuro Miyata, Masataka Kuwana, Issei Komuro, Yasuharu Tabara, Atsuhisa Ueda, Mitsuaki Isobe, Tsuneyo Mimori, Fumihiko Matsuda. Takayasu arteritis and ulcerative colitis: high rate of co-occurrence and genetic overlap. *Arthritis & rheumatology (Hoboken, N.J.)*. 2015.05; 67(8); 2226-2232
7. Suzuki J, Aoyama N, Aoki M, Tada Y, Wakayama K, Akazawa H, Shigematsu K, Hoshina K, Izumi Y, Komuro I, Miyata T, Hirata Y, Isobe M. Incidence of periodontitis in Japanese patients with cardiovascular diseases: a comparison between abdominal aortic aneurysm and arrhythmia. *Heart Vessels*. 2015.07; 30(4); 498-502
8. Daisuke Ueshima, Takashi Ashikaga, Tsukasa Shimura, Yu Hatano, Taro Sasaoka, Ken Kurihara, Shunji Yoshikawa, Yasuhiro Maejima, Mitsuaki Isobe. Popliteal Retrograde Approach is Effective and Safe for Superficial Femoral Artery Chronic Total Occlusion. *Ann Vasc Dis*. 2015.08; 8(3); 220-226
9. Suzuki J, Imai Y, Aoki M, Fujita D, Aoyama N, Tada Y, Akazawa H, Izumi Y, Isobe M, Komuro I, Nagai R, Hirata Y. High incidence and severity of periodontitis in patients with Marfan syndrome in Japan. *Heart Vessels*. 2015.09; 30(5); 692-695
10. Chisato Takamura, Jun-Ichi Suzuki, Masahito Ogawa, Ryo Watanabe, Yuko Tada, Yasuhiro Maejima, Hiroshi Akazawa, Issei Komuro, Mitsuaki Isobe. Suppression of murine autoimmune myocarditis achieved with direct renin inhibition. *J Cardiol*. 2015.10;

[Misc]

1. Yasuhiro Maejima, Yun Chen, Mitsuaki Isobe, Asa B Gustafsson, Richard N Kitsis, Junichi Sadoshima. Recent Progress in Research on Molecular Mechanisms of Autophagy in the Heart. *Am. J. Physiol. Heart Circ. Physiol.*. 2015.02; 308(4); H259-H268
2. Yasuhiro Maejima, Mitsuaki Isobe, Junichi Sadoshima. Regulation of autophagy by beclin 1 in the heart. *J. Mol. Cell. Cardiol.*. 2015.11;

[Conference Activities & Talks]

1. Yasuhiro Maejima, Natsuko Tamura, Mitsuaki Isobe. Single Nucleotide Polymorphism of MLX Gene Plays a Crucial Role in the Pathogenesis of Takayasu Arteritis Through Facilitating Inflammasome Formation of the Aorta. Basic Cardiovascular Sciences 2015 Scientific Sessions of American Heart Association 2015.07 New Orleans, Louisiana, U.S.A.

2. Yasuhiro Maejima, Yusuke Ito, Natsuko Tamura, Ryo Watanabe, Mitsuaki Isobe. Dipeptidyl peptidase-4 deteriorates cardiac function during autoimmune myocarditis by facilitating cathepsin-G activity. American Heart Association Scientific Sessions 2015 2015.11.09 Orlando, FL, USA
3. Kajikawa Y, Hosokawa S, Wakabayashi K, Maejima Y, Isobe M, Doi S. Dexmedetomidine Ameliorates Monocrotaline Induced Pulmonary Arterial Hypertension in Rats. American Heart Association Scientific Sessions 2015 2015.11.10 Orland, 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. Kawagoe I, Inada E, Ishikawa S, Matsunaga T, Takamochi K, Oh S, Suzuki K. Perioperative management of carinal pneumonectomy: a retrospective review of 13 patients J Anesth. 2015; 29; 446-449
2. Ohmori T, Shiota N, Haramo A, Masuda T, Maruyama F, Wakabayashi K, Adachi YU, Nakazawa K. Post-operative cardiac arrest induced by co-administration of amiodarone and dexmedetomidine: a case report J Intensive Care. 2015; 3; 43

3. Fujita H, Yagishita N, Aratani S, Saito-Fujita T, Morota S, Yamano Y, Hansson MJ, Inazu M, Kokuba H, Sudo K, Sato E, Kawahara K, Nakajima F, Hasegawa D, Higuchi I, Sato T, Araya N, Usui C, Nishioka K, Nakatani Y, Maruyama I, Usui M, Hara N, Uchino H, Elmer E, Nishioka K, Nakajima T. The E3 ligase synoviolin controls body weight and mitochondrial biogenesis through negative regulation of PGC-1 β EMBO J. 2015; 34; 1042-1055
4. Toyama S, Matsuoka K, Tagaito Y, Shimoyama M. Retrospective evaluation of the effect of carotid artery stenosis on cerebral oxygen saturation during off-pump coronary artery bypasses grafting in adult patients BMC Anesthesiology. 2015; 15; 180
5. Uzawa Y, Otsuji M, Nakazawa K, Fan W, Yamada Y. Derivation of recruitment function from the pressure-volume curve in an acute lung injury model Respiratory Physiology & Neurobiology. 2015; 205; 16-20
6. Fukami Nakajima, Satoko Aratani, Hidetoshi Fujita, Naoko Yagishita, Shizuko Ichinose, Koshi Makita, Yasuhiro Setoguchi, Toshihiro Nakajima. Synoviolin inhibitor LS-102 reduces endoplasmic reticulum stress-induced collagen secretion in an in vitro model of stress-related interstitial pneumonia. Int. J. Mol. Med.. 2015.01; 35(1); 110-116
7. Fukami Nakajima, Akihiro Komoda, Satoko Aratani, Hidetoshi Fujita, Mariko Kawate, Kou Nakatani, Masako Akiyama, Koshi Makita, Toshihiro Nakajima. Effects of xenon irradiation of the stellate ganglion region on fibromyalgia. J Phys Ther Sci. 2015.01; 27(1); 209-212
8. Hiroyuki Ito, Tokujiro Uchida, Koshi Makita. Ketamine causes mitochondrial dysfunction in human induced pluripotent stem cell-derived neurons. PLoS ONE. 2015.05; 10(5); e0128445
9. Hiroyuki Ito, Tokujiro Uchida, Koshi Makita. Interactions between rat alveolar epithelial cells and bone marrow-derived mesenchymal stem cells: an in vitro co-culture model Intensive Care Medicine Experimental. 2015.05; 3(15);
10. Daniel E O'Brien, Benedict J Alter, Maiko Satomoto, Clinton D Morgan, Steve Davidson, Sherri K Vogt, Megan E Norman, Graydon B Gereau, Joseph A Demaro, Gary E Landreth, Judith P Golden, Robert W Gereau. ERK2 Alone Drives Inflammatory Pain But Cooperates with ERK1 in Sensory Neuron Survival. J. Neurosci.. 2015.06; 35(25); 9491-9507
11. Tomozawa Arisa, Ishikawa Seiji, Shiota Nobuhiro, Cholvisudhi Phantila, Makita Koshi. Perioperative risk factors for acute kidney injury after liver resection surgery: an historical cohort study. Can J Anaesth. 2015.07; 62(7); 753-761
12. ZhongLiang Sun, Maiko Satomoto, Koshi Makita. Therapeutic effects of intravenous administration of bone marrow stromal cells on sevoflurane-induced neuronal apoptosis and neuroinflammation in neonatal rats. Korean J Anesthesiol. 2015.08; 68(4); 397-401

[Books etc]

1. Jiro Kurata, Shuo Zhang. Understanding neuropathic pain. Bunkodo, 2015.05 (ISBN : 978-4-8306-2840-5)
2. Jiro Kurata, Hugh C Hemmings Jr. BJA Special Issue on Memory and Awareness in Anaesthesia. Oxford University Press, 2015.07
3. 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..
4. 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. Toyama S. Hypotension during spinal anaesthesia for caesarean section *Anaesthesia* . 2015; 70; 1208-1209
2. Jiro Kurata. What you should know about "functional" oxygen saturation *Journal of the Japanese Society of Intensive Care Medicine*. 2015.05; 22(3); 186-187
3. Jiro Kurata, Hugh C Hemmings Jr. Memory and awareness in anaesthesia. *Br J Anaesth*. 2015.07; 115(suppl 1); i1-i3
4. Jiro Kurata. Minding the mind of subconscious self. *British Journal of Anaesthesia*. 2015.07; 115(suppl 1); i122
5. Hideaki Kaneko, Shuo Zhang, Miho Sekiguchi, Jiro Kurata. Shinichi Konno. The difference of nucleus accumbens activation between chronic low back pain with or without psychiatric problems. *British Journal of Anaesthesia*. 2015.07; 115(suppl 1); i142
6. Jiro Kurata. Subconscious processing and chronification of pain. *British Journal of Anaesthesia*. 2015.07; 115(suppl 1); i143
7. Jiro Kurata. Mining the hidden dysrhythmia - can machines get smarter at defining the anaesthetised state? *Anaesthesia*. 2015.12; 70(12); 1338-1341

[Conference Activities & Talks]

1. Tianjiao Li, Shuo Zhang, Eri Ikeda, Hiroyuki Kobinata, Koshi Makita, Yoshitaka Kobayashi, Shinichi Konno, Jiro Kurata. Chronic low back pain is associated with morphological alterations in the sensory and affective regions of the brain: a Voxel-Based Morphometry study. The 7th Joint Junior Inspire Symposium of the Center for Brain Integration Research and the Ochanomizu Neuroscience Association 2015.02.21 Tokyo
2. Shimoyama M, Toyama S, Shimoyama N. Comparison of the effects of tramadol, duloxetine and morphine in a murine model of chemotherapy-induced neuropathic pain. 5th International Congress on Neuropathic Pain 2015.05.14 Nice, France
3. Tianjiao Li, Shuo Zhang, Koshi Makita, Yoshitaka Kobayashi, Shinichi Konno, Jiro Kurata. Chronic low back pain is associated with morphological alterations in the sensory and affective regions of the brain: a voxel-based morphometry study. The 62nd Annual Meeting of the Japanese Society of Anesthesiologists 2015.05.28 Kobe
4. Sun Z, Cui W, Satomoto M, Aizawa H, Tanaka T, Makita K. 2. Neonatal sevoflurane exposure induces adulthood amygdala dysfunction in fear conditioning test. *Euroanesthesia* 2015 2015.06.01 Berlin
5. Adachi YU, Yoshida T, Matsuda N, Nakazawa K, Makita K. Lecithin decreased the hypnotic potency of intravenous anesthetics in ddY mice. *Euroanaesthesia* 2015.06.02 Berlin, Germany
6. Tianjiao Li, Shuo Zhang, Eri Ikeda, Hiroyuki Kobinata, Koshi Makita, Yoshitaka Kobayashi, Shinichi Konno, Jiro Kurata. Chronic low back pain is associated with morphological alterations in the sensory and affective regions of the brain: a voxel-based morphometry study. The 21st Annual Meeting of the Organization of Human Brain Mapping 2015.06.17 Honolulu, Hawaii, USA
7. Manami Tanaka, Akio Masuda, Jiro Kurata, Kazuaki Yokoyama, Yasuko Kawauchi, Yusuke Ito, Koshi Makita. Radiofrequency ablation to sacroiliac branches for low back pain of Ehlers-Danlos syndrome. The 49th Annual Meeting of the Japan Society of Pain Clinicians 2015.07.25 Osaka
8. Hiroyuki Kobinata, Eri Ikeda, Koshi Makita, Jiro Kurata. Longer duration of thermal pain stimuli magnifies offset analgesia. The 49th Annual Meeting of the Japan Society of Pain Clinicians 2015.07.25 Osaka
9. Eri Ikeda, Hiroyuki Kobinata, Koshi Makita, Jiro Kurata. Offset analgesia requires thermal stimulation above 43 degrees centigrade. The 49th Annual Meeting of the Japan Society of Pain Clinicians 2015.07.25 Osaka

10. Yonezawa N, Takei T, Toh M. Usefulness of sonographic evaluation of the diaphragm in mechanically ventilated patients with diaphragmatic paralysis: A report of two cases. 12th Congress of the World Federation of Societies of Intensive and Critical Care Medicine 2015.08.30 Seoul, Korea
11. Jiro Kurata. Sevoflurane modifies information transfer across the cerebral cortex. The 45th Annual Meeting of the Society for Neuroscience 2015.10.20 Chicago, Illinois, USA
12. Itoh Y, Kasuga T, Toyama S, Uchida T, Makita K. Retrospective analysis for intra-operative ventilatory management during general anesthesia: Is lung protective ventilation accepted as a common practice in the operating room?. Annual Meeting of American Society of Anesthesiologists 2015.10.24 San Diego, CA, USA
13. Adachi YU, Tanaka K, Kobayashi K, Kawaguchi M, Nishiwaki K, Nakazawa K, Makita k. Droperidol Showed Greater Decreases in the Bispectral Index Values than Haloperidol During General Anesthesia With Both Desflurane and Sevoflurane. Annual meeting of American Society of Anesthesiologists 2015.10.24 San Diego, CA, USA.
14. Adachi YU, Wakabayashi K, Nakazawa K, Makita K. Lecithin-enriched Formulation Decreases the Hypnotic Potency of Intravenous Anesthetics in ddY Mice. Annual meeting of American Society of Anesthesiologists 2015.10.24 San Diego, CA, USA
15. Yamamoto Y, Uchida T, Ito H, Kido K, Yamamoto M, Yamada Y, Ohno N, Asahara M, Yamaguchi O, Makita K. Perioperative Elevation in Cell Free DNA Levels in Patients Undergoing Cardiac Surgery: Possible Contribution of Neutrophil Extracellular Traps to Perioperative Renal Dysfunction: A Multicenter Observational Study. Annual Meeting of American Society of Anesthesiologists 2015.10.24 San Diego, CA, USA
16. Satomoto M, Yamamoto M, Hakusui T, Adachi YU, Makita K. 3. Droperidol Decreases the Required Dose of Inhaled Anesthetics During General Anesthesia With Desflurane and Remifentanyl in Women Breast Cancer Surgery.. Anesthesiology 2015 Annual Meeting 2015.10.25 San Diego
17. Sun Z, Satomoto M, Adachi YU, Cui W, Aizawa H, Ajioka I, Makita K. 4. Neonatal Sevoflurane Exposure Induces Adulthood Amygdala Dysfunction in Contextual Fear Conditioning Test. Anesthesiology 2015 Annual Meeting 2015.10.26 San Diego
18. Ito H, Uchida T, Makita K. Ketamine Causes Mitochondrial Dysfunction in Human Induced Pluripotent Stem Cell-derived Neurons. Anesthesiology 2015.10.26 San Diego, CA, USA

Cardiovascular Surgery

Professor Hirokuni ARAI
 Associate Professor Tomohiro MIZUNO
 Junior Associate Professor Keiji OI
 Assistant Professor Masafumi YASHIMA, Tsuyoshi HACHIMARU, Shogo SAKURAI, Tatsuki FUJIWARA,
 Masashi TAKESHITA, Eiki NAGAOKA
 Graduate Student Hidehito KUROKI, Taiju WATANABE, 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. Sakota D, Murashige T, Kosaka R, Fujiwara T, Nishida M, Maruyama O. . Real-Time Observation of Thrombus Growth Process in an Impeller of a Hydrodynamically Levitated Centrifugal Blood Pump by Near-Infrared Hyperspectral Imaging Artif Organs. 2015; 39((8)); 714-719

2. Watanabe T., Arai H., Mizuno T.. Intraoperative ultrasound imaging of coronary artery ostial stenosis J. Thorac. Cardiovasc. Surg.. 2015.04; 149(4); 1206-1207
3. Yoshiki Hitoshi, Tadano Kotaro, Ban Daisuke, Ohuchi Katsuhiko, Tanabe Minoru, Kawashima Kenji. Surgical energy device using steam jet for robotic assisted surgery. Conf Proc IEEE Eng Med Biol Soc. 2015.08; 2015; 6872-6875
4. 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. Am J Geriatr Psychiatry. 2015.09;
5. Mizuno T., Hachimaru T., Oi K., Watanabe T., Kuroki H., Fujiwara T., Sakurai S., Takeshita M., Kinoshita R., Arai H.. Easy and Safe Total Debranching of Arch Aneurysms Using Axilloaxillary Arterial Bypass Ann Thorac Surg. 2015.10; 100(4); 1476-1478

[Misc]

1. Oi K., Arai H. (Review) Stroke associated with coronary artery bypass grafting Gen Thorac Cardiovasc Surg. 2015.09; 63; 487-495

[Conference Activities & Talks]

1. Arai H.. Optimizing intraoperative decision making during CABG: Luck or science?. 2015.03.26 New York, USA
2. Takeshita M., Mizuno T., Oi K., Yashima M., Hachimaru T., Watanabe T., Kuroki H., Fujiwara T., Sakurai S., Kinoshita R., Arai H. . Left Atrioventricular Valve Plasty for Partial Atrioventricular Septal Defect Cases in Adult. Mitral Conclave 2015 2015.04.23 New York, USA
3. Arai H., Watanabe T., Kinoshita R., Takeshita M., Kuroki H., Sakurai S., Fujiwara T., Yashima H., Hachimaru T., Oi K., Mizuno T.. Mitral Valve Repair Using Auto-pericardial Patch For Extensive Leaflet Destruction Due To Active Infective Endocarditis.. AATS Mitral Conclave 2015 2015.04.23 New York, USA
4. Kinoshita R., Arai H., Oi K., Mizuno T., Watanabe T., Takeshita M., Kuroki H., Sakurai S., Fujiwara T., Yashima M., Hachimaru T. . Pericardial Patch Augmentation for severe Tricuspid Regurgitation Caused by Pacemaker and ICD Leads. AATS Mitral Conclave 2015 2015.04.24 New York, USA
5. Arai H.. Common CABG strategy in Japan.. 14th Scientific Symposium of Korean Coronary Artery Surgery Forum 2015.05 Korea
6. Arai H.. Intraoperative validation of CABG using TTFM and Epi-cardiac Ultrasound Imaging.. 23rd Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2015.05.12 Hong Kong
7. Kuroki H., Oi K., Mizuno T., Hachimaru T., Watanabe T., Fujiwara T., Sakurai S., Arai H.. Graft selection for left circumflex artery in terms of long term outcomes of coronary artery bypass grafting.. 23rd Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2015.05.13 Hong Kong
8. Arai H.. (Moderator) Adult Cardiac – Asian Perspective (Mitral Valve). 23rd Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2015.05.13 Hong Kong
9. Arai H.. (Moderator) Free Paper Session /Invited Lectures(10). 23rd Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2015.05.14 Hong Kong
10. Mizuno T., Sakai K., Oi K., Hachimaru T., Makita T., Oishi K., Arai H.. Minimally Circulatory-Assisted On-Pump Beating Coronary Artery Bypass Grafting for Patients with High Risk of Hemodynamic Deterioration during Off-Pump Grafting. 2015 ISMICS Annual Scientific Meeting 2015.06.04 Berlin, Germany
11. Arai H., Watanabe T., Oi K., Mizuno T.. Intra-operative Quality Control of CABG using High Frequency Epicardial Ultrasound Imaging in combination with Transit Time Flow Measurement.. 2015 ISMICS Annual Scientific Meeting 2015.06.04 Berlin, Germany
12. Nagaoka E., Mizuno T., Oi K., Yashima M., Hachimaru T., Kuroki H., Tasaki D., Fujiwara T., Takeshita M., Kinoshita R., Arai H. . Assessment of Reverse Remodeling after Combination Therapy for Ischemic Mitral Regurgitation. AATS International Coronary Congress 2015 2015.08.21 New York, USA

13. Mizuno T., Oi K., Yashima M., Hachimaru T., Nagaoka E., Kuroki H., Tasaki D., Fujiwara T., Takeshita M., Kinoshita R., Arai H.. Long-Term Results of Off-Pump CABG for Left Main and Complex Coronary Artery Disease. AATS International Coronary Congress 2015 2015.08.21 New York, USA
14. Arai H.. Why I always Image the Ascending Aorta Intraoperatively. AATS International Coronary Congress 2015 2015.08.22 New York, USA
15. Arai H.. High Frequency Ultrasound Interrogation of the Anastomoses. AATS International Coronary Congress 2015 2015.08.22 New York, USA
16. Arai H.. (Moderator) Graft Assessment with Transit Time Flow Measurement. AATS International Coronary Congress 2015 2015.08.22 New York, USA
17. Arai H.. (Moderator) Abstracts/Videos (Parallel Session). AATS International Coronary Congress 2015 2015.08.22 New York, USA
18. Mizuno T., Oi K., Yashima M., Hachimaru T., Nagaoka E., Kuroki H., Tasaki D., Fujiwara T., Takeshita M., Kinoshita R., Arai H.. Standardized Surgical Techniques of Off Pump Cabg to Accomplish High Complete Revascularization. AATS International Coronary Congress 2015 2015.08.23 New Yorl,USA
19. Yoshiki H, Tadano K, Ban D, Ohuchi K, Tanabe M, Kawashima K. Surgical Energy Device Using Steam Jet for Robotic Assisted Surgery. 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2015.08.28 Milan, Italy
20. Arai H.. Intraoperative Quality Control of CABG using High Resolution Epicardial Ultrasonography.. 3rd Heart Care Heart International Symposium 2015.09.04 Thailand
21. Arai H.. Challenges in Training Cardiothoracic Surgery in Current Era.. 3rd Heart Care Heart International Symposium 2015.09.06 Thailand
22. Arai H.. Pericardial Augmentation for Severe TR caused by Pace Maker Lead.. 3rd Heart Care Heart International Symposium 2015.09.06 Thailand
23. Fujiwara T., Sakota D., Ouchi K., Murashige T., Kosaka R., Nishida M., Endo S., Nagaoka E., Oi K., Mizuno T., Maruyama O., Arai H.. The Real-Time Optical Monitoring of Thrombus Formation Inside the Blood Pump During Extracorporeal Circulation Using Hyperspectral Imaging in Acute Animal Experiments. 23rd Annual Congress of the International Society for Rotary Blood Pumps 2015.09.28 Dubrovnik
24. Onishi T, Arafune T, Ohuchi K, Nomoto A, Tachiyanagi N. Normalized pulse volume on pain new findings and its application to pain monitoring. IAMPOV International Symposium 2015.10.04 Tokyo, Japan

Nephrology

Professor Shinichi UCHIDA
Tatemitsu RAI (Dept. of Nephrology and Regional Medicine (Ibaraki))
Associate Professor Tomokazu OKADO (Dept. of Blood Purification)
Eisei SOHARA
Junior Associate Professor Shotaro NAITO
Assistant Professor Naohiro NOMURA
Koichiro SUSA (Dept. of Blood Purification)
Daiei TAKAHASHI (Dept. of Blood Purification)
Moko ZENIYA (Dept. of Nephrology and Regional Medicine (Ibaraki))
Project Assistant Professor Soichiro IIMORI
Assistant Professor Takayasu MORI
Graduate Student Yuya ARAKI, Yutaro MORI, Humiaki ANDO
Yuki YOSHIZAKI, Yohei ARAI, Yuri KASAGI
Emi SASAKI, Shintaro MANDAI, Sayaka YOSHIDA
Genryu Ou, Hiroaki KIKUCHI, Wakana SHODA, Hiroko HASHIMOTO
Hospital Staff Hidehiko SATO (Dept. of Blood Purification)
Satomi SAITO, Megumi YAMAMURO, Megumi OHWADA
Resident Ryohei KAWAMOTO, Ayumu NOMIZU
Technician Chieko IJIMA, Motoko CHIGA
Secretary Asa MURANO, Yukiko ITO

(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 2015, our 12 presentations, including "top oral abstract for ASN", were adopted in the annual meeting of American society of nephrology (ASN KIDNEY WEEK). Moreover, the articles written by Moko Zeniya, assistant professor, and by Eriko Kikuchi, graduate student, were all accepted by the Journal of the American Society of Nephrology (IF: 9.34), which is the highest journal in the nephrology field. Both of them were presented in "press release", and the article written by Zeniya was selected for cover article of the Journal of the American Society of Nephrology.

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) is 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 over 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 3 to 5 students every year in the project semester, in which they are expected to participate in the forefront research together with 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 three months, which is more practical and comprehensive than that the previous lectures held in the classroom. After that, 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 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 at 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 blood purification center is one of the biggest institutions among 42 hospitals belonging to national universities. In 2014, the number of newly started dialysis patients was in 1st place, the number of plasma exchange was 1st place, the number of endotoxin absorption was 2nd place, and total number of blood purification therapy was within 3rd 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. Araki Yuya, Rai Tatemitsu, Sohara Eisei, Mori Takayasu, Inoue Yuichi, Isobe Kiyoshi, Kikuchi Eriko, Ohta Akihito, Sasaki Sei, Uchida Shinichi. Generation and analysis of knock-in mice carrying pseudohypoaldosteronism type II-causing mutations in the cullin 3 gene. *Biol Open*. 2015; 4(11); 1509-1517
2. Oi Katsuyuki, Okado Tomokazu, Togo Hisako, Iimori Soichiro, Yui Naofumi, Sohara Eisei, Kanda Eiichiro, Rai Tatemitsu, Sasaki Sei, Uchida Shinichi. Two Cases of Hemodialysis-associated Chronic Portal-systemic Shunt Encephalopathy (CPSE) with Opposite Changes in the Blood Ammonia Concentrations during Hemodialysis: A Case Report and Literature Review. *Intern Med*. 2015; 54(11); 1375-1380
3. Ihara Katsuhito, Naito Shotaro, Okado Tomokazu, Rai Tatemitsu, Mori Yutaro, Toda Takayuki, Uchida Shinichi, Sasaki Sei, Matsui Noriaki. Successful recovery from an acute kidney injury due to amniotic fluid embolism. *Intern Med*. 2015; 54(1); 49-54
4. Gotoh Yusuke, Kita Satomi, Fujii Makoto, Tagashira Hideaki, Horie Ichiro, Arai Yuji, Uchida Shinichi, Iwamoto Takahiro. Genetic knockout and pharmacologic inhibition of NCX2 cause natriuresis and hypercalciuria. *Biochem Biophys Res Commun*. 2015.01; 456(2); 670-675
5. Okado T, Iimori S, Nishida H, Yui N, Sohara E, Rai T, Uchida S, Sasaki S. Successful treatment of Mycobacterium chelonae peritoneal dialysis-related infection by a combination regimen including local thermal therapy. *Peritoneal dialysis international*. 2015.01; 35(1); 114-116
6. Miyauchi Takayuki, Yamamoto Hiroyuki, Abe Yoichiro, Yoshida Go J, Rojek Aleksandra, Sohara Eisei, Uchida Shinichi, Nielsen Soren, Yasui Masato. Dynamic subcellular localization of aquaporin-7 in white adipocytes. *FEBS Lett*. 2015.02; 589(5); 608-614
7. Hiroaki Kikuchi, Takayasu Mori, Tatemitsu Rai, Shinichi Uchida. Acute kidney injury caused by sarcoid granulomatous interstitial nephritis without extrarenal manifestations CEN case reports. 2015.03;
8. Yoshizaki Yuki, Yui Naofumi, Okado Tomokazu, Ishigami Junichi, Iimori Soichiro, Oi Katsuyuki, Sohara Eisei, Sasaki Sei, Rai Tatemitsu, Uchida Shinichi. Retroperitoneal Fibrosis in Chronic Kidney Disease General Medicine. 2015.06; 16(2); 103-106
9. Sohara Eisei, Uchida Shinichi. Kelch-like 3/Cullin 3 ubiquitin ligase complex and WNK signaling in salt-sensitive hypertension and electrolyte disorder. *Nephrol Dial Transplant*. 2015.07;
10. Kikuchi Eriko, Mori Takayasu, Zeniya Moko, Isobe Kiyoshi, Ishigami-Yuasa Mari, Fujii Shinya, Kagechika Hiroyuki, Ishihara Tomoaki, Mizushima Tohru, Sasaki Sei, Sohara Eisei, Rai Tatemitsu, Uchida Shinichi. Discovery of Novel SPAK Inhibitors That Block WNK Kinase Signaling to Cation Chloride Transporters. *J Am Soc Nephrol*. 2015.07; 26(7); 1525-1536
11. Ohkubo Atsushi, Okado Tomokazu, Kurashima Naoki, Maeda Takuma, Arai Shingo, Miyamoto Satoko, Itagaki Ayako, Seshima Hiroshi, Iimori Soichiro, Naito Shotaro, Sohara Eisei, Uchida Shinichi, Rai Tatemitsu. Removal Characteristics of Immunoglobulin G Subclasses by Conventional Plasma Exchange and Selective Plasma Exchange. *Ther Apher Dial*. 2015.08; 19(4); 361-366
12. Iimori Soichiro, Naito Shotaro, Noda Yumi, Nishida Hidenori, Kihira Hiromi, Yui Naofumi, Okado Tomokazu, Sasaki Sei, Uchida Shinichi, Rai Tatemitsu. Anaemia management and mortality risk in newly visiting patients with chronic kidney disease in Japan: The CKD-ROUTE study. *Nephrology (Carlton)*. 2015.09; 20(9); 601-608
13. Zeniya Moko, Morimoto Nobuhisa, Takahashi Daiei, Mori Yutaro, Mori Takayasu, Ando Fumiaki, Araki Yuya, Yoshizaki Yuki, Inoue Yuichi, Isobe Kiyoshi, Nomura Naohiro, Oi Katsuyuki, Nishida Hidenori, Sasaki Sei, Sohara Eisei, Rai Tatemitsu, Uchida Shinichi. Kelch-Like Protein 2 Mediates Angiotensin II-With No Lysine 3 Signaling in the Regulation of Vascular Tonus. *J Am Soc Nephrol*. 2015.09; 26(9); 2129-2138
14. Kuwahara Michio, Arai Youhei, Takehara Eriko, Sasaki Yasunori, Yoshimine Tomoharu, Kusaka Keita, Shikuma Satomi, Akita Wataru, Uchida Shinichi. Early response to erythropoiesis-stimulating agents in non-dialysis chronic kidney disease patients. *Clin Exp Nephrol*. 2015.10;

15. Arthur Julian, Huang Jianmin, Nomura Naohiro, Jin William W, Li Wei, Cheng Xiang, Brown Dennis, Lu Hua Jenny. Characterization of the putative phosphorylation sites of the AQP2 C terminus and their role in AQP2 trafficking in LLC-PK1 cells. *Am J Physiol Renal Physiol*. 2015.10; 309(8); F673-F679
16. Mori Yutaro, Mori Takayasu, Wakabayashi Mai, Yoshizaki Yuki, Zeniya Moko, Sohara Eisei, Rai Tatemitsu, Uchida Shinichi. Involvement of selective autophagy mediated by p62/SQSTM1 in KLHL3-dependent WNK4 degradation. *Biochem J*. 2015.11; 472(1); 33-41
17. Yoshizaki Yuki, Mori Yutaro, Tsuzaki Yoshihito, Mori Takayasu, Nomura Naohiro, Wakabayashi Mai, Takahashi Daiei, Zeniya Moko, Kikuchi Eriko, Araki Yuya, Ando Fumiaki, Isobe Kiyoshi, Nishida Hidenori, Ohta Akihito, Susa Koichiro, Inoue Yuichi, Chiga Motoko, Rai Tatemitsu, Sasaki Sei, Uchida Shinichi, Sohara Eisei. Impaired degradation of WNK by Akt and PKA phosphorylation of KLHL3. *Biochem Biophys Res Commun*. 2015.11; 467(2); 229-234
18. Kikuchi H, Ishigami J, Inoue Y, Mori T, Susa K, Iimori S, Nomura N, Naito S, Kuwana H, Yui N, Sohara E, Okado T, Rai T, Uchida S. A subacute kidney injury with hyperkalemia manifested 3 weeks after adrenalectomy 2015.11; 42; 42-45
19. Mandai Shintaro, Mori Takayasu, Sohara Eisei, Tatemitsu Rai, Uchida Shinichi. Generation of Hypertension-Associated STK39 Polymorphism Knockin Cell Lines With the Clustered Regularly Interspaced Short Palindromic Repeats/Cas9 System. *Hypertension*. 2015.12; 66(6); 1199-1206
20. Yuichi Inoue. Aberrant glycosylation and localization of polycystin-1 caused polycystic kidney in an AQP11 knockout model 2015.12; 57(8); 1316-1318

[Misc]

1. Mori Takayasu, Uchida Shinichi. Causative genetic variants of pseudohypoaldosteronism type II and essential hypertension *Nihon Jinzo Gakkai Shi*. 2015.05; 57(4); 751-757
2. Kikuchi Eriko, Mori Takayasu, Uchida Shinichi. WNK-SPAK-SLC12A signal cascade is a new therapeutic target for hypertension *Nihon Rinsho*. 2015.09; 73(9); 1597-1605

[Conference Activities & Talks]

1. Kikuchi H, Kanda E, Mandai S, Akazawa M, Iimori S, Oi K, Toda T, Tamura T, Sasaki S, Okado T, Rai T, Uchida S. Low Serum Albumin and Body Mass Index Predicts Chronic Kidney Disease Progression. The 4th Chronic Kidney Disease Frontier Meeting 2015.02.28 Nagoya
2. Rai T. Chronic kidney disease (CKD) and preventive medicine - Screening for drugs with novel actions. TMU-TMDU Joint Symposium 2015.03.14 Tokyo
3. Low body mass index and low serum albumin level are associated with the progression of chronic kidney disease. 2015.06.05
4. Yuichi Inoue. Aberrant glycosylation and localization of polycystin-1 caused polycystic kidney in an AQP11 knockout model. 2015.08.29
5. A Case of chronic kidney disease acutely exacerbated by rhabdomyolysis, in which CT scan was useful for the diagnosis.. 2015.10.02
6. A case of nephropathy induced by Sunitinib. 2015.10.02
7. Yui Naofumi, Sasaki Sei, Uchida Shinichi. Dephosphorylation at Ser-261 is a determinant for the regulated AQP2 apical accumulation. The 48th Annual Meeting of American Society of Nephrology 2015.11 San Diego, USA
8. Yuya Araki, Tatemitsu Rai, Eisei Sohara, Takayasu Mori, Yuichi Inoue, Eriko Kikuchi, Shinichi Uchida. Generation and Analysis of Knock-In Mice Carrying Pseudohypoaldosteronism Type II-Causing Mutations in the Cullin 3 Gene. ASN 2015.11.05 San Diego
9. Nomura Naohiro, Shoda Wakana, Sohara Eisei, Rai Tatemitsu, Uchida Shinichi. Potassium-induced dephosphorylation of renal sodium-chloride cotransporter is NOT dependent on the anions. The 48th Annual Meeting of the American Society of Nephrology 2015.11.05 San Diego, USA

10. Mandai S, Kanda E, Iimori S, Naito S, Sohara E, Okado T, Sasaki S, Rai T, Uchida S. Association of Serum Chloride Level with Mortality and Cardiovascular Events in Chronic Kidney Disease: The CKD-ROUTE Study. The 48th Annual Meeting of American Society of Nephrology 2015.11.05 San Diego
11. Mandai S, Mori T, Sohara E, Rai T, Uchida S. Generation of Hypertension-Associated STK39 Polymorphism Knockin Cell Lines with the CRISPR/Cas9 System. The 48th Annual Meeting of American Society of Nephrology 2015.11.05 San Diego
12. Susa Koichiro, Sohara Eisei, Takahashi Daiei, Rai Tatemitsu, Uchida Shinichi. The Major Contribution of WNK4 to the Pathogenesis of Pseudohypoaldosteronism Type II (PHAII) Caused by the KLHL3 Mutation R528H. The 48th Annual Meeting of American Society of Nephrology 2015.11.05 San Diego
13. Kikuchi H, Kanda E, Iimori S, Naito S, Sasaki S, Sohara E, Okado T, Rai T, Uchida S. Combination of low body mass index and serum albumin level leads to chronic kidney disease progression: the chronic kidney disease—research of outcomes in treatment and epidemiology study. The 48th Annual Meeting of American Society of Nephrology 2015.11.05 San Diego, USA
14. Naito S, Iimori S, Sohara E, Okado T, Sasaki S, Uchida S, Rai T. The Effects of Diuretics on the Progression of CKD and Incidence of Cardiovascular Events: Results from the CKD-ROUTE Study – A Prospective Cohort Study of Newly Visiting CKD Patients in Japan. The 48th Annual Meeting of American Society of Nephrology 2015 2015.11.05 San Diego
15. Shoda W, Yui N, Naito S, Iimori S, Susa K, Mori T, Nomura N, Sohara E, Okado T, Rai T, Uchida S. Sunitinib-Induced Nephrotic Syndrome and Acute Kidney Injury in a Malignant Insulinoma Patient: A Case Report. The 48th Annual Meeting of American Society of Nephrology 2015 2015.11.07 San Diego
16. Takehara Eriko, Mandai Shintaro, Uchida Shinichi . Reversal of Dialysis-Dependent Renal Failure and Nephrotic Syndrome after Conservative Therapy in an Adult with Proliferative Glomerulonephritis with C3-Dominant Deposition. 2015.11.07 San Diego, USA
17. Uchida Shinichi. The KLHL proteins, the WNKs and renal Na⁺ transport.. 8Th FAOPS (Federation of the Asian and Oceanian Physiological Societies) Congress 2015.11.23 Bangkok, Thailand

[Awards & Honors]

1. Young Investigator Award, 2015.08

Comprehensive Reproductive Medicine

Professor : Toshiro KUBOTA

Associate Professor : Satoshi OBAYASHI

Project Professor : Naoyuki MIYASAKA

Junior Associate Professor : Naoyuki YOSHIKI, Tatsuya HARADA

Project Associate Professor : Masakazu TERAUCHI

Project Junior Associate Professor: Akira WAKABAYASHI

Assistant Professor : Kimio WAKANA, Tomonori ISHIKAWA, Mikayo TOBA, Makiko EGAWA, Yuki IWAHARA,

Noriko OSHIMA- SUDO, Shiro HIRAMITSU, Mayumi YOKOTA, Atsushi YAMAMOTO, Takafumi TSUKADA

Hospital Staff : Mayumi ONIZUKA, Kotoi TSURANE, Chiaki MOCHIZUKI, Yoko FUJIOKA

Graduate Student : Reiko SHIRAI, Makoto IIZUKA, Kiyotaka TAKAGI, Izumi HONDA, Aiko TAKATA,

Asuka HIROSE, Takashi NAKASUJI, Kazuki SAITO, Akiko FURUSAWA, Takuto MATSUURA, Rie OI,

Takayuki TATSUMI, Masaki SEKIGUCHI, Ayumi YAMAGUCHI, Yuri SUKENOBE

(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. Yasui Toshiyuki, Hayashi Kunihiro, Nagai Kazue, Mizunuma Hideki, Kubota Toshiro, Lee Jung-Su, Suzuki Shosuke. Risk profiles for endometriosis in Japanese women: results from a repeated survey of self-reports. *J Epidemiol.* 2015; 25(3); 194-203
2. Nagai Kazue, Hayashi Kunihiro, Yasui Toshiyuki, Katanoda Kota, Iso Hiroyasu, Kiyohara Yutaka, Wakatsuki Akihiko, Kubota Toshiro, Mizunuma Hideki. Disease history and risk of comorbidity in women's life course: a comprehensive analysis of the Japan Nurses' Health Study baseline survey. *BMJ Open.* 2015; 5(3); e006360
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17. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Prevalence and predictors of storage lower urinary tract symptoms in perimenopausal and postmenopausal women attending a menopause clinic. *Menopause*. 2015.10; 22(10); 1084-1090
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[Conference Activities & Talks]

1. Masakazu Terauchi. Pharmacological Treatment of Depression in Peri- and Early Post-Menopausal Women. World Congress on Women' s Mental Health 2015.03.24 Tokyo
2. Saito K, Kubota T, Kuwahara A, Saito H.. Hormone replacement in the frozen-thawed embryo transfer cycle is a risk factor of caesarean section. The IFFS/JSRM International Meeting 2015 2015.04.26 Yokohama
3. Masakazu Terauchi. Symposium 14: STD "Screening and treatment of Chlamydia trachomatis genital infection". 24th Asian & Oceanic Congress of Obstetrics & Gynecology 2015.06.06 Kuching, Malaysia

4. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Feeling of Unattractiveness in Peri- and Postmenopausal Women is Associated with Depressed Mood, Poor Memory, and Unsatisfactory Sexual Relationship. North American Menopause Society 26th Annual Meeting 2015.10.01 Las Vegas, NV
5. Iizuka M, Yamaguchi A, Ohkura Y, Obayashi S, Kubota T. . Effect of gamma-oryzanol purified from rice bran oil on quality of vascular endothelial function.. 26th Annual Meeting of North American Menopause Society (NAMS), 2015.10.01 LasVegas, Nevada
6. Furusawa A, Mochizuki C, Kohri Y, Fusegi A, Yoshida T, Tsugata M, Umeki H, Kubota T, Somekawa Y.. Tumorectomy for recurrent uterine body cancer. . 19th International Meeting of the European Society of Gynaecological Oncology (ESGO) 2015.10.25 Nice

Urology

Professor and Chairman: Kazunori Kihara

Associate Professor: Yasuhisa Fujii

Junior Associate Professor: Kazutaka Saito,

Noboru Numao (Department of Insured Medical Care Management), Yoh Matsuoka,

Junichiro Ishioka (-March Center for Minimally Invasive Surgery, April-)

Assistant Professor: Minato Yokoyama, Soichiro Yoshida, Manabu Tatokoro (-March), Masaya Ito, Masaharu Inoue (April-)

Hospital Staff: Naoko Kawamura, Masaharu Inoue (-March), Hajime Tanaka, Takayuki Nakayama, Shingo Moriyama, Yuma Waseda, Masaki Kobayashi (April-September), Yuki Nakamura (April-), Motohiro Fujiwara (April-)

Graduate Student Naoko Kawamura, Sachi Kitayama, Toshihiro Kanda, Masaharu Inoue (-March), Hajime Tanaka (-March), Takayuki Nakayama (-March), Saori Araki, Yosuke Yasuda, Sho Uehara, Yuma Waseda (April-), Hiroshi Fukushima (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 CO2 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. Sho Uehara, Takeshi Yuasa, Yasuhisa Fujii, Akihiro Yano, Shinya Yamamoto, Hitoshi Masuda, Iwao Fukui, Junji Yonese. Prior administration of a non-steroidal anti-androgen failed to prevent the flare-up caused by a luteinizing hormone-releasing hormone agonist in a patient with metastatic prostate cancer. *BMC Res Notes*. 2015; 8; 335
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3. Masashi Nagata, Yasuyoshi Ishiwata, Yutaka Takahashi, Hiromitsu Takahashi, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara, Masato Yasuhara. Pharmacokinetic-pharmacodynamic analysis of sunitinib-

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 5. Yasuda Yosuke, Fujii Yasuhisa, Yuasa Takeshi, Yamamoto Shinya, Yonese Junji, Fukui Iwao. Do testosterone levels have prognostic significance in patients with metastatic prostate cancer treated with combined androgen blockade? *Int J Urol.* 2015.01; 22(1); 132-133
 6. Yamamoto Shinya, Masuda Hitoshi, Urakami Shinji, Fujii Yasuhisa, Sakamoto Kimihiko, Kozuka Takuyo, Oguchi Masahiko, Fukui Iwao, Yonese Junji. Patient-perceived Satisfaction After Definitive Treatment for Men With High-risk Prostate Cancer: Radical Prostatectomy vs Intensity-modulated Radiotherapy With Androgen Deprivation Therapy. *Urology.* 2015.02; 85(2); 407-414
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 8. Kazunori Kihara, Fumitaka Koga, Yasuhisa Fujii, Hitoshi Masuda, Manabu Tatokoro, Minato Yokoyama, Yoh Matsuoka, Noboru Numao, Junichiro Ishioka, Kazutaka Saito. Gasless laparoendoscopic single-port clampless sutureless partial nephrectomy for peripheral renal tumors: perioperative outcomes. *Int. J. Urol.* 2015.04; 22(4); 349-355
 9. Soichiro Yoshida, Masaya Ito, Manabu Tatokoro, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Multitask Imaging Monitor for Surgical Navigation: Combination of Touchless Interface and Head-Mounted Display. *Urol. Int.* 2015.04;
 10. Soichiro Yoshida, Naotaka Fukui, Kazutaka Saito, Yasuhisa Fujii, Yukio Kageyama, Kazunori Kihara. Novel image monitoring system using a head-mounted display for assistants in da Vinci surgery. *Int. J. Urol.* 2015.05; 22(5); 520-521
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 15. Masaharu Inoue, Yasuhisa Fujii, Minato Yokoyama, Kazutaka Saito, Noboru Numao, Kazunori Kihara. Progression of hypertension after partial nephrectomy in patients with renal tumors: A preliminary report. *Int. J. Urol.* 2015.08; 22(8); 797-798
 16. Masanori Murakami, Takanobu Yoshimoto, Isao Minami, Ryotaro Bouchi, Kyoichiro Tsuchiya, Koshi Hashimoto, Hajime Izumiyama, Yasuhisa Fujii, Takashi Endo, Takumi Akashi, Koshiro Nishimoto, Kuniaki Mukai, Kazunori Kihara, Yoshihiro Ogawa. A Novel Somatic Deletion Mutation of ATP2B3 in Aldosterone-Producing Adenoma. *Endocr. Pathol.* 2015.10;
 17. Shinji Urakami, Takeshi Yuasa, Shinya Yamamoto, Mizuaki Sakura, Hajime Tanaka, Tatsuro Hayashi, Sho Uehara, Yasushi Inoue, Yasuhisa Fujii, Hitoshi Masuda, Iwao Fukui, Junji Yonese. Clinical response to induction chemotherapy predicts improved survival outcome in urothelial carcinoma with clinical lymph nodal metastasis treated by consolidative surgery. *Int. J. Clin. Oncol.* 2015.12; 20(6); 1171-1178

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[Books etc]

1. Kazunori Kihara, Yasuhisa Fujii, Kazutaka Saito, Fumitaka Koga, Noboru Numao, Yoh Matsuoka, Junichiro Ishioka, Minato Yokoyama, Hitoshi Masuda, Tatsuya Nagai, Soichiro Yoshida, Manabu Tatokoro, Toshiki Kijima, Naoko Kawamura, Masaharu Inoue, Masaya Ito. *Gasless Single-Port RoboSurgeon Surgery in Urology*. Springer, 2015.09 (ISBN : 978-4-431-54504-0)

[Misc]

1. Manabu Tatokoro, Fumitaka Koga, Soichiro Yoshida, Kazunori Kihara. Heat shock protein 90 targeting therapy: state of the art and future perspective. *EXCLI J.* 2015; 14; 48-58
2. Yasuhisa Fujii. Editorial Comment from Dr Fujii to Early unclamping might reduce the risk of renal artery pseudoaneurysm after robot-assisted laparoscopic partial nephrectomy. *Int. J. Urol.* 2015.12; 22(12); 1103

[Conference Activities & Talks]

1. Masaharu Inoue, Yasuhisa Fujii, Minato Yokoyama, Masaya Ito, Manabu Tatokoro, Soichiro Yoshida, Junichiro Ishioka, Yoh Matsuoka, Noboru Numao, Kazutaka Saito, Kazunori Kihara. Progression of hypertension after partial nephrectomy in Japanese patients with renal tumors. 30th Annual EAU Congress 2015.03.21 Madrid, Spain
2. Nakayama T., Saito K., Fujii Y., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Numao N, Kihara K. Prognostic comparison of serum biomarkers for cancer-specific survival of renal cell carcinoma undergoing nephrectomy: C-reactive protein has the highest predictive ability on survival. The 30th Annual Congress of the European Association of Urology 2015.03.21 Madrid, Spain
3. Numao N., Ito M., Uchida Y., Yoshida S., Nakayama T., Inoue M., Tatokoro M., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Fujii Y., Kihara K. Optimal number of sampling cores in MRI-targeted biopsy. The 30th Annual Congress of the European Association of Urology 2015.03.21 Madrid, Spain
4. Tanaka H, Fujii Y, Ito M, Tatokoro M, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Numao N, Saito K, Yonese J, Kihara K. Novel prediction model for fat-poor angiomyolipoma in small renal masses based on radiological and clinical features. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
5. Tatokoro M., Nakanishi Y., Komai Y., Matsuoka Y., Ishioka J., Numao N., Yoshimoto K., Saito K., Fujii Y., Ogawa Y., Kihara K. Impaired glucose tolerance predicts the development of hypoglycemia after removal of pheochromocytoma. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
6. Moriyama S., Saito K., Ishioka J., Kageyama Y., Morimoto S., Arisawa C., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Matsuoka Y., Numao N., Fujii Y., Kihara K. Preoperative prediction algorithm for the selection of candidates for neoadjuvant chemotherapy in upper tract urothelial carcinomas. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
7. Fujii, Y., Kihara, K., Numao, N., Matsuoka, Y., Ishioka, J., Saito, K. Gasless single-port RoboSurgeon partial cystectomy: A hybrid technique combining an intravesical and extravesical approach. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain

8. Fujii, Y., Kihara, K., Numao, N., Tanaka H., Tatokoro M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Numao N., Saito K. Selective bladder-sparing protocol consisting of low-dose chemoradiotherapy and consolidative partial cystectomy against muscle-invasive bladder cancer: oncological and functional outcome. The 30th Annual Congress of the European Association of Urology 2015.03.22 Madrid, Spain
9. Ishioka J, Yokoyama M, Waseda Y, Kawamura N, Ito M, Tatokoro M, Yoshida S, Matsuoka Y, Numao N, Saito K, Arisawa C, Morimoto S, Kageyama Y, Fujii Y, Kihara K. Preoperative prediction of postoperative renal function for upper tract urothelial carcinoma patients: Concerning issues of perioperative renal impairment and the use of cisplatin-based chemotherapy. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
10. Kawamura N., Yokoyama M., Fujii Y., Ishioka J., Numao N., Matsuoka Y., Saito K, Arisawa C., Okuno T., Noro A., Morimoto S., Kihara K. Longitudinal change and risk factors of severe deterioration in renal function after radical nephrectomy. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
11. Nakamura Y. , Numao N. , Yoshida S. , Komai Y. , Ito M. , Tatokoro M. , Yokoyama M. , Ishioka J. , Matsuoka Y. , Saito K. , Fujii Y. , Kihara K.. Transrectal 12-core prostate biopsy and MRI have a comparable risk of missing significant prostate cancer in men with PSA less than 10ng/ml and normal DRE. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
12. Fujii, Y., Moriyama S., Yokoyama M., Yonese J., Noro A., Arisawa C., Morimoto S., Okuno T., Kitahara S., Koga F., Sakai Y., Suzuki M., Nagahama K., Izutani T., Saito K., Kihara K. Bladder neck involvement predicts progression in patients with primary non-muscle-invasive bladder cancer: A multicenter validation study. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
13. Yoshida S., Fukuyo T., Ito M., Tatokoro M., Yokoyama M, Ishioka J., Matsuoka Y., Numao N., Saito K., Fujii Y., Kihara K. A novel three-dimensional image display system for transurethral surgery. The 30th Annual Congress of the European Association of Urology 2015.03.23 Madrid, Spain
14. Moriyama S., Saito K., Ishioka J., Kageyama Y., Morimoto S., Arisawa C., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Matsuoka Y., Numao N., Fujii Y., Kihara K. Preoperative selection algorithm for eligible neoadjuvant chemotherapy patients in upper tract urothelial carcinomas. The 111th annual meeting of the American Urological Association 2015.05.15 New Orleans, USA
15. Tanaka H., Fujii Y., Ito M., Tatokoro M., Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Numao N., Saito K., Yonese J., Kihara K. Development and validation of a novel prediction model for fat-poor angiomyolipoma in small renal masses based on radiological and clinical features. The 111th annual meeting of the American Urological Association 2015.05.15 New Orleans, USA
16. Tatokoro M., Nakanishi Y., Komai Y., Matsuoka Y., Ishioka J., Numao N., Yoshimoto K., Saito K., Fujii Y., Ogawa Y., Kihara K. Impact of impaired glucose tolerance on the development of hypoglycemia following removal of pheochromocytoma. 111th annual meeting of the American Urological Association 2015.05.15 New Orleans, USA
17. Waseda Y., Ishikawa Y., Kawano K., Kihara K., Morimoto S. Simple prediction of postoperative renal function with dynamic CT before nephroureterectomy: the ratio of renal cortex enhancement on diseased to contralateral kidney. The 111th annual meeting of the American Urological Association 2015.05.15 New Orleans, USA
18. Fujii, Y., Moriyama S., Yokoyama M., Yonese J., Noro A., Arisawa C., Morimoto S., Okuno T., Kitahara S., Koga F., Sakai Y., Suzuki M., Nagahama K., Izutani T., Saito K., Kihara K, TMDU NMIBC group.. Impact of bladder neck involvement on progression in patients with primary non-muscle-invasive bladder cancer: A multicenter validation study. The 111th annual meeting of the American Urological Association 2015.05.16 New Orleans, USA
19. Yoshida S., Fukuyo T., Ito M., Tatokoro M., Ishioka J., Matsuoka Y., Numao N., Saito K., Fujii Y., Kihara K. Development of new three-dimensional image system for transurethral surgery. The 111th annual meeting of the American Urological Association 2015.05.16 New Orleans, USA
20. Yoshida S., Fukuda S., Kanda T., Fukui N., Saito K., Fujii Y., Kageyama Y, Kihara K. Novel image monitoring system using a head-mounted display for assistants in da Vinci surgery. The 111th annual meeting of the American Urological Association 2015.05.16 New Orleans, USA,

21. Numao N., Ito M., Uchida Y., Yoshida S., Nakayama T., Inoue M., Tatokoro M., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Fujii Y., Kihara K. Optimal MRI-targeted biopsy sampling number. The 111th annual meeting of the American Urological Association 2015.05.17 New Orleans, USA
22. Kawamura N., Yokoyama M., Fujii Y., Ishioka J., Numao N., Matsuoka Y., Saito K., Arisawa C., Okuno T., Noro A., Morimoto S., Kihara K. Recovery in renal function after radical nephrectomy and its negative predictive factors: a multicenter longitudinal study. The 111th annual meeting of the American Urological Association 2015.05.18 New Orleans, USA
23. Fujii Y., Kihara K., Tanaka H., Tatokoro M., Yoshida S. Yokoyama M., Ishioka J., Matusoka Y., Numao N., Saito K. Oncological and functional outcomes in muscle-invasive bladder cancer patients undergoing bladder-sparing treatment consisting of low-dose chemoradiotherapy and consolidative partial cystectomy. The 111th annual meeting of the American Urological Association 2015.05.18 New Orleans, USA
24. Yoshida S., Tanabe K., Koga F., Inoue M., Kobayashi S., Ishioka J., Tamura T., Sugawara E., Saito K., Akashi T., Fujii Y., Kihara K. Favorable survival outcomes after a chemoradiation-based multimodal approach against muscle-invasive bladder cancer with high Ki-67 expression. The 111th annual meeting of the American Urological Association 2015.05.18 New Orleans, USA
25. Matsuoka Y, Numao N, Saito K, Tanaka H, Ito M, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Kihara K. Eligibility analysis for focal therapy based on prostatectomy findings: Does intermediate-risk cancer have a higher likelihood of undertreatment than low-risk cancer?. 8th International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer 2015.06.21 Amsterdam, Netherland
26. Numao N, Ito M, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y, Kihara K. Efficient sampling methods in systematic biopsy that could be performed in combination with MRI-guided biopsy. 8th International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer 2015.06.21 Amsterdam, Netherland
27. Saito K, Matsuoka Y, Numao N, Hayashi K, Yoshida S, Yokoyama M, Ishioka J, Fujii Y, Yoshimura R, Kihara K. Focal therapy for prostate cancer with hemi-gland low dose rate brachytherapy. 8th International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer 2015.06.21 Amsterdam, Netherland
28. Saito K. Focal therapy for Prostate Cancer with Hemi-gland Brachytherapy. Dr.Grimm Online Workshop 2015.08.25 Tokyo

[Awards & Honors]

1. Reviewer of the Month, 2015.02
2. Poster Award: 30th Anniversary Congress of EAU (EAU 2015), European Association of Urology, 2015.03
3. Poster Award: 30th Anniversary Congress of EAU (EAU 2015), European Association of Urology, 2015.03
4. Poster Award: 30th Anniversary Congress of EAU (EAU 2015), European Association of Urology, 2015.03
5. Reviewer of the Year 2014, International Journal of Urology, 2015.04
6. 3rd prize of best poster award, International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer, 2015.06

Gastrointestinal Surgery

Professor

Tatsuyuki KAWANO

Project Professor

Masahiro TSUBAKI

Associate Professor

Masamichi YASHUNO, Mikito INOKUCHI, Yasuaki NAKAJIMA

Junior Associate Professor

Kenro KAWADA

Assistant Professor

Yutaka TOKAIRIN, Sho Otuki, Akifumi KIKUCHI,
Yoshitake FUJIMORI, Akihiro HOSHINO, Shinichi YAMAUCHI,
Takuya OKADA

Project Assistant Professor

Yutaka MIYAWAKI / Tetsuma CHIBA

Graduate Student

Hideaki MURASE, Tairo RYOTOKUJI, Toshio TANIOKA,
Naot FUJIWARA, Kenta KOBAYASHI, Katsumasa SAITO,
Yasunori SOMENO, Kyoko HIGUCHI, Hisashi FUJIWARA,
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 KAWAMURA, Kazuya Yamaguchi, Megumi SASAKI,
Rei GH0, 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. Hiroyuki Uetake , Masamichi Yasuno, Megumi Ishiguro, Shingo Kameoka, Yasuhiro Shimada, Keiichi Takahashi, Toshiaki Watanabe, Kei Muro, Hideo Baba, Junji Yamamoto, Nobuyuki Mizunuma, , Izumi Mochizuki, Yusuke Kinugasa, Takashi Kikuchi, Kenichi Sugihara. A Multicenter Phase II Trial of mFOL-FOX6 Plus Bevacizumab to Treat Liver-Only Metastases of Colorectal Cancer that are Unsuitable for Upfront Resection (TRICC0808) *Annals of Surgical Oncology*. 2015; 22(3); 908-915
2. Kobayashi H, Kikuchi A, Okazaki S, Ishiguro M, Ishikawa T, Iida S, Uetake H, Sugihara K. Diagnostic performance of multidetector row computed tomography for assessment of lymph node metastasis in patients with distal rectal cancer. *Ann Surg Oncol*. 2015.01; 22(1); 203-208
3. Yutaka Tokairin, Kagami Nagai, Hisashi Fujiwara, Taichi Ogo, Masafumi Okuda, Yasuaki Nakajima, Kenro Kawada, Yutaka Miyawaki, Hisayo Nasu, Keiichi Akita, Tatsuyuki Kawano. Mediastinoscopic subaortic and tracheobronchial lymph node dissection with a new cervico-hiatal crossover approach in thiel-embalmed cadavers. *Int Surg*. 2015.04; 100(4); 580-588
4. Nakagawa M, Inokuchi M, Takagi Y, Kato K, Sugita H, Otsuki S, Kojima K, Uetake H, Sugihara K.. Erythropoietin-Producing Hepatocellular A1 is an Independent Prognostic Factor for Gastric Cancer. *Ann Surg Oncol*. 2015.07; 22(2); 2329-2335
5. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Yutaka Miyawaki, Takuya Okada, Kagami Nagai & Tatsuyuki Kawano. Endoscopic assessment 1 day after esophagectomy for predicting cervical esophagogastric anastomosis-relating complications. *Surg Endosc* (Epub ahead of print). 2015.07;
6. 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).
7. 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).

[Books etc]

1. Kawada K, Kawano T, Sugimoto T, et al. Observation of the pharynx to the cervical esophagus using transnasal endoscopy with blue laser imaging.. Somchai Amornytin(eds) : *Endoscopy-Innovative Uses and Emerging Technologies*, 1st ed, INTECH, Croatia, 2015

[Conference Activities & Talks]

1. Treatment and Strategy for superficial carcinoma of Barrett's Esophagus. 2015.05.15
2. Usefulness of magnifying endoscopy with Blue Laser Imaging for superficial esophageal cancer. 2015.05.17
3. Nakajima Y, Kawada K, Tokairin Y, Miyawaki Y, Okada T, Kawano T. Invasion into Adjacent Structures and the Speed of Growth of Recurrent Tumors are Useful Prognostic Markers for the Post-recurrence Survival of Esophageal Squamous Cell Carcinoma: A Retrospective Analysis of 114 Patients.. ESSR2015 2015.06.12 Liverpool
4. Yutaka Nakajima, Yasuaki Nakajima, Toshihiro Matsui, Yuichiro Kume, Naoto Fujiwara, Tairo Ryotokuji, Yutaka Miyawaki, Yutaka Tokairin, Kenro Kawada, Tatsuyuki Kawano. Stent Treatment as Therapeutic Strategy for Advanced Esophageal Cancer. The 69th Annual Meeting of the Japan Esophageal Society 2015.07.03 Yokohama

5. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Yutaka Miyawaki, Takuya Okada, Tairo Ryotokuji, Naoto Fujiwara, Hisashi Fujiwara, Taichi Ogo, Masafumi Okuda, Katsumasa Saito, Yuichiro Kume, Yutaka Nakajima, Toshihiro Matsui, kagami Nagai, Keiichi Akita, Tatsuyuki Kawano. Mediastinoscopic subaortic and tracheobronchial lymph node dissection with a crossover approach. The 70th General Meeting of the Japanese Society of Gastroentological Surgery 2015.07.16 Hamamatsu
6. Masafumi Okuda, Kenro Kawada, Toshihiro Matsui, Yuichiro Kume, Yutaka Nakajima, Naoto Fujiwara, Takuya Okada, Akihiro Hoshino, Tetsuma Chiba, Yutaka Tokairin, Yasuaki Nakajima, Tatsuyuki Kawano. Removal of a “huge” foreign object using Esophagogastroduodenoscopy combined with a curved laryngoscope.. OESO 13th World Conference 2015.08.31 Monaco
7. Kenro Kawada, Takuya Okada, Toshihiro Matsui, Yuichiro Kume, Yutaka Nakajima, Taichi Ogo, Akihiro Hoshino, Tetsuma Chiba, Yutaka Tokairin, Tatsuyuki Kawano. Salvage endoscopic submucosal dissection in patients with local failure after chemoradiotherapy for esophageal squamous cell carcinoma. OESO 13th World conference 2015.08.31 Monaco
8. Yutaka Nakajima, Kenro Kawada, Toshihiro Matsui, Yuichiro Kume, Taichi Ogo, Masafumi Okuda, Takuya Okada, Akihiro Hoshino, Tetsuma Chiba, Yutaka Tokairin, Yasuaki Nakajima, Tatsuyuki Kawano. Five cases of squamous cell carcinoma arising from esophageal diverticula treated with argon plasma coagulation. OESO 13th World Conference 2015.09.01 Monaco
9. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Tetsuma Chiba, Akihiro Hoshino, Takuya Okada, Hisashi Fujiwara, Yuichiro Kume, Yutaka Nakajima, Taichi Ogo, Masafumi Okuda, Toshihiro Matsui, Kagami Nagai, Keiichi Akita, Tatsuyuki Kawano. Mediastinoscopic subaortic and tracheobronchial LN dissection with a cervicohiatal crossover approach in radical esophagectomy. 2015 Congress of the European Society for Diseases of the Esophagus 2015.11.06 Stockholm
10. Nakajima Y, Kawada K, Tokairin Y, Chiba T, Hoshino A, Miyawaki Y, Okada T, Kawano T. Esophageal bypass surgery for an esophagorespiratory fistula.. Asian Pacific Digestive Week 2015 2015.12.05 Taipei
11. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Masafumi Okuda, Taichi Ogo, Katsumasa Saito, Naoto Fujiwara, Tairo Ryotokuji, Takuya Okada, Yutaka Miyawaki, Yuichi 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

Epigenetics

Associate Professor Takashi KOHDA
Professor Fumitoshi ISHINO
Assistant Professor Hirosuke SHIURA
Tokunin Lecturer Jiyoun LEE
Adjunct Lecturer Shin KOBAYASHI,
Graduate students Kiyotaka TAKAGI, Moe KITAZAWA, Ayumi Matsuzawa

(1) 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.

(2) Lectures & Courses

“Epigenetics” coupled with “Genetics” enables us to elucidate several ‘genomic functions’ in inheritance, development and evolution of organisms including our human beings. Genomic imprinting is one of the mammalian specific gene regulation mechanisms 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’. These studies show us how Epigenetics is important in mammalian biology. Our department focuses these mammalian specific genomic functions to elucidate how these genomic functions work and how new genomic functions have been evolved during evolution. Our final goal is to contribute to the 21st’s medicine and human biology by novel understanding of genomic functions.

(3) Publications

[Original Articles]

1. Ito M, Sferruzzi-Perri A N, Edwards C A, Adalsteinsson B T, Allen S E, Loo T-H, Kitazawa M, Kaneko-Ishino T, Ishino F, Stewart C L and Ferguson-Smith A C.. A trans-homologue interaction between reciprocally imprinted miR-127 and Rtl1 regulates placenta development. *Development*. 2015.07; 142(14); 2425-2430
2. Ono R, Ishii M, Fujihara Y, Kitazawa M, Usami T, Kaneko-Ishino T, Kanno J, Ikawa M and Ishino F.. Double strand break repair by capture of retrotransposon sequences and reverse-transcribed spliced mRNA sequences in mouse zygotes. *Scientific Reports*. 2015.07; 5; 12281
3. Irie M, Yoshikawa M, Ono R, Iwafune H, Furuse T, Yamada I, Wakana S, Yamashita Y, Abe T, Ishino F and Kaneko-Ishino T. Cognitive function related to the Sirh11/Zcchc16 gene acquired from an LTR retrotransposon in eutherians. *PLoS Genetics*. 2015.09; 11(9); 1005521

4. Kagami M, Kurosawa K, Miyazaki O, Ishino F, Matsuoka K, Ogata T.. Comprehensive clinical studies in 34 patients with molecularly defined UPD(14)pat and related conditions (Kagami-Ogata syndrome). *Eur J Hum Genet* . 2015.11; 23(11); 1488-1498

[Conference Activities & Talks]

1. Matsuzawa A, Lee J, Takahashi S and Ishino F.. Culture condition affect DNA methylation status of genomic imprinting in ES cells. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
2. Kawasaki Y, Tohda T, Kuroda Y and Ishino F.. Analysis of cytosine modifications by EnIGMA method. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
3. Lee J, Takahashi S, Kohda T, Matsuzawa A, Kawasumi M, Kanai M, Kaneko-Ishino T and Ishino F.. Stable culture of haploid ES cells by regulating cell cycle. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
4. Kitazawa M, Ono R, Oka S, Kaneko-Ishino T and Ishino F.. Effects of eutherian-specific Peg11 gene on pups and placentas. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
5. Kobayashi S, Hosoi Y, Shinohara Y, Okabe M and Ishino F. Live imaging of X chromosome re-activation and reprogramming of stem cells. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
6. Fumitoshi Ishino and Tomoko Kaneko-Ishino.. Mammalian evolution promoted by LTR retrotransposon-derived genes.. The International Conference of the Korean Society for Molecular and Cellular Biology (KSMCB) 2015 2015.09.23 COEX, Seoul
7. Ishino F. Beyond the Genomic imprinting. 2015.10.23
8. Ishino F. Beyond the genomic imprinting-its origin, relation to viviparity and retrotransposon-derived genes. 2015.11.05
9. Ishino F. Placental functions of LTR-retrotransposon-derived genes. 2015.11.05
10. Ishino F. Mammalian-specific genomic functions in development and evolution. 2015.11.25
11. Kiyotaka Takagi, Tatsuya Harada, Toshiro Kubota, Fumitoshi Ishino, Takashi Kohda. The age-dependent gene expression profiles of human blastocysts. The 38th Annual Meeting of the Molecular Biology Society of Japan 2015.12.01 Kobe Port Island, Hyogo
12. Yui Goto, Kenji Suzuki, Asuka Furuta, Takashi Kohda, Masahiro Ikawa, Toshinobu Nakamura. Critical function of Klf17 for zygotic gene activation in mice. The 38th Annual Meeting of the Molecular Biology Society of Japan 2015.12.01 Kobe Port Island, Hyogo
13. Ishino F and Kaneko-Ishino T. Mechanism of endogenization from LTR retrotransposons. 2015.12.02
14. Irie M, Ishino F and Kaneko-Ishino T. LTR retrotransposon-derived SIRH genes in mammals. 2015.12.04
15. Fumitoshi Ishino. Mammalian evolution by acquired genes. 2015.12.22 The University of Tokyo

Thoracic Surgery

Professor Kenichi Okubo
Junior Associate Professor Hironori Ishibashi
Assistant Professor Masashi Kobayashi
Hospital assistant professor
Graduate Student Chihiro Takasaki
Graduate Student Sachiko Kumazawa
Graduate Student Akiko Ui
Graduate Student Ken Takahashi
Graduate Student Katsutoshi Seto
Graduate Student Ryo Wakejima

(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
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. Sato T, Watanabe A, Kondo H, Kanzaki M, Okubo K, Yokoi K, Matsumoto K, Marutsuka T, Shinohara H, Teramukai S, Kishi K, Ebina M, Sugiyama Y, Meinoshin O, Date H. Japanese Association for Chest Surgery. Long-term results and predictors of survival after surgical resection of patients with lung cancer and interstitial lung diseases. *J Thorac Cardiovasc Surg.* 2015; 149(1); 64-69
2. Ishibashi H, Takasaki C, Okubo K . Phrenic nerve paralysis from recurrence of stage I thymoma with myasthenia gravis 10 years after complete resection. *Gen Thorac Cardiovasc Surg,* . 2015.06; 63(6); 365-368
3. Ishibashi H, Kobayashi M, Takasaki C, Okubo K . Interim results of pleurectomy/decortication and intra-operative intrapleural hyperthermic cisplatin perfusion for patients with malignant pleural mesothelioma intolerable to extrapleural pneumonectomy. *Gen Thorac Cardiovasc Surg,* . 2015.07; 63(7); 395-400
4. Sowa T, Menju T, Sonobe M, Nakanishi T, Shikuma K, Imamura N, Motoyama H, Hijiya K, Aoyama A, Chen F, Sato T, Kobayashi M, Yoshizawa A, Haga H, Sozu T. Association between epithelial-mesenchymal transition and cancer stemness and their effect on the prognosis of lung adenocarcinoma. *Cancer Med.* 2015.12; 4(12); 1853-1862
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* 2015 Sep.3(Epub ahead of print).

Igakuken Disease-oriented Molecular Biology

Visiting Professor	Takahiko Hara
Visiting Professor	Masanari Itokawa
Visiting Professor	Masato Hasegawa
Visiting Professor	Haruo Okado
Graduate Student	Takahiko Sugimoto, Seiji Kanzaki, Mai Kanokoda (April~), Marino Nakajima (April~), Rena Takahashi (April~), Natsumi Yokote (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. Y. Kodaka, K. Tanaka, K. Kitajima, K. Tanegashima, R. Matsuda, and T. Hara. LIM homeobox transcription factor Lhx2 inhibits skeletal muscle differentiation in part via transcriptional activation of *Msx1* and *Msx2*. **Exp. Cell Res.**, 331: 309-319, 2015.
2. K. Kitajima, M. Kawaguchi, K. Miyashita, M. Nakajima, M. Kanokoda, and T. Hara. Efficient production of T cells from mouse pluripotent stem cells by controlled expression of Lhx2. **Genes Cells**, 20: 720-738, 2015.
3. K. Tsuji, K. Tanegashima, K. Sato, K. Sakamoto, A. Shigenaga, T. Inokuma, *T. Hara, and *A. Otaka. Efficient one-pot synthesis of CXCL14 and its derivative using an N-sulfanylethylanilide peptide as a

peptide thioester equivalent and their biological evaluation. *Bioorg. Med. Chem.*, 23: 5909-5914, 2015.

*Corresponding authors.

4. K. Kitajima, M. Nakajima, M. Kanokoda, M. Kyba, A. Dandapat, J. Tolar, M. K. Saito, M. Toyoda, A. Umezawa, and T. Hara. GSK3b inhibition activates the CDX/HOX pathway and promotes hemogenic endothelial progenitor differentiation from human pluripotent stem cells. *Exp. Hematol.*, Published on October 23, 2015 as doi:10.1016/j.exphem.2015.09.007.
5. K. Uno, D. Nishizawa, S. Seo, K. Takayama, S. Matsumura, N. Sakai, K. Ohi, T. Nabeshima, R. Hashimoto, N. Ozaki, J. Hasegawa, N. Sato, F. Tanioka, H. Sugimura, K. I. Fukuda, S. Higuchi, H. Ujike, T. Inada, N. Iwata, I. Sora, M. Iyo, N. Kondo, M. J. Won, N. Naruse, K. Uehara-Aoyama, M. Itokawa, M. Yamada, K. Ikeda, Y. Miyamoto, and A. Nitta. The piccolo intronic single nucleotide polymorphism rs13438494 regulates dopamine and serotonin uptake and shows associations with dependence-like behavior in genomic association study. *Curr. Mol. Med.*, 15: 265-274, 2015.
6. S. Koike, T. Kayama, M. Arai, Y. Horiuchi, A. Kobori, M. Miyashita, M. Itokawa, and Y. Ogasawara Y. Characterization of modified proteins in plasma from a subtype of schizophrenia based on carbonyl stress: Protein carbonyl is a possible biomarker of psychiatric disorders. *Biochem. Biophys. Res. Commun.*, 467: 361-366, 2015.
7. M. Maekawa, K. Yamada, M. Toyoshima, T. Ohnishi, Y. Iwayama, C. Shimamoto, T. Toyota, Y. Nozaki, S. Balan, H. Matsuzaki, Y. Iwata, K. Suzuki, M. Miyashita, M. Kikuchi, M. Kato, Y. Okada, W. Akamatsu, N. Mori, Y. Owada, M. Itokawa, H. Okano, and T. Yoshikawa. Utility of scalp hair follicles as a novel source of biomarker genes for psychiatric illnesses. *Biol. Psychiatry*, 78: 116-125, 2015.
8. D. Nishizawa, S. Kasai, J. Hasegawa, N. Sato, H. Yamada, F. Tanioka, M. Nagashima, R. Katoh, Y. Satoh, M. Tagami, H. Ujike, N. Ozaki, T. Inada, N. Iwata, I. Sora, M. Iyo, M. Yamada, N. Kondo, M. Won, N. Naruse, K. Uehara-Aoyama, M. Itokawa, K. Ohi, R. Hashimoto, K. Tanisawa, T. Arai, S. Mori, M. Sawabe, M. Naka-Mieno, Y. Yamada, M. Yamada, N. Sato, M. Muramatsu, M. Tanaka, Y. Irukayama-Tomobe, Y. Saito, T. Sakurai, M. Hayashida, H. Sugimura, and K. Ikeda. Associations between the orexin (hypocretin) receptor 2 gene polymorphism Val308Ile and nicotine dependence in genome-wide and subsequent association studies. *Molecular Brain*, 8: 50, 2015.
9. R. Saiga, S. Takekoshi, C. Inomoto, N. Nakamura, A. Tsuboi, M. Osawa, M. Arai, K. Oshima, M. Itokawa, K. Uesugi, A. Takeuchi, Y. Terada, Y. Suzuki, and R. Mizutani. Three-Dimensional Neuronal Structure of Human Cerebral Cortex Determined by Synchrotron-Radiation Microtomography. *Microsc. Microanal.*, 21(Suppl 3): 919-920, 2015.
10. F. N. Bangel, M. Yamada, M. Arai, Y. Iwayama, S. Balan, T. Toyota, Y. Iwata, K. Suzuki, M. Kikuchi, T. Hashimoto, N. Kanahara, N. Mori, M. Itokawa, O. Stock, and T. Yoshikawa. Genetic analysis of the glyoxalase system in schizophrenia. *Prog. Neuropsychopharmacol. Biol. Psychiatry.*, 59: 105-110, 2015.
11. M. Takahashi, H. Miyata, F. Kametani, T. Nonaka, H. Akiyama, S. Hisanaga, M. Hasegawa. Extracellular association of APP and tau fibrils induces intracellular aggregate formation of tau. *Acta Neuropathol.*, 29: 895-907, 2015.
12. S. Matsumoto, Y. Motoi, K. Ishiguro, T. Tabira, F. Kametani, M. Hasegawa, N. Hattori. The twenty-four KDa C-terminal tau fragment increases with aging in tauopathy mice: implications of prion-like properties. *Hum. Mol. Genet.*, 24: 6403-6416, 2015.
13. M. Hosokawa, T. Arai, M. Masuda-Suzukake, H. Kondo, T. Matsuwaki, M. Nishihara, M. Hasegawa, H. Akiyama. Progranulin Reduction Is Associated With Increased Tau Phosphorylation in P301L Tau Transgenic Mice. *J. Neuropathol. Exp. Neurol.*, 74: 158-165, 2015.
14. A. Baborie, T. D. Griffiths, E. Jaros, R. Perry, I. G. McKeith, D. J. Burn, M. Masuda-Suzukake, M. Hasegawa, S. Rollinson, S. Pickering-Brown, A. C. Robinson, Y. S. Davidson, and D. M. Mann. Accumulation of dipeptide repeat proteins predates that of TDP-43 in Frontotemporal Lobar Degeneration associated with hexanucleotide repeat expansions in C9ORF72 gene. *Neuropathol. Appl. Neurobiol.*, 41: 601-612, 2015.
15. K. Okamoto, Y. Fujita, E. Hoshino, Y. Tamura, T. Fukuda, M. Hasegawa, M. Takatama. An autopsy case of familial amyotrophic lateral sclerosis with a TARDBP Q343R mutation. *Neuropathology*, 35: 462-468, 2015.
16. K. Nakajima, S. Hirai, T. Morio, and H. Okado. Benzodiazepines induce sequelae in immature mice with inflammation-induced status epilepticus. *Epilepsy Behavior*, 52:180-186, 2015.
17. T. Udagawa, Y. Fujioka, M. Tanaka, D. Honda, S. Yokoi, Y. Riku, D. Ibi, T. Nagai, K. Yamada, H. Watanabe, M. Katsuno, T. Inada, K. Ohno, M. Sokabe, H. Okado, S. Ishigaki, and G. Sobue. Fus regulates AMPA receptor function and FTLD/ALS-associated behavior via GluA1 mRNA

stabilization. *Nat. Commun.*, 6: 7098, 2015.

18. J. I. Heng, Z. Qu, C. Ohtaka-Maruyama, H. Okado, M. Kasai, D. Castro, F. Guillemot, S. S. Tan. The Zinc Finger Transcription Factor RP58 Negatively Regulates Rnd2 for the Control of Neuronal Migration During Cerebral Cortical Development. *Cereb. Cortex.*, 25: 806-16. 2015.

[Review Articles]

1. Y. Kouidrat, A. Amad, M. Arai, M. Miyashita, J. D. Lalau, G. Loas, and M. Itokawa. Advanced glycation end products and schizophrenia: A systematic review. *J. Psychiatr. Res.*, 66-67C: 112-117, 2015.
2. C. Ohtaka-Maruyama and H. Okado. Molecular Pathways Underlying Projection Neuron Production and Migration during Cerebral Cortical Development. *Front Neurosci.*, 9: 447, 2015.

[Conference Activities & Talks]

1. K. Kitajima, M. Nakajima, M. Kanokoda, and T. Hara. Efficient induction method of hematopoietic cells from human induced pluripotent stem cells. BMB2015, 2015.12.1-4, Kobe.
2. M. Hasegawa. Molecular analyses of pathological tau in tauopathy brains. Brain Protein Aging and Dementia Control. 1st International Symposium. Molecular bases of brain protein aging. 2015.10.9, Nagoya.

Clinical Anatomy

Professor Keiichi AKITA
 Junior Associate Professor Akimoto NIMURA
 Kumiko YAMAGUCHI
 (Department of Professional Development in Health Science)
 Assistant Professor Masayo HARADA
 Research Technician Hisayo NASU, Kiyomi SAIKAWA, Sadaaki HEIMA
 Graduate Student Kazuhiro SAKAMOTO(∼ March), Sachiyuki TUKADA(∼ March),
 Yasuo NAKAJIMA, Kazuhito SEKIZAWA, Hitomi FUJISHIRO, Keiko OKUMURA,
 Tatsuya TAMAKI, Ryuhei OKADA, Eichirou KAGAWA, Motoki TANAKA,
 Kotaro EGUCHI, Nobuaki KAWAI, Saya HORIUCHI, Pawaree Nonthasaen,
 Natnicha Kampan, Kentaro AMAHA(April ∼), Yusuke UEDA(April ∼),
 Yasunori TATARA(April ∼), Shota HOSHIKA(April ∼), Phichaya BARAMEE(October ∼)

(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. Kazuaki Sakamoto, Hisayo Nasu, Akimoto Nimura, Junichiro Hamada, Keiichi Akita. An anatomic study of the structure and innervation of the pronator quadratus muscle. *Anatomical Science International*. 2015.03; 90(2); 82-88
2. Yasuyuki Kawaguchi, Eiji Kondo, Ryo Takeda, Keiichi Akita, Kazunori Yasuda, Andrew A Amis. The role of fibers in the femoral attachment of the anterior cruciate ligament in resisting tibial displacement. *Arthroscopy*. 2015.03; 31(3); 435-444
3. Taiki Nozaki, Akimoto Nimura, Hitomi Fujishiro, Tomoyuki Mochizuki, Kumiko Yamaguchi, Ryuichi Kato, Hiroyuki Sugaya, Keiichi Akita. The anatomic relationship between the morphology of the greater tubercle of the humerus and the insertion of the infraspinatus tendon. *J Shoulder Elbow Surg*. 2015.04; 24(4); 555-560
4. Yutaka Tokairin, Kagami Nagai, Hisashi Fujiwara, Taichi Ogo, Masafumi Okuda, Yasuaki Nakajima, Kenro Kawada, Yutaka Miyawaki, Hisayo Nasu, Keiichi Akita, Tatsuyuki Kawano. Mediastinoscopic subaortic and tracheobronchial lymph node dissection with a new cervico-hiatal crossover approach in thiel-embalmed cadavers. *Int Surg*. 2015.04; 100(4); 580-588
5. Mika Okazawa, Aki Murashima, Masayo Harada, Naomi Nakagata, Masafumi Noguchi, Mitsuru Morimoto, Tadashi Kimura, David M Ornitz, Gen Yamada. Region-specific regulation of cell proliferation by FGF receptor signaling during the Wolffian duct development. *Dev Biol*. 2015.04; 400(1); 139-147
6. Atsushi Tasaki, Akimoto Nimura, Taiki Nozaki, Akira Yamakawa, Mamoru Niitsu, Wataru Morita, Yoshimitsu Hoshikawa, Keiichi Akita. Quantitative and qualitative analyses of subacromial impingement by kinematic open MRI. *Knee Surg Sports Traumatol Arthrosc*. 2015.05; 23(5); 1489-1497
7. Yoshihiro Hagiwara, Kenji Kanazawa, Akira Ando, Akimoto Nimura, Takashi Watanabe, Kazuhiro Majima, Keiichi Akita, Eiji Itoi. Blood flow changes of the anterior humeral circumflex artery decrease with the scapula in internal rotation. *Knee Surg Sports Traumatol Arthrosc*. 2015.05; 23(5); 1467-1472
8. Masayo Harada, Akiko Omori, Chiaki Nakahara, Naomi Nakagata, Keiichi Akita, Gen Yamada. Tissue-specific roles of FGF signaling in external genitalia development *Dev Dyn*. 2015.06; 244(6); 759-773
9. Atsushi Tasaki, Akimoto Nimura, Tomoyuki Mochizuki, Kumiko Yamaguchi, Ryuichi Kato, Hiroyuki Sugaya, Keiichi Akita. Anatomic observation of the running space of the suprascapular nerve at the suprascapular notch in the same direction as the nerve. *Knee Surg Sports Traumatol Arthrosc*. 2015.09; 23(9); 2667-2673
10. Hisayo Nasu, Akimoto Nimura, Kumiko Yamaguchi, Keiichi Akita. Distribution of the axillary nerve to the subacromial bursa and the area around the long head of the biceps tendon. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2015.09; 23(9); 2651-2657

[Books etc]

1. Akimoto Nimura, Keiichi Akita, Hiroyuki Sugaya. Normal and Pathological Anatomy of the Shoulder. Springer Berlin Heidelberg, 2015.01

[Conference Activities & Talks]

1. Akimoto Nimura, Taiki Nozaki, Keiichi Akita. The Anatomic Relationship Between The Morphology Of The Greater Tubercle Of The Humerus And The Insertion Of The Infraspinatus Tendon. 61st the Orthopaedic Research Society 2015.03.28 Las Vegas, USA
2. Ryuhei Okada , Kyoko Ito , Kazuchika Ohno. Ischemic colitis during concurrent radiotherapy and cetuximab therapy: A case report. 4th Congress of Asian Society of Head and Neck Oncology 2015.06 Kobe Japan
3. Masayo Harada, Akiko Omori, Keiichi Akita, Gen Yamada. Tissue-specific roles of FGF signaling in external genitalia development. 48th Annual Meeting of the Japanese Society of Developmental Biologists 2015.06.03 Tsukuba, Japan
4. Akimoto Nimura, Masataka Nakazawa, Hiroyuki Sugaya, Takeshi Muneta, Keiichi Akita. Based on its anatomic configuration, the posterior bundle of the acromioclavicular ligament plays a role in joint stabilization. Biennial ISAKOS Congress 2015.06.06 Lyon, France
5. Itsuko Okuda, Keiichi Akita, Yasuo Nakajima. Anatomic imaging analysis for the facial structures affect facial aging. 32nd Annual Meeting American Association of Clinical Anatomists 2015.06.10 Las Vegas, USA
6. Hisayo Nasu, Sara Sugiura, Akimoto Nimura, Keiichi Akita. Anatomic study regarding the attachment of the joint capsule in the posterolateral side of the knee. 13th Congress of European Association of Clinical Anatomy 2015.06.24 Rouen, France
7. Akimoto Nimura, Keiichi Akita. Anatomic study for the stability of the lateral side of the elbow joint based on the capsule complex. International Congress of Clinical Anatomy 2015.06.24 Rouen, France
8. Hitomi Fujishiro, Sathiyuki Tsukada, Akimoto Nimura, Kumiko Yamaguchi, Keiichi Akita. Anatomic relationship between lateral meniscus and anterior cruciate ligament on Tibia. International Congress of Clinical Anatomy 2015.06.24 Rouen, France
9. Tomomi Sakaguchi-Kuma , Hitomi Hujishiro, Kazuo Shimazaki, Kumiko Yamaguchi, Takashi Ono, Keiichi Akita. The anatomic study of the ridge on condylar process of mandible. International Congress of Clinical Anatomy 2015.06.24 Rouen, France
10. Kumiko Yamaguchi, Nao Hayashi, Itsuko Okuda, Kosuke Matsunaga, Keiichi Akita. Distribution of the temporalis and orbicularis oculi at the lateral region to orbit. International Congress of Clinical Anatomy 2015.06.24
11. Masayo Harada, Akiko Omori, Keiichi Akita, Gen Yamada. Spatiotemporally regulated FGF signaling plays tissue-specific roles in multiple processes of external genitalia development. Mouse Molecular Genetics 2015.09.16 Cambridge, UK
12. Kumiko Yamaguchi, Keiichi Akita. Distribution of the masticatory and facial muscles at the lateral region to orbit. Congreso argentino de anatomia clinica 2015.09.24 Buenos Aires, Argentina
13. Mari Uomizu, Kumiko Yamaguchi, Keiichi Akita. Anatomical variations in the insertion of the pectoralis minor tendon associated with the coracohumeral ligament. Congreso argentino de anatomia clinica 2015.09.24 Buenos Aires, Argentina
14. Keiichi Akita. Recent Progresses of the clinical anatomy of the shoulder joint with special reference to the rotator cuff muscles. Congreso argentino de anatomia clinica 2015.09.24 Buenos Aires, Argentina

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

- The function of non-coding RNA in development and diseases will be examined.
- Development and regeneration using genome editing technologies, such as TALEN and CRISPR/Cas9 will be analyzed.
- Genome dynamics during embryogenesis will be monitored by new techniques.
- Novel systems approaches will be established and applied for developmental biology and medicine.
- Dysregulation of bone homeostasis under the microgravity
- Molecular mechanism underlying pathogenesis of osteoporosis
- Molecular understanding of the physiological homeostasis controlled by bone tissue

In this year, We studied it on the following themes.

- MiRNA which regulates cartilage homeostasis was identified.
- We developed screening system for miRNA target genes using reporter vector library.
- A to I RNA editing of microRNA was detected by next generation sequencing in synovium derived from patients with rheumatoid arthritis and clarified to regulate arthritis using animal model.
- Comparative analysis of evolutionary conservation of SOX9 targets in cartilage and sex differentiation.
- We investigated the molecular mechanisms underlying post-transcriptional regulation of IL-6 by RNA binding protein.
- The Screening of novel Damage-associated molecular patterns proteins.
- Protein localization analysis by High-throughput microscope system.
- Analysis for the effects of gravity on bone homeostasis
- Analysis of the molecular basis for osteocyte-controlled bone homeostasis
- Identification of the bone-derived molecules responsible for energy homeostasis
- Establishment of human genetic disease models through CRISPR/Cas9 system.
- Cell competition selects those cells that fit environment better. A new therapeutic approach using this phenomena for chromosomal anomalies such as Down syndrome is being sought.

(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. Satoshi Hara, Moe Tamano, Satoshi Yamashita, Tomoko Kato, Takeshi Saito, Tetsushi Sakuma, Takashi Yamamoto, Masafumi Inui, Shuji Takada. Generation of mutant mice via the CRISPR/Cas9 system using FokI-dCas9. *Sci Rep.* 2015; 5; 11221
2. Koji Otabe, Hiroyuki Nakahara, Akihiko Hasegawa, Tetsuya Matsukawa, Fumiaki Ayabe, Naoko Onizuka, Masafumi Inui, Shuji Takada, Yoshiaki Ito, Ichiro Sekiya, Takeshi Muneta, Martin Lotz, Hiroshi Asahara. Transcription factor Mohawk controls tenogenic differentiation of bone marrow mesenchymal stem cells in vitro and in vivo. *J. Orthop. Res.* 2015.01; 33(1); 1-8
3. Matsubara Y, Kato T, Kashimada K, Tanaka H, Zhi Z, Ichinose S, Mizutani S, Morio T, Chiba T, Ito Y, Saga Y, Takada S, Asahara H.. TALEN-Mediated Gene Disruption on Y Chromosome Reveals Critical Role of EIF2S3Y in Mouse Spermatogenesis. *Stem Cells Dev.* 2015.05;
4. Matsubara Y, Kato T, Kashimada K, Tanaka H, Zhi Z, Ichinose S, Mizutani S, Morio T, Chiba T, Ito Y, Saga Y, Takada S, Asahara H. TALEN-Mediated Gene Disruption on Y Chromosome Reveals Critical Role of EIF2S3Y in Mouse Spermatogenesis. *Stem Cells Dev.* 2015.05; 1164-1170
5. Sumiya E, Negishi-Koga T, Nagai Y, Suematsu A, Suda T, Shinohara M, Sato K, Sanjo H, Akira S, Takayanagi H. Phosphoproteomic analysis of kinase-deficient mice reveals multiple TAK1 targets in osteoclast differentiation. *Biochem Biophys Res Commun.* 2015.08; 463; 1284-1290
6. Tateishi R, Akiyama N, Miyauchi M, Yoshinaga R, Sasanuma H, Kudo T, Shimbo M, Shinohara M, Obata K, Inoue J, Shirakawa M, Shiba D, Asahara H, Yoshida N, Takahashi S, Morita H, Akiyama T. Hypergravity Provokes a Temporary Reduction in CD4+CD8+ Thymocyte Number and a Persistent Decrease in Medullary Thymic Epithelial Cell Frequency in Mice *PLoS One.* 2015.10;
7. Gernapudi R, Wolfson B, Zhang Y, Yao Y, Yang P, Asahara H, Zhou Q. MicroRNA 140 Promotes Expression of Long Noncoding RNA NEAT1 in Adipogenesis *Mol Cell Biol.* 2015.10;
8. Ryosuke Tateishi, Nobuko Akiyama, Maki Miyauchi, Riko Yoshinaga, Hiroki Sasanuma, Takashi Kudo, Miki Shimbo, Masahiro Shinohara, Koji Obata, Jun-ichiro Inoue, Masaki Shirakawa, Dai Shiba, Hiroshi Asahara, Nobuaki Yoshida, Satoru Takahashi, Hironobu Morita, Taishin Akiyama. Hypergravity Provokes a Temporary Reduction in CD4+CD8+ Thymocyte Number and a Persistent Decrease in Medullary Thymic Epithelial Cell Frequency in Mice. *PLoS One.* 2015.10; 10;
9. Ogura Y, Miyake N, Kou I, Iida A, Nakajima M, Takeda K, Fujibayashi S, Shiina M, Okada E, Toyama Y, Iwanami A, Ishii K, Ogata K, Asahara H, Matsumoto N, Nakamura M, Matsumoto M, Ikegawa S. Identification of HOXD4 Mutations in Spinal Extradural Arachnoid Cyst *PLoS One.* 2015.11;
10. 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

[Books etc]

1. microRNA as a keeper of bones and joints. 2015.12

[Misc]

1. Yoko Watanabe-Tanaka, Hiroshi Asahara. The role of microRNAs in the pathogenesis of rheumatoid arthritis Inflammation and Regeneration. 2015.06; 35(3); 148-153
2. Takahide Matsushima, Hiroshi Asahara. Exosome and miRNA Rheumatology. 2015.10; 54(4); 468-472

[Conference Activities & Talks]

1. Asahara H, Tempei Sato, Masafumi Inui. The Critical role of miRNAs at the edge of Hox-code during skeletal development. Gordon Research Conference 2015.03.23 Houston
2. Hiroshi Asahara. The Role of Mxk in Tendon and Spinal Disc Homeostasis and Regeneration. The ICMRS Conference and Xiangya Osteoporosis Forum 2015.04.06 China
3. Hiroshi Asahara. Regulation of Hox-code at RNA level during skeletal development.. The ICMRS Conference and Xiangya Osteoporosis Forum 2015.04.10 China
4. Tempei Sato. Functional analysis of microRNA/target gene interaction and its requirement of the axial body patterning. 20st Annual Meeting of the RNA Society 2015.07.16 Sapporo
5. Koda N, Shinohara M, Nakamichi R, Ito Y, Ichinose S, Moriyama K, Asahara H. ROLES OF TRANSCRIPTIONAL FACTOR MOHAWK IN PERIODONTAL LIGAMENT. Australian New Zealand Bone&Mineral Society Annual Scientific Meeting 2015 2015.11.01 Hobart
6. Hiroshi Asahara, Tomoki Chiba, Kentaro Abe, Yoshiaki Ito. Inflammatory signal regulation at RNA level. Biochemistry and Molecular Biology 2015.12.01 Hyogo

[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
 Assistant Professor Morito KURATA (on administrative leave)
 Kouhei YAMAMOTO, Shinya ABE, Shiho ABE,
 Laboratory Technician Miori INOUE
 Technical Assistant Sachiko ISHIBASHI
 Graduate Students Yuko KINOWAKI,
 Atsushi KIHARA, Kenichi MIYAMOTO,
 Kazuhito SUZUKI, Masafumi INOUE,
 Kenichiro KATO, Xiao Hai JIN
 Momoko Yamada, Takuya Maeda,
 Miu katsuyama, Abudushalamu Muyashaer,
 Vilayvong Sulideyh, Luangxay Thitsamay,
 Masae Yanai, Mariko Muto,
 Sumito Shingaki

(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 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).

(4) Publications

[Original Articles]

1. Jinta M, Imadome K, Komatsu H, Yoshimori M, Kurata M, Fujiwara S, Miura O, Arai A.. L-Asparaginase monotherapy for EBV-positive T/NK lymphoproliferative diseases: A pilot Study. *Journal of Medical and Dental Sciences*. 2015.03; 62(1); 1-9
2. Abe S, Yokomizo N, Kobayashi Y, Yamamoto K.. Confirmation of immunoglobulin heavy chain rearrangement by polymerase chain reaction using surgically obtained, paraffin-embedded samples to diagnose primary palate mucosa-associated lymphoid tissue lymphoma: A case study. *Int J Surg Case Rep*.. 2015.03; 10; 129-133
3. Yoshimori M, Takada H, Imadome KI, Kurata M, Yamamoto K, Koyama T, Shimizu N, Fujiwara S, Miura O, Arai A.. P-glycoprotein is expressed and causes resistance to chemotherapy in EBV-positive T-cell lymphoproliferative diseases. *Cancer Med*.. 2015.07;
4. Shinya Abe, Kouhei Yamamoto, Morito Kurata, Shiho Abe-Suzuki, Rie Horii, Futoshi Akiyama, Masanobu Kitagawa. Targeting MCM2 function as a novel strategy for the treatment of highly malignant breast tumors. *Oncotarget*. 2015.10; 6(33); 34892-34909
5. Yoshimori M, Takada H, Imadome K, Kurata M, Yamamoto K, Koyama T, Shimizu N, Fujiwara S, Miura O, Arai A.. P-glycoprotein is expressed and causes resistance to chemotherapy in EBV-positive T-cell lymphoproliferative diseases. *Cancer Medicine*. 2015.10; 4(10); 1494-1504

[Conference Activities & Talks]

1. Ayako Arai, Hiroshi Takase, Kouhei Yamamoto, Hiroki Akiyama, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. The 77th Annual Meeting of the Japanese Society of Hematology 2015.10.17 Kanazawa
2. Ayako Arai, Hiroshi Takase, Kouhei Yamamoto, Hiroki Akiyama, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. 57th ASH Annual Meeting and Exposition 2015.12.05 Orlando

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 malignant progression for clinical application of cancer prevention, diagnosis and treatment.

(2) Research

1. Molecular analysis of refractory malignancies including liver, pancreatic and scirrhou 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 targted theratpy
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. 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*. 2015; 7(4); 3966-3983
2. Nakao K, Tanaka S, Miura T, Sato K, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Arii S, Tanabe M. A novel Aurora/VEGFR dual kinase inhibitor as treatment for hepatocellular carcinoma *Cancer Science*. 2015; 106(8); 1016-1022
 3. Matsunaga H, Tanaka S, Aihara A, Ogawa K, Matsumura S, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Arii S, Tanabe M. A novel therapeutic combination targeting sequentially Aurora B and Bcl-xL in hepatocellular carcinoma *Annals of Surgical Oncology*. 2015; 22(9); 3079-3086
 4. Miura T, Ban D, Tanaka S, Mogushi K, Kudo A, Matsumura S, Mitsunori Y, Ochiai T, Tanaka H, Tanabe M. Distinct clinicopathological phenotype of hepatocellular carcinoma with EOB-MRI hyperintensity: association with gene expression signature *American Journal of Surgery*. 2015; 210(3); 561-569
 5. Sakamoto A, Akiyama Y, Shimada S, Zhu WG, Yuasa Y, Tanaka S. DNA methylation in the exon 1 region and complex regulation of Twist1 expression in gastric cancer *PLoS ONE*. 2015; 10(12); e0145630
 6. Okajima C, Arii S, Tanaka S, Matsumura S, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Tanabe M. Prognostic role of Child-Pugh score 5 and 6 in hepatocellular carcinoma patients who underwent curative hepatic resection *American Journal of Surgery*. 2015; 209(1); 199-205
 7. Ban D, Kudo A, Ito H, Mitsunori Y, Matsumura S, Aihara A, Ochiai T, Tanaka S, Tanabe M, Itano O, Kaneko H, Wakabayashi G. The difficulty of laparoscopic liver resection *Updates in Surgery*. 2015; 67(2); 123-128
 8. Yasui K, Konishi C, Gen Y, Endo M, Dohi O, Tomie A, Kitaichi T, Yamada N, Iwai N, Nishikawa T, Yamaguchi K, Moriguchi M, Sumida Y, Mitsuyoshi H, Tanaka S, Arii S, Itoh Y. EVI1, a target gene for amplification at 3q26, antagonizes TGF-beta-mediated growth inhibition in hepatocellular carcinoma *Cancer Science*. 2015; 106(7); 929-937
 9. Watanabe Y, Yamamoto H, Oikawa R, Toyota M, Yamamoto M, Kokudo N, Tanaka S, Arii S, Yotsuyanagi H, Koike K, Itoh F. DNA methylation at hepatitis B viral integrants is associated with methylation at flanking human genomic sequences *Genome Research*. 2015; 25(3); 328-337
 10. Hiroko Matsunaga, Shinji Tanaka, Arihiro Aihara, Kousuke Ogawa, Satoshi Matsumura, Daisuke Ban, Takanori Ochiai, Takumi Irie, Atsushi Kudo, Noriaki Nakamura, Shigeki Arii and Minoru Tanabe. . A Novel Therapeutic Combination Sequentially Targeting Aurora B and Bcl-xL in Hepatocellular Carcinoma. *Ann. Surg. Oncol*. 2015.09; 22(9); 3079-3086
 11. 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*, in press.
 12. 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*, in press.
 13. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Sayuri 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. *Journal of Gastroenterology*, in press.
 14. Akahoshi K, Tanaka S, Mogushi K, Shimada S, Matsumura S, Akiyama Y, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Arii S, Tanabe M. Expression of connective tissue growth factor in the livers of non-viral hepatocellular carcinoma patients with metabolic risk factors. *Journal of Gastroenterology*, in press.

[Misc]

1. Tanaka S. Cancer stem cells as therapeutic targets of hepato-biliary-pancreatic cancers *Journal of Hepato-Biliary-Pancreatic Sciences*. 2015; 22(7); 531-537

2. Ban D, Kudo A, Irie T, Ochiai T, Aihara A, Matusmura S, Tanaka S, Tanabe M. Advances in reduced port laparoscopic liver resection *Asian Journal of Endoscopic Surgery*. 2015; 8(1); 11-15
3. Tanaka S. Molecular pathogenesis and targeted therapy of pancreatic cancer. *Annals of Surgical Oncology*, in press.
4. Tanaka S. Cancer stem cells as therapeutic targets. *Human Stem Cell Toxicity*, 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 of annotated compounds. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08 Nagoya
2. Tanaka S, Aihara A, Tanabe M. Molecular pathogenesis and targeted therapy for major vascular invasiveness of hepatocellular carcinoma (symposium). The 13th General Meeting of the Japanese Society of Gastroenterological Surgery 2015.10.08 Tokyo
3. Fukamachi H, Shimada S, Akiyama Y, Yuasa Y, Tsuchiya K, Tanaka S. Features of poorly-differentiated gastric tumor-initiating cells from patient-derived tumor xenograft tissues. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.09 Nagoya
4. Akiyama Y, Koda Y, Nishikawaji T, Shimada S, Sakamoto A, Yuasa Y, Tanaka S. Transcriptional regulatory mechanism of SET7/9 in gastric cancer. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.09 Nagoya
5. Tanaka S. Surgical oncology for identification of novel molecular targets in refractory cancers (symposium). The 74th Annual Meeting of the Japanese Cancer Association 2015.10.09 Nagoya
6. Nishikawaji T, Akiyama Y, Shimada S, Yuasa Y, Tanaka S. Oncogenic roles of SETDB2, a histone methyltransferase, in human gastric carcinogenesis. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.09 Nagoya
7. Sakamoto A, Shimada S, Akiyama Y, Yuasa Y, Tanaka S. Epigenetic regulation of Twist1 in diffuse-type gastric cancer cell lines of an E-cadherin/p53-deficient mouse model. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.09 Nagoya

[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 : Makoto Kodama, Yuan Bae, Emiko SUGAWARA

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. 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.* 2015; (in press);
2. Toru Shuta, Uchihara Toshiki, Hara Makoto, Mae Sunao, Toru Michio, Hirokawa Katsuiku, Endo Takashi, Sugawara Emiko, Kitagawa Masanobu, Kobayashi Takayoshi. An Autopsy Case of Dementia with Lewy Bodies with Vocal Cord Abductor Paralysis. *Eur Neurol.* 2015; 74(3-4); 186-187
3. Kana Minegishi, Takayasu Watanabe, Asuka Furukawa, Keisuke Uchida, Yoshimi Suzuki, Takumi Akashi, Fumito Maruyama, Ichiro Nakagawa, Yoshinobu Eishi. Genetic profiles of *Propionibacterium acnes* and identification of a unique transposon with novel insertion sequences in sarcoid and non-sarcoid isolates. *Sci Rep.* 2015; 5; 9832
4. Blair K Gage, Ali Asadi, Robert K Baker, Travis D Webber, Rennian Wang, Masayuki Itoh, Masaharu Hayashi, Rie Miyata, Takumi Akashi, Timothy J Kieffer. The Role of ARX in Human Pancreatic Endocrine Specification. *PLoS ONE.* 2015; 10(12); e0144100
5. Shunsuke Ohta, Kenro Kawada, Jirawat Swangsri, Naoto Fujiwara, Katsumasa Saito, Hisashi Fujiwara, Tairo Ryotokuji, Takuya Okada, Yutaka Miyawaki, Yutaka Tohkairin, Yasuaki Nakajima, Youichi Kumagai, Kagami Nagai, Takashi Ito, Yoshinobu Eishi, Tatsuyuki Kawano. Relationships between Micro-Vascular and Iodine-Staining Patterns in the Vicinity of the Tumor Front of Superficial Esophageal Squamous Carcinoma. *PLoS ONE.* 2015; 10(8); e0126533
6. Risa Nomura, Kentaro Miyai, Michiyo Okada, Michiko Kajiwara, Makoto Ono, Tsutomu Ogata, Ichiro Onishi, Mana Sato, Masaki Sekine, Takumi Akashi, Shuki Mizutani, Kenichi Kashimada. A 45,X/46,XY DSD (Disorder of Sexual Development) case with an extremely uneven distribution of 46,XY cells between lymphocytes and gonads. *Clin Pediatr Endocrinol.* 2015.01; 24(1); 11-14
7. Sugimoto H, Nagahara M, Bae Y, Nakagawa T, Ishikawa T, Sato T, Uetake H, Eishi Y, Sugihara K. Clinicopathologic relevance of claudin 5 expression in breast cancer. *Am. J. Clin. Pathol.* 2015.04; 143(4); 540-546
8. Ichiro Yamada, Naoyuki Miyasaka, Keigo Hikishima, Yutaka Tokairin, Tatsuyuki Kawano, Eisaku Ito, Daisuke Kobayashi, Yoshinobu Eishi, Hideyuki Okano. Ultra-high-resolution MR imaging of esophageal carcinoma at ultra-high field strength (7.0T) ex vivo: correlation with histopathologic findings. *Magn Reson Imaging.* 2015.05; 33(4); 413-419
9. Keita Fukushima, Kiichiro Tsuchiya, Yoshihito Kano, Nobukatsu Horita, Shuji Hibiya, Ryohei Hayashi, Keisuke Kitagaki, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Shigeru Oshima, Takashi Nagaishi, Okamoto Ryuichi, Tetsuya Nakamura, Mamoru Watanabe. Atonal homolog 1 protein stabilized by tumor necrosis factor α induces high malignant potential in colon cancer cell line. *Cancer Sci.* 2015.05; 106(8); 1000-1007

10. Ichiro Yamada, Keigo Hikishima, Naoyuki Miyasaka, Yutaka Tokairin, Eisaku Ito, Tatsuyuki Kawano, Daisuke Kobayashi, Yoshinobu Eishi, Hideyuki Okano. Esophageal carcinoma: Evaluation with q-space diffusion-weighted MR imaging ex vivo. *Magn Reson Med*. 2015.06; 73(6); 2262-2273
11. Ichiro Yamada, Naoyuki Miyasaka, Keigo Hikishima, Keiji Kato, Kazuyuki Kojima, Tatsuyuki Kawano, Eisaku Ito, Daisuke Kobayashi, Yoshinobu Eishi, Hideyuki Okano. Gastric Carcinoma: Ex Vivo MR Imaging at 7.0 T-Correlation with Histopathologic Findings. *Radiology*. 2015.06; 275(3); 841-848
12. Kawachi H, Eishi Y, Ueno H, Nemoto T, Fujimori T, Iwashita A, Ajioka Y, Ochiai A, Ishiguro S, Shimoda T, Mochizuki H, Kato Y, Watanabe H, Koike M, Sugihara K. A three-tier classification system based on the depth of submucosal invasion and budding/sprouting can improve the treatment strategy for T1 colorectal cancer: a retrospective multicenter study. *Mod. Pathol*. 2015.06; 28(6); 872-879
13. Pariko Yorozu, Asuka Furukawa, Keisuke Uchida, Takumi Akashi, Tomoya Kakegawa, Tomohisa Ogawa, Junko Minami, Yoshimi Suzuki, Nobuyasu Awano, Haruhiko Furusawa, Yasunari Miyazaki, Naohiko Inase, Yoshinobu Eishi. Propionibacterium acnes catalase induces increased Th1 immune response in sarcoidosis patients. *Respir Investig*. 2015.07; 53(4); 161-169
14. Tsutsui T, Miyazaki Y, Kuramochi J, Uchida K, Eishi Y, Inase N. The amount of avian antigen in household dust predicts the prognosis of chronic bird-related hypersensitivity pneumonitis. *Ann Am Thorac Soc*. 2015.07; 12(7); 1013-1021
15. Kenji Tanabe, Soichiro Yoshida, Fumitaka Koga, Masaharu Inoue, Shuichiro Kobayashi, Junichiro Ishioka, Tomoki Tamura, Emiko Sugawara, Kazutaka Saito, Takumi Akashi, Yasuhisa Fujii, Kazunori Kihara. High Ki-67 Expression Predicts Favorable Survival in Muscle-Invasive Bladder Cancer Patients Treated With Chemoradiation-Based Bladder-Sparing Protocol. *Clin Genitourin Cancer*. 2015.08; 13(4); e243-e251
16. Yoshimitsu Akiyama, Yuki Koda, Sun-Ju Byeon, Shu Shimada, Taketo Nishikawaji, Ayuna Sakamoto, Yingxuan Chen, Kazuyuki Kojima, Tatsuyuki Kawano, Yoshinobu Eishi, Dajun Deng, Woo Ho Kim, Wei-Guo Zhu, Yasuhito Yuasa, Shinji Tanaka. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. *Oncotarget*. 2015.12;

[Conference Activities & Talks]

1. Yuan Bae, Takatoshi Matsuyama, Hiroyuki Uetake, Takumi Akashi, Yoshinobu Eishi. An autopsy case of rectal primary adenocarcinoma with solitary metastasis to the cervical vertebra. 2015.05.02 Nagoya Congress Center
2. Yoshinobu Eishi. Screening for early gastric cancer. 46th World Congress of Surgery 2015.08.25 Bangkok, Thailand

Experimental Animal Model for Human Disease

Professor	Masami Kanai-Azuma
Junior Associate Professor	Yoshikazu Hirate
Assistant Professor	Shu Endo
Assistant Professor	Hitomi Suzuki
Assistant Professor	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 failure.
- 5)Study of the molecular events involved in the regulation of spermatogonial stem cells.

(2) Publications

[Original Articles]

1. Suzuki Hitomi, Kanai-Azuma Masami, Kanai Yoshiakira. From Sex Determination to Initial Folliculogenesis in Mammalian Ovaries: Morphogenetic Waves along the Anteroposterior and Dorsoventral Axes. *Sex Dev.* 2015; 9(4); 190-204
2. Uemura Mami, Igarashi Hitomi, Ozawa Aisa, Tsunekawa Naoki, Kurohmaru Masamichi, Kanai-Azuma Masami, Kanai Yoshiakira. Fate mapping of gallbladder progenitors in posteroventral foregut endoderm of mouse early somite-stage embryos. *J Vet Med Sci.* 2015.01;
3. Aiyama Yoshimi, Tsunekawa Naoki, Kishi Kasane, Kawasumi Miyuri, Suzuki Hitomi, Kanai-Azuma Masami, Kurohmaru Masamichi, Kanai Yoshiakira. A Niche for GFRalpha1-Positive Spermatogonia in the Terminal Segments of the Seminiferous Tubules in Hamster Testes. *Stem Cells.* 2015.09; 33(9); 2811-2824

[Conference Activities & Talks]

1. Kanai-Azuma Masami, Yoshikazu Hirate, Miyuri Kawasumi, Hitomi Suzuki, Yoshiakira Kanai. A possible involvement of a dose-dependent Sox17 activity of uterine epithelia in mouse implantation processes. 7th International Symposium Biology of Vertebrate Sex Determination 2015.04.13 Kona, Hawaii
2. Yoshikazu Hirate,Hitomi Suzuki,Miyuri Kawasumi,Yoshiakira Kanai,Masami Kanai-Azuma. Sox17 heterozygous female mice show haploinsufficiency in implantation.. The 62nd Annual Meeting of Japanese Association for Laboratory Animal Science 2015.05.28 Kyoto TERRSA

3. Ikuo Nobuhisa, Mitsujiro Osawa, Mami Uemura, Kaho Harada, Maha Anani, Kiyoka Saito, Haruna Takagi, Satomi Takahashi, Masami Kanai-Azuma, Yoshiakira Kanai, Atsushi Iwama, Tetsuya Taga. Sox17 is critical for the maintenance of stem cell phenotype of intra-aortic hematopoietic clusters of cells in the aorta-gonad-mesonephros region. International Society for Experimental Hematology 2015.09.17 Kyoto

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. Noriko Funato, Masataka Nakamura, James A. Richardson, Deepack Srivastava, Hiromi Yanagisawa.. Loss of Tbx1 induces bone phenotypes similar to cleidocranial dysplasia. *Hum Mol Genet.* . 2015.01; 24(2); 424-435
2. T Tsukahara, N Iwase, K Kawakami, M Iwasaki, C Yamamoto, K Ohmine, R Uchibori, T Teruya, H Ido, Y Saga, M Urabe, H Mizukami, A Kume, M Nakamura, R Brentjens, K Ozawa. The Tol2 transposon system mediates the genetic engineering of T-cells with CD19-specific chimeric antigen receptors for B-cell malignancies. *Gene Ther.* 2015.02; 22(2); 209-215
3. Yusuke Onaka, Norihito Shintani, Takanobu Nakazawa, Ryota Haba, Yukio Ago, Hyper Wang, Takuya Kanoh, Atsuko Hayata-Takano, Hiroyuki Hirai, Kin-Ya Nagata, Masataka Nakamura, Ryota Hashimoto, Toshio Matsuda, James A Waschek, Atsushi Kasai, Kazuki Nagayasu, Akemichi Baba, Hitoshi Hashimoto. CRTH2, a prostaglandin D2 receptor, mediates depression-related behavior in mice. *Behav. Brain Res.* 2015.02; 284; 131-137
4. Toshifumi Hara, Mariko Mizuguchi, Masahiro Fujii, Masataka Nakamura. Krüppel-like factor 2 represses transcription of the telomerase catalytic subunit human telomerase reverse transcriptase (hTERT) in human T cells. *J. Biol. Chem.* 2015.04; 290(14); 8758-8763
5. S Kinpara, S Ito, T Takahata, Y Saitoh, A Hasegawa, M Kijiyama, A Utsunomiya, M Masuda, Y Miyazaki, M Matsuoka, M Nakamura, S Yamaoka, T Masuda, M Kannagi. Involvement of double-stranded RNA-dependent protein kinase and antisense viral RNA in the constitutive NF κ B activation in adult T-cell leukemia/lymphoma cells. *Leukemia.* 2015.06; 29(6); 1425-1429

6. Yuetsu Tanaka, Mariko Mizuguchi, Yoshiaki Takahashi, Hideki Fujii, Reiko Tanaka, Takuya Fukushima, Takeaki Tomoyose, Aftab A Ansari, Masataka Nakamura. Human T-cell leukemia virus type-I Tax induces the expression of CD83 on T cells. *Retrovirology*. 2015.07; 12; 56

[Misc]

1. Noriko Funato, Masataka Nakamura, Hiromi Yanagisawa. Molecular basis of cleft palates in mice. *World J Biol Chem*. 2015.08; 6(3); 121-138

[Conference Activities & Talks]

1. Funato N. Gene Ontology Analysis for Cleft Palate. 2015.09.12
2. Mariko Mizuguchi, Yuetsu Tanaka, Takuya Fukushima, Masataka Nakamura . Regulation of hTERT gene expression in HTLV-1 infected T-cells. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08
3. Funato N, Yanagisawa H, Nakamura M.. Gene Ontology Analysis for Cleft Palate.

Material Biofunctions

Akiko Nagai (Associate Professor)
 Kosuke Nozaki (Assistant Professor)
 Hiroshi Masuda (Project Associate Professor)
 Minako Segawa (Technical Assistant)
 Kasumi Yamanaka (Technical Assistant)
 Hiromi Shigematsu (Technical Assistant)

(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. HIROSHI MASUDA, SHOGO HIROTA, AKIRA USHIYAMA, AKIMASA HIRATA, TAKUJI ARIMA, HIROSHI WATANABE, KANAKO WAKE, SOICHI WATANABE, MASAO TAKI, AKIKO NAGAI, CHIYOJI OHKUBO. No Changes in Cerebral Microcirculatory Parameters in Rat During Local Cortex Exposure to Microwaves In Vivo. 2015; 29; in press
2. N. Horiuchi, J. Endo, N. Wada, K. Nozaki, M. Nakamura, A. Nagai, K. Katayama and K. Yamashita. Dielectric properties of fluorine substituted hydroxyapatite: the effect of the substitution on configuration of hydroxide ion chains Journal of Materials Chemistry B. 2015; 3(33); 6790-6797

3. N. Wada, N. Horiuchi, M. Nakamura, K. Nozaki, T. Hiyama, A. Nagai and K. Yamashita. Controlled calcite nucleation on polarized calcite single crystal substrates in the presence of polyacrylic acid J. Cryst. Growth. 2015; 415; 7-14
4. N. Horiuchi, Y. Tsuchiya, N. Wada, K. Nozaki, M. Nakamura, A. Nagai, T. Okura and K. Yamashita. Polarization-assisted surface engineering for low temperature degradation-proof in yttria-stabilized zirconia ceramics J. Asian Ceram. Soc.. 2015; 3(2); 156-159
5. Kosuke Nozaki, Hiroki Koizumi, Naohiro Horiuchi, Miho Nakamura, Toshinori Okura, Kimihiro Yamashita, Akiko Nagai. Suppression effects of dental glass-ceramics with polarization-induced highly dense surface charges against bacterial adhesion. Dent Mater J. 2015; 34(5); 671-678
6. Natsuno Matsui, Kosuke Nozaki, Kazuhiko Ishihara, Kimihiro Yamashita, Akiko Nagai. Concentration-dependent effects of fibronectin adsorbed on hydroxyapatite surfaces on osteoblast adhesion. Mater Sci Eng C Mater Biol Appl. 2015.03; 48; 378-383
7. Nozaki K, Shinonaga T, Ebe N, Horiuchi N, Nakamura M, Tsutsumi Y, Hanawa T, Tsukamoto M, Yamashita K, Nagai A. Hierarchical periodic micro/nano-structures on nitinol and their influence on oriented endothelialization and anti-thrombosis Mater Sci Eng C Mater Biol Appl. 2015.12; 57; 1-6
8. Ishizaka M, Nagai A, Iwanaga M, Imamura M, Azuma H. Possible involvement of enhanced arginase activity due to up-regulated arginases and decreased hydroxyarginine in accelerating intimal hyperplasia with hyperglycemia. Vascul Pharmacol. 47(5-6); 272-280
9. Hiroshi Masuda, Akira Ushiyama, Shogo Hirota, Kanako Wake, Soichi Watanabe, Yukio Yamanaka, Masao Taki, Chiyoji Ohkubo. Effects of subchronic exposure to a 1439 MHz electromagnetic field on the microcirculatory parameters in rat brain. In Vivo. 21(4); 563-570
10. Hiroshi Masuda, Akira Ushiyama, Shogo Hirota, Kanako Wake, Soichi Watanabe, Yukio Yamanaka, Masao Taki, Chiyoji Ohkubo. Effects of acute exposure to a 1439 MHz electromagnetic field on the microcirculatory parameters in rat brain. In Vivo. 21(4); 555-562
11. Hiroshi Masuda, Akira Ushiyama, Shogo Hirota, George F Lawlor, Chiyoji Ohkubo. Long-term observation of pial microcirculatory parameters using an implanted cranial window method in the rat. In Vivo. 21(3); 471-479
12. Akira Ushiyama, Hiroshi Masuda, Shugo Hirota, Chiyoji Ohkubo. Subchronic effects on leukocyte-endothelial interactions in mice by whole body exposure to extremely low frequency electromagnetic fields. In Vivo. 18(4); 425-432

[Books etc]

1. Nozaki K, Ebe N, Yamashita K, Nagai A. Mineral Scales and Deposits: Scientific and Technological Approaches. Elsevier, 2015.06

[Conference Activities & Talks]

1. K. Shibata, N. Horiuchi, K. Nozaki, M. Nakamura, A. Nagai, K. Yamashita. Hydrothermal synthesis of fibrous hydroxyapatite. The 5th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-5) 2015.06.09 Tokyo, Japan
2. K. Watanabe, N. Horiuchi, K. Nozaki, M. Makamura, A. Nagai, K. Yamashita. Dielectric evaluation of chlorine substituted hydroxyapatite. The 5th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-5) 2015.06.09 Tokyo, Japan
3. Nozaki K, Fujita K, Ebe N, Miura H, Yamashita K, Nagai A. Bioresorbable and osteoconductive properties of porous carbonated apatite implanted in cortical and cancellous bone tissues. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09
4. Iwata N, Nozaki K, Miura H, Yamashita K, Nagai A. The effect of titania nanotube surfaces on osteoblast behavior. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09

5. T. Masutani, N. Horiuchi, K. Nozaki, M. Nakamura, K. Yamashita, A. Nagai. Polarization influences on cell dynamics via ERK signaling pathways. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09
6. Nozaki K, Fujita K, Yamashita K, Miura H, Nagai A. Evaluation of bone formation and degradation of porous carbonated apatite block. 2015.10.03
7. Donghe Shen, Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita, Michiyo Miyashin. Osteoblastic responses to OCP and carbonate-containing OCP in vitro. The 37th annual meeting of the Japanese society for biomaterials 2015.11.09 Kyoto, Japan
8. Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Dielectric Study on Reorientation Phenomena of Hydroxide Ion in Hydroxyapatite. 17th US-Japan Seminar on Dielectric and Piezoelectric Ceramics 2015.11.17 Matsumoto, Japan
9. Yuta Kuwamura, Naohiro Horiuchi, Hirobumi Shibata, Kazuaki Hashimoto, Kimihiro Yamashita, Akiko Nagai. Osteoclast formation on carbonate substituted apatite. 15th Asian BioCeramics symposium 2015.12.09 Tokyo, Japan
10. Naohiro Horiuchi, Norio Wada, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Dielectric Phenomena in Monoclinic and Hexagonal Hydroxyapatite. 15th Asian BioCeramics symposium 2015.12.09 Tokyo, Japan
11. Donghe Shen, Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita, Michiyo Miyashin. Carbonate-containing Octacalcium Phosphate enhanced osteoblast proliferation and differentiation. 15th Asian BioCeramics symposium 2015.12.09 Tokyo, Japan
12. Natsuko Iwata, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita, Akiko Nagai. The effect of titania nanotube surfaces on osteoblast behavior. 15th Asian Bioceramics Symposium 2015.12.10
13. Risa Yamada, Kosuke Nozaki, Hiroyuki Miura, Kimihiro Yamashita and Akiko Nagai. Study on antimicrobial activity by silver doped yttria-stabilized zirconia. 15th Asian Bioceramics Symposium 2015.12.10
14. Kazuhisa Fujita, Kosuke Nozaki, Kimihiro Yamashita, Hiroyuki Miura, and Akiko Nagai. Alkaline Phosphatase Activity of Periodontal Ligament Cell on Hydroxyl- and Carbonated-Apatites. 15th Asian Bioceramics Symposium 2015.12.10
15. T. Endo, K. Nozaki, K. Hashimoto, K. Yamashita, A. Nagai. Characterization of structure stability of β -tricalcium phosphate doped Na ion by electrical analysis. 15th Asian Bioceramics Symposium 2015.12.10
16. Kazuki Igeta, Kosuke Nozaki, Mamoru Aizawa, Kimihiro Yamashita, Akiko Nagai. Comparison of cytokines secretions from macrophage cultured on hydroxyapatite and carbonated apatite dense ceramics. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.16
17. Yuta Kuwamura, Naohiro Horiuchi, Kazuaki Hashimoto, Kimihiro Yamashita, Akiko Nagai. Effect of carbonated apatite on osteoclast differentiation of RAW264. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.16

Genetic Regulation

Professor Akinori KIMURA
Associate Professor Takeharu HAYASHI
Assistant Professor Daisuke SAKURAI
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.

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 Kosuke Tanimoto 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. S Komatsu, D Ichikawa, S Hirajima, H Nagata, Y Nishimura, T Kawaguchi, M Miyamae, W Okajima, T Ohashi, H Konishi, A Shiozaki, H Fujiwara, K Okamoto, H Tsuda, I Imoto, J Inazawa, E Otsuji. Overexpression of SMYD2 contributes to malignant outcome in gastric cancer. Br. J. Cancer. 2015.01; 112(2); 357-364
2. Hosoda F, Arai Y, Okada N, Shimizu H, Miyamoto M, Kitagawa N, Katai H, Taniguchi H, Yanagihara K, Imoto I, Inazawa J, Ohki M, Shibata T. Integrated genomic and functional analyses reveal glyoxalase I as a novel metabolic oncogene in human gastric cancer. Oncogene. 2015.02; 34(9); 1196-1206

3. Shin Hayashi, Mariko Yagi, Ichijiro Morisaki, Johji Inazawa. Identical deletion at 14q13.3 including PAX9 and NKX2-1 in siblings from mosaicism of unaffected parent. *J. Hum. Genet.*. 2015.04; 60(4); 203-206
4. Yoh Dobashi, Hiroyoshi Tsubochi, Hirochika Matsubara, Jun Inoue, Johji Inazawa, Shunsuke Endo, Akishi Ooi. Diverse involvement of isoforms and gene aberrations of Akt in human lung carcinomas. *Cancer Sci.*. 2015.06; 106(6); 772-781
5. Reiko Iwadate, Jun Inoue, Hitoshi Tsuda, Masashi Takano, Kenichi Furuya, Akira Hirasawa, Daisuke Aoki, Johji Inazawa. High Expression of p62 Protein Is Associated with Poor Prognosis and Aggressive Phenotypes in Endometrial Cancer. *Am. J. Pathol.*. 2015.09; 185(9); 2523-2533
6. Naoto Fujiwara, Jun Inoue, Tatsuyuki Kawano, Kousuke Tanimoto, Ken-Ichi Kozaki, Johji Inazawa. miR-634 Activates the Mitochondrial Apoptosis Pathway and Enhances Chemotherapy-Induced Cytotoxicity. *Cancer Res.*. 2015.09; 75(18); 3890-3901
7. 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. *PLOS One*. 2015.11; 10(11); e0140480
8. Yoshimitsu Yanaka, Tomoki Muramatsu, Hiroyuki Uetake, Ken-ichi Kozaki, Johji Inazawa. miR-544a induces epithelial-mesenchymal transition through the activation of WNT signaling pathway in gastric cancer. *Carcinogenesis*. 2015.11; 36(11); 1363-1371
9. Yumi Ozaki, Kyoko Fujiwara, Maki Ikeda, Toshinori Ozaki, Tadashi Terui, Masayoshi Soma, Johji Inazawa, Hiroki Nagase. The oncogenic role of GASC1 in chemically induced mouse skin cancer. *Mamm. Genome*. 2015.12; 26(11-12); 591-597

[Conference Activities & Talks]

1. Morishita M, Muramatsu T, Hayashi S, Hirai M, Suto Y, Konishi T, Moriyama K, Inazawa J. Exploration of mechanisms for chromothripsis by irradiation.. American Association for Cancer Research, 106th Annual Meeting 2015 2015.04 Philadelphia, USA.
2. Muramatsu T, Kozaki K, Imoto S, Yamaguchi R, Tsuda H, Kawano T, Morishita M, Miyano S, Inazawa J. The hypusine cascade promotes cancer progression and metastasis through the regulation of RhoA in squamous cell carcinoma. . American Association for Cancer Research, 106th Annual Meeting 2015 2015.04 Philadelphia, USA.
3. Inazawa J. Function-based screening of cancer-related miRNAs. . 2015 Seoul National University, Cancer Research Institute, Cancer Symposium. 2015.04.03 Hwasun Kunho Resort, Korea
4. Michelle N, Inoue J, Kawano T, Inazawa J. Inactivation of LPTM5 gene in human cancer. The 34th Sapporo International Cancer Symposium. . The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan
5. Morishita M, Muramatsu T, Hayashi S, Hirai M, Suto Y, Konishi T, Moriyama K, Inazawa J. Chromothripsis-like pattern in cancer-cell genome after irradiation by a focused vertical micro-beam system SPICE. . The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan
6. Hiramoto H, Muramatsu T, Ichikawa D, Othuji E, Inazawa J. Exploring EMT-related miRNAs using cell-based reporter system in pancreatic cancer. The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan
7. Sato T, Muramatsu T, Tanabe M, Inazawa J. Characterization of circulating tumor cell phenotype in pancreatic cancer. The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan
8. Sujata S, Muramatsu T, Inazawa J. Highly metastatic cancer cell exosomes contribute to cancer cell growth and metastatic traits . The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan
9. Muramatsu T, Kozaki K, Imoto S, Yamaguchi R, Tsuda H, Kawano T, Fujiwara N, Morishita M, Miyano S, Inazawa J. The hypusine cascade promotes cancer progression and metastasis through the regulation of RhoA in squamous cell carcinoma . The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan

10. Inoue J, Inazawa J. Screening of autophagy modulators for cancer therapy using high-content imaging system. The 34th Sapporo International Cancer Symposium 2015.06.26 Sapporo, Japan
11. Johji Inazawa. High expression of SQSTM1/p62 protein is associated with poor prognosis in epithelial ovarian cancer. Second Annual Meeting of the International Ovarian Cancer Consortium in conjunction with International Symposium on Tumor Microenvironment and Therapy Resistance 2015.08.17 Oklahoma City, USA
12. Johji Inazawa. Function-based screening of cancer-related miRNAs. . The 20th Japan-Korea Cancer Research Workshop. 2015.12.01 Tokyo, Japan

Biochemical Genetics

Professor	Shigetaka Kitajima MD, PhD
Associate Professor	Yujiro Tanaka MD, PhD
Graduate Student	Natsuki Arai Akihisa Fujisawa
Research Student	Shota Saitoh Natsumi Sakai
Technical Assistant	Makoto Inoue Yohei Uchida

(1) Outline

Transcriptional regulation is one of the most important processes by which genome information is expressed from DNA to mRNA to protein. The faithful synthesis of mRNA is achieved by transcriptional machinery comprised of RNA polymerase II, basal factors and many other protein factors, whose dysfunction is implicated in various human diseases. Our research interest is focused on the basic mechanism of transcription cycle and implication of early response transcription factors in determining cell fate in stress response.

Key words

- To provide novel paradigm of transcriptional regulation
- To understand role of transcription factor in cell fate determination

(2) Research

Research Subjects

- 1) Transcription
 - Elongin A plays dual roles in stress response
 - A novel function of FCP1
- 2) Cell fate determination by activating transcription factor (ATF) 3
 - Pro-apoptotic role of ATF3 and its implication in anti-cancer therapy
 - Genome-wide screen of the role of ATF3 in stress response and human cancer
 - ATF3 complex; transcriptional repressor or activator
 - ATF3 transcriptionally regulates microRNA
- 3) H3K36-specific histone methyltransferase ASH1.

(3) Publications

[Original Articles]

1. Inoue M et al. ATF3 is a direct target of the Wnt classical pathway and its anti-invasive role in human colon cancer cells. manuscript in preparation 2015;
2. Uchida Y et al. Systems analysis of DNA damage response of p53-ATF3 pathway in a mouse model. manuscript in preparation 2015;
3. Fukasawa K et al. ATF3 deficiency protects against RANKL-induced osteoporosis by suppressing proliferation of osteoclast precursors. revised 2015;
4. Iezaki T, Ozaki K, et al. ATF3 deficiency in chondrocytes alleviates osteoarthritis development. revised 2015;

Hematology

Professor Osamu Miura

Junior Associate Professor Ayako Arai

Assistant Professor Tetsuya Fukuda, Masahide Yamamoto, Gaku Oshikawa, Ken Watanabe

Project Assistant Professor Chizuko Sakashita

Senior Resident Ayako Nogami, Sayaka Suzuki, Keisuke Tanaka, Jyunichi Mukae
Graduate Student Minako Junta, Yoshihiro Umezawa, Hiroki Akiyama, Shinya Ishida,
Keigo Okada, Emi Uchida, 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 thrombocytopenia, with chemotherapeutics, molecularly-targeted drugs, immunosuppressive agents, and hematopoietic cell transplantation.

(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. Hiroki Akiyama, Masahide Yamamoto, Chizuko Sakashita, Yoshihiro Umezawa, Tetsuya Kurosu, Naomi Murakami, Osamu Miura. Therapy-related Leukemia with Inv(16)(p13.1q22) and Type D CBFB/MYH11 Developing after Exposure to Irinotecan-containing Chemoradiotherapy. *Intern. Med.* 2015; 54(6); 651-655
2. T Nagao, G Oshikawa, S Ishida, H Akiyama, Y Umezawa, A Nogami, T Kurosu, O Miura. A novel MYD88 mutation, L265RPP, in Waldenström macroglobulinemia activates the NF- κ B pathway to upregulate Bcl-xL expression and enhances cell survival. *Blood Cancer J.* 2015; 5; e314
3. Kudo D, Ohashi K, Komeno K, Nakamura Y, Shinagawa A, Yoshida C, Katsura Y, Ota I, Kakihana K, Kobayashi T, Kawai N, Kato A, Arai A, Yamamoto K, Toyota S, Kumagai T, Ohwada A, Miki T, Hori M, Okoshi Y, Kojima H, and Sakamaki H.. Efficacy and safety of bortezomib-containing induction chemotherapy for autologous stem cell transplantation-eligible Japanese multiple myeloma patients -A phase 2 multicenter trial *International Journal of Myeloma.* 2015; 5(3); 12-22
4. Shihoko Suwa, Aya Kasubata, Miyu Kato, Megumi Iida, Ken Watanabe, Osamu Miura, Tetsuya Fukuda. The tryptophan derivative, tranilast, and conditioned medium with indoleamine 2,3-dioxygenase-expressing cells inhibit the proliferation of lymphoid malignancies. *Int. J. Oncol.* 2015.01;
5. Takaaki Hattori, Ayako Arai, Takanori Yokota, Ken-Ichi Imadome, Hiroyuki Tomimitsu, Osamu Miura, Hidehiro Mizusawa. Immune-mediated neuropathy with Epstein-Barr virus-positive T-cell lymphoproliferative disease. *Intern. Med.* 2015.01; 54(1); 69-73
6. Youko Suehiro, Atsuhiko Hasegawa, Tadafumi Iino, Amane Sasada, Nobukazu Watanabe, Masao Matsuo, Ayako Takamori, Ryuji Tanosaki, Atae Utsunomiya, Ilseung Choi, Tetsuya Fukuda, Osamu Miura, Shigeo Takaishi, Takanori Teshima, Koichi Akashi, Mari Kannagi, Naokuni Uike, Jun Okamura. Clinical outcomes of a novel therapeutic vaccine with Tax peptide-pulsed dendritic cells for adult T cell leukaemia/lymphoma in a pilot study. *Br. J. Haematol.* 2015.01;
7. Masahide Yamamoto, Keigo Okada, Hiroki Akiyama, Tetsuya Kurosu, Osamu Miura. Evaluation of the efficacy of maintenance therapy for low-to-intermediate-risk acute promyelocytic leukemia in molecular remission: A retrospective single-institution study. *Mol Clin Oncol.* 2015.03; 3(2); 449-453
8. Jinta M, Imadome K, Komatsu H, Yoshimori M, Kurata M, Fujiwara S, Miura O, Arai A.. L-Asparaginase monotherapy for EBV-positive T/NK lymphoproliferative diseases: A pilot Study. *Journal of Medical and Dental Sciences.* 2015.03; 62(1); 1-9

9. Ayako Nogami, Gaku Oshikawa, Keigo Okada, Shusaku Fukutake, Yoshihiro Umezawa, Toshikage Nagao, Tetsuya Kurosu, Osamu Miura. FLT3-ITD confers resistance to the PI3K/Akt pathway inhibitors by protecting the mTOR/4EBP1/Mcl-1 pathway through STAT5 activation in acute myeloid leukemia. *Oncotarget*. 2015.04; 6(11); 9189-9205
10. Gaku Oshikawa, Kazuhiko Kakihana, Makoto Saito, Jun Aoki, Yuho Najima, Takeshi Kobayashi, Noriko Doki, Hisashi Sakamaki, Kazuteru Ohashi. Post-transplant maintenance therapy with azacitidine and gemtuzumab ozogamicin for high-risk acute myeloid leukaemia. *British Journal of Haematology*. 2015.06; 169(5); 756-759
11. Makoto Hirokawa, Kenichi Sawada, Naohito Fujisima, Masanao Teramura, Masami, Bessho, Kazuo Dan, Hisashi Tsurumi, Shinji Nakao, Akio Urabe, Shin Fujisawa, Yuji Yonemura, Fumio Kawano, Kazuo Oshimi, Koichi Sugimoto, Akira Matsuda, Masamitsu Karasawa, Ayako Arai, Norio Komatsu, Hideo Harigae, Mitsuhiro Omine, Keiya Ozawa, Mineo Kurokawa for the PRCA Collaborative Study Group.. Long-term outcome of patients with acquired chronic pure red cell aplasia following immunosuppressive therapy *Br J Haematol*. 2015.06; 169(6); 879-886
12. Emi Uchida, Ken Watanabe, Reina Arai, Masahide Yamamoto, Masayoshi Souri, Tsukasa Osaki, Akitada Ichinose, Osamu Miura, Takatoshi Koyama. Autoimmune Hemorrhaphilia Resulting from Autoantiboy against the A Subunit of Factor XIII. *Internal Medicine*. 2015.09; 54(18); 2383-2387
13. Oshikawa G, Yoshioka K, Takahashi Y, Shingai N, Ikegawa S, Kobayashi T, Doki N, Kakihana K, Ohashi K, Sakamaki H. Impact of prior azacitidine on the outcome of allogeneic hematopoietic transplantation for myelodysplastic syndrome *Pathology and Oncology Research*. 2015.09; 21(4); 1037-1043
14. Yoshimori M, Takada H, Imadome K, Kurata M, Yamamoto K, Koyama T, Shimizu N, Fujiwara S, Miura O, Arai A.. P-glycoprotein is expressed and causes resistance to chemotherapy in EBV-positive T-cell lymphoproliferative diseases. *Cancer Medicine*. 2015.10; 4(10); 1494-1504

[Misc]

1. Ayako Arai. Molecular mechanisms of Epstein-Barr virus-induced lymphoid neoplasms *Rinsho Ketsueki*. 2015.03; 56(3); 269-277
2. The molecular mechanisms of Epstein-Barr virus-induced T-or NK-lymphoid neoplasms development *Intensivist*. 2015.04; 7(2); 357-362
3. Ayako Arai. Epstein-Barr virus and Burkitt lymphoma *Hamatology*. 2015.08; 71(2); 214-219
4. Ayako Arai. The molecular mechanisms of Epstein-Barr virus-induced T-or NK-lymphoid neoplasms development *Nippon Rinsho*. 2015.10; 73(8); 55-59

[Conference Activities & Talks]

1. Retrospective analysis of autologous stem cell transplantation for relapse/refractory diffuse large B-cell lymphoma after R-CHOP chemotherapy. The 37th Annual Meeting of the Japan Society for Hematopoietic Cell Transplantation 2015.03.06 Kobe
2. Makoto Arai, Ayako Arai, Shun-ichiro Izumi. Postgraduate education in Kampo (traditional Japanese) medicine: A current survey of clinical training hospitals. An International Association of Medical Education (AMEE) 2015.09.08 Glasgow
3. Ayako Nogami, Keigo Okada, Gaku Oshikawa, Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Tetsuya Kurosu, Osamu Miura. FLT3-ITD confers resistance to Bortezomib by protecting the mTOR pathway via STAT5 and Pim-1. The 77th Annual Meeting of the Japanese Society of Hematology 2015.10.16 Ishikawa Ongakudo
4. Yoshihiro Umezawa, Hiroki Akiyama, Keigo Okada, Shinya Ishida, Ayako Nogami, Gaku Oshikawa, Tetsuya Kurosu, Osamu Miura. PECAM — 1 enhances SDF-1-induced chemotaxis mediated through activation of the PI3K/Akt/mTORC1 pathway. The 77th annual meeting of the japanese society of hematology 2015.10.17

5. Ayako Arai, Hiroshi Takase, Kouhei Yamamoto, Hiroki Akiyama, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. The 77th Annual Meeting of the Japanese Society of Hematology 2015.10.17 Kanazawa
6. Gaku Oshikawa, Shinya Ishida, Toshikage Nagao, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Ayako Nogami, Osamu Miura. A novel MYD88 mutation, L265RPP, activates NF- κ B to enhance Bcl-xL expression and cell survival. The 77th Annual Meeting of the Japanese Society of Hematology 2015.10.18 Kanazawa
7. Akira Toriihara, Reiko Nakajima, Ayako Arai, Masashi Nakadate, Koichiro Abe, Kazunori Kubota, Ukihide Tateishi. FDG-PET/CT of Epstein-Barr virus-related lymphoproliferative disorders: knowledge for rapid and appropriate diagnosis.. 102nd Scientific Assembly and Annual Meeting of Radiological Society of North America 2015.11.29 Chicago
8. Ayako Nogami, Keigo Okada, Gaku Oshikawa, Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Tetsuya Kurosu, Osamu Miura. FLT3-ITD Confers Resistance to Bortezomib By Protecting the mTOR/4EBP1 Pathway through Activation of STAT5 and Induction of Pim-1 Expression. 57th ASH Annual Meeting and Exposition 2015.12.05 Orange County Convention Center, Orlando
9. Ayako Arai, Hiroshi Takase, Kouhei Yamamoto, Hiroki Akiyama, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. 57th ASH Annual Meeting and Exposition 2015.12.05 Orlando

[Awards & Honors]

1. Certificate of Merit, Radiological Society of North America, 2015.12

Molecular Endocrinology and Metabolism

Professor: Yoshihiro Ogawa

Associate Professor: Takanobu Yoshimoto, Hajime Izumiyama

Assistant Professor: Isao Minami, Kyoichiro Tsuchiya, Ryotaro Bouchi

Clinical Fellow: Norihiko Ohara, Yujiro Nakano, Takato Takeuchi, Masahiro Asakawa, Yuriko Sasahara

Resident: Mitsuyuki Numasawa

Project Assistant Professor: Rumi Hachiya, Misa Saijo, Masanori Murakami, Takeru Sakai, Xunmei Yuan¹, Ibuki Shirakawa¹

JSPS RPD Fellow: Michiko Itoh

Graduate Students (Doctor' s course): Chikara Komiya, Yasutaka Chiba, Kazutaka Tsujimoto, Yasutaka Miyachi, Hideaki Kato, Kumiko Shiba, Kenichi Kawahori, Maki Kawasaki, Toshihiro Goto, Takuya Ohmura, Ryo Sakai, Megumi Hatano

Graduate Students (Master' s course): Takuya Shiihashi

Project Associate Professor: Koshi Hashimoto², Kyoko Shirakabe¹

¹Department of Organ Network and Metabolism, ²Department 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. Konuma Kuniha, Itoh Michiko, Suganami Takayoshi, Kanai Sayaka, Nakagawa Nobutaka, Sakai Takeru, Kawano Hiroyuki, Hara Mitsuko, Kojima Soichi, Izumi Yuichi, Ogawa Yoshihiro. Eicosapentaenoic acid ameliorates non-alcoholic steatohepatitis in a novel mouse model using melanocortin 4 receptor-deficient mice. *PLoS One*. 2015; 10(3); e0121528
2. Muramatsu-Kato Keiko, Itoh Hiroaki, Kohmura-Kobayashi Yukiko, Ferdous Urmi J, Tamura Naoaki, Yaguchi Chizuko, Uchida Toshiyuki, Suzuki Kazunao, Hashimoto Koshi, Suganami Takayoshi, Ogawa Yoshihiro, Kanayama Naohiro. Undernourishment in utero Primes Hepatic Steatosis in Adult Mice Offspring on an Obesogenic Diet; Involvement of Endoplasmic Reticulum Stress. *Sci Rep*. 2015; 5; 16867
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11. Fukuda Tatsuya, Bouchi Ryotaro, Minami Isao, Ohara Norihiko, Nakano Yujiro, Nishitani Rie, Murakami Masanori, Takeuchi Takato, Akihisa Momoko, Fujita Masamichi, Izumiyama Hajime, Hashimoto Koshi, Yoshimoto Takanobu, Ogawa Yoshihiro. Retrograde pyelonephritis and lumbar spondylitis as a result of *Salmonella typhi* in a type 2 diabetes patient with neurogenic bladder. *J Diabet Investig*. 2015.06;
12. Masanori Murakami, Takanobu Yoshimoto, Isao Minami, Ryotaro Bouchi, Kyoichiro Tsuchiya, Koshi Hashimoto, Hajime Izumiyama, Yasuhisa Fujii, Takashi Endo, Takumi Akashi, Koshiro Nishimoto, Kuniaki Mukai, Kazunori Kihara, Yoshihiro Ogawa. A Novel Somatic Deletion Mutation of ATP2B3 in Aldosterone-Producing Adenoma. *Endocr. Pathol.*. 2015.10;

13. Hashimoto Koshi, Tagami Tetsuya, Yamakage Hajime, Muranaka Kazuya, Tanaka Masashi, Odori Shinji, Kono Shigeo, Shimatsu Akira, Ogawa Yoshihiro, Satoh-Asahara Noriko. Serum free thyroxine levels is associated with the efficacy of weight reduction therapy in obese female patients. *Endocr J.* 2015.12;
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15. Bouchi Ryotaro, Takeuchi Takato, Akihisa Momoko, Ohara Norihiko, Nakano Yujiro, Nishitani Rie, Murakami Masanori, Fukuda Tatsuya, Fujita Masamichi, Minami Isao, Mihara Masatomo, Yoshimoto Takanobu, Ogawa Yoshihiro. 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 Diabet Investig.* 2015.12;

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

Satoshi Matsumura MD, PhD

Yusuke Mitsunori MD, PhD

Satoshi Matsumura MD, PhD

Hiromitsu Ito MD (since April)

Taku Sato MD (until September)

Graduate School Students

Hiromitsu Ito MD (until March)

Eriko Katsuta MD (until March)

Keisuke Nakao MD (until March)

Takaki Furuyama MD (until March)

Keiichi Akakhoshi MD

Atsushi Ohba MD

Yasuhito Iwao MD (joining April)

Hiroki Ueda MD

Yoshiteru Ohata MD

Taku Sato MD (since October)

Yuki Mizuno MD

Norimichi Chiyonobu MD

Haku Liu MD

Shuichi Watanabe (joining April)

Yoshiya Ishikawa (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.

(5) Publications

[Original Articles]

1. Shinoda Masahiro, Kishida Norihiro, Itano Osamu, Ei Shigenori, Ueno Akihisa, Kitago Minoru, Abe Yuta, Hibi Taizo, Yagi Hiroshi, Masugi Yohei, Tanabe Minoru, Aiura Koichi, Sakamaoto Michiie, Tanimoto Akihiro, Kitagawa Yuko. Long-term complete response of advanced hepatocellular carcinoma treated with multidisciplinary therapy including reduced dose of sorafenib: case report and review of the literature. *World J Surg Oncol.* 2015; 13; 144
2. Ei Shigenori, Shinoda Masahiro, Itano Osamu, Obara Hideaki, Kitago Minoru, Hibi Taizo, Yagi Hiroshi, Abe Yuta, Matsubara Kentaro, Ono Yoshihiro, Kawachi Shigeyuki, Hoshino Ken, Kuroda Tatsuo, Tanabe Minoru, Kitagawa Yuko. Effects of Addition of Early Enteral Nutritional Support During the Postoperative Phase in Patients after Living-Donor Liver Transplantation. *Ann Transplant.* 2015; 20; 357-365
3. Okajima C, Arai S, Tanaka S, Matsumura S, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Tanabe M.. Prognostic role of Child-Pugh score 5 and 6 in hepatocellular carcinoma patients who underwent curative hepatic resection. *Am. J. Surg.* 2015.01; 209(1); 199-205
4. X Dong, Q lin, A Aihara, Y Li, C Huang, W Chung, Q Tang, X Chen, R Carlson, C Nadolny, G Gabriel, M Olsen, J Wands. Aspartate beta-Hydroxylase expression promotes a malignant pancreatic cellular phenotype. *Oncotarget.* 2015.01; 6(2); 1231-1248
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- Taizo, Abe Yuta, Kitago Minoru, Obara Hideaki, Itano Osamu, Takeuchi Hiroya, Sakamoto Michiie, Tanabe Minoru, Maruyama Ikuro, Kitagawa Yuko. Gene transfer of high-mobility group box 1 box-A domain in a rat acute liver failure model. *J Surg Res.* 2015.04; 194(2); 571-580
6. Ei Shigenori, Hibi Taizo, Tanabe Minoru, Itano Osamu, Shinoda Masahiro, Kitago Minoru, Abe Yuta, Yagi Hiroshi, Okabayashi Koji, Sugiyama Daisuke, Wakabayashi Go, Kitagawa Yuko. Cryoablation provides superior local control of primary hepatocellular carcinomas of > 2 cm compared with radiofrequency ablation and microwave coagulation therapy: an underestimated tool in the toolbox. *Ann Surg Oncol.* 2015.04; 22(4); 1294-1300
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 8. Ban Daisuke, Kudo Atsushi, Ito Hiromitsu, Mitsunori Yusuke, Matsumura Satoshi, Aihara Arihiro, Ochiai Takanori, Tanaka Shinji, Tanabe Minoru, Itano Osamu, Kaneko Hironori, Wakabayashi Go. The difficulty of laparoscopic liver resection. *Updates Surg.* 2015.06; 67(2); 123-128
 9. Nakao Keisuke, Tanaka Shinji, Miura Tomoya, Sato Kota, Matsumura Satoshi, Aihara Arihiro, Mitsunori Yusuke, Ban Daisuke, Ochiai Takanori, Kudo Atsushi, Arii Shigeki, Tanabe Minoru. Novel Aurora/vascular endothelial growth factor receptor dual kinase inhibitor as treatment for hepatocellular carcinoma. *Cancer Sci.* 2015.08; 106(8); 1016-1022
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 11. Hiroko Matsunaga, Shinji Tanaka, Arihiro Aihara, Kousuke Ogawa, Satoshi Matsumura, Daisuke Ban, Takanori Ochiai, Takumi Irie, Atsushi Kudo, Noriaki Nakamura, Shigeki Arii and Minoru Tanabe. . A Novel Therapeutic Combination Sequentially Targeting Aurora B and Bcl-xL in Hepatocellular Carcinoma. *Ann. Surg. Oncol.* 2015.09; 22(9); 3079-3086
 12. Miura Tomoya, Ban Daisuke, Tanaka Shinji, Mogushi Kaoru, Kudo Atsushi, Matsumura Satoshi, Mitsunori Yusuke, Ochiai Takanori, Tanaka Hiroshi, Tanabe Minoru. Distinct clinicopathological phenotype of hepatocellular carcinoma with ethoxybenzyl-magnetic resonance imaging hyperintensity: association with gene expression signature. *Am J Surg.* 2015.09; 210(3); 561-569
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 14. 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.[Epub ahead of print] *J Gastroenterol.* 2015.11;
 15. Hibi Taizo, Shinoda Masahiro, Itano Osamu, Obara Hideaki, Kitago Minoru, Abe Yuta, Yagi Hiroshi, Tanaka Masayuki, Hoshino Ken, Fujino Akihiro, Kuroda Tatsuo, Kawachi Shigeyuki, Tanabe Minoru, Shimazu Motohide, Kitagawa Yuko. Steroid minimization immunosuppression protocol using basiliximab

in adult living donor liver transplantation for hepatitis C virus-related cirrhosis. *Hepatol Res.* 2015.12; 45(12); 1178-1184

16. Hayashi Kosuke, Uchida Hiroyuki, Takaoka Chie, Izawa Yuka, Shinoda Masahiro, Obara Hideaki, Itano Osamu, Shirahase Joichiro, Tanabe Minoru, Kitagawa Yuko, Mimura Masaru. Discrepancy in Psychological Attitudes Toward Living Donor Liver Transplantation Between Recipients and Donors. *Transplantation.* 2015.12; 99(12); 2551-2555

[Misc]

1. Daisuke Ban, Atsushi Kudo, Takumi Irie, Takanori Ochiai, Arihiro Aihara, Satoshi Matsumura, Shinji Tanaka, Minoru Tanabe. Advances in reduced port laparoscopic liver resection. *Asian J Endosc Surg.* 2015.02; 8(1); 11-15

[Conference Activities & Talks]

1. T. Ochiai, T. Sato , Y. Ohata , H. Ueda , A Oba , K. Akahoshi , K. Nakao , T. Furuyama , E. Katsuta , H. Ito , S. Matsumura , A. Aihara, D.Ban , T.Irie , A Kudo , S.Tanaka, M. Tanabe. Treatment strategy for hepatocellular carcinoma with portal vein tumor thrombosis. 10th Annual Academic Surgical Congress 2015.02.04 Las Vegas, USA
2. K. Akahoshi , T. Ochiai, S.Matsumura ,A. Aihara , D. Ban, T. Irie , A. Kudo ,S. Tanaka ,M . Tanabe. The Management of Cholecystectomy in Patients Receiving Anticoagulant and/or Antiplatelet Therapy. 10th Annual Academic Surgical Congress 2015.02.04 Las Vegas, USA
3. A cell surface β -hydroxylase is a novel therapeutic target for HCC. 2015.04.17
4. Minoru Tanabe. SILS laparoscopic cholecystectomy. IRCAD Advanced Course in Hepatobiliary and Pancreatic Surgery 2015.05.28 Taiwan
5. Minoru Tanabe. State of the Art in radiofrequency, micro-wave, and cryoablation. IRCAD Advanced Course in Hepatobiliary and Pancreatic Surgery 2015.05.30 Taiwan
6. Aihara A, Matsunaga M, NakaoK, Ito H, Mitsunori M, Matsumura M, Ban D, Ochiai T, Kudo A, Tanabe M, Tanaka S. Aurora B kinase is a promising therapeutic target for hepatocellular carcinoma. The 6th Asia-Pacific Primary liver Cancer Expert Meeting 2015.07.04 Osaka
7. Minoru Tanabe. One port laparoscopic cholecystectomy. IRCAD Advanced Course in Hepatobiliary and Pancreatic Surgery 2015.07.30 Brazil
8. Minoru Tanabe. State of the Art in radiofrequency, micro-wave, and cryoablation. IRCAD Advanced Course in Hepatobiliary and Pancreatic Surgery 2015.08.01 Brazil
9. Tanaka S, Aihara A, Tanabe M. Molecular pathogenesis and targeted therapy for major vascular invasiveness of hepatocellular carcinoma. JDDW2015 2015.10.08 Tokyo
10. Akahoshi K, Tanaka S, Tanabe M. Characteristics of Non-B Non-C hepatocellular carcinoma and lifestyle related diseases as its risk factors. JDDW2015 2015.10.09 Tokyo
11. OchiaiT, Ito H, Mitsunori M, AiharaA, Ban D, Kudo A, Tanaka S, Tanabe M. Minimizing intraoperative blood loss during hepatectomy –practical use of multiple energy devices-. APDW2015 2015.12.06 Taipei, Taiwan
12. Minoru Tanabe. Single port cholecystectomy. IRCAD New Perspectives in Hepatobiliary and Pancreatic Surgery Advanced Course 2015.12.17 Strasbourg, France
13. Minoru Tanabe. State of the Art in ablation therapy (radiofrequency, micro-wave,and cryoablation) . IRCAD New Perspectives in Hepatobiliary and Pancreatic Surgery Advanced Course 2015.12.19 Strasbourg, France

[Patents]

1. ORGAN FUNCTION MAINTAINING AND AMELIORATING SOLUTION, Patent Number:PCT/JP2006/304269

Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa

Associate Professor: Shinichi Sotome, Yoshinori Asou

Assistant Professor: Tsuyoshi Kato, Toshitaka Yoshii, Hiroyuki Inose, Mitsuhiro Enomoto

(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 charactorised 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 revolutional measurering 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 sectiones, 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. Masato Yuasa, Tsuyoshi Yamada, Takashi Taniyama, Tomokazu Masaoka, Wei Xuetao, Toshitaka Yoshii, Masaki Horie, Hiroaki Yasuda, Toshimasa Uemura, Atsushi Okawa, Shinichi Sotome. Dexamethasone enhances osteogenic differentiation of bone marrow- and muscle-derived stromal cells and augments ectopic bone formation induced by bone morphogenetic protein-2. *PLoS ONE*. 2015; 10(2); e0116462
2. Kokoro Ozaki, Nobuo Sanjo, Kinya Ishikawa, Miwa Higashi, Takaaki Hattori, Naoyuki Tanuma, Rie Miyata, Masaharu Hayashi, Takanori Yokota, Atsushi Okawa, Hidehiro Mizusawa. Elevation of 8-hydroxy-2'-deoxyguanosine in the cerebrospinal fluid of three patients with superficial siderosis *Neurology and Clinical Neuroscience*. 2015;
3. Joshua N Farr, Matthew M Roforth, Koji Fujita, Kristy M Nicks, Julie M Cunningham, Elizabeth J Atkinson, Terry M Therneau, Louise K McCready, James M Peterson, Matthew T Drake, David G Monroe, Sundeep Khosla. Effects of Age and Estrogen on Skeletal Gene Expression in Humans as Assessed by RNA Sequencing. *PLoS ONE*. 2015; 10(9); e0138347
4. Toshitaka Yoshii, Takashi Hirai, Tsuyoshi Yamada, Satoshi Sumiya, Renpei Mastumoto, Tsuyoshi Kato, Mitsuhiro Enomoto, Hiroyuki Inose, Shigenori Kawabata, Kenichi Shinomiya, Atsushi Okawa. Lumbar pedicle screw placement using a fluoroscopic pedicle axis view and a cannulated tapping device. *J Orthop Surg Res*. 2015; 10; 79
5. Funauchi Yuki, Tanikawa Chizu, Yi Lo Paulisally Hau, Mori Jinichi, Daigo Yataro, Takano Atsushi, Miyagi Yohei, Okawa Atsushi, Nakamura Yusuke, Matsuda Koichi. Regulation of iron homeostasis by the p53-ISCU pathway. *Sci Rep*. 2015; 5; 16497
6. Kobayashi Keiji, Nojiri Hidetoshi, Saita Yoshitomo, Morikawa Daichi, Ozawa Yusuke, Watanabe Kenji, Koike Masato, Asou Yoshinori, Shirasawa Takuji, Yokote Koutaro, Kaneko Kazuo, Shimizu Takahiko. Mitochondrial superoxide in osteocytes perturbs canalicular networks in the setting of age-related osteoporosis. *Sci Rep*. 2015; 5; 9148
7. Gaku Koyano, Tetsuya Jinno, Daisuke Koga, Chisato Hoshino, Takeshi Muneta, Atsushi Okawa. Is closed suction drainage effective in early recovery of hip joint function? Comparative evaluation in one-stage bilateral total hip arthroplasty. *J Arthroplasty*. 2015.01; 30(1); 74-78
8. Imajo Yasuaki, Taguchi Toshihiko, Yone Kazunori, Okawa Atsushi, Otani Koji, Ogata Tadanori, Ozawa Hiroshi, Shimada Yoichi, Neo Masashi, Iguchi Tetsuhiro. Japanese 2011 nationwide survey on complications from spine surgery. *J Orthop Sci*. 2015.01; 20(1); 38-54

9. Pilar Peris, Matthew M Roforth, Kristy M Nicks, Daniel Fraser, Koji Fujita, Robert L Jilka, Sundeep Khosla, Ulrike McGregor. Ability of circulating human hematopoietic lineage negative cells to support hematopoiesis. *J. Cell. Biochem.* 2015.01; 116(1); 58-66
10. Iwata Munetaka, Aikawa Takeshi, Hakozaiki Takaharu, Arai Kiyotaka, Ochi Hiroki, Haro Hirotaka, Tagawa Masahiro, Asou Yoshinori, Hara Yasushi. Enhancement of Runx2 expression is potentially linked to beta-catenin accumulation in canine intervertebral disc degeneration. *J Cell Physiol.* 2015.01; 230(1); 180-190
11. Chengshan Ma, Toru Fukuda, Hiroki Ochi, Satoko Sunamura, Cheng Xu, Ren Xu, Atsushi Okawa, Shu Takeda. Genetic determination of the cellular basis of the ghrelin-dependent bone remodeling. *Mol Metab.* 2015.03; 4(3); 175-185
12. Takashi Taniyama, Tomokazu Masaoka, Tsuyoshi Yamada, Xuetao Wei, Hiroaki Yasuda, Toshitaka Yoshii, Yuko Kozaka, Tomoji Takayama, Masahiro Hirano, Atsushi Okawa, Shinichi Sotome. Repair of Osteochondral Defects in a Rabbit Model Using a Porous Hydroxyapatite Collagen Composite Impregnated With Bone Morphogenetic Protein-2. *Artif Organs.* 2015.04;
13. Matthew M Roforth, Joshua N Farr, Koji Fujita, Louise K McCready, Elizabeth J Atkinson, Terry M Therneau, Julie M Cunningham, Matthew T Drake, David G Monroe, Sundeep Khosla. Global transcriptional profiling using RNA sequencing and DNA methylation patterns in highly enriched mesenchymal cells from young versus elderly women. *Bone.* 2015.07; 76; 49-57
14. Yuasa Masato, Mignemi Nicholas A, Nyman Jeffry S, Duvall Craig L, Schwartz Herbert S, Okawa Atsushi, Yoshii Toshitaka, Bhattacharjee Gourab, Zhao Chenguang, Bible Jesse E, Obremskey William T, Flick Matthew J, Degen Jay L, Barnett Joey V, Cates Justin M M, Schoenecker Jonathan G. Fibrinolysis is essential for fracture repair and prevention of heterotopic ossification. *J Clin Invest.* 2015.08; 125(8); 3117-3131
15. Ryohei Takada , Tetsuya Jinno , Daisuke Koga , Masanobu Hirao , Takeshi Muneta , Atsushi Okawa . Is Drain Tip Culture Prognostic of Surgical Site Infection? Results of 1380 Drain Tip Cultures in Total Hip Arthroplasty. *J Arthroplasty.* 2015.08; 30(8); 1407-1409
16. Yoshii Toshitaka, Nyman Jeffry S, Yuasa Masato, Esparza Javier M, Okawa Atsushi, Gutierrez Gloria E. Local application of a proteasome inhibitor enhances fracture healing in rats. *J Orthop Res.* 2015.08; 33(8); 1197-1204
17. Kristy M Nicks, Koji Fujita, Daniel Fraser, Ulrike McGregor, Matthew T Drake, Meghan E McGee-Lawrence, Jennifer J Westendorf, David G Monroe, Sundeep Khosla. Deletion of Estrogen Receptor Beta in Osteoprogenitor Cells Increases Trabecular but Not Cortical Bone Mass in Female Mice. *J. Bone Miner. Res.* 2015.09;
18. Kawabata Atsuyuki, Inose Hiroyuki, Ukegawa Dai, Kawabata Shigenori, Yamada Tsuyoshi, Okawa Atsushi. A foreign body granuloma after the usage of polyglycolic acid mesh and fibrin glue for dural repair. A case report. *J Orthop Sci.* 2015.09;
19. Sakai Kenichiro, Yoshii Toshitaka, Hirai Takashi, Arai Yoshiyasu, Torigoe Ichiro, Tomori Masaki, Sato Hirokazu, Okawa Atsushi. CERVICAL SAGITTAL IMBALANCE IS A PREDICTOR OF KYPHOTIC DEFORMITY AFTER LAMINOPLASTY IN CERVICAL SPONDYLOTIC MYELOPATHY PATIENTS WITHOUT PREOPERATIVE KYPHOTIC ALIGNMENT. *Spine (Phila Pa 1976).* 2015.09;
20. Yuasa Masato, Mignemi Nicholas A, Nyman Jeffry S, Duvall Craig L, Schwartz Herbert S, Okawa Atsushi, Yoshii Toshitaka, Bhattacharjee Gourab, Zhao Chenguang, Bible Jesse E, Obremskey William T, Flick Matthew J, Degen Jay L, Barnett Joey V, Cates Justin M M, Schoenecker Jonathan G. Fibrinolysis is essential for fracture repair and prevention of heterotopic ossification. *J Clin Invest.* 2015.09; 125(9); 3723
21. Toru Fukuda, Hiroki Ochi, Satoko Sunamura, Akina Haiden, Waka Bando, Hiroyuki Inose, Atsushi Okawa, Yoshinori Asou, Shu Takeda. MicroRNA-145 regulates osteoblastic differentiation by targeting the transcription factor Cbfb. *FEBS Lett.* 2015.10; 589(21); 3302-3308
22. Ailixiding Maierhaba, Aibibula Zulpiya, Iwata Munetaka, Piao Jinying, Hara Yasushi, Koga Daisuke, Okawa Atsushi, Morita Sadao, Asou Yoshinori. Pivotal role of Sirt6 in the crosstalk among ageing, metabolic syndrome and osteoarthritis. *Biochem Biophys Res Commun.* 2015.10; 466(3); 319-326

23. Okamoto Sawako, Kawahara Kazuo, Okawa Atsushi, Tanaka Yujiro. Values and risks of second opinion in Japan's universal health-care system. *Health Expect.* 2015.10; 18(5); 826-838
24. 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.* 2015.12; 1-19
25. Kazumasa Miyatake, Tetsuya Jinno, Daisuke Koga, Yuki Yamauchi, Takeshi Muneta, Atsushi Okawa. Comparison of Different Materials and Proximal Coatings Used for Femoral Components in One-Stage Bilateral Total Hip Arthroplasty. *J Arthroplasty.* 2015.12; 30(12); 2237-2241

[Conference Activities & Talks]

1. Hirai T., Arai Y., Sakai K., Torigoe I., Maehara H., Tomori M., Soma M., Yoshii T., Sato H., & Okawa A. Two-year follow-up evaluation of alternative surgical treatments for cervical spondylotic myelopathy patients with cervical mis-alignment and/or large anterior impingement.. 6th annual meeting of the Cervical Spine Research Society– Asia Pacific Section 2015.03.26 Yokohama
2. Toshitaka Yoshii, Takashi Hirai, Hiroyuki Inose, Tsuyoshi Kato, Kenichiro Sakai, Shigenori Kawabata, Kenichi Shinomiya, Atsushi Okawa. A Prospective, Randomized Study Comparing Selective Laminectomy and Conventional Laminoplasty for Cervical Spondylotic Myelopathy: A Minimum of 2-year Follow-up . 6th CSRS Asia Pacific Section 2015.03.26 Yokohama
3. Hiroyuki Inose, et al.. Bone remodeling ratio (BRR) as a predicting factor for non-union after spinal fusion.. WCO-IOF-ESCEO 2015.03.27 MILAN
4. Shingo Sato, Qingxia Wei, Makoto Hirata, Yuning Tang, Shu Takeda, Jay S. Wunder, Benjamin Alman. Microarray and RNA sequencing analysis of pericyte-derived sarcomas in a novel sarcoma mouse model. Orthopaedic Research Society Annual Meeting 2015 2015.03.28 Las Vegas
5. Tsuyoshi Yamada, Shinichi Sotome, Toshitaka Yoshii, Atsushi Okawa. After Repeated Division, Bone Marrow Stromal Cells Express Inhibitory Factors With Osteogenic Capabilities, And EphA5 Is A Primary Candidate. . Orthopaedic Research Society 2015 Annual Meeting 2015.03.28 Las Vegas
6. Yasuda H, Masaoka T, Taniyama T, Yamada T, Wei X, Yoshii T, Takayama T, Kozaka Y, Nakajima T, Okawa A, Sotome S. Spinal fusion with bone morphogenetic protein-2 delivered by hydroxyapatite/collagen in a rabbit.. Orthopaedic Research Society 2015 Annual Meeting 2015.03.28 Las Vegas, Nevada
7. Maierhaba Ailixiding, Zulipiya Aibibula, Munetaka Iwata, Jinying Piao, Jin Guangwen, Daisuke Koga, Atsushi Okawa, Sadao Morita, Yoshinori Asou. Potent role of Sirt6 in the crosstalk between metabolic syndrome and osteoarthritis. ORS 2015 Annual Meeting 2015.03.28 Las Vegas, Nevada
8. Toshitaka Yoshii, Jeffry S. Nyman, Javier Esparza, Atsushi Okawa, Gloria E. Gutierrez. Local Application of a Proteasome Inhibitor Enhances Fracture Healing in Rats . Orthopaedic Research Society 2015 Annual Meeting 2015.03.28 Las Vegas
9. Yoto Oh, Atsuhiko Tano, Yoshiro Kurosa, Atsushi Okawa. Can temporary external fixator for the initial treatment of lower extremity fractures be used in the operative field of the internal fixation safely?. 16th European Congress of Trauma & Emergency Surgery (ECTES) 2015.05.10 Amsterdam, Netherlands
10. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Takeshi Muneta, Atsushi Okawa. Drain tip culture cannot be prognostic of surgical site infection after total hip arthroplasty. 16th EFORT 2015.05.27 Praha, CZE
11. Yuko Tokunaga Segawa, Makoto Kamegaya, Takashi Saisu, Jun Kakizaki, Mitsuaki Morita, Yasuhiro Oikawa, Reiko Tanaka, Yuta Tsukagoshi, Tetsuya Jinno, Atsushi Okawa. Treatment outcome of poor prognostic group of patients with Legg-Calvé-Perthes disease. The Asia Pacific Paediatric Orthopaedic Society (APPOS) 2015 2015.06.05 Hong Kong
12. Tsuyoshi Kato, Toshitaka Yoshii, Hiroyuki Inose, Takashi Hirai, Tsuyoshi Yamada, Takashi Taniyama, Shigenori Kawabata, Atsushi Okawa. Long-term outcome of surgery for lumbar degenerative spondylolisthesis in a prospective randomized clinical trial. ISSLS 2015.06.08 San Francisco

13. Takuya Oyaizu, Mitsuhiro Enomoto, Masaki Horie, Yasushi Kojima, Kazuyoshi Yagishita. Acceleration of muscle volume reduction and recovery from hypoxia of injured skeletal muscle by hyperbaric oxygen. Undersea & Hyperbaric Medical Society 2015.06.18 Montreal
14. Toshitaka Yoshii. Anterior Decompression with Fusion vs Posterior Decompression with Fusion for Massive Cervical Ossification of Posterior Longitudinal Ligament with 50% Canal Occupying Ratio or More. Spine Across the Sea 2015.07.26 Kohala Coast, Hawaii
15. Toshitaka Yoshii. Complications in Cervical Spine, My Worst Case. Spine Across the Sea 2015.07.26 Kohala Coast ,Hawaii
16. Hiroyuki Inose, Masanori Saito, Philipp Kaldis, Atsushi Okawa. The cell cycle regulation of chondrocyte development. ASBMR 2015 Annual Meeting 2015.10.09 Seattle
17. Hirai T., Mulpuri Y., Spigelman I. & Nishimura I.. Differential accumulation of Nav1.8 mRNA with de novo long 3' UTR in sensory axons after peripheral nerve injury. 45th annual meeting of the Society for Neuroscience 2015.10.17 Chicago
18. Satoshi Sumiya, Shigenori Kawabata, Syuta Ushio, Toshitaka Yoshii, Tsuyoshi Kato, Atsushi Okawa. Noninvasive Evaluation By Magnetospinography Of Electrophysiological Activity In The Cervical Spine After Peripheral Nerve Stimulation In Humans. 43rd CSRS 2015.12.03 San Diego
19. Toshitaka Yoshii, Takashi Hirai, Satoshi Sumiya, Tsuyoshi Kato, Shigenori Kawabata, Atsushi Okawa, Kenichi Shinomiya. Anterior Decompression with Fusion vs. Posterior Decompression with Fusion for Massive Cervical Ossification of Posterior Longitudinal Ligament with 50% Canal Occupying Ratio or More: Retrospective Multi-Center Study. 43rd CSRS 2015.12.03 San Diego

Biofunctional Molecular Science

Associate Professor Tomoya Hirano

(1) Outline

Our group is working on the developments of functional molecules, which can “modulate” or “sense” the physiological functions, such as enzyme inhibitors and fluorescent sensors for elucidating intracellular or extracellular signal transduction pathway. In addition, we also focus on the development of novel drug and diagnostic tools for various diseases.

(2) Research

1) Construction of a facile method to develop various fluorescent sensors for elucidating physiological functions
We construct a facile method to develop various fluorescent sensors, which can sense the change of the concentration or activity of each biologically important analyte.

2) Development of histone methyltransferase inhibitors
Post-translational modification of histone proteins plays an important role in the regulation of gene expression, and can be controlled by histone modifying enzymes, such as histone methyltransferase (HMT). We are developing some inhibitors against these HMTs.

(3) Education

In this course, students are taught and trained several knowledgnes and techniques for the development of functional molecules.

(4) Lectures & Courses

Through this course, students are expected to understand and train the experimental techniques related to organic chemistry, analytical chemistry, medicinal chemistry and chemical biology.

(5) Publications

[Original Articles]

1. Kazumi Inoue, Ko Urushibara, Misae Kanai, Kei Yura, Shinya Fujii, Mari Ishigami-Yuasa, Yuichi Hashimoto, Shuichi Mori, Emiko Kawachi, Mio Matsumura, Tomoya Hirano, Hiroyuki Kagechika, Aya Tanatani. Design and synthesis of 4-benzyl-1-(2H)-phthalazinone derivatives as novel androgen receptor antagonists. *Eur J Med Chem.* 2015.09; 102; 310-319
2. Takuya Shiraishi, Hiroyuki Kagechika, Tomoya Hirano. 6-Arylcoumarins: versatile scaffolds for fluorescent sensors *New Journal of Chemistry.* 2015.10; 39; 8389-8396

[Conference Activities & Talks]

1. Tomoya Hirano, Takuya Shiraishi, Yuuki Noji, Toshki Saito, Hiroyuki Kagechika. Development of fluorescent sensors for environmental change. Grant-in-Aid for Scientific Research on Innovative Area “HD Physiology” The Final HD Physiology Symposium 2015.03 Osaka
2. Naoki Hinata, Tomoya Hirano, Hiroyuki Kagechika, Ayumi Ohsaki. Fluorescent compounds from *Quassia amara*. Inaugural Symposium of the Phytochemical Society of Asia 2015 (ISPSA 2015) 2015.08 Tokushima
3. Michitake Hirano, Tomoya Hirano, Takashi Fujiwara, Kasumi Ohira, Akihiro Ito, Minoru Yoshida, Hiroyuki Kagechika. Study for the development of inhibitors for Set7/9. 3rd International Conference on Retinoids 2015.10 Gifu

Biomechanics

Kenji Kawashima
Takahiro Kanno

(1) Outline

Kawashima Lab. mainly working on the development of medical devices and systems based on control engineering, robotics and fluid dynamics.

Key word is integration such as hardware and software, electrical and pneumatics, human and machine.

(2) Research

- 1)Surgical robot system
- 2)Haptic device using biological and visual information
- 3)Forceps manipulator for minimally invasive surgery
- 4)Development of power assist devices using pneumatic actuators

(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. T. Kanno, D. Haraguchi, M. Yamamoto, K. Tadano, and K. Kawashima. A Forceps Manipulator With Flexible 4-DOF Mechanism for Laparoscopic Surgery IEEE/ASME Transactions on Mechatronics. 2015; 20(3); 1170-1178
2. In Kim, Kotaro Tadano, Kenji Kawashima. Research on a Master Manipulator Using an Isometric Interface for Translation in Robotic Surgery International Journal of Advanced Robotic Systems. 2015;

3. Daisuke Haraguchi, Takahiro Kanno, Kotaro Tadano, Kenji Kawashima. A Pneumatically-Driven Surgical Manipulator with a Flexible Distal Joint Capable of Force Sensing IEEE/ASME Transactions on Mechatronics. 2015; 20(6); 2950-2961
4. Jun Li, Kenji Kawashima, Toshiharu Kagawa. A method to suppress temperature increase in pneumatic artificial rubber muscles Experimental Thermal and Fluid Science. 2015.02; 61; 59-65
5. Daisuke Haraguchi, Takahiro Kanno, Kotaro Tadano, Kenji Kawashim. A Pneumatically-Driven Surgical Manipulator with a Flexible Distal Joint Capable of Force Sensing IEEE/ASME Transactions on Mechatronics (TMECH). 2015.04; 20(6); 2950-2961
6. Kotaro Tadano, Kenji Kawashim. A Pneumatic Laparoscope Holder controlled by Head Movement The International Journal of Medical Robotics and Computer Assisted Surgery. 2015.09; 11(3); 331-340
7. Hongbing Li, Kenji Kawashima. Achieving Stable Tracking in Wave-Variable-Based Teleoperation. (ACCEPT) IEEE/ASME Transactions on Mechatronics (TMECH).

[Conference Activities & Talks]

1. Ryoken Miyazaki, Takahiro Kanno, Gen Endo, Kenji Kawashima. Pneumatically Driven Handheld Forceps with Force Display Operated by Motion Sensor. 2015 IEEE International Conference on Robotics and Automation 2015.05.27 Seattle
2. Takahiro Kanno, Daisuke Morisaki, Ryouken Miyazaki, Gen Endo, Kenji Kawashima. A Walking Assistive Device with Intention Detection using Back-driven Pneumatic Artificial Muscles. 2015 IEEE 11th International Conference on Rehabilitation Robotics 2015.08.12 Singapore
3. Ryoken Miyazaki, Tomohisa Terata, Takahiro Kanno, Toshiaki Tsuji, Gen Endo, Kenji Kawashima. Wide-range in-air Haptic Device Using a Pneumatic Bellows and Its Application to Master-slave Surgical Robot. 2015 IEEE/RSJ International Conference on Intelligent Robots and Systems 2015.09.30 Hamburg
4. Ryoken Miyazaki, Takahiro Kanno, Kyohei Takikawa, Kenji Kawashima. Dexterous and Lightweight Robotic Hand-held Forceps for Laparoscopy Surgery. 6th International Conference on Advanced Mechatronics 2015.12.06
5. Kyouhei Takikawa, Kanno Takahiro, Gen Endo, Kenji Kawashima. Development of Surgical Forceps Manipulator Using Flexible Joint and Two Pneumatic Cylinder to Two Degree-of-Freedom Flexion. 6th International Conference on Advanced Mechatronics 2015.12.06
6. Daisuke Morisaki, Hiroshi Suzuki, Sho Yoshida, Takashi Fujioka, Takahiro Kanno, Gen Endo, Kenji Kawashima. Pneumatic Walking Assistive System with a Soft Exoskeleton and a Follower Robot for Power Source. 6th International Conference on Advanced Mechatronics 2015.12.07

Structural Biology

Associate Professor Teikichi IKURA

(1) Outline

We are investigating the relationship between structure and function of biopolymers such as proteins and nucleic acids from the physicochemical viewpoint. Our lab deals with the fundamental issues on protein folding and stability, and various folding-diseases such as Alzheimer's disease.

(2) Research

Research Subjects

1. Analysis of interactions between tau protein and Pin1
2. Structural analyses of potential drug targets

(3) Education

Lecture on Structural Biology

The goal of this lecture is to provide the ability to understand and analyze the relationship between structure and function of biopolymers such as proteins and nucleic acids. This lecture deals with the fundamental contents on protein folding and stability, and then takes an overview on various folding-diseases such as Alzheimer's disease from the physicochemical viewpoint.

(4) Lectures & Courses

The purpose of this course is to provide the ability to understand and analyze the relationship between structure and function of biopolymers such as proteins and nucleic acids. Students learn fundamental contents through the lecture, fundamental techniques through the practice, and then acquire various techniques essential to bio-science through lab experiments.

The goal of this lecture is to provide the ability to understand and analyze the relationship between structure and function of biopolymers such as proteins and nucleic acids. This lecture deals with the fundamental contents on protein folding and stability, and then takes an overview on various folding-diseases such as Alzheimer's disease from the physicochemical viewpoint.

In this practice, students learn how to read scientific journal related to folding-diseases, and understand fundamental techniques to elucidate the inherent functions of the proteins and the mechanism of the diseases.

In the lab experiments, students learn various techniques for physicochemical study on proteins such as gene cloning, protein expression and purification, structural analysis and interaction analysis.

(5) Publications

[Original Articles]

1. Morooka, S., Hoshina, M., Kii, I., Okabe, T., Kojima, H., Inoue, N., Okuno, Y., Denawa, M., Yoshida, S., Fukuhara, J., Ninomiya, K., Ikura, T., Furuya, T., Nagano, T., Noda, K., Ishida, S., Hosoya, T., Ito, N., Yoshimura, N., Hagiwara*, M.. Identification of a dual inhibitor of SRPK1 and CK2 that attenuates pathological angiogenesis of macular degeneration in mice. *Molecular Pharmacology*. 2015.08; 88(2); 316-325
2. Anami, Y., Sakamaki, Y., Itoh, T., Inaba, Y., Nakabayashi, M., Ikura, T., Ito, N., Yamamoto, K.. Fine tuning of agonistic/antagonistic activity for vitamin D receptor by 22-alkyl chain length of ligands: 22S-hexyl compound unexpectedly restored agonistic activity. *Bioorganic & Medicinal Chemistry*. 2015.11; 23(22); 7274-7281
3. Watarai, Y., Ishizawa, M., Ikura, T., Zacconi, F. C. M., Uno, S., Ito, N., Mourino, A., Tokiwa, H., Makishima, M., Yamada, S.. Synthesis, biological activities, and X-ray crystal structural analysis of 25-hydroxy-25(or 26)-adamantyl-17-[20(22),23-diynyl] -21-norvitamin D compounds *Journal of Medical Chemistry*. 2015.12; 58(24); 9510-9521

[Conference Activities & Talks]

1. Nobutaka Numoto, Satomi Inaba, Hisayuki Morii, Teikichi Ikura, Masayuki Oda, Nobutoshi Ito. Molecular recognition mechanisms of T-cell activator CD28 and SH2 domains of Gads and PI3-kinase. The 15th Annual Meeting of the Protein Society of Japan 2015.06 Tokushima
2. Satomi Inaba, Nobutaka Numoto, Hisayuki Morii, Teikichi Ikura, Ryo Abe, Nobutoshi Ito, Masayuki Oda. Molecular interaction between PI3-kinase and co-stimulation receptor ICOS. The 15th Annual Meeting of the Protein Society of Japan 2015.06 Tokushima
3. Ikura, T., Naoya Tochio, N., Kawasaki, R., Tate, S., Ito, N.. Pin1 doesn't isomerize pT231-P232 of tau peptide, but prevents the peptide from aggregating. The 15th Annual Meeting of the Protein Society of Japan 2015.06 Tokushima
4. Inaba S., Numoto N., Morii H., Ikura T., Abe R., Ito N., Oda M.. Structural and thermodynamic analysis of co-stimulation receptor CD28 phosphopeptide interactions with Grb2, Gads, and PI3-kinase SH2 domains. The 29th Annual Symposium of The Protein Society 2015.07 Palau de Congressos de Barcelona, Barcelona (Spain)
5. Ikura, T., Ito, N.. Functional conversion from peptidyl-prolyl isomerase to protease by a single amino acid substitution. The 53rd Annual Meeting of the Biophysical Society of Japan 2015.09 Kanazawa

Diagnostic Radiology and Nuclear Medicine

Professor Ukihide Tateishi
Project Professor Yukihsa Saida
Associate Professors Ichiro Yamada
Lecturers Mitsuhiro Kishino, Yoshio Kitazume(Feb ~)
Research Associates Yoshio Kitazume(~ Jan), Yoshiaki Katada,
 Makiko Honda(Aug ~), Akira Troriihara,
 Kaori Okazawa, Masashi Nakadate,
 Akiyuki Matuhisa(~ Mar), Tomoyuki Fujioka(Feb ~)
Hospital Staff members Makiko Honda(Apr ~ Jul), Tomoyuki Fujioka(~ Jan),
 Yoshihiro Iwasa, Youko Shirakawa(Apr ~), Namiko Matsui(Oct ~),
Resident Jun Ooyama(Oct ~), Namiko Matsui(Apr ~ Sep),
 Kenji Nishida(Apr ~ Sep), Emi Yamaga(Apr ~), Ken Yamagiwa(Apr ~)

(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 radiology 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. 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), 18F-FACBC (amino acid metabolism), 62/64Cu-ATSM (redox, hypoxia), 18F-FLT (DNA synthesis), 18F-NaF (bone metabolism), and 68Ga-DOTA-PEG-RGD (angiogenesis). The usefulness of 18F-FDG in the discipline of oncology has been observed in numerous carcinomas. 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. One SPECT scanner and one PET/CT scanner were renewed respectively.

(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. 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.* 2015; (in press);
2. 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.* 2015; (in press);

3. Akira Toriihara, Yoshio Kitazume, Hidenori Nishida, Kazunori Kubota, Masashi Nakadate, Ukihide Tateishi. Comparison of FDG-PET/CT images between chronic renal failure patients on hemodialysis and controls. *Am J Nucl Med Mol Imaging*. 2015; 5(2); 204-211
4. Yoshihiro Iwasa, Yoshio Kitazume, Ukihide Tateishi, Yukihisa Saida, Daisuke Ban, Minoru Tanabe, Akira Takemoto. Hepatocellular carcinoma histological grade prediction: A quantitative comparison of diffusion-weighted, T2-weighted, and hepatobiliary-phase magnetic resonance imaging *J Comput Assist Tomogr*. 2015; in press;
5. Akira Toriihara, Atsunobu Tsunoda, Akira Takemoto, Kazunori Kubota, Youichi Machida, Ukihide Tateishi. Dual-time-point FDG-PET/CT of temporal bone chondroblastoma: two cases *Asia Oceania Journal of Nuclear Medicine & Biology*. 2015; 3; 120-124
6. Hirata Yasuhide, Inaba Yutaka, Kobayashi Naomi, Ike Hiroyuki, Yukizawa Yohei, Fujimaki Hiroshi, Tezuka Taro, Tateishi Ukihide, Inoue Tomio, Saito Tomoyuki. Correlation between mechanical stress by finite element analysis and 18F-fluoride PET uptake in hip osteoarthritis patients. *J Orthop Res*. 2015.01; 33(1); 78-83
7. Kobayashi Naomi, Inaba Yutaka, Tateishi Ukihide, Ike Hiroyuki, Kubota So, Inoue Tomio, Saito Tomoyuki. Comparison of 18F-fluoride positron emission tomography and magnetic resonance imaging in evaluating early-stage osteoarthritis of the hip. *Nucl Med Commun*. 2015.01; 36(1); 84-89
8. Katahira-Suzuki Ryoko, Hata Masaharu, Tateishi Ukihide, Taguchi Takahide, Takano Shoko, Omura-Minamisawa Motoko, Inoue Tomio. Definitive chemo-radiotherapy for squamous cell carcinoma of the pharynx: impact of baseline low hemoglobin level (< 12 g/dL) and post-radiation therapy F-18 FDG-PET/CT. *Ann Nucl Med*. 2015.01; 29(1); 37-45
9. Toriihara A, Kitazume Y, Nishida H, Kubota K, Nakadate M, Tateishi U. Comparison of FDG-PET/CT images between chronic renal failure patients on hemodialysis and controls. *American Journal of Nuclear Medicine and Molecular Imaging*. 2015.02; 5(2); 204-211
10. Tateishi Ukihide, Tatsumi Mitsuaki, Terauchi Takashi, Ando Kiyoshi, Niitsu Nozomi, Kim Won Seog, Suh Cheolwon, Ogura Michinori, Tobinai Kensei. Prognostic significance of metabolic tumor burden by positron emission tomography/computed tomography in patients with relapsed/refractory diffuse large B-cell lymphoma. *Cancer Sci*. 2015.02; 106(2); 186-193
11. Motoko Watanabe, Yojiro Umezaki, Anna Miura, Yukiko Shinohara, Tatsuya Yoshikawa, Tomomi Sakuma, Chisa Shitano, Ayano Katagiri, Miho Takenoshita, Akira Toriihara, Akihito Uezato, Toru Nishikawa, Haruhiko Motomura, Akira Toyofuku. Comparison of cerebral blood flow in oral somatic delusion in patients with and without a history of depression: a comparative case series. *BMC Psychiatry*. 2015.03; 15(1); 422
12. Yoshiaki Katada, Shunichi Kondo, Eitoshi Tsuboi, Ken Nakamura, Kyu Rokkaku, Yoshihito Irie. Type IA endoleak embolization after TEVAR via direct transthoracic puncture. *Jpn J Radiol*. 2015.03; 33(3); 169-172
13. Tomita Naoto, Hattori Yukako, Fujisawa Shin, Hashimoto Chizuko, Taguchi Jun, Takasaki Hirotaka, Sakai Rika, Tateishi Ukihide, Ishigatsubo Yoshiaki. Post-therapy (1)(8)F-fluorodeoxyglucose positron emission tomography for predicting outcome in patients with peripheral T cell lymphoma. *Ann Hematol*. 2015.03; 94(3); 431-436
14. Tezuka D, Terashima M, Kato Y, Toriihara A, Hirasawa K, Sasaoka T, Yoshikawa S, Maejima Y, Ashikaga T, Suzuki J, Hirao K, Isobe M.. Clinical characteristics of definite or suspected isolated cardiac sarcoidosis: Application of cardiac magnetic resonance imaging and (18)F-fluoro-2-deoxyglucose positron-emission tomography/computerized tomography. *Journal of Cardiac Failure*. 2015.04; 21(4); 313-322
15. Ichiro Yamada, Naoyuki Miyasaka, Keigo Hikishima, Yutaka Tokairin, Tatsuyuki Kawano, Eisaku Ito, Daisuke Kobayashi, Yoshinobu Eishi, Hideyuki Okano. Ultra-high-resolution MR imaging of esophageal carcinoma at ultra-high field strength (7.0T) ex vivo: correlation with histopathologic findings. *Magn Reson Imaging*. 2015.05; 33(4); 413-419

16. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Masakazu Nagahori, Toshimitsu Fujii, Eiko Saito, Tomoyuki Fujioka, Katsuyoshi Matsuoka, Makoto Naganuma, Mamoru Watanabe. Correlation of the Endoscopic and Magnetic Resonance Scoring Systems in the Deep Small Intestine in Crohn's Disease. *Inflamm Bowel Dis.* 2015.05; 21(8); 1832-1838
17. Ichiro Yamada, Keigo Hikishima, Naoyuki Miyasaka, Yutaka Tokairin, Eisaku Ito, Tatsuyuki Kawano, Daisuke Kobayashi, Yoshinobu Eishi, Hideyuki Okano. Esophageal carcinoma: Evaluation with q-space diffusion-weighted MR imaging ex vivo. *Magn Reson Med.* 2015.06; 73(6); 2262-2273
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19. Kubota So, Inaba Yutaka, Kobayashi Naomi, Tateishi Ukihide, Ike Hiroyuki, Inoue Tomio, Saito Tomoyuki. Prediction of femoral head collapse in osteonecrosis using 18F-fluoride positron emission tomography. *Nucl Med Commun.* 2015.06; 36(6); 596-603
20. Morita Yuka, Nozaki Taiki, Starkey Jay, Okajima Yuka, Ohde Sachiko, Matsusako Masaki, Yoshioka Hiroshi, Saida Yukihiisa, Kurihara Yasuyuki. Radiology of Fractures in Intoxicated Emergency Department Patients: Locations, Mechanisms, Presentation, and Initial Interpretation Accuracy. *Medicine (Baltimore).* 2015.06; 94(24); e980
21. Youichi Machida, Masashi Nakadate. Breast Shape Change Associated with Aging: A Study Using Prone Breast Magnetic Resonance Imaging. *Plast Reconstr Surg Glob Open.* 2015.06; 3(6); e413
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23. Nozaki Taiki, Tasaki Atsushi, Horiuchi Saya, Osakabe Chiharu, Ohde Sachiko, Saida Yukihiisa, Yoshioka Hiroshi. Quantification of Fatty Degeneration Within the Supraspinatus Muscle by Using a 2-Point Dixon Method on 3-T MRI. *AJR Am J Roentgenol.* 2015.07; 205(1); 116-122
24. Ochi Junko, Nozaki Taiki, Okada Masato, Suyama Yasuhiro, Kishimoto Mitsumasa, Akaike Gensuke, Tasaki Atsushi, Ohde Sachiko, Saida Yukihiisa, Yoshioka Hiroshi. MRI findings of the shoulder and hip joint in patients with polymyalgia rheumatica. *Mod Rheumatol.* 2015.09; 25(5); 761-767
25. Jun Oyama, Kouichi Mori, Masatoshi Imamura, Yukiko Mizushima, Ukihide Tateishi. Size of the intracranial optic nerve and optic tract in neonates at term-equivalent age at magnetic resonance imaging. *Pediatric Radiology.* 2015.12;

[Misc]

1. Masashi Nakadate, Akira Toriihara, Ukihide Tateishi. The role of FDG-PET/CT for the treatment of relapsed/refractory DLBCL Hematology. 2015.07; 71(1); 128-133

[Conference Activities & Talks]

1. Tomoyuki Fujioka, Kazunori Kubota, Akira Toriihara, Yukihiisa Saida, Ukihide Tateishi. Feasibility of [F-18] FDG-PET/CT for Clinicopathological Evaluation in Patients with Ductal Carcinoma In-Situ (DCIS) of the Breast. *European Congress of Radiology* 2015.03 Viena
2. Masashi Nakadate, Youichi Machida, Yoshihiro Iwasa, Yoshio Kitazume, Ukihide Tateishi. Post-processing subtraction of T1-weighted image from T2-weighted image: evaluation of theoretical signal intensity and comparison with a STIR image. *European Congress of Radiology* 2015.03 Vienna, Austria
3. Masashi Nakadate, Yoshihiro Iwasa, Mitsuhiro Kishino, Ukihide Tateishi. Detectability of unruptured intracranial aneurysms on thin-slice non-contrast-enhanced CT. *European Congress of Radiology* 2015.03 Vienna, Austria

4. Kitazume Y, Takenaka K, Ohtsuka K, Fujioka T, Fujii T, Tateishi U, Saida Y, Watanabe M. Can Magnetic Resonance Enterocolonography Scoring System derived from Simplified Endoscopic Activity Score for Crohn' Disease be alternative to MaRIA score?. European Congress of Radiology 2015.03.04 Vienna
5. Yoshihiro Iwasa, Yoshio Kitazume, Yukihisa Saida, Ukihide Tateishi, Daisuke Ban, Minoru Tanabe. Prediction of the histological grade of hepatocellular carcinoma: quantitative comparisons among DW, T2W, and hepatobiliary phase of Gd-EOB-DTPA enhanced MRI.. European congress of radiology 2015 2015.03.04 Vienna
6. Yoshihiro Iwasa, Yoshio Kitazume, Yukihisa Saida, Ukihide Tateishi, Daisuke Ban, Minoru Tamura . Prediction of the histological grade of hepatocellular carcinoma: quantitativ e comparison among DW, T2W, and hepatobilliary phase of Gd-EOB-DTPA enhance d MRI. Japanese Congress of Radiology 2015 2015.04
7. Fujioka T, Kubota K, Toriihara A, Saida Y, Tateishi U. Feasibility of [F-18] FDG-PET/CT for Clinicopathological Evaluation in Patients with Ductal Carcinoma In-Situ (DCIS) of the Breast . Japan radiological society 2015.04
8. Masashi Nakadate, Makoto Kimura, Hiroshi Ogura, Jun Isogai, Ukihide Tateishi. Hippocampal neurotoxicity in a patient with glyphosate-based herbicide ingestion. American Society of Neuroradiology 2015.04 Chicago, U.S.A.
9. Yoshihiro Iwasa, Yoshio Kitazume, Yukihisa Saida, Ukihide Tateishi, Daisuke Ban, Minoru Tanabe. Prediction of the histological grade of hepatocellular carcinoma: quantitative comparisons among DW, T2W, and hepatobiliary phase of Gd-EOB-DTPA enhanced MRI.. The 74th Annual Meeting of the Japan Radiological Society 2015.04.17 Yokohama, Japan
10. Yoshio Kitazume, Mayuko Sato, Shuichiro Nakaminato, Shinichi Taura, Susumu Isogai. A pulmonary lesion consisting of squamous cell carcinoma with a small proportion of adenocarcinoma preoperatively revealed to have these mixed histology by CT-guided biopsy: a case report. The 44th annual meeting of the Japanese Society of Interventional Radiology (JSIR), the 12th International symposium of Interventional Radiology (ISIR), the 4th Asia-Pacific Confefence of Interventional Radiology (APCIO) 2015.05.28 Miyazaki
11. Akira Toriihara, Tsukasa Okamoto, Takahiro Mistumura, Ukihide Tateishi. Evaluation of idiopathic interstitial pneumonias by FDG-PET/CT and methods for managing respiratory motions during the imaging.. SNMMI 62nd Annual Meeting 2015.06.06
12. Shinya Kotaki, Junichiro Sakamoto, Shin Nakamura, Takahide Taguchi, Hiroyuki Harada, Akira Toriihara, Tohru Kurabayashi. Perineural spread of malignant tumor : a case of Diffuse large B-cell lymphoma. 2015.06.07
13. Akira Toriihara, Masashi Nakadate, Tomoyuki Fujioka, Jun Oyama, Atsunobu Tsunoda, Takuro Sumi, Ukihide Tateishi. Pretherapeutic evaluation of cancer of the external auditory canal using FDG-PET/CT.. SNMMI 62nd Annual Meeting 2015.06.09
14. Akira Toriihara, Ukihide Tateishi, Mitsuaki Tatsumi, Takashi Terauchi, Ryoichi Yoshimura. Prognostic significance of volumetric parameters of FDG PET/CT in patients with malignant lymphoma.. SNMMI 62nd Annual Meeting 2015.06.10
15. Motoko Watanabe, Yojiro Umezaki, Anna Miura, Yukiko Shinohara, Tatsuya Yoshikawa, Miho Takenoshita, Akira Toriihara, Akihito Uezato, Toru Nishikawa, Haruhiko Motomura, Akira Toyofuku. Comparison of cerebral blood flow in oral somatic delusion in patients with and without a history of depression. 23rd World Congress on Psychosomatic Medicine 2015.08.21
16. Yoshio Kitazume, Kento Takenaka, Tomoyuki Fujioka, Toshimitsu Fujii, Masashi Nakadate, Kazuo Ohtsuka, Yukihisa Saida, Ukihide Tateishi. Development of a Simplified Magnetic Resonance Enterocolonography Scoring System for Crohn's Disease: Comparison with MaRIA. JSMRM 2016, the 43th annual meeting of the Japanese Society for Magnetic Resonance in Medicine 2015.09.11
17. Akira Toriihara, Reiko Nakajima, Ayako Arai, Masashi Nakadate, Koichiro Abe, Kazunori Kubota, Ukihide Tateishi. FDG-PET/CT of Epstein-Barr virus-related lymphoproliferative disorders: knowledge for rapid and appropriate diagnosis.. RSNA 101st Scientific Assembly and Annual Meeting 2015.11.29

[Awards & Honors]

1. Akira Toriihara, Reiko Nakajima, Ayako Arai, Masashi Nakadate, Koichiro Abe, Kazunori Kubota, Ukihide Tateishi, FDG-PET/CT of Epstein-Barr virus-related lymphoproliferative disorders: knowledge for rapid and appropriate diagnosis. Certificate of Merit, RSNA, 2015.12

Disease Genomics

Shumpei Ishikawa: Professor
 Takayuki Isagawa: Assistant Professor
 Hiroto Kato: Assistant Professor
 Yasunari Satou: Collaborative Researcher
 Reiko Sato: Technical Assistant
 Satoko Aihara: Technical Assistant
 Asami Yamamoto: Technical Assistant
 Kazuki Kishi: Technical Assistant
 Ryouhei Suzuki: Technical Assistant
 Miharuru Tamukai: Secretary
 Miki Fujihashi: Graduate Student

(1) Outline

Tumor tissue is a complex system composed of tumor cells and multiple types of stromal cells. Our purpose is to understand the dynamic multicellular interactions in such a complexed biological system by measuring a large amount of data at the genomic level, which leads the identifications of therapeutic targets and biomarkers. Another objective in the graduate course is to learn the applications, methods and interpretations of the disease genomics and to understand how to apply disease genomics to clinical fields through analyzing clinical human samples.

(2) Research

- ① Genomic approach for cancer - stromal interaction
- ② Functional genomic screening in cancer
- ③ Functional analysis of cancer associated molecules
- ④ Genomic analysis of clinical cancer samples

(3) Publications

[Original Articles]

1. Saito S, Morishima K, Ui T, Hoshino H, Matsubara D, Ishikawa S, Aburatani H, Fukayama M, Hosoya Y, Sata N, Lefor AK, Yasuda Y, Niki T.. The role of HGF/MET and FGF/FGFR in fibroblast-derived growth stimulation and lapatinib-resistance of esophageal squamous cell carcinoma. BMC Cancer. 2015.02;
2. Ushiku T, Ishikawa S, Kakiuchi M, Tanaka A, Katoh H, Aburatani H, Lauwers GY, Fukayama M. RHOA mutation in diffuse-type gastric cancer: a comparative clinicopathology analysis of 87 cases Gastric Cancer. 2015.04; 19(2); 403-411
3. Maeda D, Akiyama Y, Morikawa T, Kunita A, Ota Y, Katoh H, Niimi A, Nomiya A, Ishikawa S, Goto A, Igawa Y, Fukayama M, Homma Y. Hunner-Type (Classic) Interstitial Cystitis: A Distinct Inflammatory Disorder Characterized by Pancystitis, with Frequent Expansion of Clonal B-Cells and Epithelial Denudation PLoS One. 2015.11; 10(11); e0143316

[Conference Activities & Talks]

1. Daisuke Komura, Takashi Ichimura, Hiroto Katoh, Stark Markus, Hiroyuki Aburatani, Masashi Fukayama, Shumpei Ishikawa. Transcriptome Analysis across diverse biological species in the human gastric environment. 2015.04.20
2. Hiroto Katoh, Miwako Kakiuchi, Masashi Fukayama, Shumpei Ishikawa. Discovery of Altered Protein-Protein Interactions Involving RHOA in Diffuse Type Gastric Carcinoma. The 104th Annual Meeting of the Japanese Society of Pathology 2015.04.20
3. Shumpei Ishikawa, Miwako Kakiuchi, Hiroto Katoh, Ryouhei Suzuki, Atsushi Tanaka, Akimasa Hayashi, Tetsuo Ushiku, Masashi Fukayama, Hiroyuki Aburatani. RHOA mutations in diffuse-type gastric carcinoma. 2015.04.20
4. Shumpei Ishikawa. Cancer Genomics. Distinct genomic profile and driver mutation of diffuse-type gastric carcinoma. The 11th International Workshop on Advanced Genomics 2015.05.20
5. Shumpei Ishikawa. RhoA driver mutations in diffuse-type gastric carcinoma. The 34th Sapporo International Cancer Symposium 2015 2015.06.25
6. Shumpei Ishikawa. RHOA driver mutations in diffuse-type gastric carcinoma. The Japanese Society of Medical Oncology 2015 Annual Meeting 2015.07.16
7. Ishikawa S, Kakiuchi M, Fukayama M, Aburatani H.. RHOA driver mutations in diffuse-type gastric carcinoma. The 24th Annual Meeting of The Japanese Association of Metastasis Research 2015.07.23
8. Hiroto Katoh, Daisuke Komura, Hiroki Konishi, Asami Yamamoto, Masashi Fukayama, Shumpei Ishikawa. IMMUNE PROFILING IN HEALTH AND DISEASE. 2015.09.09 Seattle, USA
9. Hiroto Katoh, Daisuke Komura, Hiroki Konishi, Asami Yamamoto, Masashi Fukayama, Shumpei Ishikawa. Immunogenomic Characterization of Tumor Infiltrating TCR Repertoire in the Gastric Carcinoma Environments using Archived Histopathological Specimens. 3rd Annual immungenomics 2015 Shaping the Future of Human Health 2015.09.28 HUNTSVILLE, ALABAMA, USA
10. Kei-ichi Morita, Yu Oikawa, Kou Kayamori, Kei Sakamoto, Shumpei Ishikawa, Johji Inazawa, Hiroyuki Harada. Targeted resequencing of cancer-related genes in oral cancer. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08
11. Shigeya Hayashi, Miwako Kakiuchi, Amane Tagashira, Hiroto Katoh, Hiroki Ueda, Shogo Yamamoto, Kenji Tatsuno, Takashi Ohshima, Yasushi Rino, Atsushi Nakajima, Masashi Fukayama, Shumpei Ishikawa, Hiroyuki Aburatani. Genomic profiling for target therapy of gastric cancer. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08
12. Akihiro Suzuki, Amane Tagashira, Hiroto Katoh, Hiroki Ueda, Shogo Yamamoto, Kenji Tatsuno, Eiji Sakai, Takashi Ohshima, Yasushi Rino, Atsushi Nakajima, Masashi Fukayama, Shumpei Ishikawa, Hiroyuki Aburatani. Genomic landscape of gastric cancer. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08
13. Daisuke Matsubara, Takeshi Ito, Ichidai Tanaka, Shumpei Ishikawa, Yasushi Goto, Tomoyuki Nakano, Yoh Dobashi, Jun Nakajima, Shunsuke Endo, Masashi Fukayama, Yoshitaka Sekido, Toshiro Niki, Yoshinori Murakami. Loss of YAP1 defines neuroendocrine differentiation of lung tumor. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08
14. Shumpei Ishikawa . Genomic Profiling and Discovery of Driver Mutations in Diffuse-type Gastric Carcinoma. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08
15. Miwako Kakiuchi, Shigeya Hayashi, Amane Tagashira, Hiroto Katoh, Hiroki Ueda, Shogo Yamamoto, Kenji Tatsuno, Takashi Ohshima, Yasushi Rino, Atsushi Nakajima, Masashi Fukayama, Shumpei Ishikawa, Hiroyuki Aburatani. RHOA mutation and CLDN18-ARHGAPs rearrangements of diffuse-type gastric cancer. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08
16. Amane Tagashira, Shinichi Yachida, Miwako Kakiuchi, Hirofumi Rokutan, Akimasa Hayashi, Kenji Tatsuno, Shogo Yamamoto, Genta Nagae, Hiroyuki Abe, Shumpei Ishikawa, Tatsuhiro Shibata, Masashi Fukayama, Hiroyuki Aburatani. Multi lesion analysis of alpha fetoprotein producing gastric cancer. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.08

17. Keiichi Morita, Yu Oikawa, Kou Kayamori, Kei Sakamoto, Kousuke Tanimoto, Shumpei Ishikawa, Johji Inazawa, Hiroyuki Harada. Targeted resequencing of cancer related genes in oral cancer. The 60th Annual Meeting of the Japan Society of Human Genetics 2015.10.14
18. Keiichi Morita, Yu Oikawa, Kou Kayamori, Kei Sakamoto, Kousuke Tanimoto, Shumpei Ishikawa, Johji Inazawa, Hiroyuki Harada. A case of Melanotic neuroectodermal tumor of infancy. The 60th Annual Meeting of the Japan Society of Human Genetics 2015.10.14
19. Miki Fujihashi, Hiroto Katoh, Reiko Sato, Ryohei Suzuki, Kazuki Kishi, Daisuke Komura, Shumpei Ishikawa. Establishment of a functional genomics screening method to identify novel therapeutic targets for gastric carcinoma. The 60th Annual Meeting of the Japan Society of Human Genetics 2015.10.14
20. Hiroto Katoh, Daisuke Komura, Ryohei Suzuki, Asami Yamamoto, Masashi Fukayama, Hiroyuki Aburatani, Shumpei Ishikawa. Next-generation sequencing analysis for antigen-receptor structures of tumor infiltrating lymphocytes. The 60th Annual Meeting of the Japan Society of Human Genetics 2015.10.14
21. Takayuki Isagawa, Daisuke Komura, Reiko Sato, Kazuki Kishi, Ryohei Suzuki, Shumpei Ishikawa. Comprehensive analysis of tumor-stromal interactions. The 60th Annual Meeting of the Japan Society of Human Genetics 2015.10.14

Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka

Tenure Track Junior Associate Professor, Yukinori Okada

Tenure Track Junior Associate Professor, Kevin Urayama

(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. Diogo Dorothee, Bastarache Lisa, Liao Katherine P, Graham Robert R, Fulton Robert S, Greenberg Jeffrey D, Eyre Steve, Bowes John, Cui Jing, Lee Annette, Pappas Dimitrios A, Kremer Joel M, Barton Anne, Coenen Marieke J H, Franke Barbara, Kiemeny Lambertus A, Mariette Xavier, Richard-Miceli Corrine, Canhao Helena, Fonseca Joao E, de Vries Niek, Tak Paul P, Crusius J Bart A, Nurmohamed Michael T, Kurreeman Fina, Mikuls Ted R, Okada Yukinori, Stahl Eli A, Larson David E, Deluca Tracie L, O’Laughlin Michelle, Fronick Catrina C, Fulton Lucinda L, Kosoy Roman, Ransom Michael, Bhangale Tushar R, Ortmann Ward, Cagan Andrew, Gainer Vivian, Karlson Elizabeth W, Kohane Isaac, Murphy Shawn N, Martin Javier, Zhernakova Alexandra, Klareskog Lars, Padyukov Leonid, Worthington Jane, Mardis Elaine R, Seldin Michael F, Gregersen Peter K, Behrens Timothy, Raychaudhuri Soumya, Denny Joshua C, Plenge Robert M. TYK2 protein-coding variants protect against rheumatoid arthritis and autoimmunity, with no evidence of major pleiotropic effects on non-autoimmune complex traits. PLoS One. 2015; 10(4); e0122271
2. Terao Chikashi, Ohmura Koichiro, Kochi Yuta, Ikari Katsunori, Okada Yukinori, Shimizu Masakazu, Nishina Naoshi, Suzuki Akari, Myouzen Keiko, Kawaguchi Takahisa, Takahashi Meiko, Takasugi Kiyoshi, Murasawa Akira, Mizuki Shinichi, Iwahashi Mitsuhiro, Funahashi Keiko, Natsumeda Masamitsu, Furu Moritoshi, Hashimoto Motomu, Ito Hiromu, Fujii Takao, Ezawa Kazuhiko, Matsubara Tsukasa, Takeuchi Tsutomu, Kubo Michiaki, Yamada Ryo, Taniguchi Atsuo, Yamanaka Hisashi, Momohara Shigeki, Yamamoto Kazuhiko, Mimori Tsuneyo, Matsuda Fumihiko. Anti-citrullinated peptide/protein antibody

- (ACPA)-negative RA shares a large proportion of susceptibility loci with ACPA-positive RA: a meta-analysis of genome-wide association study in a Japanese population. *Arthritis Res Ther.* 2015; 17(1); 104
3. Shigemizu D, Aiba T, Nakagawa H, Ozaki K, Miya F, Satake W, Toda T, Miyamoto Y, Fujimoto A, Suzuki Y, Kubo M, Tsunoda T, Shimizu W, and Tanaka T . Exome analyses of long QT syndrome reveal candidate pathogenic mutations in calmodulin-interacting genes *PLoS One* . 2015;
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[Misc]

1. Kazuhiko Yamamoto, Yukinori Okada, Akari Suzuki, Yuta Kochi. Genetics of rheumatoid arthritis in Asia-present and future. *Nat Rev Rheumatol.* 2015.02;
2. Ozaki Kouichi, Tanaka Toshihiro. Molecular genetics of coronary artery disease. *J Hum Genet.* 2015.07;

[Conference Activities & Talks]

1. Yukinori Okada. Human genetics contribute to disease biology, medicine, and drug discovery. The 6th International Symposium of IFReC 2015.02.23
2. Yukinori Okada. Perspective of Human Genetics towards Preventive Medicine of Rheumatic Diseases. TMU-TMDU Joint Symposium 2015.03.14
3. Higuchi C, Tanaka T and Okada Y. Systematic comparison of machine learning methods for identification of miRNA species as disease biomarkers. The IWBBIO 2015 (3rd International Work-Conference on Bioinformatics and Biomedical Engineering) 2015.04 Spain Granada
4. Yukinori Okada. Identification of the risk HLA variants of Graves' disease by applying the HLA imputation method to large scale Japanese genome-wide association study date. The 59th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2015.04.23 Nagoya Congress Center
5. Ozaki K, Ebana Y, Furukawa T, Kubo M, Tanaka T. Identification and Analyses of Novel Atrial Fibrillation Susceptible Molecules. The 79th Annual Scientific Meeting of Japanese Circulation Society 2015.04.25 Osaka Nakanoshima
6. Ebana Y, Ozaki K, Okada Y, Tanaka T, Isobe M, Furukawa T. SY19-1 Arrhythmia, A Post-GWAS Analysis, MAGENT, Identified Novel Pathways for Atrial Fibrillation. The 79th Annual Scientific Meeting of Japanese Circulation Society 2015.04.26 Osaka Nakanoshima

7. Aiba T, Makimoto H, Makiyama T, Watanabe H, Hayashi K, Nakano Y, Morita H, Aonuma K, Hagiwara N, Fukuda K, Yoshinaga M, Horigome H, Sumitomo N, Tanaka T, Sekine A, Kamakura S, Miyamoto Y, Kusano K, Makita N, Horie M, Shimizu W. FRS-117Arrhythmia, Diverse Gender Difference of Arrhythmic Risk in Patients with Congenital Long QT Syndrome: From Japanese Congenital LQTS Multicenter Registry. The 79th Annual Scientific Meeting of Japanese Circulation Society 2015.04.26 Osaka Nakanoshima
8. Okada Y. Encounter of Big Data and Human Genetics. 12th Meeting of Bone Biology Forum 2015.08.22
9. Okada Y, Momozawa Y, Ashikawa K, Kanai M, Matsuda K et al. Identification of the risk HLA variants of Graves' disease by applying the HLA imputation method to large scale Japanese genome-wide association study data. 17th Asia Pacific League of Associations for Rheumatology Congress 2015.09.09
10. El Rouby N, McDonough CW, Gong Y, McClure LA, Mitchell BD, Horenstein RB, Talbert RL, Takahashi A, Tanaka T, Kubo M, Pepine CJ, Cooper-DeHoff RM, Benavente OR, Shuldiner AR, Johnson JA. Novel genetic loci for resistant hypertension discovered through a genome-wide association approach (GWAS) in the INternational VErapamil SR-Trandolapril Study (INVEST) and the Secondary Prevention of Sub-cortical Strokes (SPS3) Study. American Society of Human Genetics 2015.10
11. Okada Y. Statistical Genetics in the era of BIG DATA. Mini-Workshop between IMS RIKEN and Institutions of Luxembourg 2015.10.08
12. Okada Y. Close Encounters of the BIG DATA. The 74th Annual Meeting of the Japanese Cancer Association 2015.10.10
13. Okada Y. Asian GWAS Databases for Uric Acid/Gout and RA Experience. G-CAN 2015 Annual Meeting 2015.11.06
14. Okada Y. Significant impact of miRNA-target gene networks on the genetics of rheumatoid arthritis. International RA Genetics Meeting 2015.11.07
15. Okada Y. Statistical Genetics for Drug Discovery. Tokyo Medical & Dental University 14th Surugadai International Symposium 2015.11.26

[Others]

1. 2015.11
ACR Session:Utilizaing Big Data to Advance Rheumatology.American Colledge of Rheumatology Annual Meeting 2015

Applied Regenerative Medicine

Professor: Ichiro SEKIYA

Assistant Professor: Masafumi HORIE, Koji OTABE, Hisako KATANO

Project Assistant Professor: Nobutake OZEKI

Project Researcher: Keiichiro KOMORI, Mitsuru MIZUNO

Graduate Student: Kenta KATAGIRI, Yuji KONO

Technical Staff : Miyoko OJIMA, Yukie MATSUMOTO, Fumika KAWAMATA
Shizuka FUJII

Assistant Clerk: Mika WATANABE, Rei NISHIDA, 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 started transplantation of synovial stem cells to enhance meniscus healing after meniscus suture.

(4) Publications

[Original Articles]

1. Koji Otabe, Hiroyuki Nakahara, Akihiko Hasegawa, Tetsuya Matsukawa, Fumiaki Ayabe, Naoko Onizuka, Masafumi Inui, Shuji Takada, Yoshiaki Ito, Ichiro Sekiya, Takeshi Muneta, Martin Lotz, Hiroshi Asahara. Transcription factor Mohawk controls tenogenic differentiation of bone marrow mesenchymal stem cells in vitro and in vivo. *J. Orthop. Res.* 2015.01; 33(1); 1-8
2. Yu Matsukura, Takeshi Muneta, Kunikazu Tsuji, Kazumasa Miyatake, Jun Yamada, Kahaer Abula, Hideyuki Koga, Makoto Tomita, Ichiro Sekiya. Mouse synovial mesenchymal stem cells increase in yield with knee inflammation. *J. Orthop. Res.* 2015.02; 33(2); 246-253
3. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Posterolateral Bundle Graft Fixation Angles on Clinical Outcomes in Double-Bundle Anterior Cruciate Ligament Reconstruction: A Randomized Controlled Trial. *Am J Sports Med.* 2015.05; 43(5); 1157-1164

4. Kahaer Abula, Takeshi Muneta, Kazumasa Miyatake, Jun Yamada, Yu Matsukura, Makiko Inoue, Ichiro Sekiya, Daniel Graf, Aris N Economides, Vicki Rosen, Kunikazu Tsuji. Elimination of BMP7 from the developing limb mesenchyme leads to articular cartilage degeneration and synovial inflammation with increased age. *FEBS Lett.* 2015.05; 589(11); 1240-1248
5. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Initial Graft Tension on Knee Stability and Graft Tension Pattern in Double-Bundle Anterior Cruciate Ligament Reconstruction. *Arthroscopy.* 2015.05; 31(9); 1756-1763
6. Yusuke Nakagawa, Takeshi Muneta, Shinpei Kondo, Mitsuru Mizuno, Kazuo Takakuda, Shizuko Ichinose, Takeshi Tabuchi, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Synovial mesenchymal stem cells promote healing after meniscal repair in microminipigs. *Osteoarthritis Cartilage.* 2015.06; 23(6); 1007-1017
7. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Evaluation of a behind-remnant approach for femoral tunnel creation in remnant-preserving double-bundle anterior cruciate ligament reconstruction - Comparison with a standard approach. *Knee.* 2015.06; 22(3); 249-255
8. Nobutake Ozeki, Takeshi Muneta, Seiya Matsuta, Hideyuki Koga, Yusuke Nakagawa, Mitsuru Mizuno, Kunikazu Tsuji, Yo Mabuchi, Chihiro Akazawa, Eiji Kobayashi, Tomoyuki Saito, Ichiro Sekiya. Synovial mesenchymal stem cells promote meniscus regeneration augmented by an autologous Achilles tendon graft in a rat partial meniscus defect model. *Stem Cells.* 2015.06; 33(6); 1927-1938
9. Yusuke Ogata, Yo Mabuchi, Mayu Yoshida, Eriko Grace Suto, Nobuharu Suzuki, Takeshi Muneta, Ichiro Sekiya, Chihiro Akazawa. Purified Human Synovium Mesenchymal Stem Cells as a Good Resource for Cartilage Regeneration. *PLoS ONE.* 2015.06; 10(6); e0129096
10. Ichiro Sekiya, Takeshi Muneta, Masafumi Horie, Hideyuki Koga. Arthroscopic Transplantation of Synovial Stem Cells Improves Clinical Outcomes in Knees With Cartilage Defects. *Clin. Orthop. Relat. Res.* 2015.07; 473(7); 2316-2326
11. Toshifumi Watanabe, Takeshi Muneta, Ichiro Sekiya, Scott A Banks. Intraoperative joint gaps and mediolateral balance affect postoperative knee kinematics in posterior-stabilized total knee arthroplasty. *Knee.* 2015.12; 22(6); 527-534
12. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Shizuka Fujii, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Akifumi Matsuyama, Ichiro Sekiya. Platelet-derived growth factor (PDGF)-AA/AB in human serum are potential indicators of the proliferative capacity of human synovial mesenchymal stem cells. *Stem Cell Res Ther.* 2015.12; 6(1); 243

[Conference Activities & Talks]

1. Ichiro Sekiya. Synovial Mesenchymal Stem Cells to Repair/Reverse Knee OA: From Bench to Clinic. Orthopaedic Research Society 2015 Annual Meeting 2015.03.28 Las Vegas, USA
2. Ichiro Sekiya. Arthroscopic transplantation of synovial stem cells for cartilage injury. APKAS Summit 2015.05.08 taipei, TAIWAN
3. Masafumi Horie. Synovial Stem Cell Therapy for Meniscus Regeneration. ISAKOS2015 2015.06.07 Lyon, France
4. Ichiro Sekiya. Cartilage and meniscus regeneration by synovial stem cells: from bench to clinic. Japan visit program for Dutch delegation on Sport Science 2015.11.12 Tokyo, Japan

JFCR Cancer Biology

Collaborative Professor	Takuro NAKAMURA
Collaborative Professor	Kiyotaka SHIBA
Collaborative Professor	Akihiro TOMIDA
Collaborative Professor	Toru HIROTA
Associate Professor	Kengo TAKEUCHI
Graduate Student	Yuki TOGASHI

(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. Sato, S., Ikemi, M., Kikuchi, T., Matsumura, S., Shiba, K., Fujita, M. Bridging adhesion of a protein onto an inorganic surface using self-assembled dual-functionalized spheres. *J Am Chem Soc* 137, 12890-12896, 2015.
2. Yudasaka, M., Zhang, M., Matsumura, S., Yuge, R., Ichihashi, T., Irie, H., Shiba, K., Iijima, S. Not nanocarbon but dispersant induced abnormality in lysosome in macrophages in vivo. *Nanotechnology* 26, 195102, 2015. Mashima T, Ushijima M, Matsuura M, Tsukahara S, Kunimasa K, Furuno A, Saito S, Kitamura M, Soma-Nagae T, Seimiya H, Dan S, Yamori T, Tomida A. Comprehensive transcriptomic analysis of molecularly targeted drugs in cancer for target pathway evaluation. *Cancer Sci*, 106:909-920, 2015.
3. Tsukumo Y, Tsukahara S, Furuno A, Iemura S, Natsume T, Tomida A. The endoplasmic reticulum-localized protein TBL2 interacts with the 60S ribosomal subunit. *Biochem Biophys Res Commun*, 462:383-388, 2015.
4. Tanaka M, Yamaguchi S, Yamazaki Y, Kinoshita H, Kuwahara K, Nakao K, Jay PY, Noda T, Nakamura T. Somatic chromosomal translocation between *Ewsr1* and *Fli1* loci leads to dilated cardiomyopathy in a mouse model. *Sci Rep*, 5:7826, 2015.
5. Yoshioka K, Oda A, Notsu C, Ohtsuka T, Kawai Y, Suzuki S, Nakamura T, Mabuchi Y, Matsuzaki Y, Goitsuka R. Loss of homeodomain transcription factor *Prepl* perturbs adult hematopoiesis in the bone marrow. *PLoS One*, 10:e0136107, 2015.
6. Abe, Y., Sako, K., Takagaki, K., Hirayama, Y., Uchida, KSK., Herman, J., DeLuca, J., Hirota, T. HP1-assisted Aurora B kinase activity prevents chromosome segregation errors. *Dev. Cell* 36: 487-497, 2016.
7. Takahashi, M., Tanaka, K., Wakai, T., Hirota, T. Phosphoproteomic analysis of human mitotic

- chromosomes identified a chromokinesin KIF4A. *Biomed. Res.* 37: 161-165, 2016.
8. Nagasaka, K., Hirota, T. Clarifying the role of condensins in shaping chromosomes. *Nature Cell Biol.* 17: 711-713, 2015.
 9. Minamino, M., Ishibashi, M., Nakato, R., Akiyama, K., Tanaka, H., Kato, Y., Negishi, L., Hirota, T., Sutani, T., Bando, M., Shirahige, K. Escol acetylates cohesin via a mechanism different from that of Escol2. *Curr. Biol.* 25: 1694-1706, 2015.
 10. Kataoka K, Nagata Y, Kitanaka A, Shiraishi Y, Shimamura T, Yasunaga J, Totoki Y, Chiba K, Sato-Otsubo A, Nagae G, Ishii R, Muto S, Kotani S, Watatani Y, Takeda J, Sanada M, Tanaka H, Suzuki H, Sato Y, Shiozawa Y, Yoshizato T, Yoshida K, Makishima H, Iwanaga M, Ma G, Nosaka K, Hishizawa M, Itonaga H, Imaizumi Y, Munakata W, Ogasawara H, Sato T, Sasai K, Muramoto K, Penova M, Kawaguchi T, Nakamura H, Hama N, Shide K, Kubuki Y, Hidaka T, Kameda T, Nakamaki T, Ishiyama K, Miyawaki S, Yoon SS, Tobinai K, Miyazaki Y, Takaori-Kondo A, Matsuda F, Takeuchi K, Nureki O, Aburatani H, Watanabe T, Shibata T, Matsuoka M, Miyano S, Shimoda K, Ogawa S. Integrated molecular analysis of adult T cell leukemia/lymphoma. *Nat Genet.* 2015;47:1304-1315.
 11. Aoki T, Suzuki R, Kuwatsuka Y, Kako S, Fujimoto K, Taguchi J, Kondo T, Ohata K, Ito T, Kamoda Y, Fukuda T, Ichinohe T, Takeuchi K, Izutsu K, Suzumiya J. Long-term survival following autologous and allogeneic stem cell transplantation for blastic plasmacytoid dendritic cell neoplasm. *Blood.* 2015;125:3559-3562.
 12. Lin SY, Chuang SS, Jhuang JY, Sakamoto K, Takeuchi K, Bahrami A, Tsai CC. ALK positive large B-cell lymphoma with a massive neutrophilic infiltrate: report of a case mimicking epithelioid inflammatory myofibroblastic tumour. *J Clin Pathol.* 2015;68:496-498.
 13. Nitta H, Terui Y, Yokoyama M, Mishima Y, Nishimura N, Ueda K, Kusano Y, Tsuyama N, Takeuchi K, Kanda Y, Hatake K. Absolute peripheral monocyte count at diagnosis predicts central nervous system relapse in diffuse large B-cell lymphoma. *Haematologica.* 2015;100:87-90.
 14. Nakada T, Okumura S, Kuroda H, Uehara H, Mun M, Takeuchi K, Nakagawa K. Imaging Characteristics in ALK Fusion-Positive Lung Adenocarcinomas by Using HRCT. *Ann Thorac Cardiovasc Surg.* 2015;21:102-108.
 15. Sakurai H, Sugimoto KJ, Shimada A, Imai H, Wakabayashi M, Sekiguchi Y, Ota Y, Izutsu K, Takeuchi K, Komatsu N, Noguchi M. Primary CNS CCND1/MYC-Positive Double-Hit B-Cell Lymphoma: A Case Report and Review of the Literature. *J Clin Oncol.* 2015;33:e79-83.
 16. Tomita N, Kodama F, Tsuyama N, Sakata S, Takeuchi K, Ishibashi D, Koyama S, Ishii Y, Yamamoto W, Takasaki H, Hagihara M, Kuwabara H, Tanaka M, Hashimoto C, Yamazaki E, Koharazawa H, Fujimaki K, Sakai R, Fujisawa S, Ishigatsubo Y. Biweekly THP-COP therapy for newly diagnosed peripheral T-cell lymphoma patients. *Hematol Oncol.* 2015;33:9-14.

[Review Articles]

1. Nakamura T. The role of Trib1 in myeloid leukaemogenesis and differentiation. *Biochem Soc Trans,* 43:1104-1107, 2015.
2. Uchida, KSK, Hirota, T. Spindle assembly checkpoint: its control and aberration. *DNA Replication, Recombination and Repair - Molecular Mechanisms and Pathology.* Hanaoka and Sugawasa ed. pp 429-447. 2015.

[Conference Activities & Talks]

1. Shiba K. The distinct adsorption profiles of exosomes on various inorganic materials . MRS (San Francisco) April, 2015
2. Nakamura T. Molecular dissection of leukemic cell expansion in vivo. 2015 SNUCRI Cancer Symposium (Hwasan Kumho Resort, South Korea) April, 2015
3. Nakamura T. The role of Trib1 in myeloid leukemogenesis and differentiation. Tribbles pseudokinases at the crossroads of metabolism, cancer, immunity and development (Budapest, Hungary) April, 2015
4. Nakamura T. Osteochondrogenic progenitors of mouse embryo as an Ewing sarcoma cell-of-origin. ASSET-ENCCA Ewing Meeting (Paris, France) May, 2015
5. Nakamura T. The mechanism of sarcoma metastasis. in vivo Imaging Forum 2015 (Tokyo) September, 2015
6. Nakamura T. Mouse models for fusion gene-associated sarcoma: a comprehensive approach The 74th Annual Meeting of the Japanese Cance Association (Nagoya) October, 2015
7. Nakamura T. Modeling Ewing's sarcoma and fusion gene-associated sarcoma: Tools to investigate

- cell-of-origin, metastatic mechanisms and genetic pathways Japan Sarcoma Association Symposium (Kyoto) December, 2015
8. Hirota T. Dynamic deformation of kinetochores controls mitotic progression. EMBO Workshop Dynamic Kinetochore (Copenhagen) May, 2015
 9. Hirota T. An origin of chromosome missegregation in mitosis. The 27th International Conference of the Korean Society for Molecular and Cellular Biology (Seoul) September, 2015
 10. Hirota T. A system level deficiency of the chromosomal passenger complex in cancer cells. The Annual Meeting of the Japanese Cancer Association (Nagoya) October, 2015

[Patent]

The compounds composed of peptidic aptamer and phosphocholine copolymer that binds to EpCAM. JPN patent 5824596.

Minimally Invasive Medical Treatment

Professor Kazuyuki Kojima Center for minimally invasive surgery

(1) Outline

1. Investigation and research for the social needs identification of minimally invasive medical treatment in the next generation of medical and dental area.
2. Medical equipment and development of treatment to meet the needs of minimally invasive medical treatment in the next generation of medical and dental field.
3. Research and development of the education curriculum and evaluation methods of minimally invasive treatment in the medical and dental field.
4. Development and operation of minimally invasive treatment of industry-academia cooperation in the medical and dental field.
5. Development and operation of technology certification strategy of minimally invasive treatment in medical and dental area

(2) Publications

[Original Articles]

1. Nakagawa M, Inokuchi M, Takagi Y, Kato K, Sugita H, Otsuki S, Kojima K, Uetake H, Sugihara K.. Erythropoietin-Producing Hepatocellular A1 is an Independent Prognostic Factor for Gastric Cancer. Ann Surg Oncol. 2015.07; 22(2); 2329-2335

Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi
Junior Associate Professor: Takahiro Arakawa
Assistant Professor: Koji Toma
Lecturer (part-time): Kazuyoshi Yano
Lecturer (part-time): Hiroji Shimomura
Postdoctoral Researcher: Kumiko Miyajima
Research Staff: Ming Ye

(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. "Sniffer-camera" using enzyme reaction for visualization of transpired ethanol from palm skin 2015; 26(3); 20-22
2. Takahiro Arakawa, Kenta Iitani, Xin Wang, Takumi Kajiro, Koji Toma, Kazuyoshi Yano, Kohji Mitsubayashi. A sniffer-camera for imaging of ethanol vaporization from wine: the effect of wine glass shape. *Analyst*. 2015.04; 140(8); 2881-2886
3. Takahiro Arakawa, Kazutaka Kita, Xin Wang, Kumiko Miyajima, Koji Toma, Kohji Mitsubayashi. Chemiluminescent imaging of transpired ethanol from the palm for evaluation of alcohol metabolism. *Biosens Bioelectron*. 2015.05; 67; 570-575
4. Munkhbayar Munkhjargal, Kohdai Hatayama, Yuki Matsuura, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Glucose-driven chemo-mechanical autonomous drug-release system with multi-enzymatic amplification toward feedback control of blood glucose in diabetes *Biosens Bioelectron*. 2015.05; 67; 315-320
5. Tomoko Gessei, Takahiro Arakawa, Hiroyuki Kudo, Kohji Mitsubayashi. A fiber-optic sorbitol biosensor based on NADH fluorescence detection toward rapid diagnosis of diabetic complications *Analyst*. 2015.09; 140(18); 6335-6342
6. Koji Toma, Daisuke Miki, Chisato Kishikawa, Naoyuki Yoshimura, Kumiko Miyajima, Takahiro Arakawa, Hiromi Yatsuda, Kohji Mitsubayashi. Repetitive immunoassay with a surface acoustic wave device and a highly stable protein monolayer for on-site monitoring of airborne dust mite allergens. *Analytical Chemistry*. 2015.10; 87(20); 10470-10474
7. Ming Ye, Po-Jen Chien, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. An acetone bio-sniffer (gas phase biosensor) enabling assessment of lipid metabolism from exhaled breath. *Biosensors and Bioelectronics*. 2015.11; 73; 208-213
8. Koji Toma, Yurika Suzuki, Chisato Kishikawa, Mana Saito, Kumiko Miyajima, Takahiro Arakawa, Hiromi Shimomura, Kohji Mitsubayashi. Chemifluorescent optical fiber immunosensor for on-site bioaerosol monitoring system *Sensors and Materials*. 2015.12; 27(11); 1113-1122
9. Kumiko Miyajima, Kon Hiromi, Takahiro Arakawa, Kiyoko Shiba, Kohji Mitsubayashi. Fluoroimmunoassay system for fiber-optic measurement of house dust mite allergen (Der f1) *Sensors and Materials*. 2015.12; 27(9); 871-880
10. Yuki Suzuki, Ye Ming, Kumiko Miyajima, Takahiro Arakawa, Shin-ichi Sawada, Hiroyuki Kudo, Kazunari Akiyoshi, Kohji Mitsubayashi. A fluorometric biochemical gas sensor (biosniffer) for acetaldehyde vapor based on catalytic reaction of aldehyde dehydrogenase *Sensors and Materials*. 2015.12; 27(11); 1123-1130

[Books etc]

1. Agnes T. Reiner, Koji Toma, Alain R. Brisson, Dietmar Pils, Wolfgang Knoll, Jakub Dostalek. Plasmonic Exosome Biosensors for Medical Diagnostics. Springer, 2015.04 (ISBN : 978-981-287-626-3)
2. Advanced Sports Bioscience and Gear Development. 2015.06
3. Advanced Sports Bioscience and Gear Development, the opening. 2015.06
4. Advanced Sports Bioscience and Gear Development, Part1 Chapter5. 2015.06

[Conference Activities & Talks]

1. Toma K, Kano H, Offenhausser A. Label-free measurement of cell-gold cleft gap distance using surface plasmon microscopy. Pittcon 2015 2015.03.08 New Orleans, USA
2. Toma K, Ye M, Sawada S, Arakawa T, Kudo H, Akiyoshi K, Mitsubayashi K. Biochemical gas sensor (Bio-Sniffer) for detection of formaldehyde from food sample. Pittcon 2015 2015.03.08 New Orleans, USA
3. Mitsubayashi K. Chemo-mechanical energy converter "Organic engine" for autonomous blood sugar control system in diabetes. Smart Systems Integration 2015 2015.03.11 Copenhagen, Denmark
4. Munkhjargal M, Toma K, Arakawa T, Mitsubayashi K. Organic engine" (chemo-mechanical machine) with artificial active transportation for autonomous drug release system (novel artificial pancreas). 2015 MRS Spring Meeting & Exhibit 2015.04.06 San Francisco, USA
5. Mitsubayashi K. Cavitas (cavity) sensors for bio/chemical monitoring no wearable, no implantable approach. 2015 International Conference on Electronics Packaging & iMAPS All Asia Conference 2015.04.15 Kyoto, Japan
6. Arakawa T, Sato T, Iitani K, Toma K, Mitsubayashi K. Fluorometric biosniffer camera (gas-imaging system) with UV-LED excitation sheet for transdermal ethanol vapor from palm skin surface. 4th International Conference on Bio-Sensing Technology 2015.05.10 Lisbon, Portugal
7. Arakawa T, Kuroki Y, Nitta H, Toma K, Takeuchi S, Sekita T, Minakuchi S, Mitsubayashi K. Mouth guard biosensor for non-restraint monitoring of saliva glucose with telemetry system. 4th International Conference on Bio-Sensing Technology 2015.05.10 Lisbon, Portugal
8. Toma K, Miki D, Yoshimura N, Miyajima K, Arakawa T, Yatsuda H, Mitsubayashi K. Repetitive measurement of house dust mites (Der f1) with surface acoustic wave (SAW) immunosensor for on-site monitoring of indoor allergens. 4th International Conference on Bio-Sensing Technology 2015.05.10 Lisbon, Portugal
9. Toma K, Suzuki Y, Saito M, Miyajima K, Arakawa T, Shimomura H, Mitsubayashi K. Fiber-optic immunosensor for detection of airborne influenza viruses. 4th International Conference on Bio-Sensing Technology 2015.05.10 Lisbon, Portugal
10. Arakawa T, Iitani K, Sato T, Toma K, Mitsubayashi. Sniff-Camera For Imaging of Gaseous Ethanol From Palm Skin After Drinking. 4th International Symposium on Sensor Science (ISS 2015) 2015.07.13 Basel, Switzerland
11. Toma K, Miki D, Yoshimura N, Miyajima K, Arakawa T, Yatsuda H, Mitsubayashi K. Repetitive immunoassay with a regeneration resistant protein and surface acoustic wave device for allergen monitoring. EuroAnalysis 2015 2015.09.06 Bordeaux, France
12. Mitsubayashi K, Wang X, Kajiro T, Toma K, Yano K, Arakawa T. Wine aroma behavior and glass effect analyzed by sniff-camera. EuroAnalysis 2015 2015.09.06 Bordeaux, France
13. Sato T, Iitani K, Toma K, Arakawa T, Mitsubayashi K. Sniff-camera for imaging of ethanol vapor in human body gases after drinking. ICAVS 2015 : 17th International Conference on Animal and Veterinary Sciences 2015.09.07 Geneva, Switzerland
14. Toma K, Miki D, Suzuki Y, Kishikawa C, Miyajima K, Yoshimura N, Arakawa T, Yatsuda H, Mitsubayashi K. A new approach using a SAW device-based immunosensor for semi-continuous measurement of mite allergens. 2015.10.05

15. Arakawa T, Iitani K, Sato T, Toma K, Mitsubayashi K. A two-dimensional fluorometric imaging “sniffer camera” of ethanol vapor for evaluation of alcohol metabolism using enzymatic reaction. IEEE SENSORS 2015 2015.11.01 Busan, South Korea
16. Arakawa T, Kuroki Y, Nitta H, Toma K, Takeuchi S, Sekita T, Minakuchi S, Mitsubayashi K. Mouth guard type biosensor “cavitous sensor” for monitoring of saliva glucose with telemetry system. The 9th International Conference on Sensing Technology, ICST 2015 2015.12.08 Auckland, New Zealand
17. Toma K, Miki D, Kishikawa C, Yoshimura N, Miyajima K, Arakawa T, Yatsuda H, Mitsubayashi K. A surface acoustic wave biosensor allowing repetitive immunoassay for dust mite allergen monitoring. International Conference on BioSensors, BioElectronics, BioMedical Devices, BioMEMS/NEMS and Applications (Bio4Apps) 2015 2015.12.09 Fukuoka, Japan
18. Hashimoto Y, Minamide T, Kon T, Toma K, Arakawa T, Saito H, Mitsubayashi K. An optical bio-sniffer for dimethyl sulfide in the gas phase. International Conference on BioSensors, BioElectronics, BioMedical Devices, BioMEMS/NEMS and Applications (Bio4Apps) 2015 2015.12.09 Fukuoka, Japan
19. Toma K, Miki D, Yoshimura N, Miyajima K, Arakawa T, Yatsuda H, Mitsubayashi K. Repetitive immunosensing with a highly stable protein monolayer and surface acoustic wave device for allergen monitoring. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA
20. Toma K, Kano H, Offenhausser A. Label-free high resolution surface plasmon microscopy for quantitative cell-gold interface investigation. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA
21. Mitsubayashi K. Cavitas sensor and Sniff-camera for human biosensing. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA
22. Arakawa T, Kuroki Y, Nitta H, Takeuchi S, Sekita T, Mizukuchi S, Mitsubayashi K. Non-invasive mouth guard biosensor for continuous measurement of saliva glucose. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA
23. Chien PJ, Ye M, Iitani K, Sato T, Toma K, Arakawa T, Mitsubayashi K. Ethanol vapor imaging system “sniffer camera” with UV-LED excitation sheet for monitoring of alcohol metabolism from human. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA
24. Chien PJ, Ye M, Toma K, Arakawa T, Mitsubayashi K. 2-Propanol fluorometric biosensor based on secondary-alcohol dehydrogenase (S-ADH) for clinical diagnosis of ketoacidosis. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA
25. Xie R, Kurihara K, Munkhbayar M, Toma K, Arakawa T, Mitsubayashi K. Glucose-driven chemo-mechanical autonomous drug-release system toward feedback control of blood glucose in diabetes. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA
26. Ye M, Chien PJ, Toma K, Arakawa T, Mitsubayashi K. Fiber-optic biochemical acetone gas sensor (bio-sniffer) for assessment of lipid metabolism from exhaled breath. The 2015 International Chemical Congress of Pacific Basin Societies (Pacifichem) 2015 2015.12.15 Hawaii, USA

[Awards & Honors]

1. Poster Presentation Runner Up Award, 4th International Conference on Bio-Sensing Technology, 2015.05
2. Best Presentation Award, The 9th International Conference on Sensing Technology, ICST 2015, 2015.12

Biomedical Information

Professor Kenji YASUDA
Associate Professor Fumimasa NOMURA
Assistant Professor Hideyuki TERAZONO

(1) Research

- 1) Studies on Epigenetic Information Stored Living System.
- 2) Constructing “On-chip Organ Model” using Nano-Bio Technology.
- 3) Bio-computing using “Real Neural Network on Chip” .
- 4) New Drug Discovery Technology applying Single Molecule Measurement.

(2) Education

Medical instrument(Biomedical information)is a branch of institute of biomaterials and bioengineering which deals with the measurement of epigenetic information and memorization stored in living system such as brain(neural network system), immune system, and cardio systems caused by environmental hystereisis. Main objective of medical instrument in the graduate course is to provide students opportunity to study fusion of latest technologies of nano-and bio-tech, and to develop artificial organ model on chip for drug discovery and toxicology use.

(3) Publications

[Original Articles]

1. Odaka M, Kim H, Girault M, Hattori A, Terazono H, Matsuura K, Yasuda K. Evaluation of Imaging Biomarkers for Identification of Single Cancer Cells in Blood Jpn J Appl Phys. 2015.05; 54(6S1); 06FN04
2. Kim H, Terazono H, Takei H, Yasuda K. Depletion effect on concave microstructure at size-specific target particle collection Japanese Journal of Applied Physics . 2015.05; 54; 06FL02
3. Nomura F, Matsuura K, Hattori A, Odaka M, Sugio Y, Kurotobi H, Terazono H, Yasuda K. Development of impedance/external field potential dual measurement system for evaluation of electrophysiological properties of cells on micro electrodes Japanese Journal of Applied Physics. 2015.05; 54; 06FN06

[Books etc]

1. Kenji Yasuda. Chapter 2 Non-Destructive On-Chip Imaging Cytometry Assay for Constructive On-Chip Cellomics Studies. Flow Cytometry in Microbiology: Technology and Applications. Martin G. Wilkinson . Caister Academic Press, 2015.09 (ISBN : 978-1-910190-11-1)

[Conference Activities & Talks]

1. Kenji Yasuda. On-chip Cellomics System: Re-constructive Approach of Single Cells for Functional quasi in vivo Tissue/Organ Models on a Chip for Drug Discovery and Toxicology. 2nd NeuroCMOS Workshop 2015.01.20 Kobe, Japan
2. F. Nomura, T. Kaneko, H. Terazono, K. Yasuda. On-chip quasi-in vivo predictive cardiotoxicity assay using spatiotemporal fluctuation measurement on human cardiomyocyte cell-network. Biophysical Society 59th Annual Meeting 2015.02.08 Baltimore, USA
3. Kenji Yasuda, Fumimasa Nomura, Hideyuki Terazono. On-chip Cellomics Assay: Re-constructive approach of single cells for functional quasi-in vivo tissue/Organ models on a chip for drug discovery and toxicology. 9th Asian Biophysics Association (ABA) Symposium 2015.05.11 Hangzhou, China
4. Hideyuki Terazono, Fumimasa Nomura, Akihiro Hattori, Kenji Yasuda. Constructive approach to understand neuronal communication by controlling spatial patterns using microprocessing and cell-sheet technique. 2015 The Bridging Biomedical Worlds From Neural Circuitry to Neurotechnology 2015.05.11 Tokyo, Japan
5. F. Nomura, H. Kurotobi, Y. Sugio, H. Terazono, K. Yasuda. Cardiotoxicity Prediction Analysis Using Electrophysiological Signals in Lined Up Cardiomyocyte-network . 28th International Microprocesses and Nanotechnology Conference 2015.11.11 Toyama, Japan
6. M. Girault, A. Hattori, H. Kim, S. Kawada, K. Matsuura, M. Odaka, H. Terazono, K. Yasuda. Morphology Imaging Microdroplet Sorting System for Identification and Acquisition of Target Objects in Droplets. 28th International Microprocesses and Nanotechnology Conference 2015.11.12 Toyama, Japan
7. M. Odaka, H. Kim, M. Girault, A. Hattori, H. Terazono, K. Matsuura, F. Nomura, K. Yasuda. Identification of Cell Clusters in Cancer Cell-implanted Rat Bloods Based on Measurements of Imaging Biomarkers Using on-chip Multi-imaging Flow Cytometry System . 28th International Microprocesses and Nanotechnology Conference 2015.11.12 Toyama, Japan
8. H. Kim, M. Odaka, M. Girault, A. Hattori, H. Terazono, K. Yasuda . Bright Field/Fluorescent Dual Imaging Cell Sorter System for Precise Purification of Circulating Tumor Cells. 28th International Microprocesses and Nanotechnology Conference 2015.11.12 Toyama, Japan
9. H. Terazono, H. Kim, A. Hattori, F. Nomura, K. Yasuda. Development of a Micropatterning Technique Using Cell-surface Specific Binding DNA Aptamer. 28th International Microprocesses and Nanotechnology Conference 2015.11.13 Toyama, Japan
10. A. Hattori, F. Nomura, H. Kim, H. Terazono, K. Matsuura, M. Odaka, M. Girault, K. Yasuda. Predictive Human Cardiotoxicity Measurement Assay Using a Lined-Up Thousand Cardiomyocyte Cell Network . 28th International Microprocesses and Nanotechnology Conference 2015.11.13 Toyama, Japan
11. M. Girault, A. Hattori, H. Kim, K. Matsuura, M. Odaka, H. Terazono, K. Yasuda. Automatic sorting system and incubation at single cell level using microfluidic devices. The 16th Japanese-French Oceanography Symposium 2015.11.20 Shiogama, Japan
12. H. Terazono, H. Kim, F. Nomura, A. Hattori, K. Yasuda. A micropatterning technique using a cell - surface specific binding DNA aptamer. . ASCB2015 2015.12.13 San Diego, USA

Bioelectronics

Staff

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(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. Mai Sanjoh, Daisuke Iizuka, Akira Matsumoto, Yuji Miyahara. Boronate Based Metal-Free Platform for Diphosphate-Specific Molecular Recognitions. *Org Lett.* 2015.01; 17(3); 588-591
2. Tatsuro Goda. Specific interaction of phospholipid polymer with C-reactive protein *Journal of Photopolymer Science and Technology.* 2015.10; 28(5); 715-718
3. Tatsuro Goda, Daiki Higashi, Akira Matsumoto, Toru Hoshi, Takashi Sawaguchi, Yuji Miyahara. Dual aptamer-immobilized surfaces for improved affinity through multiple target binding in potentiometric thrombin biosensing. *Biosensors and Bioelectronics.* 2015.11; 73; 174-180
4. Tatsuro Goda, Masahiro Toya, Akira Matsumoto, Yuji Miyahara. Poly(3,4-ethylenedioxythiophene) bearing phosphorylcholine groups for metal-free, antibody-free, and low-impedance biosensors specific for C-reactive protein. *ACS Applied Materials and Interfaces.* 2015.11; 7(49); 27440-27448

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1. Tatsuro Goda, Kazuhiko Ishihara, Yuji Miyahara. Critical Update on 2-Methacryloyloxyethyl Phosphorylcholine (MPC) *Polymer Science. Journal of Applied Polymer Science.* 2015.01; 132(16); 41766
2. Tatsuro Goda, Miyuki Tabata, Yuji Miyahara. Electrical and Electrochemical Monitoring of Nucleic Acid Amplification. *Frontiers in Bioengineering and Biotechnology.* 2015.03; 3; 29

[Conference Activities & Talks]

1. Goda T. Biomimetic Interface Reveals Activation Dynamics of C-Reactive Protein. The 6th Taiwan-Japan Symposium on Nanomedicine 2015.01.08 Taipei, Taiwan
2. Miyahara Y, Matsumoto A, Goda T, Tabata M, Yao B. Chronocoulometric detection of isothermal nucleic acid amplification. 1st COINS International Symposium 2015.02.27 Tokyo, Japan
3. Matsumoto A, Ishii T, Matsumoto H, Suganami T, Tanaka M, Ogawa Y, Kataoka K, Miyahara Y. Synthetic gel based approach toward "electronics-free" artificial pancreas. City of Hope Seminar 2015.03.06 Pasadena, USA

4. Tabata M, Yuitoo I, Katou K, Sekiguchi T, Goda T, Matsumoto A, Miyahara Y. Design and fabrication of functional solid-state electrodes for liquid biopsy. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09 Tokyo, Japan
5. Tabata M, Yang H, Mannan F, Katayama Y, Goda T, Matsumoto A, Seichi A, Suzuki K, Miyahara Y. Electrochemical real-time monitoring of isothermal nucleic acid amplification for quantitative analysis. The 18th International Conference on Solid-State Sensors, Actuators and Microsystems (TRANSDUCERS 2015) 2015.06.22 Anchorage, Alaska
6. Goda T. Specific Interaction of Phospholipid Polymer with C-reactive Protein. The 32nd International Conference on Photopolymer Science and Technology 2015.06.24 Chiba, Japan
7. Matsumoto A. Synthetic gel based approach toward "electronics-free" artificial pancreas. City of Hope Seminar 2015.08.05 Pasadena, USA
8. Goda T. MPC as a Synthetic Ligand in C-Reactive Protein Biosensing. 2nd International Conference on Bioinspired and Zwitterionic Materials (ICBZM 2015) 2015.08.13 Seattle, USA
9. Goda T, Miyahara Y. Phospholipid polymer interfaces reveal activation dynamics of C-reactive protein. 250th American Chemical Society National Meeting & Exposition 2015.08.16 Westin Boston Waterfront, Boston, USA
10. Tabata M, Goda T, Matsumoto A, Miyahara Y. Electrochemical label-free degranulation monitoring for in-situ evaluation of cellular function. the 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2015.08.25 Milan, Italy
11. Matsumoto A, Miyahara Y. "Borono-lectin" based strategies for biosensing and smart drug delivery systems. 12th International Symposium on Stimuli-responsive Materials 2015.10.25 Sonoma, USA
12. Seichi A, Kozuka N, Kashima Y, Tabata M, Goda T, Matsumoto A, Iwasawa N, Citterio D, Miyahara Y, Suzuki K. Real-time monitoring and detection of primer generation-rolling circle amplification of DNA using an ethidium ion selective electrode. The 16th Beijing Conference and Exhibition on Instrumental Analysis (BCEIA2015) 2015.10.27 Beijing, China
13. Goda T, Matsumoto A, Miyahara Y. DNA Aptamer-based Label-free Protein Sensing Using Extended Gate Field-effect Transistors. 8th International Microprocesses and Nanotechnology Conference (MNC 2015) 2015.11.10 Toyama, Japan
14. Miyahara Y. Detection of Biomolecular Recognition and Cell Functions using Biotransistors. The 7th Takayanagi Kenjiro Memorial Symposium 2015.11.18 Shizuoka University
15. Matsumoto A, Tabata M, Yang H, Mannan F, Katayama Y, Goda T, Seichi A, Suzuki K, Miyahara Y. Electrochemical quantitative monitoring of isothermal nucleic acid amplification. 2nd COINS International Symposium 2015.11.24 Tokyo, Japan
16. Matsumoto A, Tabata M, Yang H, Mannan F, Katayama Y, Goda T, Seichi A, Suzuki K, Miyahara Y. Electrochemical quantitative monitoring of isothermal nucleic acid amplification. 2nd COINS International Symposium 2015.11.24 Tokyo, Japan
17. Goda T. Detection of Molecularly Sized Pores on Plasma Membranes. 3rd International Symposium on Nanomedicine Molecular Science Toward Medical Biophysics 2015.11.25 Tokyo, Japan
18. Goda T, Richter-Dahlfors A, Miyahara Y. Engineered Biomimetic Microenvironments using Organic Bio-electronic Ion Pumps for Inflammation and Infection Studies. 2015 MRS Fall Meeting & Exhibit 2015.11.29 Boston, USA
19. Goda T. Plasma Membrane-mimicked Polymers for Biosensing and Bioengineering. 14th Pacific Polymer Conference 2015.12.09
20. Imaizumi Y, Goda T, Matsumoto A, Miyahara Y. Direct evaluation of cell membrane integrity using ion-sensitive field-effect transistor. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.15 Honolulu, Hawaii

21. Iizuka D, Goda T, Matsumoto A, Miyahara Y, Sanjoh M. Boronate-based pyrophosphate-specific molecular recognitions. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.15 Honolulu,Hawaii
22. Tabata M, Goda T, Matsumoto A, Miyahara Y. Development of mixed nano-structure composed of self-assembled monolayer and ultra-thin silver chloride for electrochemical biosensing. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.15 Honolulu,Hawaii
23. Goda T, Miyahara Y. Organic bioelectronics create ionic microenvironments mimicking inflammation and infection for elucidating activation dynamics of C-reactive protein. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.15 Honolulu, Hawaii
24. Matsumoto A, Ishii T, Kataoka K, Matsumoto H, Suganami T, Tanaka M, Ogawa Y, Miyahara Y. Synthetic gel based approach toward "electronics-free" artificial pancreas. The International Chemical Congress of Pacific Basin Societies 2015 2015.12.15 Hawaii, USA
25. Naito M, Yoshinaga N, Ishii T, Matsumoto A, Miyahara Y, Miyata K, Kataoka K. Intracellular ATP-responsive release of siRNA from polyion complex micelles. 13th US-Japan Symposium on Drug Delivery Systems 2015.12.16 Hawaii, USA
26. Seichi A, Kozuka N, Kashima Y, Tabata M, Goda T, Matsumoto A, Iwasawa N, Citterio D, Miyahara Y, Suzuki K. Real-time monitoring and detection of primer generation-rolling circle amplification of DNA using an ethidium ion selective electrode. RSC Tokyo International Conference 2015 Tokyo, Japan

[Patents]

1. Sugar-responsive gel and medicine administering device, Patent Number : 5696961
2. Block copolymer having phenylboronic acid group Introduced therein,and use thereof, Patent Number : 9,114,177(US patent)

Material-Based Medical Engineering

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(1) Outline

In our laboratory, we treat many research topics from the basic study of biomaterials from the point of view 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 science".

(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 areas 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 an 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”, “human environment medical engineering”, and “functional materials science”.

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

1. A. Matsuhashi, K. Nam, T. Kimura, A. Kishida. Fabrication of fibrillized collagen microspheres with microstructure resembling extracellular matrix *Soft Matter*. 2015.04; 11(14); 2844-2851
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 PartB*. 2015.05;
3. Y. Hashimoto, S. Funamoto, S. Sasaki, J. Negishi, T. Honda, S. Hattori, K. Nam, T. Kimura, M. Mochizuki, H. Kobayashi, A. Kishida. Corneal regeneration by deep anterior lamellar keratoplasty (DALK) using decellularized corneal matrix *PLOS ONE*. 2015.07; 10(7); e0131989
4. P. Wu, N. Nakamura, T. Kimura, K. Nam, T. Fujisato, S. Funamoto, T. Higami, A. Kishida. Decellularized porcine aortic intima-media as a potential cardiovascular biomaterial *Interact Cardiovasc Thorac Surg*. 2015.08; 21(2); 189-194
5. Jun Negishi, Seiichi Funamoto, Tsuyoshi Kimura, Kwangwoo Nam, Tetsuya Higami, Akio Kishida. Porcine radial artery decellularization by high hydrostatic pressure. *J Tissue Eng Regen Med*. 2015.11; 9; E114-E151
6. M. Tabuchi, J. Negishi, A. Yamashita, T. Higami, A. Kishida, S. Funamoto. Effect of decellularized tissue powders on a rat model of acute myocardial infarction *Mater. Sci. Eng. C-Mater. Biol. Appl.*. 2015.11; 56; 494-500
7. J. Negishi, S. Funamoto, T. Kimura, K. Nam, T. Higami, A. Kishida. Porcine radial artery decellularization by high hydrostatic pressure *J. Tissue Eng. Regen. Med.*. 2015.11; 9(11); 144-151
8. K. Nam, T. Kimura, A. Kishida. Preparation fibrillized collagen-glycosaminoglycan complex matrix using fibrillogenesis *Macromolecular Symposia*. 2015.12; 358(1); 95-105

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1. Y. Sawa, K. Matsuda, E. Tatsumi, G. Matsumiya, T. Abe, K. Fukunaga, A. Kishida, K. Kokubo, T. Masuzawa, A. Myoui, M. Nishimura, T. Nishimura, T. Nishinaka. Journal of Artificial Organs 2014:the year in review *Journal of Artificial Organs*. 2015.03; 18(1); 1-7

[Conference Activities & Talks]

1. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. Preparation and physical properties of a small diameter decellularized vascular graft covered with electrospun fibers. SFB 2015 Annual Meeting and Exposition 2015.04.15 Charlotte, USA
2. N. Nakamura, A. Ito, K. Nam, T. Kimura, T. Fujisato, T. Tsuji, A. Kishida. Preparation of decellularized mandible bone with periodontal membrane for periodontal reconstruction. SFB 2015 Annual Meeting and Exposition 2015.04.15 Charlotte, USA
3. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. Preparation of a small diameter decellularized vessel covered with nanofibers by electrospinning. The 5th Asian Biomaterials Congress 2015.05.06 Taipei, Taiwan
4. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. Preparation of a small diameter decellularized blood vessel covered with electrospun nanofibers. Biomaterials International 2015 2015.06.01 Kenting, Taiwan
5. Y. Hashimoto, J. Negishi, M. Tabuchi, A. Yamashita, A. Kishida, S. Funamoto. Evaluation of decellularized tissue powder using a rat myocardial infarct model. 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2015.08.25 Milano, Italy

6. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. Preparation of a small diameter decellularized blood vessel covered with SPU fibers by electrospinning. 27th European Conference on Biomaterials 2015.08.30 Krakow, Poland
7. N. Nakamura, T. Kimura, A. Ito, T. Fujisato, T. Tsuji, A. Kishida. Acellular periodontal ligament matrix for artificial tooth implant. 27th European Conference on Biomaterials 2015.08.30 Krakow, Poland
8. A. Kishida, N. Nakamura, A. Ito, K. Nam, T. Kimura, T. Fujisato, T. Tsuji. Periodontal reconstruction using decellularized periodontal tissue combined with artificial tooth. 4th TERMIS World Congress 2015.09.08 Boston, USA
9. N. Nakamura, T. Kimura, K. Nam, T. Fujisato, T. Tsuji, H. Iwata, A. Kishida. Artificial microenvironment of decellularized bone marrow induced hematopoiesis. 4th TERMIS World Congress 2015.09.08 Boston, USA
10. T. Kimura, H. Morita, P. Wu, N. Nakamura, K. Nam, T. Fujisato, A. Kishida. A small-diameter decellularized vascular graft covered with electrospun fibers. 4th TERMIS World Congress 2015.09.08 Boston, USA
11. Y. Zhang, K. Nam, T. Kimura, A. Kishida. Preparation of gradient decellularized dermis-polymer complex for tissue interlinking device. 4th TERMIS World Congress 2015.09.08 Boston, USA
12. T. Kimura, N. Nakamura, N. Sasaki, S. Sakaguchi, S. Kimura, A. Kishida. Preparation of interface for specific capture of targets cells. Bio4Apps 2015 2015.12.09 Fukuoka, Japan
13. T. Kimura, N. Nakamura, H. Morita, P. Wu, K. Nam, T. Fujisato, A. Kishida.. Fabrication of decellularized aorta with electrospun fibers for small-diameter vascular grafts. Pacificchem 2015 2015.12.15 Hawaii, USA

Organic and Medicinal Chemistry

Professor Hiroyuki KAGECHIKA
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 Yumeto Yamauchi
 Hidekazu Yokoo
 Hiroto Inuma
 Kazuhiro Imaida
 Ryohei Iwashita
 Tsuyoshi Oikawa
 Yuki Noji
 Mititake Hirano
 Takahiro Miura

(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. Brun, P.-J., Grijalva, A., Rausch, R., Watson, E., Yuen, J. J., Das, B. C., Shudo, K., Kagechika, H., Leibel, R. L., Blaner, W. S.. Retinoic acid receptor signaling is required to maintain glucose-stimulated insulin secretion and β -cell mass FASEB Journal. 2015; 26; 671-683
2. Mori, S., Takeuchi, Y., Tanatani, A., Kagechika, H., Fujii, S.. Development of 1,3-diphenyladamantane derivatives as nonsteroidal progesterone receptor antagonists Bioorganic Medicinal Chemistry. 2015; 23; 803-809
3. Shiraishi, T.; Kagechika, H.; Hirano, T.. 6-Arylcoumarins: versatile scaffolds for fluorescent sensors New Journal of Chemistry. 2015; 39; 8389-8396
4. Tsuji, M.; Shudo, K.; Kagechika, H.. Docking simulations suggest that all-trans retinoic acid could bind to retinoid X receptors Journal of Computer Aided Molecular Design. 2015; 29; 975-988
5. Qin, X.-Y.; Fujii, S.; Shimizu, A.; Kagechika, H.; KOJIMA, S.. Carboxylic derivatives of vitamin K2 inhibit hepatocellular carcinoma cell growth through caspase/transglutaminase-related signaling pathways Journal of Nutritional Science and Vitaminology. 2015; 61; 285-290
6. Nishiyama, S.; Urushibara, K.; Masu, H.; Azumaya, I.; Kagechika, H. Tanatani, A.. Conformational and chiral properties of cyclic-tri(N-methyl-meta-benzamide) bearing amidino groups Chirality. 2015; 27; 487-491
7. Fujii, S.; Shimizu, A.; Takeda, N.; Oguchi, K.; Katsurai, T.; Shirakawa, H.; Komai, M.; Kagechika, H.. Systematic synthesis and anti-inflammatory activity of ω -carboxylated menaquinone derivatives - Investigations on identified and putative vitamin K2 metabolites - Bioorganic Medicinal Chemistry. 2015; 23; 2344-2352
8. Kikuchi Eriko, Mori Takayasu, Zeniya Moko, Isobe Kiyoshi, Ishigami-Yuasa Mari, Fujii Shinya, Kagechika Hiroyuki, Ishihara Tomoaki, Mizushima Tohru, Sasaki Sei, Sohara Eisei, Rai Tatsumitsu, Uchida Shinichi. Discovery of Novel SPAK Inhibitors That Block WNK Kinase Signaling to Cation Chloride Transporters. J Am Soc Nephrol. 2015.07; 26(7); 1525-1536
9. Manami Kodaka, Zeyu Yang, Kentaro Nakagawa, Junichi Maruyama, Xiaoyin Xu, Aradhan Sarkar, Ayana Ichimura, Yusuke Nasu, Takeaki Ozawa, Hiroaki Iwasa, Mari Ishigami-Yuasa, Shigeru Ito, Hiroyuki Kagechika, Yutaka Hata. A new cell-based assay to evaluate myogenesis in mouse myoblast C2C12 cells. Exp. Cell Res.. 2015.08; 336(2); 171-181
10. Kazumi Inoue, Ko Urushibara, Misae Kanai, Kei Yura, Shinya Fujii, Mari Ishigami-Yuasa, Yuichi Hashimoto, Shuichi Mori, Emiko Kawachi, Mio Matsumura, Tomoya Hirano, Hiroyuki Kagechika, Aya Tanatani. Design and synthesis of 4-benzyl-1-(2H)-phthalazinone derivatives as novel androgen receptor antagonists. Eur J Med Chem. 2015.09; 102; 310-319
11. Shodai Kawano, Junichi Maruyama, Shunta Nagashima, Kazutoshi Inami, Wenzhe Qiu, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiroshi Nishina, Yutaka Hata. A cell-based screening for TAZ activators identifies ethacridine, a widely used antiseptic and abortifacient, as a compound that promotes dephosphorylation of TAZ and inhibits adipogenesis in C3H10T1/2 cells. J. Biochem.. 2015.11; 158(5); 413-423

12. Saito-Hakoda, A.; Uruno, A.; Yokoyama, A.; Shimizu, K.; Parvin, R.; Kudo, M.; Saito-Ito, T.; Sato, I.; Kogure, N.; Suzuki, D.; Shimada, H.; Yoshikawa, T.; Fujiwara, I.; Kagechika, H.; Iwasaki, Y.; Kure, S.; Ito, S.; Sugawara, A.. Effects of RXR Agonists on Cell Proliferation/Apoptosis and ACTH Secretion/Pomc Expression Plos ONE. 2015.11; 10; e0141960
13. Yu. R.; Miyamura, N.; Okamoto-Uchida, Y.; Arima, N.; Ishigami-Yuasa, M.; Kagechika, H.; Nishina, H.. A Modified Murine Embryonic Stem Cell Test for Evaluating the Teratogenic Effects of Drugs on Early Embryogenesis Plos ONE. 2015.11; 10; e0145286
14. Shrestha, R.; Tatsukawa, H.; Shrestha, R.; Ishibashi, N.; Matsuura, T.; Kagechika, H.; Kose, S.; Hitomi, K.; Imamoto, N.; Kojima, S.. Molecular mechanism by which acyclic retinoid induces nuclear localization of transglutaminase 2 in human hepatocellular carcinoma cells. Cell Death & Disease. 2015.12; 6; e2002

[Conference Activities & Talks]

1. Masuno, H., Fujii, S., Hirano, T.; Kawachi, E.; Tanatani, A.; Kagechika, H.. Development of carborane-based non-secosteroidal vitamin D analogs. 18th Workshop on Vitamin D 2015.04.21 Delft, Nederland
2. Kagechika, H., Fujii, S., Shirakawa, H., Komai, M., Qin, X.-Y., Kojima, S.. Systematic synthesis and biological activities of ω -carboxylated menaquinone derivatives.. FASEB meeting on vitamin K 2015.06.12 Chicago, USA
3. Fukasawa, H., Shudo, K., Kagechika, H.. Therapeutic potential of tamibarotene for Alzheimer's disease and COPD. 3rd International conference on retinoid 2015.10.21 Gifu, Japan
4. Ishigami-Yuasa, M., Ekimoto, H., Kagechika, H.. Synergistic inhibition of viable human cancer cells by a synthetic retinoid tamibarotene (Am80) in combination with DNA methyltransferase or histone deacetylase inhibitors. 3rd International conference on retinoid 2015.10.21 Gifu, Japan
5. 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-catalyzed reaction. 3rd International conference on retinoid 2015.10.21 Gifu, Japan
6. Hirano, M., Hirano, T., Fujiwara, T., Ohira, K., Kagechika, H., Ito, A., Yoshida, M.. Study for the development of inhibitors for Set7/9. 3rd International conference on retinoid 2015.10.21 Gifu, Japan
7. Oya, Y., Suganuma, M., Iida, K., Sakai, R., Kagechika, H., Shudo, K., Fujiki, H. . Combination of EGCG and Am80 is an innovative cancer treatment mediated through induction of GADD153 and DR5 gene expressions caused by inhibition of histone deacetylase 4 and 5. 3rd International conference on retinoid 2015.10.21 Gifu, Japan
8. Shiraishi, T., Hirano, T., Noji, Y., Saito, T., Kagechika, H.. Development of various fluorescent sensors based on coumarin scaffold. Pacificchem 2015 2015.12.15 Hawaii, USA
9. Yuasa, M., Mori, T., Fujii, S., Watanabe, Y., Suzuyama, H., Kikuchi, E., Uchida, S., Kagechika, H.. Development of WNK signaling inhibitors as new class of antihypertensive drugs. Pacificchem 2015 2015.12.15 Hawaii, USA
10. Ainiwaer, D., Ito, S., Nakagawa, K., Zeyu, Y., Yuasa, M., Hata, Y., Kagechika, H.. Development of novel activators for transcriptional co-activator TAZ involved in Hippo pathway. Pacificchem 2015 2015.12.15 Hawaii, USA

Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Suguru YOSHIDA
Assistant Professor	Yoshitake Nishiyama, Takahisa YANO
PD	Fumika KARAKI
Technical Assistant	Yoshihiro MISAWA, Yuki Hazama, Tomoko Kuribara
Graduate Students	Takamoto MORITA, Kazuya KANEMOTO, Keisuke UCHIDA, Ken SHIMOMORI, Tomohiro MEGURO, Sayuri GOTO, Kei AKIYAMA, Kazuhiro Oya, Akira NAGAI, Hana NAKAJIMA, Yu NAKAMURA, Naoaki MAKIO, Kotaro Mutsuura
Collaborators	Yasuyuki SUGIMURA, Shonan CHIN, Youngchan KIM, Tsubasa MATSUZAWA, Yuya TAMURA

(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. Yoshida M, Kataoka N, Miyauchi K, Ohe K, Iida K, Yoshida S, Nojima T, Okuno Y, Onogi H, Usui T, Takeuchi A, Hosoya T, Suzuki T, Hagiwara M. Rectifier of aberrant mRNA splicing recovers tRNA modification in familial dysautonomia. *Proc Natl Acad Sci USA*. 2015.03; 112(9); 2764-2769
2. Yoshida S, Uchida K, Hosoya T. Generation of Arynes Using Trimethylsilylmethyl Grignard Reagent for Activation of *ortho*-Iodoaryl or *ortho*-Sulfinylaryl Triflates. *Chem Lett*. 2015.05; 44(5); 691-693

3. Yoshida S, Karaki F, Uchida F, Hosoya T. Generation of cycloheptynes and cyclooctynes *via* a sulfoxide-magnesium exchange reaction of readily synthesized 2-sulfinylcycloalkenyl triflates. *Chem Commun.* 2015.05; 51(42); 8745-8748
4. Yoshida S, Hazama Y, Sumida Y, Yano T, Hosoya T. An Alternative Method for Generating Arynes from *ortho*-Silylaryl Triflates: Activation by Cesium Carbonate in the Presence of a Crown Ether. *Molecules.* 2015.06; 20(6); 10131-10140
5. Morooka, S., Hoshina, M., Kii, I., Okabe, T., Kojima, H., Inoue, N., Okuno, Y., Denawa, M., Yoshida, S., Fukuhara, J., Ninomiya, K., Ikura, T., Furuya, T., Nagano, T., Noda, K., Ishida, S., Hosoya, T., Ito, N., Yoshimura, N., Hagiwara*, M.. Identification of a dual inhibitor of SRPK1 and CK2 that attenuates pathological angiogenesis of macular degeneration in mice. *Molecular Pharmacology.* 2015.08; 88(2); 316-325
6. Masaki S, Kii I, Sumida Y, Kato-Sumida T, Ogawa Y, Ito N, Nakamura M, Sonamoto R, Kataoka N, Hosoya T, Hagiwara M. Design and synthesis of a potent inhibitor of class 1 DYRK kinases as a suppressor of adipogenesis. *Bioorg Med Chem.* 2015.08; 23(15); 4434-4441
7. Hosoya T, Iimori R, Yoshida S, Sumida Y, Sahara-Miura Y, Sato J, Inouye S. Concise Synthesis of *o*-Coelenterazines. *Org Lett.* 2015.08; 17(15); 3888-3891
8. Sonamoto R, Kii I, Koike Y, Sumida Y, Kato-Sumida T, Okuno Y, Hosoya T, Hagiwara M. Identification of a DYRK1A Inhibitor that Induces Degradation of the Target Kinase using Co-chaperone CDC37 fused with Luciferase nanoKAZ. *Sci Rep.* 2015.08; 5; 12728
9. Yoshida S, Shimomori K, Nonaka T, Hosoya T. Facile Synthesis of Diverse Multisubstituted *ortho*-Silylaryl Triflates via C–H Borylation. *Chem Lett.* 2015.10; 44(10); 1324-1326
10. Okamoto M, Hidaka A, Toyama M, Hosoya T, Yamamoto M, Hagiwara M, Baba M. Selective inhibition of HIV-1 replication by the CDK9 inhibitor FIT-039. *Antiviral Res.* 2015.11; 123; 1-4
11. Niwa T, Ochiai H, Watanabe Y, Hosoya T. Ni/Cu-Catalyzed Defluoroborylation of Fluoroarenes for Diverse C–F Bond Functionalizations. *J Am Chem Soc.* 2015.11; 137(45); 14313-14318
12. Yoshida S, Yano T, Misawa Y, Sugimura Y, Igawa K, Shimizu S, Tomooka K, Hosoya T. Direct thioamination of arynes *via* reaction with sulfilimines and migratory *N*-arylation. *J Am Chem Soc.* 2015.11; 137(44); 14071-14074
13. Yoshida S, Sugimura Y, Hazama Y, Nishiyama Y, Yano T, Shimizu S, Hosoya T. A mild and facile synthesis of aryl and alkenyl sulfides *via* copper-catalyzed deborylthiolation of organoborons with thiosulfonates. *Chem Commun.* 2015.12; 51(93); 16613-16616

[Misc]

1. Yoshida S, Hosoya T. The Renaissance and Bright Future of Synthetic Aryne Chemistry. *Chem Lett.* 2015.11; 44(11); 1450-1460

[Conference Activities & Talks]

1. Morita T, Yoshida S, Hosoya T. Synthesis of Diverse Multisubstituted Benzo[*b*] thiophenes Based on Transformations *via* Thienobenzyne Intermediates. The 13th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-13) 2015.11 Kyoto, Japan
2. Uetake Y, Niwa T, Hosoya T. Rh-Catalyzed *Ipso*-Borylation of Methylthioarenes *via* C–SMe Bond Cleavage. The 13th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-13) 2015.11 Kyoto, Japan
3. Sumida Y, Sumida T, Hosoya T. Generation of Arynes and Formation of Aryne–Nickel Complexes from *o*-Borylaryl Triflates. The 13th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-13) 2015.11 Kyoto, Japan
4. Meguro T, Yoshida S, Hosoya T. Cycloaddition of Thiophene *S,S*-Dioxide Derivatives with Strained Cycloalkynes. The 13th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-13) 2015.11 Kyoto, Japan

5. Yoshida S, Shimomori K, Kim Y, Hosoya T. Selective C–F Bond Cleavage via a Silylium Intermediate. The 13th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-13) 2015.11 Kyoto, Japan
6. Hosoya T, Hatakeyama Y, Karaki F, Johmoto K, Uekusa H, Yoshida S. Transient Protection of Strained Alkynes from Click Reaction via Complexation with Copper. The 13th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-13) 2015.11 Kyoto, Japan
7. Hosoya T, Yoshida S, Misawa Y. Formal C–H azidation-based shortcut to diazido building blocks for the versatile preparation of photoaffinity labeling probes of natural products and pharmaceuticals. PACIFICHEM 2015 2015.12 Honolulu, Hawaii, USA
8. Yoshida S, Uchida K, Karaki F, Hosoya T. Generation of arynes and cycloalkynes via a sulfoxide–magnesium exchange reaction of readily synthesized precursors. PACIFICHEM 2015 2015.12 Honolulu, Hawaii, USA
9. Uchida K, Yoshida S, Igawa K, Tomooka K, Hosoya T. Efficient generation method and remarkable reactivities of 3-triflyloxyaryne. PACIFICHEM 2015 2015.12 Honolulu, Hawaii, USA
10. Hosoya T, Yoshida S, Shiraishi A, Kanno K, Kii I, Johmoto K, Uekusa H, Hagiwara M. Azido-type selective reactions for molecular conjugation. PACIFICHEM 2015 2015.12 Honolulu, Hawaii, USA
11. Yoshida S, Hatakeyama Y, Johmoto K, Uekusa H, Hosoya T. Transient Protection of strained alkynes from click reaction via complexation with copper. PACIFICHEM 2015 2015.12 Honolulu, Hawaii, USA

[Patents]

1. Method for screening substance capable of inhibiting abnormal splicing causative of onset or progress of disease, Announcement Number : WO 2015/005491
2. Pain-related compound and medicinal composition, Announcement Number : WO 2015/093567
3. Process for producing substituted benzo[f]imidazo[1,2-a]quinoxalin-3(11H)-ones, Patent Number : US 8975403
4. Medicinal composition inhibiting neovascularization proliferation factor, Announcement Number : WO 2015/147204
5. Coelenterazine analogues and coelenteramide analogues, Patent Number : US 9056840
6. Process for producing substituted benzo[f]imidazo[1,2-a]quinoxalin-3(11H)-ones, Announcement Number : US 2015/0266833
7. Coelenterazine analogues and coelenteramide analogues, Patent Number : US 9075058

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. Nobuyuki Shimizu, Shizuka Ishitani, Atsushi Sato, Hiroshi Shibuya, Tohru Ishitani. Hipk2 and PP1c cooperate to maintain Dvl protein levels required for Wnt signal transduction. *Cell Rep.* 2014.09; 8(5); 1391-1404
2. 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.*.

[Conference Activities & Talks]

1. Shimizu N, Ishitani S, Sato A, Shibuya H, Ishitani T. Hipk2 and PP1c-mediated dephosphorylation of Dishevelled sustains Wnt signal transduction. 11th International Conference on Zebrafish Development and Genetics 2014.06.27 Madison, Wisconsin, USA

Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D.
Associate Professor Jun Hirayama, Ph.D.
Assistant Professor Yoichi Asaoka, Ph.D.
Postdoctoral fellow Norio Miyamura, Ph.D.
Technical Assistants Misako Namae
Secretary Keiko Otaka

(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. Koichi Fujisawa, Shuji Terai, Toshihiko Matsumoto, Taro Takami, Naoki Yamamoto, Hiroshi Nishina, Makoto Furutani-Seiki, Isao Sakaida. Evidence for a Role of the Transcriptional Regulator Maf in Tumorigenesis and Aging. *PLoS ONE*. 2015; 10(6): e0129950
2. Yuta Mochimaru, Morio Azuma, Natsuki Oshima, Yuta Ichijo, Kazuhiro Satou, Kouhei Matsuda, Yoichi Asaoka, Hiroshi Nishina, Takashi Nakakura, Chihiro Mogi, Koichi Sato, Fumikazu Okajima, Hideaki Tomura. Extracellular acidification activates ovarian cancer G-protein-coupled receptor 1 and GPR4 homologs of zebra fish. *Biochem. Biophys. Res. Commun.* 2015.02; 457(4): 493-499
3. Sean Porazinski, Huijia Wang, Yoichi Asaoka, Martin Behrndt, Tatsuo Miyamoto, Hitoshi Morita, Shoji Hata, Takashi Sasaki, S.F. Gabby Krens, Yumi Osada, Satoshi Asaka, Akihiro Momoi, Sarah Linton, Joel B. Miesfeld, Brian A. Link, Takeshi Senga, Atahualpa Castillo-Morales, Araxi O. Urrutia, Nobuyoshi Shimizu, Hideaki Nagase, Shinya Matsuura, Stefan Bagby, Hisato Kondoh, Hiroshi Nishina, Carl-Philipp Heisenberg and Makoto Furutani-Seiki. YAP is essential for tissue tension to ensure vertebrate 3D body shape *Nature*. 2015.04;

4. Shodai Kawano, Junichi Maruyama, Shunta Nagashima, Kazutoshi Inami, Wenzhe Qiu, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiroshi Nishina, Yutaka Hata. A cell-based screening for TAZ activators identifies ethacridine, a widely used antiseptic and abortifacient, as a compound that promotes dephosphorylation of TAZ and inhibits adipogenesis in C3H10T1/2 cells. *J. Biochem.*. 2015.11; 158(5); 413-423
5. Yu. R.: Miyamura, N.; Okamoto-Uchida, Y.; Arima, N.; Ishigami-Yuasa, M.; Kagechika, H.; Nishina, H.. A Modified Murine Embryonic Stem Cell Test for Evaluating the Teratogenic Effects of Drugs on Early Embryogenesis *Plos ONE*. 2015.11; 10; e0145286

Immunology

Professor:	Takeshi TSUBATA, M.D., Ph.D.
Associate Professor:	Takahiro ADACHI, Ph.D.
Assistant Professors:	Mitsuhiro SUZUKI, Ph.D., Naoko MATSUBARA Ph.D.
Assistant Professors:	Miduo XU, Chizuru AKATSU
Lecturer:	Ji-Yang WANG
Researcher:	Zhihong LIU
Technicians:	Yukie KURUSU, Shigeko NAKANO
Secretaries:	Hiroko TAKAHASHI, Hiromi NAITOH
Graduate Students:	Miao TANG, Toshitaro TAKATA, Aslam MOHAMMAD, Nazim MEDZHIDOV, Xuyang JIAO, Mayo YOSHIOKA, Yang-Yang FENG, Amin ALBORZIAN DEH SHEIKH, Sundararaman RENGARAJAN

(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 known 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.

- 1) Elucidation of the mechanisms for humoral immune responses to glycans, glyco-lipids and nucleic acids-related antigens.
- 2) Elucidation of the role of glycan signals in the regulation of humoral immune responses, and application of glycan signals to therapy.
- 3) Analysis of pathogenesis of autoimmune diseases such as systemic lupus erythematosus (SLE) and immuno-neurological disorders.

(2) Education

Lecture course on immunology at the master's program 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 on biomedical sciences at the PhD program 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 the master's and PhD programs aim at training the students to acquire basic research skills 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. Muro. R., Nitta. T., Okada. T., Ideta. H., Tsubata. T. and Suzuki. H.. The Ras GTPase-activating protein Rasal3 supports survival of naive T cells PLoS ONE. 2015.03; 10(3); e0119898
2. Ouchida. R., Lu. Q., Liu. J., Li. Y., Chu. Y., Tsubata. T. and Wang, J.-Y.. Fc μ R interacts and cooperates with the B cell receptor to promote B cell survival J. Immunol. 2015.04; 194; 3096-3101

[Conference Activities & Talks]

1. P. A. Koni., Ren, M., Tsubata, T., Khleif, S., Maverakis, E. and Shimoda, M.. A mouse model for chronic inflammatory diseases spontaneously develops CD4/CD8 double-positive T cell leukemia/lymphoma. . The 54th Midwinter Conference of Immunologists at Asilomar. 2015.01.24 Big Bear Lake, California (USA)
2. Tsubata, T.. CD22-binding synthetic sialosides as a tool to elucidate the role of CD22 cis-ligand and as a novel immunostimulant. DRFZ 2015.03.16 Berlin
3. Tsubata, T.. CD22-binding synthetic sialosides as a tool to elucidate the role of CD22 cis-ligand and as a novel immunostimulant. TRR130 2015.03.18 Erlangen
4. Tsubata, T.. CD22-binding synthetic sialosides as a tool to elucidate the role of CD22 cis-ligand and as a novel immunostimulant. 2015.03.23 Freiburg
5. Aslam, M., Adachi, T., Weigert, M. G. and Tsubata, T.. CD72 regulates self-reactive B cells to nuclear antigens. The 30th Autoimmune Conference 2015.07.11 Tokyo
6. Onodera, T., Adachi, T., Tsubata, T., Ato, M. and Takahashi, Y.. Visualization of anti-nuclear Ab producing B cells by flow-cytometry in a SLE mouse model. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.18 Sapporo
7. Akatsu, C., Aslam, M., Adachi, T. and Tsubata, T.. Interaction of CD72 and SLE-related antigen negatively regulates self-reactive B cells. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.20 Sapporo
8. Aslam, M., Adachi, T. and Tsubata, T.. CD72 regulates self-reactive B cells to nuclear antigens. The 44th Annual Meeting of The Japanese Society for Immunology 2015.11.20 Sapporo
9. Tsubata, T.. B lymphocyte co-receptors and systemic lupus erythematosus. Fudan University 2015.12.16 Shainghai

[Patents]

1. Method for promoting immune response comprising inhibiting CD22 function in B cells, Patent Number : US 9,018,245 B2

Epigenetics

Professor Fumitoshi Ishino
Associate Professor Takashi Kohda
Assistant Professor Hirosuke Shiura
Assistant Professor Yuki Kawasaki
Project Lecturere Jiyoung Lee
Project Assistant Professor Masahito Irie
Adjunct Lecturere Shin Kobayashi

(1) Outline

“Epigenetics” coupled with “Genetics” enables us to elucidate several ‘genomic functions’ in inheritance, development and evolution of organisms including our human beings. Genomic imprinting is one of the mammalian specific gene regulation mechanisms 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’. These studies show us how Epigenetics is important in mammalian biology. Our department focuses these mammalian specific genomic functions to elucidate how these genomic functions work and how new genomic functions have been evolved during evolution. Our final goal is to contribute to the 21st’s medicine and human biology 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. Ito M, Sferruzzi-Perri A N, Edwards C A, Adalsteinsson B T, Allen S E, Loo T-H, Kitazawa M, Kaneko-Ishino T, Ishino F, Stewart C L and Ferguson-Smith A C.. A trans-homologue interaction between reciprocally imprinted miR-127 and Rtl1 regulates placenta development. *Development*. 2015.07; 142(14); 2425-2430
2. Ono R, Ishii M, Fujihara Y, Kitazawa M, Usami T, Kaneko-Ishino T, Kanno J, Ikawa M and Ishino F.. Double strand break repair by capture of retrotransposon sequences and reverse-transcribed spliced mRNA sequences in mouse zygotes. *Scientific Reports*. 2015.07; 5; 12281
3. Irie M, Yoshikawa M, Ono R, Iwafune H, Furuse T, Yamada I, Wakana S, Yamashita Y, Abe T, Ishino F and Kaneko-Ishino T. Cognitive function related to the Sirh11/Zcchc16 gene acquired from an LTR retrotransposon in eutherians. *PLoS Genetics*. 2015.09; 11(9); 1005521
4. Kagami M, Kurosawa K, Miyazaki O, Ishino F, Matsuoka K, Ogata T.. Comprehensive clinical studies in 34 patients with molecularly defined UPD(14)pat and related conditions (Kagami-Ogata syndrome). *Eur J Hum Genet* . 2015.11; 23(11); 1488-1498

[Conference Activities & Talks]

1. Matsuzawa A, Lee J, Takahashi S and Ishino F.. Culture condition affect DNA methylation status of genomic imprinting in ES cells. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
2. Kawasaki Y, Tohda T, Kuroda Y and Ishino F.. Analysis of cytosine modifications by EnIGMA method. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
3. Lee J, Takahashi S, Kohda T, Matsuzawa A, Kawasumi M, Kanai M, Kaneko-Ishino T and Ishino F.. Stable culture of haploid ES cells by regulating cell cycle. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
4. Kitazawa M, Ono R, Oka S, Kaneko-Ishino T and Ishino F.. Effects of eutherian-specific Peg11 gene on pups and placentas. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
5. Kobayashi S, Hosoi Y, Shinohara Y, Okabe M and Ishino F. Live imaging of X chromosome re-activation and reprogramming of stem cells. The 9th Annual Meeting of the Japanese Society for Epigenetics 2015.05.25
6. Fumitoshi Ishino and Tomoko Kaneko-Ishino.. Mammalian evolution promoted by LTR retrotransposon-derived genes.. The International Conference of the Korean Society for Molecular and Cellular Biology (KSMCB) 2015 2015.09.23 COEX, Seoul
7. Ishino F. Beyond the Genomic imprinting. 2015.10.23
8. Ishino F. Beyond the genomic imprinting-its origin, relation to viviparity and retrotransposon-derived genes. 2015.11.05
9. Ishino F. Placental functions of LTR-retrotransposon-derived genes. 2015.11.05
10. Ishno F. Mammalian-specific genomic functions in development and evolution. 2015.11.25

11. Ishino F and Kaneko-Ishino T. Mechanism of endogenization from LTR retrotransposons. 2015.12.02
12. Irie M, Ishino F and Kaneko-Ishino T. LTR retrotransposon-derived SIRH genes in mammals. 2015.12.04
13. Fumitoshi Ishino. Mammalian evolution by acquired genes. 2015.12.22 The University of Tokyo

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. Akihiro Ito, Tadahiro Shimazu, Satoko Maeda, Asad Ali Shah, Tatsuhiko Tsunoda, Shun-Ichiro Iemura, Toru Natsume, Takafumi Suzuki, Hozumi Motohashi, Masayuki Yamamoto, Minoru Yoshida. The sub-cellular localization and activity of cortactin is regulated by acetylation and interaction with Keap1. *Sci Signal*. 2015; 8(404); ra120
2. Ronesh Sharma, Abdollah Dehzangi, James Lyons, Kuldip Paliwal, Tatsuhiko Tsunoda, Alok Sharma. Predict Gram-Positive and Gram-Negative Subcellular Localization via Incorporating Evolutionary Information and Physicochemical Features Into Chou's General PseAAC. *IEEE Trans Nanobioscience*. 2015.12; 14(8); 915-926

[Misc]

1. Tatsuhiko Tsunoda. Big data analysis and mathematical research in medical science *Clinical Immunology & Allergy*. 2015.12; 64(6); 565-571

[Conference Activities & Talks]

1. Tatsuhiko Tsunoda. Genomic Medicine with omic big data analysis. Japanese Society of Human Genetics Symposium 2015.10.15 Tokyo
2. Tatsuhiko Tsunoda. Personalized and preemptive medicine with omic big data analysis and artificial intelligence. 19th Biomedical workshop 2015.10.30 Osaka
3. Tatsuhiko Tsunoda. Omic big data drives personalized/preemptive medicine. 14th Surugadai International Symposium 2015.11.26 Tokyo

Structural Biology

Professor Nobutoshi ITO
Associate Professor Teikichi IKURA
Assistant Professor Nobutaka NUMOTO
Technical Assistant Michiko HATTORI
Graduate Student Kenrou SHINAGAWA

(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. Morooka, S., Hoshina, M., Kii, I., Okabe, T., Kojima, H., Inoue, N., Okuno, Y., Denawa, M., Yoshida, S., Fukuhara, J., Ninomiya, K., Ikura, T., Furuya, T., Nagano, T., Noda, K., Ishida, S., Hosoya, T., Ito, N., Yoshimura, N., Hagiwara, M.. Identification of a dual inhibitor of SRPK1 and CK2 that attenuates pathological angiogenesis of macular degeneration in mice. *Molecular Pharmacology*. 2015.08; 88(2); 316-325
2. Masaki S, Kii I, Sumida Y, Kato-Sumida T, Ogawa Y, Ito N, Nakamura M, Sonamoto R, Kataoka N, Hosoya T, Hagiwara M. Design and synthesis of a potent inhibitor of class 1 DYRK kinases as a suppressor of adipogenesis. *Bioorg Med Chem*. 2015.08; 23(15); 4434-4441
3. Manjiri R Kulkarni, Monirul M Islam, Nobutaka Numoto, Montasir Elahi, Mamunur R Mahib, Nobutoshi Ito, Yutaka Kuroda. Structural and biophysical analysis of sero-specific immune responses using epitope grafted Dengue ED3 mutants. *Biochim. Biophys. Acta*. 2015.10; 1854(10 Pt A); 1438-1443
4. Anami, Y., Sakamaki, Y., Itoh, T., Inaba, Y., Nakabayashi, M., Ikura, T., Ito, N., Yamamoto, K.. Fine tuning of agonistic/antagonistic activity for vitamin D receptor by 22-alkyl chain length of ligands: 22S-hexyl compound unexpectedly restored agonistic activity. *Bioorganic & Medicinal Chemistry*. 2015.11; 23(22); 7274-7281
5. Watarai, Y., Ishizawa, M., Ikura, T., Zacconi, F. C. M., Uno, S., Ito, N., Mourino, A., Tokiwa, H., Makishima, M., Yamada, S.. Synthesis, biological activities, and X-ray crystal structural analysis of 25-hydroxy-25(or 26)-adamantyl-17-[20(22),23-diylnyl] -21-norvitamin D compounds *Journal of Medical Chemistry*. 2015.12; 58(24); 9510-9521

[Misc]

1. Nobutaka Numoto, Taro Nakagawa, Yoshihiro Fukumori, Kunio Miki. Deoxygenated Structure of Invertebrate Giant Hemoglobin Seibutsu Butsuri. 2015.09; 55(5); 266-268

[Conference Activities & Talks]

1. Nobutaka Numoto. Diversity of hemoglobin molecules. Seminar at Organization for Promotion of Tenure Track, University of Miyazaki 2015.03.23 Miyazaki
2. Nobutaka Numoto, Satomi Inaba, Hisayuki Morii, Teikichi Ikura, Masayuki Oda, Nobutoshi Ito. Molecular recognition mechanisms of T-cell activator CD28 and SH2 domains of Gads and PI3-kinase. The 15th Annual Meeting of the Protein Society of Japan 2015.06 Tokushima
3. Satomi Inaba, Nobutaka Numoto, Hisayuki Morii, Teikichi Ikura, Ryo Abe, Nobutoshi Ito, Masayuki Oda. Molecular interaction between PI3-kinase and co-stimulation receptor ICOS. The 15th Annual Meeting of the Protein Society of Japan 2015.06 Tokushima
4. Inaba S., Numoto N., Morii H., Ikura T., Abe R., Ito N., Oda M.. Structural and thermodynamic analysis of co-stimulation receptor CD28 phosphopeptide interactions with Grb2, Gads, and PI3-kinase SH2 domains. The 29th Annual Symposium of The Protein Society 2015.07 Palau de Congressos de Barcelona, Barcelona (Spain)
5. Ikura, T., Ito, N.. Functional conversion from peptidyl-prolyl isomerase to protease by a single amino acid substitution. The 53rd Annual Meeting of the Biophysical Society of Japan 2015.09 Kanazawa
6. Nobutaka Numoto, Taro Nakagawa, Akiko Kita, Nobutoshi Ito, Yoshihiro Fukumori, Kunio Miki. Ligand-free form of giant hemoglobin from *Oligobranchia mashikoi*. Annual Meeting 2015 of the Crystallographic Society of Japan 2015.10 Osaka
7. Nobutoshi Ito. Diseases and Drug Development from Protein Structure. 2015.10.23 Tokyo
8. Nobutoshi Ito. Protein Data Bank and Structure Deposition at PDBj. OIST-CCP4 Workshop 2015.11 Okinawa, Japan

Neuroscience

Professor Kohichi Tanaka
Associate Professor Hidenori Aizawa (2015/5/31)
Tomomi Aida (2015/7/1)
Assistant Professor Tomomi Aida (2015/6/30)
Project Assistant Professor Masashi Ohmachi(2015/6/15)
Graduate Student (doctor course)
Cui Wanpeng
Zhao Zhuoyang
Kaori Sugiyama
Graduate Student (master course)
Mina Kusunose
Moeko Tanaka
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. In the cerebellum, both GLAST, a glial glutamate transporter, and CDC42EP4 the small GTPase-effector protein, is exclusively expressed in Bergmann glia and localizes beneath specific membrane domains enwrapping dendritic spines of Purkinje cells. We show that CDC42EP4 forms complexes with septin hetero-oligomers, which interact with GLAST. In *Cdc42ep4* $-/-$ mice, GLAST is dissociated from septins and is delocalized away from the parallel fibre-Purkinje cell synapses. The excitatory postsynaptic current exhibits a protracted decay time constant, reduced sensitivity to a competitive inhibitor of the AMPA-type glutamate receptors (γ DGG) and excessive baseline inward current in response to a subthreshold dose of a nonselective inhibitor of the glutamate transporters/EAAT1–5 (DL-TBOA). We propose that the CDC42EP4/septin-based glial scaffold facilitates perisynaptic localization of GLAST and optimizes the efficiency of glutamate-buffering and clearance. Glutamate-mediated excitotoxicity that occurs due to a deficiency of the glial glutamate transport GLT is one of several potential pathogenic mechanisms of motor neuron death in amyotrophic lateral sclerosis (ALS). However, it remains unknown whether this deficiency is a primary cause or a secondary consequence of motor neuron degeneration. Here, we generated conditional knockout mice that lacked GLT1 specifically in the spinal cord

(GLT1-cKO mice) using the Cre/LoxP system. GLT1-cKO mice showed motor deficits, motor neuron loss and nuclear TDP-43 loss. Thus, dysfunction of glial glutamate transporters is sufficient to phenocopy ALS in mice.

2. Development of genome editing technologies

Genetically modified mice such as knockout and knockin mice have drastically improved our understanding of the functions of genes in vivo. However, the generation of genetically modified mice relies on homologous recombination in ES cells, which is a time-consuming, laborious, and expensive process. Recent development of genome editing technologies has enabled direct manipulation of the genome in mouse zygotes with out ES cells, thereby providing new avenues for simple, convenient, highly efficient, and ultra-rapid production of genetically modified mice. We developed highly efficient cloning-free CRISPR/Cas system for the production of genetically modified mice, especially for knockin mice carrying functional gene cassettes. Our novel method provides ultra convenient and highly efficient CRISPR/Cas-mediated genome editing and accelerates functional genomic research in vivo.

(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. Nakamori, T., Sato, K., Kinoshita, M., Kanamatsu, T., Sakagami, H., Tanaka, K., Ohki-Hamazaki, H. . Positive feedback of NR2B-containing NMDA receptor activity is the initial step toward visual imprinting: a model for juvenile learning. *J Neurochem.* 2015.01; 132(1); 110-123
2. Kimura, A., Guo, X., Noro, T., Harada, C., Tanaka, K., Namekata, K., Harada, T. Valproic acid prevents retinal degeneration in a murine model of normal tension glaucoma. *Neurosci Lett.* 2015.02; 588; 108-113
3. Yanagisawa, M., Aida, T., Takeda, T., Namekata, K., Harada, T., Shinagawa, R., Tanaka, K. . Arundic acid attenuates retinal ganglion cell death by increasing glutamate/aspartate transporter expression in a model of normal tension glaucoma. *Cell Death Dis.* 2015.03; 6; e1693
4. Aida T, Chiyo K, Usami T, Ishikubo H, Imahashi R, Wada Y, Tanaka KF, Sakuma T, Yamamoto T, Tanaka K.. Cloning-free CRISPR/Cas system facilitates functional cassette knock-in in mice. *Genome Biol.* 2015.04; 16; 87

5. Aida, T., Yoshida, J., Nomura, M., Tanimura, A., Iino, Y., Soma, M., Bai, N., Ito, Y., Cui, W., Aizawa, H., Yanagisawa, M., Nagai, T., Takata, N., Tanaka, K.F., Takayanagi, R., Kano, M., Gotz, M., Hirase, H., Tanaka, K.. Astroglial glutamate transporter deficiency increases synaptic excitability and leads to pathological repetitive behaviors in mice. *Neuropsychopharmacology*. 2015.06; 40(7); 1569-1579
6. Ishii, K., Kubo, K., Endo, T., Yoshida, K., Benner, S., Ito, Y., Aizawa, H., Aramaki, M., Yamanaka, A., Tanaka, K., Takata, N., Tanaka, K., Mimura, M., Tohyama, C., Kakeyama, M., Nakajima, K.. Neuronal heterotopias affect the activities of distant brain areas and lead to behavioral deficits. *J Neurosci*. 2015.09; 35(36); 12432-12445
7. Ageta-Ishihara, N., Yamazaki, M., Konno, K., Nakayama, H., Abe, M., Hashimoto, K., Nishioka, T., Kaibuchi, K., Hattori, S., Miyakawa, T., Tanaka, K., Huda, F., Hrai, H., Hashimoto, K., Watanabe, M., Sakimura, K., Kinoshita, M.. A CDC42EP4/septin-based perisynaptic glial scaffold facilitates glutamate clearance. *Nature Commun*. 2015.12; 6; 10090

Bio-informational Pharmacology

Associate Professor Junko KUROKAWA
 RPD Gaku-Shin Researcher Masami KODAMA
 Technical Support Staff Tomoko ANDO
 Technical Support Staff Reiko KIMURA

(1) Outline

Bio-informational pharmacology treats diverse area of life sciences by using pharmacological tools. This laboratory focuses on understanding fundamental physiological roles of ion channels and transporters in cardiovascular system. We employ multidisciplinary approach (patch-clamp, cell biology, fluorescent imaging, and comprehensive analysis) in order to seek novel regulatory mechanisms and modulatory molecules/compounds of ion channels and transporters in cardiovascular organs.

Our ultimate goal is to discover novel diagnostic and therapeutic strategy for intractable cardiovascular diseases, such as sudden death, life-threatening arrhythmias, and atherosclerosis, by modulating ion channels and transporters.

(2) Research

- (1) Gender specific medicine in cardiovascular diseases
- (2) Cardiac arrhythmias and iPS cells
 - (A) Cardiac disease models of iPS-derived cardiomyocytes from long QT syndrome patients
 - (B) Drug safety screening system using human iPS cells-derived cardiomyocytes
- (3) New technologies in cardiovascular research
 - (A) In vitro cardiomyocyte contraction assay system using the motion vector technology
 - (B) Generation of 3-D simulator for cardiac electrical activity

(3) Education

Physiology, Pharmacology.

(4) Publications

[Original Articles]

1. SaitoY, Nakamura K, Yoshida M, Sugiyama H, Ohe T, Kurokawa J, Furukawa T, Takano M, Nagase S, Morita H, Kusano KF, Ito H.. Enhancement of Spontaneous Activity by HCN4 overexpression in Mouse Embryonic Stem Cell-derived Cardiomyocytes - a Possible Biological Pacemaker. PLoS ONE. 2015; 10; e0138193
2. Yamakawa H, Muraoka N, Miyamoto K, Sadahiro T, Isomi M, Haginiwa S, Kojima H, Umei T, Akiyama M, Kuishi Y, Kurokawa J, Furukawa T, Fukuda K, Ieda M. . Fibroblast Growth Factors and Vascular Endothelial Growth Factor Promote Cardiac Reprogramming under Defined Conditions. Stem Cell Rep. 2015; 5; 1128-1142

3. Takahashi K, Sasano T, Sugiyama K, Kurokawa J, Tamura N, Soejima Y, Sawabe M, Isobe M, Furukawa T. . High-Fat Diet Increases Vulnerability to Atrial Arrhythmia by Conduction Disturbance via miR-27b. *J Mol Cell Cardiol.* 2015; 90; 38-46
4. Okada J, Yoshinaga T, Kurokawa J, Washio T, Furukawa T, Sawada K, Sugiura S, Hisada T. . Screening system for drug-induced arrhythmogenic risk combining patch clamp and a heart simulator. *Science Advances.* 2015.05; 1; 1400142
5. Kurokawa J, Sasano T, Kodama M, Li M, Ebana Y, Harada N, Honda SI, Nakaya H, Furukawa T. Aromatase knockout mice reveal an impact of estrogen on drug-induced alternation of murine electrocardiography parameters. *Journal of Toxicological Sciences.* 2015.06; 40;

[Conference Activities & Talks]

1. Kurokawa J, Okada J, Hayashi E, Ashihara T, Yoshinaga T, Sugiura S, Li M, Kanda Y, Sekino Y, Sawada K, Hisada T, Furukawa T. . A multidisciplinary approach for evaluation of drug-induced QT prolongation using human induced pluripotent stem cell-derived cardiomyocytes.. 59th Biophysical Society Annual Meeting 2015.02.11
2. Erina Hayashi, Miki Fujitsuka, Tetsushi Furukawa, Junko Kurokawa. Pharmacological analysis of doxorubicin in genetically engineered human iPS cell-derived cardiomyocytes. . 88th Japanese Pharmacological Society Annual Meeting 2015.03.18 Nagoya
3. Kurokawa J, Fujizuka M, Hayashi E, Ashihara T, Kanda Y, Sekino Y, Furukawa T. Effects of hydrogel culture substrate on contractile properties and gene expression profiles of human iPS cell-derived cardiomyocytes.. 135th annual meeting of the Pharmaceutical Society of Japan 2015.03.25
4. Ashihara T, Haraguchi R, Kurokawa J, Nakazawa K, Horie M. Antiarrhythmic drug efficacy in induced pluripotent stem cell-derived myocardium may be different from that in original heart: A simulation study.. The 79th Annual Scientific Meeting of Japanese Circulation Society 2015.04.24 Osaka
5. Furukawa T, Okata S, Yuasa S, Suzuki T, N Makita, J Kurokawa, T Egashira, H Yamanaka, T Seki, Y Aizawa, H Hashimoto, Y Kuroda, A Tanaka, K Yae, M Murata, T Aiba, W Shimizu, M Horie, K Kamiya, K Fukuda. Study of long QT syndrome type 3 using human iPS-derived cardiomyocytes. The 32nd Annual Scientific Meeting of the Japanese Society of Electrophysiology 2015.07.31 Kyoto
6. Junko Kurokawa. Non-genomic action of sex steroid hormones and cardiac repolarization. . The annual meeting of the International Society of Gender Medicine 2015.09.23 Berlin, Germany

Epigenetic Epidemiology

Professor: Masaaki MURAMATSU
Associate Professor : Noriko SATO
Assistant Professor : Shinobu IKEDA

Adjunct Instructor : Katsuko SUDO, Fumihiro SATA, Jun-ichi TAGUCHI, Kaoru MOGUSHI

Graduate Student: Sariya Dechamethakun, Kaung Si Thu,
Khin Thet Thet Zaw, Yuko Maeda, Fujitani,
Tay Zar Kyaw, Tadaaki Katsuta, Jyun-ya Hagiwara, Shilpa Pavethynath
Norihiko Satake, Riya Tamura, Kenji Suzuki, Hirokazu Sakamoto
Research Student: Yui Tsubota
Research Resident: Maidina Abudushataer, Ake Ko Ko Minn, 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: Clinical Informatics
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. Yamada M, Sato N, Ikeda S, Arai T, Sawabe M, Mori S, Yamada Y, Muramatsu M, Tanaka M.. Association of the chromodomain helicase DNA-binding protein 4 (CHD4) missense variation p.D140E with cancer: potential interaction with smoking. *Genes Chromosomes Cancer*.. 2015; 54; 122-128
2. Nishizawa D, Kasai S, Hasegawa J, Sato N, Yamada H, Tanioka F, Nagashima M, Katoh R, Satoh Y, Tagami M, Ujike H, Ozaki N, Inada T, Iwata N, Sora I, Iyo M, Yamada M, Kondo N, Won MJ, Naruse N, Uehara-Aoyama K, Itokawa M, Ohi K, Hashimoto R, Tanisawa K, Arai T, Mori S, Sawabe M, Nakamieno M, Yamada Y, Yamada M, Sato N, Muramatsu M, Tanaka M, Irukayama-Tomobe Y, Saito YC, Sakurai T, Hayashida M, Sugimura H, Ikeda K. Associations between the orexin (hypocretin) receptor 2 gene polymorphism Val308Ile and nicotine dependence in genome-wide and subsequent association studies. *Mol Brain*. 2015; 8; 50

[Conference Activities & Talks]

1. Noriko Sato. Inter-individual phenotypic variation and phenotypic robustness. The 60th Annual Meeting of the Japan Society of Human Genetics 2015.10.15 Tokyo
2. Noriko Sato. Prenatal exposure to an early-gestational maternal low-protein diet affects mutational stress response in the young adult mice. BMB2015 Biochemistry and Molecular Biology 2015.12.01 Kobe
3. Sariya Dechamethakun, Noriko Sato, Shinobu Ikeda, Tomio Arai, Motoji Sawabe, Masaaki Muramatsu, Masashi Tanaka. Association of CSMD2 Gene Polymorphisms with Cancer in Japanese Population. Biochemistry and Molecular Biology BMB2015 2015.12.02

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 Lecturer	Takeshi Nakano
Visiting Lecturer	Kenji Ogawa
Visiting Lecturer	Go Hirai
Visiting Lecturer	Yutaka Furutani
Visiting Lecturer	Qin Xian-Yang
Visiting Lecturer	Akiko Hashimoto-Tane
Visiting Lecturer	Ambara R. Pradipta
Visiting Lecturer	Masamichi Nagae
Visiting Lecturer	Nobuhiko Miyasaka
Visiting Lecturer	Tetsuya Koide
Graduate Students	D3 Motonari Sakai, Sayoko Yamasaki, Hari Prasad Dulal
	D2 Ryo Fukazawa, Kruthi Sharamjeet Suvarna
	D1 Mengqian Li
	M2 Daiki Kakumoto, Miki Sawamura
	M1 Sho Fukushima

(1) Research

Molecular and Chemical Somatology is an interdisciplinary field to understand basis of Bioorganic Chemistry, Chemical Biology, Structural Biology and Molecular Immunology 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) Molecular Cellular Pathology
 - Clarification of pathogenesis of diseases at molecular and cellular levels utilizing bioprobes.
- 2) Synthetic Organic Chemistry
 - Design and synthesis of bioactive molecules based on synthetic organic chemistry and chemical biology research.
- 3) Chemical Biology
 - Discovery, target identification and analyses of mechanism of action of bioactive compounds that regulate biological function.
- 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.

(3) Publications

[Original Articles]

1. Hirai, G., Nishizawa, E., Kakumoto, D., Morita, M., Okada, M., Hashizume, D., Nagashima, S., Sodeoka, M. Reactions of Carbonyl Compounds with Phosphorus Ylide Generated from Tribromofluoromethane and Tris (dimethylamino) phosphine. *Chemistry Letters*, 44: 1389-1391, 2015.
2. Ikeda, T., Ong, E.B.B., Watanabe, N., Sakaguchi, N., Maeda, K., and Koito, A.: Creation of chimeric human/rabbit APOBEC1 with activities of HIV-1 restriction and DNA mutation. *Sci. Rep.* 6, 19035. 2016.
3. Hara, H., Yokosuka, T., Hirakawa, H., Ishihara, C., Yasukawa, S., Yamazaki, M., Koseki, H., Yoshida, H. and Saito, T. Clustering of CARMA1 through SH3-GUK domain interactions is required for its activation of NF- κ B signaling. *Nat. Commun.* 6:5555, 2015.
4. Shrestha, R., Tatsukawa, H., Shrestha, R., Ishibashi, N., Matsuura, T., Kagechika, H., Kose, S., Hitomi, K., Imamoto, N., and Kojima, S. Molecular mechanism by which acyclic retinoid induces nuclear localization of transglutaminase 2 in human hepatocellular carcinoma cells. *Cell Death & Disease*, 6, e2002. 2015
5. Qin, X-Y., Fujii, S., Shimizu, A., Kagechika, H., and Kojima, S. Carboxylic derivatives of vitamin K2 inhibit hepatocellular carcinoma cell growth through caspase/transglutaminase-related signaling pathways. *J. Nutri. Sci. Vitaminol.*, 61:285-290, 2015.

[Review Articles]

1. Hirai, G., Sodeoka, M. Focused library with a core structure extracted from natural products and modified: application to phosphatase inhibitors and several biochemical findings. *Acc. Chem. Res.*48: 1464-73, 2015.
2. Nagae, M., and Yamaguchi, Y. Sugar recognition and protein-protein interaction of mammalian lectins conferring diverse functions. *Curr. Opin. Struct. Biol.* 34:108-115, 2015.

[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, pp43-62. 2016.

[Conference Activities & Talks]

1. Kojima, S. “Novel molecular mechanisms of nuclear localization of TG2.” 14th International Congress on Amino Acids, Peptides and Proteins, Vienna, Austria, August, 2015.

Metallic Biomaterials

Yusuke TSUTSUMI Assoc Prof
 Takao HANAWA Prof
 Maki ASHIDA Assist Prof
 Peng CHEN Assist Prof
 Hisashi DOI Assist Prof
 Toshie NAKANISHI Secretary
 Tomoko SETOGUCHI Secretary

(1) Outline

1. Bio-functionilization 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 minimalize 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. Maekawa M, Kanno Z, Wada T, Hongo T, Doi H, Hanawa T, Ono T, Uo M. Mechanical properties of orthodontic wires made of super engineering plastic Dental Materials Journal. 2015.02; 34(1); 114-119
2. Seo JH, Tsutsumi Y, Kobari A, Shimojo M, Hanawa T, Yui N. Modulation of friction dynamics in water by changing the combination of the loop- and graft-type poly(ethylene glycol) surfaces Soft Mater. 2015.02; 11(5); 936-942

3. Shinonaga T, Tsukamoto M, Kawa T, Chen P, Nagai A, Hanawa T. Formation of periodic nanostructures using a femtosecond laser to control cell spreading on titanium *Applied Physics B*. 2015.03; 119; 493-496
4. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Superplasticity in the Ti-6Al-7Nb alloy processed by high-pressure torsion *Mater. Sci. Eng. A*. 2015.06; 640; 449-453
5. Ashida M, Sugimoto T, Nomura N, Tsutsumi Y, Chen P, Doi H, Hanawa T. Microstructure and mechanical properties of large-scale ingots of the Zr-1Mo alloy *Mater. Trans.* 2015.07; 56(9); 1544-1548
6. Jang SH, Lee DH, Ha JY, Hanawa T, Kim KH, Kwon TY. Preliminary evaluation of mechanical properties of Co-Cr alloys fabricated by three new manufacturing processes *Int J Prosthodont*. 2015.07; 28(4); 396-398
7. Umezawa T, Chen P, Tsutsumi Y, Doi H, Ashida M, Suzuki S, Moriyama K, Hanawa T. Calcification of MC3T3-E1 cells on titanium and zirconium *Dental Materials Journal*. 2015.10; 34(5); 713-718
8. Fukuhara Y, Kyuzo M, Tsutsumi Y, Nagai A, Chen P, Hanawa T. The effect of different component ratios in block polymers and processing conditions on electrodeposition efficiency onto titanium *Applied Surface Science*. 2015.11; 355; 784-791
9. Nozaki K, Shinonaga T, Ebe N, Horiuchi N, Nakamura M, Tsutsumi Y, Hanawa T, Tsukamoto M, Yamashita K, Nagai A. Hierarchical periodic micro/nano-structures on nitinol and their influence on oriented endothelialization and anti-thrombosis *Mater Sci Eng C Mater Biol Appl*. 2015.12; 57; 1-6
10. Okamoto H, Tsutsumi Y, Watanabe M, Yamakage K, Ashida M, Chen P, Doi H, Miura H, Matsumura M, Hanawa T. Evaluation of release and accumulation of metal ions from titanium and nickel by accelerated dissolution test in simulated body environments *Electrochemistry*. 2015.12; 83(12); 1048-1052
11. Tsutsumi Y, Nishisaka T, Doi H, Ashida M, Chen P, Hanawa T. Reaction of calcium and phosphate ions with titanium, zirconium, niobium, and tantalum *Surf Interface anal*. 2015.12; 47(13); 1148-1154

[Books etc]

1. Hanawa T. Biofunctionalization of metals with polymers, *Advances in metallic biomaterials: Processing and applications*. Springer, New York, 2015.06
2. Hanawa T. Biofunctionalization of metallic materials: Creation of biosis-abiosis intelligent interface, *Interface Oral Health Science 2014*. Springer, New York, 2015.09

[Conference Activities & Talks]

1. Akimoto T, Ueno T, Tsutsumi Y, Doi H, Hanawa T, Wakabayashi N. The corrosion resistance of Ti-Zr binary alloy with compositional change. *IADR (The International Association for Dental Research)* 2015.03.11 Boston, USA
2. Hanawa T, Ashida M, Chen P, Doi H, Tsutsumi Y, Horita Z. Strengthening of Ti-6Al-7Nb alloy for dental narrow implants. *Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015)* 2015.04.15 NC, USA
3. Chen P, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Cellular and gene expression responses in osteoblast-like cells to metals. *Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015)* 2015.04.15 NC, USA
4. Tsutsumi Y, Niizeki N, Chen P, Ashida M, Doi H, Noda K, Hanawa T. Micro-arc oxidation treatment for improvement of antibacterial property of titanium. *Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015)* 2015.04.15 NC, USA
5. Chen P, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Extension, locomotion, and proliferation of osteoblast-like cells on metals. *Society for Biomaterials 2015 Annual Meeting and Exposition (SFB2015)* 2015.04.15 NC, USA
6. Chen P, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Osteogenic activity of MC3T3-E1 cells on sputter-deposited metals. *The 5th Asian Biomaterials Congress (ABMC5)* 2015.05.06 Taipei, Taiwan

7. Tsutsumi Y, Niizeki N, Chen P, Ashida M, Doi H, Noda K, Hanawa T. Development of multi-biofunctional surface on Ti by simple electrochemical treatment. The 5th Asian Biomaterials Congress (ABMC5) 2015.05.06 Taipei, Taiwan
8. Kajima Y, Takaichi A, Yasue T, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Evaluation of the shear bond strength of dental porcelain to Zr-14Nb alloy with low magnetic susceptibility . 4th TRI university consortium 2015.05.20 Thailand
9. Hanawa T, Fukuhara Y, Tsutsumi Y, Chen P, Doi H, Ashida M, Inoue Y, Ishihara K. Biofunctionalization of titanium with electrodeposited MPC polymer. Biomaterials International 2015 (BMI 2015) 2015.06.01 Kenting, Taiwan
10. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Improvement of bioactivity of zirconium by combination of anodic and cathodic polarization method. Biomaterials International 2015 (BMI 2015) 2015.06.01 Kenting, Taiwan
11. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T. Influence of heat treatment on mechanical properties of Ti-6Al-7Nb processed by severe plastic deformation. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09 Tokyo, Japan
12. Chen P, Ashida M, Tsutsumi Y, Doi H, Hanawa T. Effect of sputter-deposited metals on osteogenic potential of preosteoblast cells. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09 Tokyo, Japan
13. Tsutsumi Y, Chen P, Ashida M, Doi H, Nakai M, Niinomi M, Hanawa T. Micro-arc oxidation treatment for improvement of antibacterial property of titanium and its alloy. The 6th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials (AMDI-6) 2015.06.09 Tokyo, Japan
14. Tsutsumi Y, Niizeki N, Chen P, Ashida M, Doi H, Noda K, Hanawa T. Electrochemical surface treatment for achieving both hard-tissue compatibility and antibacterial property on Ti. The 13th World Conference on Titanium (Ti-2015) 2015.08.16 San Diego, California, USA
15. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Effects of grain refinement by high-pressure torsion on mechanical properties of Ti-6Al-7Nb. The 13th World Conference on Titanium (Ti-2015) 2015.08.16 San Diego, California, USA
16. Hanawa T, Nomura N, Ashida M, Tsutsumi Y, Doi H, Chen P, Itoh M. Decrease of MRI artifact in spinal instruments of zirconium alloy. 27th European Conference on Biomaterials (ESB2015) 2015.08.30 Krakow, Poland
17. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Effects of initial microstructure on the resultant microstructure and mechanical properties of Ti-6Al-7Nb alloy after HPT processing. International workshop on giant straining process for advanced materials (GSAM2015) 2015.09.03 Fukuoka, Japan
18. Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Superplasticity of biocompatible Ti-6Al-7Nb alloy after processing by high-pressure torsion. 12th International Conference on Superplasticity in Advanced Materials (ICSAM) 2015 2015.09.08 Tokyo, Japan
19. Biological properties of a-BC:H films prepared by pulsed plasma CVD. 2015.09.13
20. Hanawa T. Biomedical application of Ti and its alloys. 16th KIM-JIM Symposium 2015.09.16 Fukuoka, Japan
21. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Electrochemical surface treatments on metallic biomaterials for improvement of antibacterial property and hard tissue compatibility. XIV Brazil MRS Meeting (SBPMat2015) 2015.09.27 Rio de Janeiro, Brazil
22. Hanawa T, Tsutsumi Y, Fukuhara Y, Chen P, Ashida M, Doi H. Biofunctionalization of titanium with electrodeposited functional molecules. XIV Brazil MRS Meeting (SBPMat2015) 2015.09.27 Rio de Janeiro, Brazil

23. Nomura N, Suyalatu, Nakamoto T, Kimura T, Doi H, Tsutsumi Y, Hanawa T. Mechanical properties of selective laser melted Co-Cr-Mo alloys for biomedical applications. XIV Brazil MRS Meeting (SBPMat2015) 2015.09.27 Rio de Janeiro, Brazil
24. Washio K, Tsutsumi Y, Tsumanuma Y, Supreda S, Yano K, Ichinose S, Yamato M, Okano T, Hanawa T, Ishikawa I. New periodontal-like tissue formation on the modified titanium surface. 11th Asian Pacific Society of Periodontology Meeting (11th APSP) 2015.10.08 Bali, Indonesia
25. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Formation of multi-biofunctional surface layer on titanium by simple electrochemical treatment. International Symposium on EcoTopia Science 2015 (ISETS '15) 2015.11.27 Nagoya
26. Hanai M, Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Microstructures and mechanical properties of bi-modal Ti-6Al-7Nb alloy processed by high-pressure torsion. International Symposium on EcoTopia Science 2015 (ISETS '15) 2015.11.27 Nagoya
27. Tsutsumi Y, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T. Formation of bioactive and antibacterial ceramic layer on titanium by simple electrochemical surface treatment. 15th Asian BioCeramics Symposium (ABC 2015) 2015.12.10 Tokyo
28. Tsutsumi Y, Nishisaka T, Doi H, Ashida M, Chen P, Hanawa T. Reaction of calcium and phosphate ions with titanium, zirconium, niobium, and tantalum. 15th Asian BioCeramics Symposium (ABC 2015) 2015.12.10 Tokyo
29. Hanai M, Ashida M, Chen P, Doi H, Tsutsumi Y, Hanawa T, Horita Z. Strengthening of bi-modal Ti-6Al-7Nb alloy using high-pressure torsion. Twenty-Fourth International Symposium on Processing and Fabrication of Advanced Materials (PFAM XXIV) 2015.12.18 Osaka
30. Hanawa T, Ashida M, Tsutsumi Y, Doi H, Chen P. Zr-1Mo alloy to decrease of MRI Artifact. Twenty-Fourth International Symposium on Processing and Fabrication of Advanced Materials (PFAM XXIV) 2015.12.18 Osaka
31. Tsutsumi Y, Shimabukuro M, Ashida M, Chen P, Doi H, Hanawa T. Optimization of silver ion release from electrochemically-treated titanium surface. Twenty-Fourth International Symposium on Processing and Fabrication of Advanced Materials (PFAM XXIV) 2015.12.18 Osaka

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
 Assistant Kyoko AKATANI
 Adjunct Lecturer Yoshio HAYASHI

Graduate students

D3 Shohei TAKETOMI
 D2 Takuya KOBAYAKAWA, Hikaru TAKANO, Takayoshi HIGASHI
 D1 Kiju KONNO, Kei TOYAMA, Kenichi HIRAMATSU, Yuzuna Honda
 M2 Iyo Ohura, Misato KOTANI, Taisuke SUGII, Yuriko MARUTANI, Daisuke MIYAKI, Natsuka YATABE
 M1 Yusuke ISHIDA, Moemi KANEKO, Naoyuki KURATA, Ayumi SAITOU, Toshihiko TSUKINOKI

External Collaborators

Yuko YAMADA, Tsukasa HASHIMOTO, Takuma KAWADA

(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. Takano H, Narumi T, Nomura W, Furuta T, Tamamura H. Utilization of the Heavy Atom Effect for the Development of a Photosensitive 8-Azacoumarin-type Photolabile Protecting Group. *Org Lett.* 2015; 17(21); 5372-5375
2. Nomura W, Aikawa H, Taketomi S, Tanabe M, Mizuguchi T, Tamamura H. Exploration of Labeling of Near Infrared Dyes on the Polyproline Linker for Bivalent-Type CXCR4 Ligands. *Bioorg Med Chem.* 2015; 23(21); 6967-6973
3. Nomura W, Koseki T, Ohashi N, Mizuguchi T, Tamamura H. Trivalent Ligands for CXCR4 Bearing Polyproline Linkers Show Specific Recognition for Cells with Increased CXCR4 Expression. *Org Biomol Chem.* 2015; 13(32); 8734-8739
4. Mizuguchi T, Ohashi N, Nomura W, Komoriya M, Hashimoto C, Yamamoto N, Murakami T, Tamamura H. Anti-HIV Screening for Cell-Penetrating Peptides Using Chloroquine and Identification of Anti-HIV Peptides Derived from Matrix Proteins. *Bioorg Med Chem.* 2015; 23(15); 4423-4427
5. Nomura W, Ohashi N, Mori A, Tamamura H. An In-cell Fluorogenic Tag-probe System for Protein Dynamics Imaging Enabled by Cell-Penetrating Peptides. *Bioconjugate Chem.* 2015; 26(6); 1080-1085

6. Kobayakawa T, Narumi T, Tamamura H. Remote Stereinduction in the Organocuprate-Mediated Allylic Alkylation of Allylic gem-Dichlorides: Highly Diastereoselective Synthesis of (Z)-Chloroalkene Dipeptide Isosteres. *Org Lett.* 2015; 17(10); 2302-2305

[Books etc]

1. Nomura W, Koseki T, Mizuguchi T, Tamamura H. Design and Synthesis of Trivalent CXCR4 Ligands Utilizing Polyproline Linkers. in "Peptide Science 2014," ed. by Akira Otaka, The Japanese Peptide Society, Osaka. 2015
2. Mizuguchi T, Yamazaki Y, Kobayashi K, Ooe H, Iida M, Ninomiya R, Saito K, Akaji K, Tamamura H. Studies on Identification of Active Sites of an Inhibitory Cyclic Peptide against EGF Receptor Dimerization. in "Peptide Science 2014," ed. by Akira Otaka, The Japanese Peptide Society, Osaka. 2015
3. Kobayakawa T, Narumi T, Tamamura H. Development of Efficient Synthetic Methodologies of Chloroalkene Dipeptide Isosteres. in "Peptide Science 2014," ed. by Akira Otaka, The Japanese Peptide Society, Osaka. 2015
4. Takano H, Narumi T, Nomura W, Furuta T, Tamamura H. Development of 8-Azacoumarin-4-ylmethyl-type Photolabile Protecting Groups Based on Amide-Alkene Isosterism. in "Peptide Science 2014," ed. by Akira Otaka, The Japanese Peptide Society, Osaka. 2015
5. Honda Y, Mizuguchi T, Hashimoto C, Taketomi S, Ohashi N, Nomura W, Tamamura H. Development of Dimeric Peptide Derivatives Based on gp41 Fragments as HIV-1 Fusion Inhibitors. in "Peptide Science 2014," ed. by Akira Otaka, The Japanese Peptide Society, Osaka. 2015

[Conference Activities & Talks]

1. Tamamura H. Development of anti-HIV agents and prevention of HIV infection. Taipei Medical University-Tokyo Medical and Dental University Joint Symposium 2015: Preventive Medicine and Dentistry 2015.05.14 Tokyo, Japan
2. Ohashi N, Nomura W, Minato N, Tamamura H. Development of a FRET Based PKC Ligand Screening Method. The 19th Korean Peptide Protein Symposium 2015.07.06 Taejeon, Korea
3. Honda Y, Nomura W, Fujino M, Murakami T, Tamamura H. Dimerization of C34 Derivatives with C-Terminal Disulfide Bridge and the Addition of an N-Terminal GCGG Sequence Extremely Increase HIV-1 Inhibitory Activity. The 19th Korean Peptide Protein Symposium 2015.07.07 Taejeon, Korea
4. Tamamura H. Development of peptide-lead anti-HIV agents and chemical biology. Department of Pharmacology and Experimental Neuroscience – Seminar Series in University of Nebraska Medical Center 2015.10.02 Omaha, USA
5. Mizuguchi T, Ohashi N, Nomura W, Murakami T, Tamamura H. An anti-HIV assay method for cell-penetrating peptides using chloroquine and identification of inhibitory peptides derived from matrix proteins. The 16th Kumamoto AIDS Seminar 2015.10.08 Kumamoto, Japan
6. Kotani M, Irahara Y, Ishida Y, Harada S, Ohashi N, Yamada Y, Mizuguchi T, Miura T, Nomura W, Matsushita S, Yoshimura K, Tamamura H. New design of small CD4 mimic molecules targeting HIV-1 gp120. 2015.10.08 Kumamoto, Japan
7. Honda Y, Nomura W, Fujino M, Murakami T, Tamamura H. Development of dimeric inhibitors against HIV-1 fusion utilizing disulfide bonds derived from gp41 fragment peptides. The 16th Kumamoto AIDS Seminar 2015.10.08 Kumamoto, Japan
8. Nomura W, Honda Y, Mizuguchi T, Tamamura H. Peptidomimetic-based Mid-size Drug Research: Anti-HIV Agents. The 10th AFMC International Medicinal Chemistry Symposium 2015.10.19 Jeju, Korea
9. Nomura W, Masuda A, Tamamura H. Simultaneous digestion by site-specific nucleases for efficient gene deletion: Study of hTERT promoter function. Conference on Transposition and Genome Engineering 2015 2015.11.19 Nara. Japan
10. Tamamura H. Multivalent ligands showing specific recognition for CXCR4 expression. The Seventh Peptide Engineering Meeting (PEM7) 2015.12.07 Pune, India

11. Tamamura H. Multivalent ligands for CXCR4 with polyproline linkers showing specific recognition for its expression. The 7th International Peptide Symposium 2015.12.11 Singapore, Singapore
12. Nomura W, Masuda A, Tamamura H. Efficient conversion of genomic promoter region by genome engineering systems. Pacificchem 2015 2015.12.17 Honolulu, USA

NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA
Visiting Professor	Kenkichi MASUTOMI
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	Katsuya TSUCHIHARA
Visiting Lecturer	Koji OKAMOTO
Visiting Lecturer	Issay KITABAYASHI
Graduate Students	D3 Sachiyo MIMAKI
	D2 Kasumi OTSUBO
	D1 Yuki YAMAMOTO,
	Yoshihiro MATSUURA
	M2 Yosei RIN
	M1 Masaki NAGASATO,
	Minori YUMOTO,
	Sayaka SUGITA, Manami MIURA

(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. Tsuneki M, Nakamura Y, Kinjo T, Nakanishi R, Arakawa H. Mieap suppresses murine intestinal tumor via its mitochondrial quality control. *Sci Rep.* 5: 12472, 2015.
2. Lessmann T, Maida Y, Tomaru Y, Yasukawa M, Ando Y, Kojima M, Kasim V, Simon C, Daub C, Carninci P, Hayashizaki Y, Masutomi K. TERT regulates microRNAs. *Int J Mol Sci.* 16: 1192-1208, 2015.
3. Neri S, Ishii G, Hashimoto H, Kuwata T, Nagai K, Date H, Ochiai A. Podoplanin-expressing cancer-associated fibroblasts lead and enhance the local invasion of cancer cells in lung adenocarcinoma. *Int*

- J Cancer. 137: 784-796, 2015.
4. Takahashi A, Ishii G, Neri S, Yoshida T, Hashimoto H, Suzuki S, Umemura S, Matsumoto S, Yoh K, Niho S, Goto K, Ohmatsu H, Nagai K, Gemma A, Ohe Y, Ochiai A. Podoplanin-expressing cancer-associated fibroblasts have an inhibitory impact on the tumor growth of small cell lung cancer. *Oncotarget* 6: 9531-9541, 2015.
 5. Koga Y, Manabe S, Aihara Y, Sato R, Tsumura R, Iwafuji H, Furuya F, Fuchigami H, Fujiwara J, Hisada Y, Yamamoto Y, Yasunaga M, Matsumura Y. Antitumor effect of antitissue factor antibody-MMAE conjugate in human pancreatic tumor xenografts. *Int J Cancer*. 137: 1457-1466, 2015.
 6. Yamamoto Y, Hyodo I, Koga Y, Tsumura R, Sato R, Obonai T, Fuchigami H, Furuya F, Yasunaga M, Harada M, Kato Y, Ohtsu A, Matsumura Y. Enhanced antitumor effect of anti-tissue factor antibody-conjugated epirubicin-incorporating micelles in xenograft models. *Cancer Sci*. 106: 627-634, 2015.
 7. Totta P, Pesiri V, Enari M, Marino M, Acconcia F. Clathrin heavy chain interacts with estrogen receptor α and modulates 17β -estradiol signaling. *Mol Endocrinol*. 29: 739-755, 2015.
 8. Tajima T, Kito F, Ohta T, Kawai A, Kondo T. Interactomic approach to SBP1-binding protein in lung adenocarcinoma. *J Electrophoresis*. 59: 1-6, 2015.
 9. Narumi K, Miyakawa R, Ueda R, Hashimoto H, Yamamoto Y, Yoshida T, Aoki K. Proinflammatory proteins S100A8/S100A9 activate natural killer cells via interaction with a receptor of advanced glycation endproduct. *J Immunol*. 194: 5539-5548, 2015.

[Review Articles]

1. Maida Y, Masutomi K. Telomerase reverse transcriptase moonlights: Therapeutic targets beyond telomerase. *Cancer Sci*. 11: 1486-1492, 2015.

[Conference Activities & Talks]

1. Yauyuki Nakamura, Masayuki Tsuneki, Takashi Kinjo, and Hirofumi Arakawa. Critical role of Mieap, a p53-inducible protein, in intestinal tumor suppression. American Association for Cancer Research Annual Meeting (Philadelphia, USA), April, 2015.
2. Yoshiko Maida, Mami Yasukawa, Kenkichi Masutomi. Analysis of RdRP products synthesized by TERT. Cold Spring Harbor Laboratory Meeting "Telomere and Telomerase" (Cold Spring Harbor, NY), April, 2015.
3. Masahiro Yasunaga, Masaru Furuta, Koretsugu Ogata, Yuki Fujiwara, Yoshikatsu Koga, Yasuhiro Matsumura Y. Visualization of drug delivery by using high resolution microscopic mass spectrometry. American Association for Cancer Research Annual Meeting (Philadelphia, USA), April, 2015.
4. Masahiro Yasunaga, Masaru Furuta, Koretsugu Ogata, Yuki Fujiwara, Yoshikatsu Koga, Yasuhiro Matsumura. Molecular imaging of drug delivery by using high resolution microscopic mass spectrometry. 8th World Molecular Imaging Congress (Hawaii, USA), September, 2015.
5. Masahiro Yasunaga. Developmental Strategy of CAST (Cancer Stromal Targeting) therapy. Masahiro Yasunaga. 26th Antibody Engineering & Therapeutics Main Conference (San Diego, USA), December, 2015.
6. Yutaka Shima, Minori Yumoto, Issay Kitabayashi. MLL is essential for NUP98-HOXA9-induced leukemia. 57th Annual meeting of American Society of Hematology (Orlando, USA), December, 2015.

Cellular and Molecular Medicine

associate professor Yumiko Oishi MD., Ph.D

assistant professor Daiki Taneichi Ph.D

assistant professor Shinichiro Hayashi Ph.D

Project 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) Publications

[Original Articles]

1. Yumiko Oishi, Ichiro Manabe. Immunometabolic control of homeostasis and inflammation Inflammation and Regeneration. 2015.09; 35(4); 185-192
2. Jérôme Chal, Masayuki Oginuma, Ziad Al Tanoury, Bénédicte Gobert, Olga Sumara, Aurore Hick, Fanny Bousson, Yasmine Zidouni, Caroline Mursch, Philippe Moncuquet, Olivier Tassy, Stéphane Vincent, Ayako Miyanari, Agata Bera, Jean-Marie Garnier, Getzabel Guevara, Marie Hestin, Leif Kennedy, Shinichiro Hayashi, Bernadette Drayton, Thomas Cherrier, Barbara Gayraud-Morel, Emanuela Gussoni, Frédéric Relaix, Shahragim Tajbakhsh, Olivier Pourquié. Differentiation of pluripotent stem cells to muscle fiber to model Duchenne muscular dystrophy. Nat. Biotechnol.. 2015.09; 33(9); 962-969

[Books etc]

1. Yumiko Oishi, Ichiro Manabe. animal models. 2015.01 (ISBN : 978-4-900487-54-3)

[Misc]

1. Yumiko Oishi. Coordinated regulation of inflammatory response and cellular metabolism in macrophage Endocrinology, Diabetology & Metabolism. 2015.09; 41(3); 230-234

[Conference Activities & Talks]

1. Yumiko Oishi. Coordinated regulation of immune response and lipid homeostasis in macrophages. The 79th Annual Scientific meeting of the Japanese Circulation Society 2015.04.25

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. Sugisawa M, Yamamoto Y, Arakawa S. Evaluation of the effect of implant surface roughness on bacterial biofilm formation Journal of bio-integration society. 2015.05; 5; 85-92
2. Sugisawa M, Ueda D, Arakawa S,. Influence of metallic dental artifact causing different metallic restorations on to CT images Japanese journal of advanced implant medicine. 2015.09; 6(1); 9-15

[Misc]

1. Shinichi Arakawa. Basic characteristic and clinical application of ozone-nanobubble water (NBW3) The Journal of the Japanese Society for Dental Materials and Devices. 2015.01; 34(1); 21-24
2. Arakawa S. Application of functional waters for superaged society: Ozone nano-bubble water Bulletin of the Japanese society for dental products . 2015.09; 9(52); 2-3
3. Arakawa S. The basic knowledge of oral care Tsubasa: malignant lymphoma, pathology and latest treatment . 2015.10; 51; 36-43
4. Arakawa S. Let's start to visiting oral care 1 Dental Hygiene 2015. 2015.11; 35(11); 1232-1235
5. Arakawa S. Let's start to visiting oral care 2 Dental Hygiene 2015. 2015.12; 35(12); 1363-1367
6. Arakawa S. New Frontier for dental clinic Quint News. 2015.12; (240); 6-7
7. Shinichi Arakawa. Ozone antiseptic shows potential for treating severe gum infections Asia Research News 2015.

[Conference Activities & Talks]

1. Sugisawa M, Arakawa S, Hashimoto Y, Yamamoto Y. Evaluation of the effect of implant surface roughness on bacterial biofilm formation. 5th annual meeting of bio-integration society 2015.03.29
2. Ode T, Podyma-Inoue K, Arakawa S, Yokoyama M, Izumi Y. Intracellular cholesterol trafficking is involved in osteoblastic differentiation of MC3T3—E1 cells. 57th Annual meeting of Japanese society of periodontology, International conference 2015.05.15
3. Yoshiko MIURA1, Masayo SUNAGA, Yuki TAKEMAWARI, Wakana MIYA, . Application and evaluation of interactive computer simulation material for dental hygienists.. 2015.07.10 Kagoshima
4. Development of the IPE training program regarding oral care for aged persons who need primary nursing care.- Oral hygiene students instructed medical and dental ones. -. 2015.07.10
5. Arakawa S. The application of ozone nanobubble water to dental treatment. Seminar at Academy of photofunctionalized biomaterials 2015.08.02
6. Sugisawa M, Yamamoto Y, Arakawa S. The effect of surface roughness of implant to biofilm formation. 18th meeting of the Japanese society for advanced implant medicine 2015.09.12
7. Watanabe T, Yasuda M, Kondo K, Arakawa S. The survey for dental needs of mental patients at visiting care facilities. 10th Annual meeting of Japan dental hygienist's association 2015.09.21 Sapporo
8. The survey for dental needs of mental patients at visiting care facilities. 2015.09.21
9. Arakawa S. Application of functional waters for superaged society: Ozone nano-bubble water. Saitama implant association 2015.10.18

10. Arakawa S. Infection control and prevention in dental area and application of slightly acidic electrolytic water. 14th meeting of the japanese society for functional water: Symposium 2015.10.24
11. The cooperation system of perioperative oral management in University Hospital of Tokyo Medical and Dental University. 2015.11.07
12. Sugisawa M, Suda D, Arakawa S. Bactericidal activity of NBW3 to *S. mutans* in different working time . 7th meeting of the society for researches regarding ozone medical treatment 2015.12.06
13. Sawada K, Tan M, Otsuki M, Arakawa s, Tagami J. Effect of ozone gel on tooth bleaching. 80th meeting of the stomatological society 2015.12.26

Oral Care for Systemic Health Support

Professor YOSHIMASU Hidemi
Junior Associate Professor

ONODERA Mitsue
Visiting Lecturer
Kitahara Minoru
Visiting Lecturer
Yazawa Masato

(1) 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 pathophysiological roles of gap junction

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,
Kanao TODA,
Kyoko AKIYAMA,
Mio NAITO

(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**

[Conference Activities & Talks]

1. Mio Naito, Kayoko Shinada, Katsuko Taniyama. Survey on oral health literacy at newspaper printing factories. The 88th Annual Meeting of the Japan Society for Occupational Health 2015.05 Osaka
2. Kayoko Shinada. Oral Health Care Sciences in Japan. 5th Research Week-International Symposium of Oral Medicine College of Oral Medicine, Taipei Medical University 2015.05.17 Taipei

Oral Health Care Science for Community and Welfare

Professor Junichi FURUYA
Junior Associate Professor Keiko ENDO

(1) **Outline**

The goal of the program of Oral Health Care Science for Community and Welfare is to promote oral health optimized for hospitalized, institutionalized, and home-cared patients with inter-professional collaboration in medical treatment, long-term care, and welfare. Specifically, our researches are focused on oral function and meal support to contribute health and quality of life.

(2) **Research**

- 1) Oral hygiene care, dysphagia rehabilitation, and meal support on multidisciplinary team approach medicine.
- 2) Dysphagia, oral functional disorder, and social welfare.
- 3) Removable dentures, masticatory and swallowing function, and denture care.
- 4) Skills and outcomes of oral management by dental professions
- 5) Corporation of medical care, health, nursing-care, and welfare in regional communities.

(3) **Education**

Geriatric dentistry
Social welfare
Team approach in Nutrition Support Team and Palliative Care Team
Dysphagia Rehabilitation

(4) **Lectures & Courses**

The goal of the program of Oral Health Care Science for Community and Welfare is to develop the ability to promote oral health optimized for hospitalized, institutionalized, and home-cared patients with inter-professional collaboration in medical treatment, long-term care, and welfare.

(5) **Publications**

[Original Articles]

1. Yayoi Tanaka, Hirohiko Hirano, Keiko Endo, et al.. Nutrition support by dietitian 2015;
2. Junichi Furuya, Yasushi Tamada, Tomohide Sato, Atsushi Hara, Taro Nomura, Takuya Kobayashi, Maiko Sakai, Hisatomo Kondo. Wearing complete dentures is associated with changes in the three-dimensional shape of the oropharynx in edentulous older people that affect swallowing. Gerodontology. 2015.05;

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. Aki Kuroda, Tomoki Tanaka, Hirohiko Hirano, Yuki Ohara, Takeshi Kikutani, Hiroyasu Furuya, Shuichi P Obuchi, Hisashi Kawai, Shinya Ishii, Masahiro Akishita, Tetsuo Tsuji, Katsuya Iijima. Eating Alone as Social Disengagement is Strongly Associated With Depressive Symptoms in Japanese Community-Dwelling Older Adults. *J Am Med Dir Assoc.* 2015.02;
2. Yuki Ohara, Daisuke Takagi, Ayako Eda, Shihoh Morishita, Yutaka Watanabe, Hirohiko Hirano. Relationship between severity of dementia and oral health status, nutritional status among older people with dementia in group homes *The journal of Japan society for dental hygiene.* 2015.02; 9(2); 69-79
3. Yuki Ohara, Naomi Yoshida, Yoko Kono, Hirohiko Hirano, Hideyo Yoshida, Shiro Mataka, Kumiko Sugimoto. Effectiveness of an oral health educational program on community-dwelling older people with xerostomia. *Geriatr Gerontol Int.* 2015.04; 15(4); 481-489
4. Yuki Ohara, Hirohiko Hirano, Yutaka Watanabe, Shuichi Obuchi, Hideyo Yoshida, Yoshinori Fujiwara, Kazushige Ihara, Hisashi Kawai, Shiro Mataka. Factors associated with self-rated oral health among community-dwelling older Japanese: A cross-sectional study. *Geriatr Gerontol Int.* 2015.06; 15(6); 755-761

5. Kohji Murakami, Hirohiko Hirano, Yutaka Watanabe, Ayako Edahiro, Yuki Ohara, Hideyo Yoshida, Hunkyung Kim, Daisuke Takagi, Shouji Hironaka. Relationship between swallowing function and the skeletal muscle mass of older adults requiring long-term care. *Geriatr Gerontol Int.* 2015.08;
6. 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.* 2015.09;

[Conference Activities & Talks]

1. Yutaka Watanabe, Shiho Morishita, Shino Suma, Ayako Edahiro, Hirohiko Hirano, Keiko Motokawa, Yuki Ohara, Hidenori Arai, Takao Suzuki. The relationship between frailty and oral function in community-dwelling elderly people. The 10th IAGG Asia/Oseania Regional Congress 2015.10.20 Thai, Chiang Mai

Basic Sciences of Oral Health Care

Professor Akira Yamaguchi

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 pharmaceutics.

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 Pharmaceutics.
- Graduation thesis:

(4) Publications

[Original Articles]

1. Sakamoto Y. Spatial relationship between the palatopharyngeus and the superior constrictor of the pharynx. *Surgical and Radiologic Anatomy*. 2015; 37(6); 649-655
2. Yuriko Nishiyama, Tsutomu Matsumoto, Ji-Won Lee, Takashi Saitou, Takeshi Imamura, Keiji Moriyama, Akira Yamaguchi, Tadahiro Iimura. Changes in the spatial distribution of sclerostin in the osteocytic lacuno-canalicular system in alveolar bone due to orthodontic forces, as detected on multimodal confocal fluorescence imaging analyses. *Arch. Oral Biol.*. 2015.01; 60(1); 45-54

[Conference Activities & Talks]

1. Sakamoto Y. Gross anatomical observations on the hypoglossal nerve and the extrinsic muscles of the tongue. International Congress of Clinical Anatomy. 2015.06 Rouen, France.
2. Sakamoto Y. Interrelationships between the insertions of the infrahyoid muscles. The 32nd annual meeting American Association of Clinical Anatomists. 2015.06 Henderson, USA.

Basic Oral Health Engineering

Professor SUGIMOTO Kumiko

Associate Professor

OKI Meiko

Assistant Professor

KAMIJO Shingo

Visiting Lecturer

YANO AKIRA

Visiting Lecturer

Imai Toshiyuki

Visiting Lecturer

Iwasa Yasuyuki

Visiting Lecturer

NAKANE Ayako

Visiting Lecturer

Tsuchihashi Natsumi

Visiting Lecturer

Yamanaka Sato

(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 needs for prosthetic appliances of oral and maxillofacial regions remains high because of rapid progress of aged society in Japan. However, the objective evaluation of effects of wearing prosthetic appliances on oral functions and holistic health has not been performed thoroughly. Thus, we investigate the effects of prosthetic approach and professional intervention by a team including dental technician on stomatognathic function and holistic health from the standpoint of basic sciences such as anatomy and physiology. In addition, we promote integration of basic and clinical researches through collaboration between department faculties working on basic science and clinical field. Based on the findings obtained from these researches, we aim to support people to attain stomatognathic and systemic health and happy living.

(2) Research

Research Subjects

- 1) Changes in autonomic nerve and brain activities induced by taste stimulation
- 2) The sensitivities to taste, olfactory and capsaicin stimulations in the patients of congenital insensitivity to pain with anhidrosis
- 3) Evaluation of oral care for the elderly by dental professionals
- 4) Oral health problems relevant to menopause
- 5) Objective assessment of internal stress during dental treatment by electroencephalogram
- 6) The fabrication of facial prostheses using three dimensional rapid manufacturing method
- 7) Clinical studies of treatments and prostheses for patients with maxillofacial defects
- 8) Development of materials for facial prostheses

- 9) Involvement of dental technicians in community-based oral health care
- 10) The education of dental technician which utilized 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. Sekiya Taki, Miwa Zenzo, Tsuchihashi Natsumi, Uehara Naoko, Sugimoto Kumiko. Analysis of physiological responses associated with emotional changes induced by viewing video images of dental treatment. *Journal of Medical and Dental Sciences*. 2015.03; 62(1); 11-18
2. Yuki Ohara, Naomi Yoshida, Yoko Kono, Hirohiko Hirano, Hideyo Yoshida, Shiro Mataka, Kumiko Sugimoto. Effectiveness of an oral health educational program on community-dwelling older people with xerostomia. *Geriatr Gerontol Int*. 2015.04; 15(4); 481-489
3. Sasipin Lauvahunanon, Hidekazu Takahashi, Meiko Oki, Mansuang Arksornnukit, Masafumi Kanehira, Werner J Finger. In vitro evaluation of the wear resistance of composite resin blocks for CAD/CAM. *Dent Mater J*. 2015.08; 34(4); 495-502
4. H. Imura, M. Shimada, Y. Yamazaki, K. Sugimoto. Characteristic changes in saliva and taste in burning mouth syndrome patients *Journal of Oral Pathology and Medicine*. 2015.08; online(DOI: 10.1111/jop.12350); DOI: 10.1111/jop.12350

[Conference Activities & Talks]

1. Matsushima M, Sugimoto K. Investigation for status of oral oral health in young disabled. 93rd General Session & Exhibition of the IADR 2015.03.11 Boston, USA
2. Imura H, Shimada M, Yamazaki Y, Sugimoto K. Saliva and taste in burning mouth syndrome patients. 93rd General Session & Exhibition of the IADR 2015.03.11 Boston, USA
3. Sugimoto K, Yoshida N, Yamazaki Y, Imura H, Kono Y, Yamanaka S, Sakamaki S, Kimura A . Comparative study of saliva in women at menopause. 93rd General Session & Exhibition of the IADR 2015.03.11 Boston, USA
4. Yoshida N, Sugimoto K, Yamazaki Y, Imura H, Kono Y, Yamanaka S, Sakamaki H, Kimura A. Subjective evaluation of oral health in menopausal stage. 93rd General Session & Exhibition of the IADR 2015.03.11 Boston, USA
5. Yoko Kono, Ayako Kubota, Mika Matsushima, Masato Taira, Kumiko Sugimoto. Influences of intraoral stimulation with capsaicin on salivary secretion and neural activities. 49th Meeting of The Japanese Association for the Study on Taste and Smell 2015.09.24 Gifu, Japan

6. Lauvahutanon S, Takahashi H, Oki M, Arksornnukit M, Kanehira M, FINGER WJ. Wear resistance of CAD/CAM composite resin blocks. Annual meeting of Academy of Dental Materials 2015.10.09 Maui, Hawaii, USA
7. Kumiko Sugimoto. Stream from basic taste research to oral health science . 2015.12.26

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)
Reaserch student Chen Hsuan (July, Taipei Medical Univ.)
Reaserch 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 exerise for dental materials and prosthetic traing are also provided.
Development and evaluation of new dental materials are preformed.

(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. Applicayion 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

[Original Articles]

1. Maho Shiozawa, Hidekazu Takahashi, Yuya Asakawa, Naohiko Iwasaki. Color stability of adhesive resin cements after immersion in coffee. Clin Oral Investig. 2015.05;
2. Chowdhury RU, Churei H, Takahashi H, Shahrin S, Fukasawa S, Shrestha A, Negoro T, Ueno T. Suitable design of mouthguard for sports active person with spaced dentition Dental Traumatology. 2015.06; 31(3); 238-242
3. Sasipin Lauvahutanon, Hidekazu Takahashi, Meiko Oki, Mansuang Arksornnukit, Masafumi Kanehira, Werner J Finger. In vitro evaluation of the wear resistance of composite resin blocks for CAD/CAM. Dent Mater J. 2015.08; 34(4); 495-502
4. Rade D Paravina, Razvan Ghinea, Luis J Herrera, Alvaro D Bona, Christopher Igiel, Mercedes Linninger, Maiko Sakai, Hidekazu Takahashi, Esam Tashkandi, Maria del Mar Perez. Color difference thresholds in dentistry. J Esthet Restor Dent. 27 Suppl 1; S1-S9

[Books etc]

1. Kei-ichi Ishigami, Toshiaki Ueno, Misao Kawara, Yoshinobu Maeda, Toshikazu Yasui. Yousetsu Sports Dentistry. Igaku Joho-Sha Ltd., 2015.01 (ISBN : 978-4-903553-53-5)

[Conference Activities & Talks]

1. Takahashi H, Iwasaki N, Yuzaki K. New Evaluation Model for Marginal Edge Reproducibility of CAD/CAM Blanks.. 2015 IADR/AADR/CADR General Session 2015.03.11 Boston, USA
2. Kajima Y, Takaichi A, Yasue T, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Evaluation of the shear bond strength of dental porcelain to Zr-14Nb alloy with low magnetic susceptibility. 4th TRI university consortium 2015.05 Thailand Chulalongkorn University
3. Lauvahutanon S, Takahashi H, Oki M, Arksornnukit M, Kanehira M, FINGER WJ. Wear resistance of CAD/CAM composite resin blocks. Annual meeting of Academy of Dental Materials 2015.10.09 Maui, Hawaii, USA
4. Takaichi A, Kajima Y, Yasue T, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Evaluation of the shear bond strength of dental porcelain to Zr-14Nb alloy with low magnetic susceptibility. 6th International Conference on Mechanics of Biomaterials and Tissues 2015.12 Hawaii, USA

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. Hua Qiao, Rena Takahashi, Toru Nikaido, Syozi Nakashima, Alireza Sadr, Masaomi Ikeda, Junji Tagami. Change of dentin permeability in different storage media after resin coating Asian Pacific Journal of Dentistry. 2015; 15(2); 33-40
2. Wada I, Shimada Y, Ikeda M, Sadr A, Nakashima S, Tagami J, Sumi Y.. Clinical assessment of non carious cervical lesion using swept-source optical coherence tomography. Journal of Biophotonics.

[Misc]

1. Sahar J Khunkar, Sachiko Utaka, Ilnaz Hariri, Alireza Sadr, Masaomi Ikeda, Syozi Nakashima, Toru Nikaido, Junji Tagami. Formation and characterization of hypermineralized zone beneath dentine lesion body induced by topical fluoride in-vitro. Arch. Oral Biol.. 2015.04; 60(4); 574-581

[Conference Activities & Talks]

1. ARAOKA Daisuke, SATO Kento, TAKAHASHI Masahiro, IKEDA Masaomi, HOSAKA Keiichi, NAKAJIMA Masatoshi, TAGAMI Junji. The effect of light curing of universal primer on the bond strengths of dual cure resin cement. 2015.06.25 Kitakyusyu

Department of Pharmacovigilance

Professor
Masayoshi Harigai
Masaaki Mori

Associate Professor
Ryuji Koike
Kenji Nagasaka

Junior Associate Professor
Michi Tanaka

Assistant Professor
Ryoko Sakai

Waka Yokoyama

Graduate Student
Fumio Hirano
Mari Kihara
Shoko Kasai
Masako Utsunomiya
Sayoko Harada

Research Pharmacist
Marie Yajima

Secretary
Tomoko Takahashi

(1) Research

Studies of rheumatoid arthritis

1. Registry of Japanese rheumatoid arthritis patients on biologics for long-term safety (REAL study)
2. Clinical outcomes of Japanese rheumatoid arthritis patients in real world commencing targeted therapy (CORRECT)
3. Safety of biologics in clinical use in Japanese patients with rheumatoid arthritis in long-term (SECURE study)
4. Effectiveness and safety of abatacept in Japanese patients with rheumatoid arthritis in clinical setting
5. Analysis of gene expression in Japanese rheumatoid arthritis patients treated with abatacept
6. Population-based study of comorbidities and safety in patients with rheumatoid arthritis using Japanese health insurance database
7. Clinical epidemiological study of treat-to-target strategy in rheumatoid arthritis patients with moderate to high disease activity
8. A randomized controlled trial for efficacy and safety of programmed intensive treatment with methotrexate

as an anchor drug in patients with active rheumatoid arthritis

9. Usefulness of Rheumascan for rheumatoid arthritis and rheumatic disease

10. Efficacy and safety of treatment with moderate doses of corticosteroid and immunosuppressants in rheumatoid arthritis patients with interstitial lung diseases

11. Integrated analyses of risk factors for pneumocystis pneumonia in rheumatoid arthritis patients treated with TNF inhibitor

Studies of vasculitides

1. Revision of clinical guidelines of antineutrophil cytoplasmic antibody-associated vasculitis

2. Identification of susceptibility genes associated with anti-neutrophil cytoplasm antibody-associated vasculitis in Japanese

Study of rheumatic disease and infection

1. A randomized clinical trial on the efficacy and tolerability of dose reduction and escalation regimen of Trimethoprim/Sulfamethoxazole (TMP/SMX) in patients with rheumatic diseases

Studies of pediatric rheumatic disease and infection

1. Detection of Kawasaki disease-related protein and inspection of the usefulness as the biomarker

2. National survey about the aggravation by respiratory syncytial (RS) virus infection in the immunodeficiency child

(2) Education

Department of Pharmacovigilance has established since 2005 and dedicated to pharmacovigilance activity in the field of rheumatology. Main objective of Department of Pharmacovigilance in the graduate course is to provide students opportunity to study basics of pharmacoepidemiology including clinical statistics and to implement epidemiological studies in pharmacovigilance using some databases which have been maintained by this department.

(3) Clinical Services & Other Works

Most of the members of Department of Pharmacovigilance are rheumatologists and engaged in clinical services in the field of rheumatology as specialists.

(4) Publications

[Original Articles]

1. Ken-ei Sada, Masahiro Yamamura, Masayoshi Harigai, Takao Fujii, Yoshinari Takasaki, Koichi Amano, Shouichi Fujimoto, Eri Muso, Yohko Murakawa, Yoshihiro Arimura, Hirofumi Makino, . Different responses to treatment across classified diseases and severities in Japanese patients with microscopic polyangiitis and granulomatosis with polyangiitis: a nationwide prospective inception cohort study. *Arthritis Res. Ther.* 2015; 17; 305
2. Wataru Hirose, Takashi Uchiyama, Asuka Nemoto, Masayoshi Harigai, Kenji Itoh, Toshiaki Ishizuka, Mitsuyo Matsumoto, Kazue Yamaoka, Toshihiro Nanki. Diagnostic performance of measuring antibodies to the glycopeptidolipid core antigen specific to *Mycobacterium avium* complex in patients with rheumatoid arthritis: results from a cross-sectional observational study. *Arthritis Res. Ther.* 2015; 17; 273
3. Ryoko Sakai, Soo-Kyung Cho, Toshihiro Nanki, Kaori Watanabe, Hayato Yamazaki, Michi Tanaka, Ryuji Koike, Yoshiya Tanaka, Kazuyoshi Saito, Shintaro Hirata, Koichi Amano, Hayato Nagasawa, Takayuki Sumida, Taichi Hayashi, Takahiko Sugihara, Hiroaki Dobashi, Shinsuke Yasuda, Tetsuji Sawada, Kazuhiko Ezawa, Atsuhisa Ueda, Takao Fujii, Kiyoshi Migita, Nobuyuki Miyasaka, Masayoshi Harigai, . Head-to-head comparison of the safety of tocilizumab and tumor necrosis factor inhibitors in rheumatoid arthritis patients (RA) in clinical practice: results from the registry of Japanese RA patients on biologics for long-term safety (REAL) registry. *Arthritis Res. Ther.* 2015; 17; 74

4. Hirokazu Sasaki, Masako Inagaki, Mikio Shioda, Kenji Nagasaka. Poncet's disease with high titers of rheumatoid factor and anti-citrullinated peptide antibodies mimicking rheumatoid arthritis. *J. Infect. Chemother.* 2015.01; 21(1); 65-69
5. Kaneko Yuko, Koike Takao, Oda Hiromi, Yamamoto Kazuhiko, Miyasaka Nobuyuki, Harigai Masayoshi, Yamanaka Hisashi, Ishiguro Naoki, Tanaka Yoshiya, Takeuchi Tsutomu. Obstacles to the implementation of the treat-to-target strategy for rheumatoid arthritis in clinical practice in Japan. *Mod Rheumatol.* 2015.01; 25(1); 43-49
6. Katsuji Nishimura, Masako Omori, Yasuhiro Katsumata, Eri Sato, Takahisa Gono, Yasushi Kawaguchi, Masayoshi Harigai, Masaru Mimura, Hisashi Yamanaka, Jun Ishigooka. Neurocognitive impairment in corticosteroid-naïve patients with active systemic lupus erythematosus: a prospective study. *J. Rheumatol.* 2015.03; 42(3); 441-448
7. Yamazaki H, Sakai R, Koike R, Miyazaki Y, Tanaka M, Nanki T, Watanabe K, Yasuda S, Kurita T, Kaneko Y, Tanaka Y, Nishioka Y, Takasaki Y, Nagasaka K, Nagasawa H, Tohma S, Dohi M, Sugihara T, Sugiyama H, Kawaguchi Y, Inase N, Ochi S, Hagiyaama H, Kohsaka H, Miyasaka N, Harigai M. Assessment of risks of pulmonary infection during 12 months following immunosuppressive treatment for active connective tissue diseases: a large-scale prospective cohort study. *J Rheumatol.* 2015.04; 42(4); 614-622
8. Michi Tanaka, Ryoko Sakai, Ryuji Koike, Masayoshi Harigai. Pneumocystis Jirovecii Pneumonia in Japanese Patients with Rheumatoid Arthritis Treated with Tumor Necrosis Factor Inhibitors: A Pooled Analysis of 3 Agents. *J. Rheumatol.* 2015.09; 42(9); 1726-1728
9. Yoshiya Tanaka, Masayoshi Harigai, Tsutomu Takeuchi, Hisashi Yamanaka, Naoki Ishiguro, Kazuhiko Yamamoto, Yutaka Ishii, Hiroshi Nakajima, Daniel Baker, Nobuyuki Miyasaka, Takao Koike. Prevention of joint destruction in patients with high disease activity or high C-reactive protein levels: Post hoc analysis of the GO-FORTH study. *Mod Rheumatol.* 2015.10; 1-8
10. Sakai Ryoko, Hirano Fumio, Kihara Mari, Yokoyama Waka, Yamazaki Hayato, Harada Sayoko, Nanki Toshihiro, Koike Ryuji, Miyasaka Nobuyuki, Harigai Masayoshi. High prevalence of cardiovascular comorbidities in patients with rheumatoid arthritis from a population-based cross-sectional study of a Japanese health insurance database. *Mod Rheumatol.* 2015.12; 1-7
11. Yoshiya Tanaka, Masayoshi Harigai, Tsutomu Takeuchi, Hisashi Yamanaka, Naoki Ishiguro, Kazuhiko Yamamoto, Nobuyuki Miyasaka, Takao Koike, Daniel Baker, Yutaka Ishii, Toru Yoshinari, . Clinical efficacy, radiographic progression, and safety through 156 weeks of therapy with subcutaneous golimumab in combination with methotrexate in Japanese patients with active rheumatoid arthritis despite prior methotrexate therapy: final results of the randomized GO-FORTH trial. *Mod Rheumatol.* 2015.12; 1-10

[Misc]

1. Kenji Nagasaka. Efficacy of tocilizumab for giant cell arteritis and Takayasu arteritis *Rheumatology.* 2015.04; 53(4); 355-362
2. Kenji Nagasaka. Primary small and medium vessel vasculitis *Rheumatology.* 2015.09; 54(3); 287-295

[Conference Activities & Talks]

1. F. Hirano, W. Yokoyama, H. Yamazaki, K. Amano, Y. Kaneko, A. Kawakami, T. Matsui, R. Sakai, R. Koike, N. Miyasaka, M. Harigai. SDAI REMISSION AT WEEK 24 IS A PREDICTOR OF GOOD FUNCTIONAL AND STRUCTURAL OUTCOMES AT WEEK 72 IN A T2T IMPLEMENTING COHORT. EULAR2015 2015.06.11 Rome

Department of Nanomedicine

Associate Professor Motohiro Komaki
Lecturer Kengo Iwasaki
Project researchers Naoki Yokoyama

(1) Outline

Department of Nanomedicine has been established as endow courses in 2005 by a suggestion of Ikuo Morita (Excutive director and Excutive 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 periodontolgy (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 cell 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. Honda I, Taki A, Morioka C, Komaki M et al.. Mesenchymal stem cells ameliorate intra-amniotic inflammation-related neonatal complications in rats Inflammation and Regeneration. 2015.11; 35(5); 261-268
2. 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. 2015.12; e-pub

[Conference Activities & Talks]

1. The influence of intrauterine inflammation on umbilical cord derived mesenchymal stem cells. 2015.03.24
2. Chikako Morioka, Atsuko Taki, Manabu Sugie, Kazuyuki Ito, Tomohiro Morio, Ikuo Morita. A novel therapy for Periventricular leucomalacia using umbilical cord derived mesenchymal stem cell. The 118th Annual Meeting of the Japan Pediatric Society 2015.04.17
3. Nagata M et al.. The influence of concentration ratio of culture medium from periodontal ligament stem cells on periodontal regeneration. The 58th Spring Meeting of the Japanese Society of Periodontology 2015.05
4. Motohiro Komaki et al.. Angiogenic effects of Placenta derived mesenchymal stem cell-conditioned medium. 2015.05.15
5. The effects of mesenchymal stem cell exosomes on differentiation of dermal fibroblasts. 2015.07.21
6. Masahiro Noda, Akira Aoki, Koji Mizutani, Taichen Lin, Motohiro Komaki, Shunichi Shibata, Yuichi Izumi. Effect of low-level laser therapy on early stage of wound healing of tooth extraction socket. The 58th Autumn Meeting of the Japanese Society of Periodontology 2015.09.13 Hamamatsu
7. Culture medium from periodontal ligament stem cells enhance periodontal wound healing. 2015.11.12

Department of Liver Disease Control

Professor	Yasuhiro ASAHINA
Senior Associate Professor	Sei KAKINUMA

Graduate Student
(collaboration with Department of Gastroenterology and Hepatology in TMDU)
Satoshi OHTANI (-03/2015), Fukiko KAWAI-KITAHATA (-03/2015),
Miki TANIGUCHI (-03/2015), Fumio GOTO, Shun KANEKO,
Hiroko NAGATA, Yu ASANO, Emi INOUE, Tomoyuki TSUNODA (04/2015-),
Masato MIYOSHI (04/2015-)

(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 liver failure. Because of a serious shortage of donors, 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 chronic 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 primary goal is to train highly educated and experienced clinician-researchers in the field of hepatology.

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 study are collaboration with the Department of Gastroenterology and Hepatology in TMDU.

The final goal of our education is to promote students to become a well-developed hepatologist, and also a leading expert in the field of hepatology.

(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 focused the basic studies using viral and immunological strategy, the research for molecular mechanisms of liver tissue regeneration and fibrogenesis in liver, and the study for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells.

Research projects

- Analysis of molecular mechanisms underlying resistance to anti-viral therapy for eradication of hepatitis viruses.
- Analysis of molecular mechanisms underlying proliferation and differentiation of hepatic stem/progenitor cells.
- Exploration of liver cancer-related genes essential for disease progression.
- Regenerative medical science of liver.

(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. For the education of undergraduate and graduate students in TMDU and clinical residents in TMDU Medical Hospital, we collaborate with the Department of Gastroenterology and Hepatology in TMDU.

(4) Lectures & Courses

Our Lectures and Courses are collaboration with the Department of Gastroenterology and Hepatology in TMDU. We also educate graduate students of the Department of Gastroenterology and Hepatology in TMDU in collaboration with such department.

(5) Clinical Services & Other Works

In the clinical section, we pursue development and application of highly advanced technologies, including novel procedures, for sophisticated diagnosis and treatment of liver diseases. For the treatment of patients with liver diseases in TMDU Medical Hospital, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. We also operate a lot of multicenter study collaborating with the Department of Gastroenterology and Hepatology in TMDU. We participate in five research committees for treatment and eradication of hepatitis virus funded by the Ministry of Health, Labor and Welfare of Japan in this year. 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

Clinical projects

- Prevention of progression to hepatocellular carcinoma and liver failure in patients with chronic hepatitis based on virological treatment strategy.
- Clinical trial of innovative treatment for hepatocellular carcinoma.
- Development of novel diagnostic and therapeutic strategy valuable for validation of the individual risk for liver cancer and diagnosis of early liver cancer.

(7) Publications

[Original Articles]

1. Taniguchi M, Tasaka-Fujita M, Nakagawa M, Watanabe T, Kawai-Kitahata F, Otani S, Goto F, Nagata H, Kaneko S, Nitta S, Murakawa M, Nishimura-Sakurai Y, Azuma S, Itsui Y, Mori K, Yagi S, Kakinuma S, Asahina Y, Watanabe M. Evaluation of IFN resistance in newly established genotype 1b HCV cell culture system.(in press) *Journal of Clinical and Translational Hepatology*. 2015;
2. Miyako Murakawa, Yasuhiro Asahina, Mina Nakagawa, Naoya Sakamoto, Sayuri Nitta, Akiko Kusano-Kitazume, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Miki Taniguchi, Fumio Goto, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. Impaired induction of interleukin 28B and expression of interferon λ 4 associated with nonresponse to interferon-based therapy in chronic hepatitis C. *J Gastroenterol Hepatol*. 2015.06; 30(6); 1075-1084
3. 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.[Epub ahead of print] *Hepatol Res*. 2015.07;
4. Megumi Tasaka-Fujita, Nao Sugiyama, Wonseok Kang, Takahiro Masaski, Asako Murayama, Norie Yamada, Ryuichi Sugiyama, Senko Tsukuda, Koichi Watashi, Yasuhiro Asahina, Naoya Sakamoto, Takaji Wakita, Eui-Cheol Shin, Takanobu Kato. Amino acid polymorphisms in hepatitis C virus core affect

infectious virus production and major histocompatibility complex class I molecule expression. *Sci Rep.* 2015.09; 5; 13994

5. Nobuharu Tamaki, Masayuki Kurosaki, Mayu Higuchi, Hitomi Takada, Natsuko Nakakuki, Yutaka Yasui, Shoko Suzuki, Kaoru Tsuchiya, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Shintaro Ogawa, Yasuhito Tanaka, Yasuhiro Asahina, Namiki Izumi. Genetic polymorphisms of IL28B and PNPLA3 are predictive for HCV related rapid fibrosis progression and identify patients who require urgent antiviral treatment with new regimens. *PLoS ONE.* 2015.09; 10(9); e0137351
6. 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.[Epub ahead of print] *J Gastroenterol.* 2015.11;

[Conference Activities & Talks]

1. Asahina Y, Kawai-Kitahata F, Kaneko S, Nagata H, Goto F, Otani S, Taniguchi M, Murakawa M, Nitta S, Watanabe T, Tasaka-Fujita M, Nishimura-Sakurai Y, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Tanaka S, Tanabe M, Enomoto N, Watanabe M. Gene alterations in tert promoter, CTNNB1, and TP53 are closely associated with development and prognosis of hepatocellular carcinoma: comprehensive analyses by next generation sequencing technology. 50th The International liver congress 2015, EASL 2015.04.22 Vienna
2. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Otani, Miki Taniguchi, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Shinji Tanaka, Minoru Tanabe, Nobuyuki Enomoto and Mamoru Watanabe. Gene alterations in TERT promoter, CTNNB1, and TP53 are closely associated with development and prognosis of hepatocellular carcinoma : Comprehensive analyses by next generation sequencing technology. The 3rd JSGE International Topic Conference 2015.04.24 Sendai
3. Satoshi Otani, Sei Kakinuma, Mamoru Watanabe. Matrix Metalloproteinase(MMP)-14 regulates the differentiation of hepatic stem/progenitor cells. The 3rd JSGE International Topic Conference 2015.04.25 Sendai
4. Sayuri Nitta, Yasuhiro Asahina, Takaji Wakita, Takanobu Kato. Effects of Resistance Mutations of NS5A Inhibitor on Viral Production and Susceptibility to Anti-HCV Reagents in Recombinant Hepatitis C Viruses with NS5A of Genotype 1b. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
5. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Hiroko Nagata, Syun Kaneko, Sayuri Nitta, Takako Watanabe, Yasuhiro Itsui, Mina Nakagawa, Sei Kakinuma, Sayuki Iijima, Yasuhito Tanaka, Mamoru Watanabe, Yujiro Tanaka. Expression of IFN λ 4 in liver is closely associated with non-response to antiviral therapy through the regulation of basal expression of ISGs in chronic hepatitis C patients but not in hepatitis B patients. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
6. Takako Watanabe, Yasuhiro Asahina, Mina Nakagawa, Sei Kakinuma, Yasuhiro Itsui, Hiroko Nagata, Miyako Murakawa, Fukiko Kawai-Kitahata, Mika Miura, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Serial change of resistant associated variants during early phase of NS3/4A triple therapy and the final virological outcome: analyses by ultra-deep sequencing technology. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
7. Hiroko Nagata, Yasuhiro Itsui, Fukiko Kawai-Kitahata, Shun Kaneko, Miyako Murakawa, Sayuri Nitta, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Yasuhiro Asahina. Variations of the host genome and interaction of hepatitis B viral X protein associated with hepatocarcinogenesis. AASLD The Liver Meeting 2015 2015.11.13 San Francisco, CA
8. Kawai-Kitahata F, Asahina Y, Tanaka S, Kakinuma S, Murakawa M, Nitta S, Watanabe T, Otani S, Goto F, Nagata H, Kaneko S, 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 with clinicopathological features. AASLD The Liver Meeting 2015 2015.11.14 San Francisco, CA

9. Shun Kaneko, Sei Kakinuma, Yasuhiro Asahina, Akihide Kamiya, Sayuri Nitta, Tomoyuki Tsunoda, Masato Miyoshi, Hiroko Nagata, Fumio Goto, Satoshi Otani, Miyako Murakawa, Fukiko Kawai-Kitahata, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Mamoru Watanabe. Human induced pluripotent stem cell-derived hepatic progenitor-like cells and hepatocyte-like cells as a model for interaction between hepatitis B virus and host cells. AASLD The Liver Meeting 2015 2015.11.16 San Francisco, CA

Department of Advanced Therapeutics for GI Diseases

Professor	Tetsuya NAKAMURA
Junior Associate Professor	Katsuyoshi MATSUOKA
Assistant Professor	Tomohiro MIZUTANI

Graduate Student
Kengo NOZAKI, Taichi MATSUMOTO, Yuka MATSUMOTO, Shintaro AKIYAMA, Yuria TAKEI

(1) Outline

The goal of our department is to develop novel therapeutic strategies for inflammatory bowel diseases (IBD) in humans. With the 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. Hiroki Kiyohara, Tadakazu Hisamatsu, Katsuyoshi Matsuoka, Makoto Naganuma, Hideto Kameda, Noriyuki Seta, Tsutomu Takeuchi, Takanori Kanai. Crohn's Disease in which the Patient Developed Aortitis during Treatment with Adalimumab. *Intern Med.* 2015; 54(14); 1725-1732
2. Hayashi R, Tsuchiya K, Fukushima K, Horita N, Hibiya S, Kitagaki K, Negi M, Itoh E, Akashi T, Eishi Y, Okada E, Araki A, Ohtsuka K, Fukuda S, Ohno H, Okamoto R, Nakamura T, Tanaka S, Chayama K, Watanabe M. Reduced human α -defensin 6 in non-inflamed jejunal tissue of Crohn's disease patients. (in press) *Inflamm Bowel Dis.* 2015;
3. Yu Matsuzawa, Shigeru Oshima, Yoichi Nibe, Masanori Kobayashi, Chiaki Maeyashiki, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. RIPK3 regulates p62-LC3 complex formation via the caspase-8-dependent cleavage of p62. *Biochem Biophys Res Commun.* 2015.01; 456(1); 298-304
4. Katsuyoshi Matsuoka, Takanori Kanai. The gut microbiota and inflammatory bowel disease. *Semin Immunopathol.* 2015.01; 37(1); 47-55
5. Atsushi Sakuraba, Susumu Okamoto, Katsuyoshi Matsuoka, Toshiro Sato, Makoto Naganuma, Tadakazu Hisamatsu, Yasushi Iwao, Haruhiko Ogata, Takanori Kanai, Toshifumi Hibi. Combination therapy with infliximab and thiopurine compared to infliximab monotherapy in maintaining remission of postoperative Crohn's disease. *Digestion.* 2015.04; 91(3); 233-238
6. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Masakazu Nagahori, Toshimitsu Fujii, Eiko Saito, Tomoyuki Fujioka, Katsuyoshi Matsuoka, Makoto Naganuma, Mamoru Watanabe. Correlation of the Endoscopic and Magnetic Resonance Scoring Systems in the Deep Small Intestine in Crohn's Disease. *Inflamm Bowel Dis.* 2015.05; 21(8); 1832-1838
7. Yu Matsuzawa, Shigeru Oshima, Masahiro Takahara, Chiaki Maeyashiki, Yasuhiro Nemoto, Masanori Kobayashi, Yoichi Nibe, Kengo Nozaki, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Averil Ma, Mamoru Watanabe. TNFAIP3 promotes survival of CD4 T cells by restricting MTOR and promoting autophagy. *Autophagy.* 2015.06; 11(7); 1052-1062
8. Tetsuro Takayama, Susumu Okamoto, Tadakazu Hisamatsu, Makoto Naganuma, Katsuyoshi Matsuoka, Shinta Mizuno, Rieko Bessho, Toshifumi Hibi, Takanori Kanai. Computer-Aided Prediction of Long-Term Prognosis of Patients with Ulcerative Colitis after Cytoapheresis Therapy. *PLoS ONE.* 2015.06; 10(6); e0131197
9. Katsuyoshi Matsuoka, Eiko Saito, Toshimitsu Fujii, Kento Takenaka, Maiko Kimura, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Tacrolimus for the Treatment of Ulcerative Colitis. *Intest Res.* 2015.07; 13(3); 219-226
10. Tadakazu Hisamatsu, Nobukazu Ono, Akira Imaizumi, Maiko Mori, Hiroaki Suzuki, Michihide Uo, Masaki Hashimoto, Makoto Naganuma, Katsuyoshi Matsuoka, Shinta Mizuno, Mina T Kitazume, Tomoharu Yajima, Haruhiko Ogata, Yasushi Iwao, Toshifumi Hibi, Takanori Kanai. Decreased Plasma Histidine Level Predicts Risk of Relapse in Patients with Ulcerative Colitis in Remission. *PLoS ONE.* 2015.10; 10(10); e0140716
11. Naoki Yoshimura, Yoko Yokoyama, Katsuyoshi Matsuoka, Hiroki Takahashi, Ryuichi Iwakiri, Takayuki Yamamoto, Tomoo Nakagawa, Takumi Fukuchi, Satoshi Motoya, Reiko Kunisaki, Shingo Kato, Fumihito Hirai, Yoh Ishiguro, Satoshi Tanida, Sakiko Hiraoka, Keiichi Mitsuyama, Shunji Ishihara, Shinji Tanaka, Michiro Otaka, Taro Osada, Takashi Kagaya, Yasuo Suzuki, Hiroshi Nakase, Hiroyuki Hanai,

Kenji Watanabe, Nobuhito Kashiwagi, Toshifumi Hibi. An open-label prospective randomized multicenter study of intensive versus weekly granulocyte and monocyte apheresis in active crohn's disease. *BMC Gastroenterol.* 2015.11; 15(1); 163

12. Yasuyo Wada, Tadakazu Hisamatsu, Makoto Naganuma, Katsuyoshi Matsuoka, Susumu Okamoto, Nagamu Inoue, Tomoharu Yajima, Keisuke Kouyama, Yasushi Iwao, Haruhiko Ogata, Toshifumi Hibi, Takayuki Abe, Takanori Kanai. Risk factors for decreased bone mineral density in inflammatory bowel disease: A cross-sectional study. *Clin Nutr.* 2015.12; 34(6); 1202-1209

[Conference Activities & Talks]

1. Matsuoka K, Saito E, Fujii T, Takenaka K, Nagahori M, Ohtsuka K, Watanabe M. The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) is useful to evaluate endoscopic improvement and to predict medium-term prognosis in Ulcerative Colitis patients treated with tacrolimus. 10th Congress of ECCO - Inflammatory Bowel Diseases 2015 2015.02.20 Barcelona
2. Hibiya S, Tsuchiya K, Fukushima K, Hayashi R, Horita N, Oshima S, Okamoto R, Nakamura T, Watanabe M. Long-term stimulation with cytokines acquires irreersible accumulation of NF- κ B signaling in colonic epithelial cells. 10th Congress of ECCO - Inflammatory Bowel Diseases 2015 2015.02.20 Barcelona
3. Hibiya S, Tsuchiya K, Fukushima K, Hayashi R, Horita N, Kano Y, Okamoto R, Nakamura T, Watanabe M. Continous stimulation with cytokines leads to irreversible accumulation of NF- κ B signaling in colonic epithelial cells. The 5th International Symposium on Carcinogenic Spiral 2015.02.26 Kobe
4. Nozaki K, Mochizuki W, Matsumoto Y, Matsumoto T, Fukuda M, Mizutani T, Watanabe M, Nakamura T. Live imaging analysis of intraepithelial lymphocytes (IELs) co-cultured with intestinal epithelial organoids. Cold Spring Harbor Meeting "Fundamental Immunology and Its Therapeutic Applications" 2015.04.16 New York
5. Matsuoka K, Kuwahara E, Nishiwaki Y, Watanabe M. Epidemiology and temporal change of IBD management in Japan: Results from the Japanese IBD registry data. Annual Meeting of KASID 2015 2015.04.19 Seoul
6. Katsuyoshi Matsuoka, Makoto Naganuma, Takanori Kanai. New drug development for inflammatory bowel disease in Japan : an example of collaboration between academia, industry, and government. The 101st General Meeting of the Japanese Society of Gastroenterology 2015.04.25 Sendai
7. Hiromichi Shimizu, Kohei Suzuki, Satoru Fujii, Toru Nakata, Go Ito, Tatsuro Murano, Kiichiro Tsuchiya, Tetsuya Nakamura, Ryuichi Okamoto, Katsuto Hozumi, Mamoru Watanabe. Notch Ligands DLL1 and Dll4 Are Expressed by Distinct Population of Epithelial Cells in the Mice Intestine. DDW 2015 2015.05.16 Washington, D.C.
8. Keita Fukushima, Kiichiro Tsuchiya, Shuji Hibiya, Ryohei Hayashi, Nobukatsu Horita, Yoshihito Kano, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Atoh1 Protein Expression by TNF- α and the Acquisition of Malignant Potential in Colitis- Associated Colorectal Cancer. DDW 2015 2015.05.17 Washington, D.C.
9. Toshimitsu Fujii, Kento Takenaka, Eiko Saito, Katsuyoshi Matsuoka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Modifying and Validating Endoscopic and Magnetic Resonance Scoring Systems for the Deep Small Intestine in Crohn's Disease. DDW 2015 2015.05.17 Washington, D.C.
10. Shuji Hibiya, Kiichiro Tsuchiya, Keita Fukushima, Ryohei Hayashi, Nobukatsu Horita, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Continuous Stimulation With Cytokines Leads to Irreversible Accumulation of NF- κ B Signaling in Colonic Epithelial Cells. DDW 2015 2015.05.19 Washington, D.C.
11. Toru Nakata, Hiromichi Shimizu, Kohei Suzuki, Satoru Fujii, Go Ito, Kiichiro Tsuchiya, Tetsuya Nakamura, Ryuichi Okamoto, Katsuto Hozumi, Mamoru Watanabe. Distinct Role of Notch Ligands, DLL1 and Dll4, in Normal and in Tumor Intestinal Epithelium. DDW 2015 2015.05.19 Washington, D.C.
12. Tomoaki Shirasaki, Keita Fukushima, Kiichiro Tsuchiya, Shuui Hibiya, Ryohei Hayashi, Nobukatsu Horita, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Atoh1 protein stabilized by TNF- α acquires enhanced malignant potential in colitis-associated colorectal cancer. AOCC2015 2015.06.19 Beijing

13. Kohei Suzuki, Satoru Fujii, Toru Nakata, Ami Kawamoto, Fumiaki Ishibashi, Sayaka Ohashi Segawa, Tomohiro Mizutani, Kiichiro Tsuchiya, Kazuo Otsuka, Tetsuya Nakamura, Ryuichi Okamoto, Mamoru Watanabe. Enrichment of Intestinal Stem Cells by the 3D-Culture of IBD Patient Derived Intestinal epithelium. AOCC2015 2015.06.19 Beijing
14. Nobuyuki Horita, Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Shuji Hibiya, Masayoshi Fukuda, Tomohiro Mizutani, Ryuichi Okamoto, Tetsuya Nakamura and Mamoru Watanabe. A novel fluorescent labelling system into small intestinal organoid reveals independent long-lived intestinal stem cells in a crypt. AOCC2015 2015.06.19 Beijing
15. Katsuyoshi Matsuoka. Poster Round Group 6 (Chair) . AOCC2015 2015.06.19 Beijing
16. Katsuyoshi Matsuoka. Novel Diagnostic Criteria for Intestinal Behcet's Disease: The Reality. AOCC2015 2015.06.19 Beijing
17. Toshimitsu Fujii, Kento Takenaka, Yoshio Kitazume, Eriko Saito, Katsuyoshi Matsuoka, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Modifying and validating endoscopic and magnetic resonance scoring systems for the deep small intestine in Crohn's disease. AOCC2015 2015.06.19 Beijing
18. Tetsuya Nakamura. Epithelial Regeneration by Transplantation of Intestinal Epithelial Stem Cells. The 2nd International Meeting for Epithelial Tubulology 2015.08.22 Sapporo
19. Katsuyoshi Matsuoka, Eiko Saito, Mamoru Watanabe. Salvage therapy for corticosteroid-refractory ulcerative colitis patients: Results from the real-life clinical practice. JDDW2015 2015.10.10 Tokyo
20. Shuji Hibiya, Kiichiro Tsuchiya, Tomoaki Shirasaki, Keita Fukushima, Ryohei Hayashi, Nobukatsu Horita, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Continuous stimulation with cytokines leads to irreversible activation of NF- γ b signaling in colonic epithelial cells by organoid culture. UEGW2015 2015.10.27 Barcelona
21. Tomoaki Shirasaki, Keita Fukushima, Kiichiro Tsuchiya, Shuji Hibiya, Ryohei Hayashi, Nobukatsu Horita, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. TNF- α stabilizes atoh1 protein in colitis-associated colorectal cancer resulting in enhanced malignant potential. UEGW2015 2015.10.28 Barcelona
22. Satoru Fujii, Ryuichi Okamoto, Toru Nakata, Kohei Suzuki, Fumiaki Ishibashi, Ami Kawamoto, Sayaka Ohashi Segawa, Tomohiro Mizutani, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. Establishment of a 3D cell culture-based screening platform to identify natural products that can regulate transepithelial water transport of the human gastrointestinal tract. Pacificchem2015 2015.12.17 Hawaii

Department of Sleep Modulatory Medicine

Professor Naohiko Inase
Associate Professor Meiyo Tamaoka
Assistant Professor Mizue Hobo
Technician Megumi Sato

(1) Research

Effects of NMDA-type glutamate receptor co-agonist on gamma oscillations and sleep in schizophrenia.
Open-label trial of ramelteon for diabetes mellitus with sleep disorder.
The effect of chronotherapy with the angiotensin-antagonist in hypertension with sleep apnea syndrome.
The efficacy of home-oxygen therapy in patients with sleep apnea and pulmonary fibrosis.
Development of the evaluation system for the efficacy of oral appliances on obstructive sleep apnea syndrome.
Open-label trial of hyperbaric oxygen therapy on sleep quality

(2) Education

Education of sleep medicine for students and residents

(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. Shirai, Dr. Masuo (Pulmonary Medicine)

PM Dr. Fujie (Pulmonary Medicine)

Tuesday: AM Dr. Uezato (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)

(4) Publications

[Original Articles]

1. Tsutsui T, Miyazaki Y, Okamoto T, Tateishi T, Furusawa H, Tsuchiya K, Fujie T, Tamaoka M, Sakashita H, Sumi Y, Inase N. Antigen avoidance tests for diagnosis of chronic hypersensitivity pneumonitis Respiratory Investigation. 2015.09; 53(5); 217-224

Department of Women's Health

Associate Professor Masakazu Terauchi MD PhD; Assistant Professor Kimio Wakana 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, Maternal Nursing, and Human Genetics, 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. Aiko Takata, Masakazu Terauchi, Shiro Hiramitsu, Masaya Uno, Kimio Wakana, Toshiro Kubota. Dkk-3 induces apoptosis through mitochondrial and Fas death receptor pathways in human mucinous ovarian cancer cells *Int J Gynecol Cancer*. 2015.03; 25(3); 372-379
2. Asuka Hirose, Masakazu Terauchi, Moe Tamura, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Tomato juice intake increases resting energy expenditure and improves hypertriglyceridemia in middle-aged women: an open-label, single-arm study *Nutrition Journal*. 2015.04; 14(1); 34
3. 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*. 2015.08;
4. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Prevalence and predictors of storage lower urinary tract symptoms in perimenopausal and postmenopausal women attending a menopause clinic. *Menopause*. 2015.10; 22(10); 1084-1090

[Conference Activities & Talks]

1. Masakazu Terauchi. Pharmacological Treatment of Depression in Peri- and Early Post-Menopausal Women. World Congress on Women' s Mental Health 2015.03.24 Tokyo
2. Masakazu Terauchi. Symposium 14: STD "Screening and treatment of Chlamydia trachomatis genital infection". 24th Asian & Oceanic Congress of Obstetrics & Gynecology 2015.06.06 Kuching, Malaysia
3. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Feeling of Unattractiveness in Peri- and Postmenopausal Women is Associated with Depressed Mood, Poor Memory, and Unsatisfactory Sexual Relationship. North American Menopause Society 26th Annual Meeting 2015.10.01 Las Vegas, NV

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. Yoshiki Hitoshi, Tadano Kotaro, Ban Daisuke, Ohuchi Katsuhiro, Tanabe Minoru, Kawashima Kenji. Surgical energy device using steam jet for robotic assisted surgery. Conf Proc IEEE Eng Med Biol Soc. 2015.08; 2015; 6872-6875

[Conference Activities & Talks]

1. Yoshiki H, Tadano K, Ban D, Ohuchi K, Tanabe M, Kawashima K. Surgical Energy Device Using Steam Jet for Robotic Assisted Surgery. 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2015.08.28 Milan, Italy
2. Fujiwara T., Sakota D., Ouchi K., Murashige T., Kosaka R., Nishida M., Endo S., Nagaoka E., Oi K., Mizuno T., Maruyama O., Arai H.. The Real-Time Optical Monitoring of Thrombus Formation Inside the Blood Pump During Extracorporeal Circulation Using Hyperspectral Imaging in Acute Animal Experiments. 23rd Annual Congress of the International Society for Rotary Blood Pumps 2015.09.28 Dubrovnik
3. Onishi T, Arafune T, Ohuchi K, Nomoto A, Tachiyangi N. Normalized pulse volume on pain new findings and its application to pain monitoring. IAMPOV International Symposium 2015.10.04 Tokyo, Japan

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-nitrosogluthathione 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. Tsuzuki T, Shinozaki S, Nakamoto H, Kaneki M, Goto S, Shimokado K, Kobayashi H, Naito H.. Voluntary Exercise Can Ameliorate Insulin Resistance by Reducing iNOS-Mediated S-Nitrosylation of Akt in the Liver in Obese Rats. PLoS One.. 2015.07; 10(7);

[Conference Activities & Talks]

1. Shohei Shinozaki. Single molecular switch may contribute to major aging-related diseases. The 3rd Ochanomizu Atherosclerosis Forum 2015.02.28 Tokyo
2. Shohei Shinozaki. S-nitrosylation of SIR1 and inflammatory. The 11th Japanese Association for Food Immunology Annual Meeting. 2015.10.15 Tokyo

[Others]

1. Grant-in-Aid for Young Scientists (B), MEXT KAKENHI Grant Number 25860231
The role of S-nitrosylation in pathogenesis of metabolic syndrome. 2013-2014
2. Takeda Science Foundation for Medical Research
Identification of the missing link between chronic inflammation and pathogenesis of metabolic syndrome. 2013-2014
3. Kato Memorial Bioscience Foundation, The 25th Kato Memorial Grant
Identification of the mechanisms of metabolic syndrome. 2014-2015
4. The Towa Foundation for Food Science and Research
Verification of preventative effects of functional food against metabolic syndrome. 2014
5. Novartis Foundation for Geriatricological Research. Research grant of 2015
Investigation of glycolipid metabolism disorder and mechanism of aging through protein S-nitrosylation, a novel post transcriptional modification. 2015-2016

Department of Translational Oncology

< Department of Translational Oncology >
Associate Professor: Megumi ISHIGURO
Professor (concurrent): Hiroyuki UETAKE

(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. Shinto E, Takahashi K, Yamaguchi T, Hashiguchi Y, Kotake K, Itabashi M, Yasuno M, Kanemitsu Y, Nishimura G, Akagi Y, Sato T, Kato T, Matsumoto H, Hase K, Sugihara K.. Validation and Modification of the Japanese Classification System for Liver Metastases from Colorectal Cancer:A Multi-institutional Study. *Ann Surg Oncol*. 2015; 22; 3888-3895
2. Kobayashi H, Kikuchi A, Okazaki S, Ishiguro M, Ishikawa T, Iida S, Uetake H, Sugihara K. Diagnostic performance of multidetector row computed tomography for assessment of lymph node metastasis in patients with distal rectal cancer. *Ann Surg Oncol*. 2015.01; 22(1); 203-208
3. Sugihara K, Yoshida M, Ishiguro M.. Reply to the Letter to the Editor 'Is fluoropyrimidines without oxaliplatin optimal for the adjuvant treatment of mainstream stage III colon cancer ?' by Abali et al. *Ann Oncol*. 2015.01; 26; 245-246
4. Takahashi H, Ishikawa T, Ishiguro M, Okazaki S, Mogushi K, Kobayashi H, Iida S, Mizushima H, Tanaka H, Uetake H, Sugihara K.. Prognostic significance of Traf2-and Nck-interacting kinase (TNIK) in colorectal cancer. *BMC Cancer*. 2015.02; 15; 794
5. Uetake H, Yasuno M, Ishiguro M, Kameoka S, Shimada Y, Takahashi K, Watanabe T, Muro K, Baba H, Yamamoto J, Mizunuma N, Tamagawa H, Mochizuki I, Kinugasa Y, Kikuchi T, Sugihara K. A Multicenter Phase II Trial of mFOLFOX6 Plus Bevacizumab to Treat Liver-Only Metastases of Colorectal Cancer that are Unsuitable for Upfront Resection (TRICC0808). *Ann Surg Oncol*. 2015.03; 22(3); 908-915
6. Watanabe T, Itabashi M, Shimada Y, Tanaka S, Ito Y, Ajioka Y, Hamaguchi T, Hyodo I, Igarashi M, Ishida H, Ishihara S, Ishiguro M, Kanemitsu Y, Kokudo N, Muro K, Ochiai A, Oguchi M, Ohkura Y, Saito Y, Sakai Y, Ueno H, Yoshino T, Boku N, Fujimori T, Koinuma N, Morita T, Nishimura G, Sakata Y, Takahashi K, Tsuruta O, Yamaguchi T, Yoshida M, Yamaguchi N, Kotake K, Sugihara K.. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. *Int J Clin Oncol*. 2015.04; 20; 207-239

[Conference Activities & Talks]

1. Ishikawa T, Uetake H, Ishiguro M, Murotani K, Ueno H, Matsui S, Sugihara K, Tomita N.. MSI, 18qLOH, and clinicopathological features in stage II sporadic colon cancers: Biomarker study in a Phase III study of postoperative adjuvant chemotherapy for stage II colon cancer (SACURA trial). ACCR 2015 2015.04.22 Philadelphia (USA)
2. Kinugasa Y, Ishiguro M, Nakatani E, Endo T, Shinozaki H, Takii Y, Takahashi Y, Mochizuki H, Kotake K, Kameoka S, Takahashi K, Watanabe M, Boku N, Tomita N, Sugihara K.. S-1 as adjuvant chemotherapy for stage III colon cancer: Updated outcomes of ACTS-CC trial.. 2015 ASCO Annual Meeting 2015.06.01 Chicago (USA)

Clinical Laboratory

General Manager

-Junior Associate Professor : Naoko Tojo (January-April)

-Professor : Shuji Tohda (October-)

Associate Manager

-Associate Professor : Shuji Tohda (January-September)

Assistant Professor : Naomi Murakami

Assistant Professor : Tadashi Kanouchi

Assistant Professor : Ryoko Azuma

Medical Staff : Yuki Sakurai

(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) 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 2015, 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 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 August 2015. 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. Hiroki Akiyama, Masahide Yamamoto, Chizuko Sakashita, Yoshihiro Umezawa, Tetsuya Kurosu, Naomi Murakami, Osamu Miura. Therapy-related Leukemia with Inv(16)(p13.1q22) and Type D CBFβ/MYH11 Developing after Exposure to Irinotecan-containing Chemoradiotherapy. *Intern. Med.* 2015; 54(6); 651-655
2. Mitsuma S, Van den Bergh P, Rajabally YA, Van Parijs V, Martin-Lamb D, Sonoo M, Inaba A, Shimizu T, Iose S, Sato Y, Komori T, Misawa S, Kuwabara S, The Tokyo Metropolitan Neuromuscular Electrodiagnosis Study Group(including Kanouchi T). Effects of low frequency filtering on distal compound muscle action potential duration for diagnosis of CIDP: A Japanese-European multicenter prospective study. *Clinical Neurophysiology*. 2015; 126; 1805-1810
3. Murakawa M, Asahina Y, Nakagawa M, Sakamoto N, Nitta S, Kusano-Kitazume A, Watanabe T, Kawai-Kitahata F, Otani S, Taniguchi M, Goto F, Nishimura-Sakurai Y, Itsui Y, Azuma S, Kakinuma S, Watanabe M.. Impaired induction of IL28B and expression of IFN λ 4 associated with non-response to interferon-based therapy in chronic hepatitis C. *Journal of Gastroenterology and Hepatology*. 2015.01;
4. Miyako Murakawa, Yasuhiro Asahina, Mina Nakagawa, Naoya Sakamoto, Sayuri Nitta, Akiko Kusano-Kitazume, Takako Watanabe, Fukiko Kawai-Kitahata, Satoshi Otani, Miki Taniguchi, Fumio Goto, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. Impaired induction of interleukin 28B and expression of interferon λ 4 associated with nonresponse to interferon-based therapy in chronic hepatitis C. *J Gastroenterol Hepatol*. 2015.06; 30(6); 1075-1084
5. 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.[Epub ahead of print] *Hepatol Res*. 2015.07;

[Books etc]

1. Tadashi Kanouchi. Current Therapy in Neurological Disorders 2015-2017 (Japanese). Nankodo Co., Ltd., 2015.01 (ISBN : 978-4-524-26595-4)
2. Tadashi Kanouchi. Resident's textbook of Neurology (Japanese). 2015.01 (ISBN : 978-4-7878-2079-2)

[Conference Activities & Talks]

1. Nonami H, Kanouchi T, Ishibashi T, Yokota T. A case of multiple cranial nerve palsies with characteristic myoclonus-like involuntary movements of facial and cervical muscles (Japanese). 9th Tokyo metropolitan neuromuscular electrodiagnosis forum 2015.01.24 Tokyo
2. Kanouchi T. The basics of neurophysiological function tests (Japanese). 2015.03.07 Tokyo
3. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Hiroko Nagata, Fumio Goto, Satoshi Otani, Miki Taniguchi, Miyako Murakawa, Sayuri Nitta, Takako Watanabe, Megumi Tasaka-Fujita, Yuki Nishimura-Sakurai, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Shinji Tanaka, Minoru Tanabe, Nobuyuki Enomoto and Mamoru Watanabe. Gene alterations in TERT promoter, CTNNB1, and TP53 are closely associated with development and prognosis of hepatocellular carcinoma : Comprehensive analyses by next generation sequencing technology. The 3rd JSGE International Topic Conference 2015.04.24 Sendai

4. Kanouchi T, Sekiguchi T, Yokota T. Local progression at the onset lower limb and spread to the upper limb in ALS (Japanese). 56th Annual Meeting of The Japanese Society of Neurology 2015.05.23 Niigata
5. Kanouchi T. Nerve conduction study in the upper extremity (Japanese). 12th neuromuscular electrodiagnosis seminar 2015.07.18 Tokyo
6. Kanouchi T. The basics of nerve conduction study (Japanese). 10th Tokyo technical seminar for clinical neurophysiological tests 2015.08.02 Tokyo
7. Kanouchi T, Yokota T. Symposium 3. Electrophysiological approach to the pathomechanism of lesion spread in ALS (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.05 Osaka
8. Ono D, Kanouchi T, Sanjo N, Nishida Y, Ishikawa K, Yokota T. Somatosensory evoked potential in the patients with spinal cord atrophy in neuromyelitis optica and multiple sclerosis (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.05 Osaka
9. Narumi J, Kanouchi T, Akaza M, Aoyagi E, Yanagi N, Ohta N, Sumi Y, Yokota T, Hagihara M, Tohda S. Study for quality control in nerve conduction study (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.05 Osaka
10. Iida S, Suzuki M, Sanjo N, Nishida Y, Kanouchi T, Yokota T. Predictive factors in nerve conduction study for remission maintenance therapy in CIDP (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.06 Osaka
11. Kanouchi T, Sekiguchi T, Yokota T. Correlation between disease progression in the onset limb and symptom spread to the bulbar region in ALS (Japanese). 45th Annual Meeting of The Japanese Society of Clinical Neurophysiology 2015.11.06 Osaka

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
 Medical Technologist Yuki Shinohara

(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 2015)
 - 1) The amount of blood products used
 Red cell component products 11,251 Units (5,705 bags)
 Platelet concentration 22,725 Units (2,002 bags)
 Fresh frozen plasma 11,321 Units (4,641 bags)
 - 2) Autologous blood collection and transfusion
 Autologous blood collection 333 cases (427 times, 83 4Units)
 Autologous blood transfusion 304 cases (720 Units)
 - 3) The number of clinical tests of transfusion
 Blood typing 10,155
 Anti red blood cell antibody test 4,973
 Cross match test 9,081
 - 4) Hematopoietic stem cell harvest

Autologous peripheral blood stem cell harvest 11 cases 13 times

Allogenic peripheral blood stem cell harvest 3 cases 3 times

Autologous peripheral mononuclear cell harvest 1 case 1 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 10 cases 10 times

Allogenic peripheral blood stem cell transplantation 3 cases 3 times

Autologous peripheral mononuclear cell transplantation 1 case 1 time

Allogenic bone marrow transplantation 11 cases 11 times

Allogenic umbilical cord blood transplantation 10 cases 11 times

(4) Publications

[Original Articles]

1. Shihoko Suwa, Aya Kasubata, Miyu Kato, Megumi Iida, Ken Watanabe, Osamu Miura, Tetsuya Fukuda. The tryptophan derivative, tranilast, and conditioned medium with indoleamine 2,3-dioxygenase-expressing cells inhibit the proliferation of lymphoid malignancies. *Int. J. Oncol.* 2015.01;
2. Risa Nomura, Kentaro Miyai, Michiyo Okada, Michiko Kajiwara, Makoto Ono, Tsutomu Ogata, Iichiro Onishi, Mana Sato, Masaki Sekine, Takumi Akashi, Shuki Mizutani, Kenichi Kashimada. A 45,X/46,XY DSD (Disorder of Sexual Development) case with an extremely uneven distribution of 46,XY cells between lymphocytes and gonads. *Clin Pediatr Endocrinol.* 2015.01; 24(1); 11-14
3. Hiroaki Goto, Takashi Kaneko, Yoko Shioda, Michiko Kajiwara, Kazuo Sakashita, Toshiyuki Kitoh, Akira Hayakawa, Mizuka Miki, Keisuke Kato, Atsushi Ogawa, Yoshiko Hashii, Takeshi Inukai, Chiaki Kato, Hisashi Sakamaki, Hiromasa Yabe, Ritsuro Suzuki, Koji Kato. Hematopoietic stem cell transplantation for patients with acute lymphoblastic leukemia and Down syndrome. *Pediatr Blood Cancer.* 2015.01; 62(1); 148-152
4. Kanako Mitsui-Sekinaka, Kohsuke Imai, Hiroki Sato, Daisuke Tomizawa, Michiko Kajiwara, Masayuki Nagasawa, Tomohiro Morio, Shigeaki Nonoyama. Clinical features and hematopoietic stem cell transplantations for CD40 ligand deficiency in Japan. *J. Allergy Clin. Immunol.* 2015.10; 136(4); 1018-1024
5. Motohiro Kato, Masafumi Seki, Kenichi Yoshida, Yusuke Sato, Ryo Oyama, Yuki Arakawa, Hiroshi Kishimoto, Tomohiko Taki, Masaharu Akiyama, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Noriko Mitsui, Michiko Kajiwara, Shuki Mizutani, Masashi Sanada, Satoru Miyano, Seishi Ogawa, Katsuyoshi Koh, Junko Takita. Genomic analysis of clonal origin of Langerhans cell histiocytosis following acute lymphoblastic leukaemia. *Br. J. Haematol.* 2015.11;

[Conference Activities & Talks]

1. epilepsy in acute lymphoblastic leukemia. The 118th Annual Meeting of the Japan Pediatric Society 2015.04.18 Osaka
2. Ataxia Telangiectasia patient with intractable Cytomegalovirus encephalitis. The 118th Annual Meeting of the Japan Pediatric Society 2015.04.19 Osaka

Hyperbaric Medical Center

Center Chief and Associate Professor; Kazuyoshi YAGISHITA
 Lecturer; Mitsuhiro ENOMOTO
 Clinical fellow; Takuya OYAIKU
 Part-time Lecturer; Seiichiro TOGAWA, Yasushi KOJIMA,
 Masaharu SHIBAYAMA
 Researcher; Masaki HORIE,
 Secretary; Kiyomi ITOH

(1) Outline

Hyperbaric oxygen therapy (HBO), which can dissolve oxygen in serum in proportion to atmospheric pressure and transport oxygen to ischemic tissue, is an established therapy for treatment of several conditions, including decompression illness, carbon monoxide poisoning, acute arterial 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 2014, 6,210 times hyperbaric oxygen therapy (HBO) in 674 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. Toshitaka Yoshii, Takashi Hirai, Tsuyoshi Yamada, Satoshi Sumiya, Renpei Mastumoto, Tsuyoshi Kato, Mitsuhiro Enomoto, Hiroyuki Inose, Shigenori Kawabata, Kenichi Shinomiya, Atsushi Okawa. Lumbarosacral pedicle screw placement using a fluoroscopic pedicle axis view and a cannulated tapping device. *J Orthop Surg Res.* 2015; 10; 79
2. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Otabe K, Sekiya I.. Mid- to long-term results of single-bundle versus double-bundle anterior cruciate ligament reconstruction: randomized controlled trial. *Arthroscopy.* 2015.01; 31(1); 69-76
3. Shimoda M, Enomoto M, Horie M, Miyakawa S, Yagishita K.. Effects of hyperbaric oxygen on muscle fatigue after maximal intermittent plantar flexion exercise *J Strength Cond Res.* 2015.03; 17;
4. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Initial Graft Tension on Knee Stability and Graft Tension Pattern in Double-Bundle Anterior Cruciate Ligament Reconstruction. *Arthroscopy.* 2015.05; 31(9); 1756-1763
5. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Otabe K, Sekiya I.. Effect of posterolateral bundle graft fixation angles on clinical outcomes in double-bundle anterior cruciate ligament reconstruction: a randomized controlled trial. *Am J Sports Med.* 2015.05; 43(5); 1157-1164
6. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Evaluation of a behind-remnant approach for femoral tunnel creation in remnant-preserving double-bundle anterior cruciate ligament reconstruction - Comparison with a standard approach. *Knee.* 2015.06; 22(3); 249-255
7. Manabu Shimoda, Mitsuhiro Enomoto, Masaki Horie, Shumpei Miyakawa, Kazuyoshi Yagishita. Effects of hyperbaric oxygen on muscle fatigue after maximal intermittent plantar flexion exercise. *J Strength Cond Res.* 2015.06;
8. YASUSHI KOJIMA, MITSUHIRO ENOMOTO, TAKUYA OYAIZU, KAZUYOSHI YAGISHITA. The effects of delayed recompression treatment over 7 days after the onset of symptoms in patients with mild decompression illness *The Japanese Journal of Hyperbaric and Undersea Medicine.* 2015.09; 50(3); 129-134
9. Yoko Yamamoto, Yoshihiro Noguchi, Mitsuhiro Enomoto, Kazuyoshi Yagishita, Ken Kitamura. Otological complications associated with hyperbaric oxygen therapy. *Eur Arch Otorhinolaryngol.* 2015.12;
10. Kohei Yamakoshi, Kazuyoshi Yagishita, Hirotsugu Tsuchimochi, Tadakatsu Inagaki, Mikiyasu Shirai, David C Poole, Yutaka Kano. Microvascular oxygen partial pressure during hyperbaric oxygen in diabetic rat skeletal muscle. *Am. J. Physiol. Regul. Integr. Comp. Physiol..* 2015.12; 309(12); R1512-R1520

[Books etc]

1. YASUSHI KOJIMA. DAN Annual Diving Report. Divers Alert Network, 2015.11

[Misc]

1. Mitsuhiro Enomoto. The future of bone marrow stromal cell transplantation for the treatment of spinal cord injury. *Neural Regen Res.* 2015.03; 10(3); 383-384

[Conference Activities & Talks]

1. OYAIZU Takuya, ENOMOTO Mitsuhiro, YOSHII Toshitaka, OKAWA Atsushi. Relation between paraspinal muscle fatigue and Xray parameters in patients with spinal kyphotic deformity.. 2015.04.16
2. OYAIZU Takuya, ENOMOTO Mitsuhiro, YAGISHITA Kazuyoshi. Acceleration of muscle volume reduction and recovery from hypoxia of injured skeletal muscle by hyperbaric oxygen.. Undersea and Hyperbaric Medical Society Annual Scientific Meeting 2015 2015.06.18 Montreal, Canada
3. Tomomasa Nakamura. Comparison of short-term results between 3 approaches for femoral tunnel creation in remnant-preserved double bundle anterior cruciate ligament reconstruction. 2015.06.19
4. ENOMOTO Mitsuhiro, KABURAGI Hidetoshi, HIRAI Takashi, WAKABAYASHI Yoshiaki, YAGISHITA Kazuyoshi, YOKOTA Takanori, OKAWA Atsushi. A model of chronic pain from human prostate cancer cells implanted into the mouse tibia. The 45th annual meeting of the Society for Neuroscience 2015.10
5. OYAIZU Takuya, ENOMOTO Mitsuhiro, HORIE Masaki, OKAWA Atsushi, YAGISHITA Kazuyoshi. Hyperbaric and high-oxygen environment reduce swelling and maintain oxygen tension in skeletal muscle contusion injury.. 2015.10.22

[Awards & Honors]

1. Young Scientist/Medical Doctor Award, Undersea and Hyperbaric Medical Society, 2015.06

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 2,110 samples in year 2015 in total.

(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. Tomohito Takimoto, Hidetoshi Takada, Masataka Ishimura, Makiko Kirino, Kenichiro Hata, Osamu Ohara, Tomohiro Morio, Toshiro Hara. Wiskott-Aldrich Syndrome in a Girl Caused by Heterozygous WASP Mutation and Extremely Skewed X-Chromosome Inactivation: A Novel Association with Maternal Uniparental Isodisomy 6. *Neonatology*. 2015; 107(3); 185-190
2. Koji Otabe, Hiroyuki Nakahara, Akihiko Hasegawa, Tetsuya Matsukawa, Fumiaki Ayabe, Naoko Onizuka, Masafumi Inui, Shuji Takada, Yoshiaki Ito, Ichiro Sekiya, Takeshi Muneta, Martin Lotz, Hiroshi Asahara. Transcription factor Mohawk controls tenogenic differentiation of bone marrow mesenchymal stem cells in vitro and in vivo. *J. Orthop. Res.*. 2015.01; 33(1); 1-8
3. Oshima K, Imai K, Albert MH, Bittner TC, Strauss G, Filipovich AH, Morio T, Kapoor N, Dalal J, Schultz KR, Casper JT, Notarangelo LD, Ochs HD, Nonoyama S.. Hematopoietic stem cell transplantation for X-linked thrombocytopenia with mutations in the WAS gene *J Clin Immunol*. 2015.01; 35(1); 15-21
4. Risa Nomura, Kentaro Miyai, Michiyo Okada, Michiko Kajiwara, Makoto Ono, Tsutomu Ogata, Ichiro Onishi, Mana Sato, Masaki Sekine, Takumi Akashi, Shuki Mizutani, Kenichi Kashimada. A 45,X/46,XY DSD (Disorder of Sexual Development) case with an extremely uneven distribution of 46,XY cells between lymphocytes and gonads. *Clin Pediatr Endocrinol*. 2015.01; 24(1); 11-14
5. Hiroaki Goto, Takashi Kaneko, Yoko Shioda, Michiko Kajiwara, Kazuo Sakashita, Toshiyuki Kitoh, Akira Hayakawa, Mizuka Miki, Keisuke Kato, Atsushi Ogawa, Yoshiko Hashii, Takeshi Inukai, Chiaki Kato, Hisashi Sakamaki, Hiromasa Yabe, Ritsuro Suzuki, Koji Kato. Hematopoietic stem cell transplantation for patients with acute lymphoblastic leukemia and Down syndrome. *Pediatr Blood Cancer*. 2015.01; 62(1); 148-152
6. Yu Matsukura, Takeshi Muneta, Kunikazu Tsuji, Kazumasa Miyatake, Jun Yamada, Kahaer Abula, Hideyuki Koga, Makoto Tomita, Ichiro Sekiya. Mouse synovial mesenchymal stem cells increase in yield with knee inflammation. *J. Orthop. Res.*. 2015.02; 33(2); 246-253
7. Teppei Ohkawa, Satoshi Miyamoto, Manabu Sugie, Daisuke Tomizawa, Kohsuke Imai, Masayuki Nagasawa, Tomohiro Morio, Shuki Mizutani, Masatoshi Takagi. Transient abnormal myelopoiesis in non-Down syndrome neonate. *Pediatr Int*. 2015.02; 57(1); e14-e17
8. Ting Wu, Songmei Wang, Jinfeng Wu, Zhiguang Lin, Xianxian Sui, Xiaoping Xu, Norio Shimizu, Bobin Chen, Xuanyi Wang. Icaritin induces lytic cytotoxicity in extranodal NK/T-cell lymphoma. *J. Exp. Clin. Cancer Res.*. 2015.02; 34; 17
9. Mitsuiki N, Yang X, Bartol SJ, Grosserichter-Wagener C, Kosaka Y, Takada H, Imai K, Kanegane H, Mizutani S, van der Burg M, van Zelm MC, Ohara O, Morio T.. Mutations in Bruton's tyrosine kinase impair IgA responses. *Int. J. Hematol.*. 2015.03; 101(3); 305-313
10. Yun-Wen Chen, Tianhuan Guo, Lijun Shen, Kai-Yau Wong, Qian Tao, William W L Choi, Rex K H Au-Yeung, Yuen-Piu Chan, Michelle L Y Wong, Johnny C O Tang, Wei-Ping Liu, Gan-Di Li, Norio Shimizu, Florence Loong, Eric Tse, Yok-Lam Kwong, Gopesh Srivastava. Receptor-type tyrosine-protein phosphatase κ directly targets STAT3 activation for tumor suppression in nasal NK/T-cell lymphoma. *Blood*. 2015.03; 125(10); 1589-1600
11. Tamaki Kato, Elena Crestani, Chikako Kamae, Kenichi Honma, Tomoko Yokosuka, Takeshi Ikegawa, Naonori Nishida, Hirokazu Kanegane, Taizo Wada, Akihiro Yachie, Osamu Ohara, Tomohiro Morio, Luigi D Notarangelo, Kohsuke Imai, Shigeaki Nonoyama. RAG1 Deficiency May Present Clinically as Selective IgA Deficiency. *J. Clin. Immunol.*. 2015.04; 35(3); 280-288

12. Shumpei Yokota, Yasuhiko Itoh, Tomohiro Morio, Naokata Sumitomo, Kaori Daimaru, Seiji Minota. Macrophage Activation Syndrome in Patients with Systemic Juvenile Idiopathic Arthritis under Treatment with Tocilizumab. *J. Rheumatol.*. 2015.04; 42(4); 712-722
13. Go Matsuda, Ken-Ichi Imadome, Fuyuko Kawano, Masashi Mochizuki, Nakaba Ochiai, Tomohiro Morio, Norio Shimizu, Shigeyoshi Fujiwara. Cellular immunotherapy with ex vivo expanded cord blood T cells in a humanized mouse model of EBV-associated lymphoproliferative disease. *Immunotherapy*. 2015.04; 7(4); 335-341
14. Yohei Matsubara, Tomoko Kato, Kenichi Kashimada, Hiromitsu Tanaka, Zhou Zhi, Shizuko Ichinose, Shuki Mizutani, Tomohiro Morio, Tomoki Chiba, Yoshiaki Ito, Yumiko Saga, Shuji Takada, Hirhoshi Asahara. TALEN-mediated gene disruption on Y Chromosome reveals Critical Role of EIF2S3Y in Mouse Spermatogenesis. *Stem Cells Dev.*. 2015.05; 24(10); 1164-1170
15. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Posterolateral Bundle Graft Fixation Angles on Clinical Outcomes in Double-Bundle Anterior Cruciate Ligament Reconstruction: A Randomized Controlled Trial. *Am J Sports Med.* 2015.05; 43(5); 1157-1164
16. Kahaer Abula, Takeshi Muneta, Kazumasa Miyatake, Jun Yamada, Yu Matsukura, Makiko Inoue, Ichiro Sekiya, Daniel Graf, Aris N Economides, Vicki Rosen, Kunikazu Tsuji. Elimination of BMP7 from the developing limb mesenchyme leads to articular cartilage degeneration and synovial inflammation with increased age. *FEBS Lett.* 2015.05; 589(11); 1240-1248
17. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Initial Graft Tension on Knee Stability and Graft Tension Pattern in Double-Bundle Anterior Cruciate Ligament Reconstruction. *Arthroscopy*. 2015.05; 31(9); 1756-1763
18. Tomoya Muto, Chikako Ohwada, Atsuko Yamazaki, Yasumasa Sugita, Shokichi Tsukamoto, Shio Sakai, Yusuke Takeda, Naoya Mimura, Masahiro Takeuchi, Emiko Sakaida, Tohru Iseki, Norio Shimizu, Tomohiro Morio, Chiaki Nakaseko. Long-term complete remission by infusion of ex vivo-expanded donor-derived CD4(+) lymphocytes for treating an early relapse of Hodgkin lymphoma after cord blood transplantation. *Leuk. Lymphoma*. 2015.05; 1-11
19. Yusuke Nakagawa, Takeshi Muneta, Shinpei Kondo, Mitsuru Mizuno, Kazuo Takakuda, Shizuko Ichinose, Takeshi Tabuchi, Hideyuki Koga, Kunikazu Tsuji, Ichiro Sekiya. Synovial mesenchymal stem cells promote healing after meniscal repair in microminipigs. *Osteoarthritis Cartilage*. 2015.06; 23(6); 1007-1017
20. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Evaluation of a behind-remnant approach for femoral tunnel creation in remnant-preserving double-bundle anterior cruciate ligament reconstruction - Comparison with a standard approach. *Knee*. 2015.06; 22(3); 249-255
21. Nobutake Ozeki, Takeshi Muneta, Seiya Matsuta, Hideyuki Koga, Yusuke Nakagawa, Mitsuru Mizuno, Kunikazu Tsuji, Yo Mabuchi, Chihiro Akazawa, Eiji Kobayashi, Tomoyuki Saito, Ichiro Sekiya. Synovial mesenchymal stem cells promote meniscus regeneration augmented by an autologous Achilles tendon graft in a rat partial meniscus defect model. *Stem Cells*. 2015.06; 33(6); 1927-1938
22. Yusuke Ogata, Yo Mabuchi, Mayu Yoshida, Eriko Grace Suto, Nobuharu Suzuki, Takeshi Muneta, Ichiro Sekiya, Chihiro Akazawa. Purified Human Synovium Mesenchymal Stem Cells as a Good Resource for Cartilage Regeneration. *PLoS ONE*. 2015.06; 10(6); e0129096
23. Ichiro Sekiya, Takeshi Muneta, Masafumi Horie, Hideyuki Koga. Arthroscopic Transplantation of Synovial Stem Cells Improves Clinical Outcomes in Knees With Cartilage Defects. *Clin. Orthop. Relat. Res.*. 2015.07; 473(7); 2316-2326
24. Siok-Bian Ng, Koichi Ohshima, Viknesvaran Selvarajan, Gaofeng Huang, Shoa-Nian Choo, Hiroaki Miyoshi, Norio Shimizu, Renji Reghunathan, Hsin-Chieh Chua, Allen Eng-Juh Yeoh, Thuan-Chong Quah, Liang-Piu Koh, Poh-Lin Tan, Wee-Joo Chng. Epstein-Barr virus-associated T/natural killer-cell lymphoproliferative disorder in children and young adults has similar molecular signature to extranodal nasal natural killer/T-cell lymphoma but shows distinctive stem cell-like phenotype. *Leuk. Lymphoma*. 2015.08; 56(8); 2408-2415

25. Natsuko Inazawa, Tsukasa Hori, Naoki Hatakeyama, Masaki Yamamoto, Yuko Yoto, Masanori Nojima, Nobuhiro Suzuki, Norio Shimizu, Hiroyuki Tsutsumi. Large-scale multiplex polymerase chain reaction assay for diagnosis of viral reactivations after allogeneic hematopoietic stem cell transplantation. *J. Med. Virol.* 2015.08; 87(8); 1427-1435
26. Takao Hayakawa, Takashi Aoi, Christopher Bravery, Karin Hoogendoorn, Ivana Knezevic, Junichi Koga, Daisuke Maeda, Akifumi Matsuyama, James McBlane, Tomohiro Morio, John Petricciani, Mahendra Rao, Anthony Ridgway, Daisaku Sato, Yoji Sato, Glyn Stacey, Norihisa Sakamoto, Jean-Hugues Trouvin, Akihiro Umezawa, Masayuki Yamato, Kazuo Yano, Hiroyuki Yokote, Kentaro Yoshimatsu, Pierrette Zorzi-Morre. Report of the international conference on regulatory endeavors towards the sound development of human cell therapy products. *Biologicals*. 2015.09; 43(5); 283-297
27. Kanako Mitsui-Sekinaka, Kohsuke Imai, Hiroki Sato, Daisuke Tomizawa, Michiko Kajiwarra, Masayuki Nagasawa, Tomohiro Morio, Shigeaki Nonoyama. Clinical features and hematopoietic stem cell transplantations for CD40 ligand deficiency in Japan. *J. Allergy Clin. Immunol.* 2015.10; 136(4); 1018-1024
28. Kei Takasawa, Shigeru Takishima, Chikako Morioka, Masato Nishioka, Hirofumi Ohashi, Yoko Aoki, Masayuki Shimohira, Kenichi Kashimada, Tomohiro Morio. Improved growth velocity of a patient with Noonan-like syndrome with loose anagen hair (NS/LAH) without growth hormone deficiency by low-dose growth hormone therapy. *Am. J. Med. Genet. A*. 2015.10; 167A(10); 2425-2429
29. Shinobu Tamura, Kohei Higuchi, Masaharu Tamaki, Chizuko Inoue, Ryoko Awazawa, Noriko Mitsuki, Yuka Nakazawa, Hiroyuki Mishima, Kenzo Takahashi, Osamu Kondo, Kohsuke Imai, Tomohiro Morio, Osamu Ohara, Tomoo Ogi, Fukumi Furukawa, Masami Inoue, Koh-Ichiro Yoshiura, Nobuo Kanazawa. Novel compound heterozygous DNA ligase IV mutations in an adolescent with a slowly-progressing radiosensitive-severe combined immunodeficiency. *Clin. Immunol.* 2015.10; 160(2); 255-260
30. Keisuke Nakajima, Shinobu Hirai, Tomohiro Morio, Haruo Okado. Benzodiazepines induce sequelae in immature mice with inflammation-induced status epilepticus. *Epilepsy Behav.* 2015.10; 52(Pt A); 180-186
31. Mayumi Yoshimori, Honami Takada, Ken-Ichi Imadome, Morito Kurata, Kouhei Yamamoto, Takatoshi Koyama, Norio Shimizu, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. P-glycoprotein is expressed and causes resistance to chemotherapy in EBV-positive T-cell lymphoproliferative diseases. *Cancer Med.* 2015.10; 4(10); 1494-1504
32. Motohiro Kato, Masafumi Seki, Kenichi Yoshida, Yusuke Sato, Ryo Oyama, Yuki Arakawa, Hiroshi Kishimoto, Tomohiko Taki, Masaharu Akiyama, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Noriko Mitsuki, Michiko Kajiwarra, Shuki Mizutani, Masashi Sanada, Satoru Miyano, Seishi Ogawa, Katsuyoshi Koh, Junko Takita. Genomic analysis of clonal origin of Langerhans cell histiocytosis following acute lymphoblastic leukaemia. *Br. J. Haematol.* 2015.11;
33. Atsumi Tsuji, Kaoru Konishi, Satomi Hasegawa, Akira Anazawa, Toshikazu Onishi, Makoto Ono, Tomohiro Morio, Teruo Kitagawa, Kenichi Kashimada. Newborn screening for congenital adrenal hyperplasia in Tokyo, Japan from 1989 to 2013: a retrospective population-based study. *BMC Pediatr.* 2015.12; 15(1); 209
34. Toshifumi Watanabe, Takeshi Muneta, Ichiro Sekiya, Scott A Banks. Intraoperative joint gaps and mediolateral balance affect postoperative knee kinematics in posterior-stabilized total knee arthroplasty. *Knee.* 2015.12; 22(6); 527-534
35. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yukie Matsumoto, Shizuka Fujii, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Akifumi Matsuyama, Ichiro Sekiya. Platelet-derived growth factor (PDGF)-AA/AB in human serum are potential indicators of the proliferative capacity of human synovial mesenchymal stem cells. *Stem Cell Res Ther.* 2015.12; 6(1); 243

[Conference Activities & Talks]

1. Morio T. Cell processing facility. International regulatory endeavor towards sound development of human cell therapy products. 2015.02.18 Tokyo
2. Ichiro Sekiya. Synovial Mesenchymal Stem Cells to Repair/Reverse Knee OA: From Bench to Clinic. Orthopaedic Research Society 2015 Annual Meeting 2015.03.28 Las Vegas, USA

3. Ichiro Sekiya. Arthroscopic transplantation of synovial stem cells for cartilage injury. APKAS Summitt 2015.05.08 taipei,TAIWAN
4. Ichiro Sekiya. Cartilage and meniscus regeneration by synovial stem cells:from bench to clinic. Japan visit program for Dutch delegation on Sport Science 2015.11.12 Tokyo, Japan

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

[Original Articles]

1. Ebihara A, Iino Y, Yoshioka T, Hanada T, Sunakawa M, Sumi Y, Suda H. Apices of maxillary premolars observed by swept source optical coherence tomography SPIE Lasers in Dentistry XXI. 2015.02; 9306; 93060J-93060J-5
2. Iino Y, Yoshioka T, Hanada T, Ebihara A, Sunakawa M, Sumi Y, Suda H. Observation of the pulp horn by swept source optical coherence tomography and cone beam computed tomography SPIE Lasers in Dentistry XXI. 2015.02; 9306; 93060I-93060I-5

[Books etc]

1. Sunakawa M, Suda H. Physiological function of dentin/pulp complex and periodontal membrane. Okiji T, Suda H, Nakamura H ed. Textbook of Endodontics. Nagasueshoten, 2015.04

[Conference Activities & Talks]

1. Ebihara A, Iino Y, Yoshioka Y, Hanada T, Sunakawa M, Sumi Y, Suda H. Apices of maxillary premolars observed by swept source optical coherence tomography. SPIE 2015.02.08 San Francisco
2. Iino Y, Yoshioka T, Hanada T, Ebihara A, Sunakawa M, Sumi M, Suda H. Observation of the pulp horn by swept source optical coherence tomography and cone beam computed tomography. SPIE 2015.02.08 San Francisco
3. Kawamura J, Kaneko T, Yamanaka Y, Ito T, Sunakawa M, Okiji T. Immunohistochemical and gene-expression analysis of pulp injury-induced glial cell activation in the rat thalamus.. The 4th Tri-University Consortium 2015.05.20 Bangkok

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 2015.

The 119 consultation services concerning dental devices were performed in 2015.

(5) Publications

[Original Articles]

1. Reiko Wadachi, Toshihiko Yoshioka, Takahiro Hanada, Naoko Harada, Arata Ebihara, Hideaki Suda. The Present Situation and Problems of Tooth Fracture -The Present Demands of Dental Practice Revealed through a Survey of New Patients of an Endodontic Clinic- The Japanese Journal of Conservative Dentistry. 2015.02; 58 (1); 1-9

[Conference Activities & Talks]

1. Takahashi H, Iwasaki N, Yuzaki K. New Evaluation Model for Marginal Edge Reproducibility of CAD/CAM Blanks.. 2015 IADR/AADR/CADR General Session 2015.03.11 Boston, USA
2. Junji Tagami. Inheritance and evolution in cariology and operative dentistry. Honorary doctorate memorial lecture 2015.09.04 Mahidol University, Faculty of Dentistry
3. Kazuo TAKAKUDA, Hazuki KOSHITOMAE, Naoko HARADA, Kazuko IRIMURA. Failure Rate Estimation of Medical Devices by Bayesian statistics. Oromaxillofacial Biomechanics Association 2015.11.16

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 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.

(4) Publications

[Original Articles]

1. Toshitaka Yoshii, Takashi Hirai, Tsuyoshi Yamada, Satoshi Sumiya, Renpei Mastumoto, Tsuyoshi Kato, Mitsuhiro Enomoto, Hiroyuki Inose, Shigenori Kawabata, Kenichi Shinomiya, Atsushi Okawa. Lumbarosacral pedicle screw placement using a fluoroscopic pedicle axis view and a cannulated tapping device. *J Orthop Surg Res.* 2015; 10; 79
2. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Otabe K, Sekiya I.. Mid- to long-term results of single-bundle versus double-bundle anterior cruciate ligament reconstruction: randomized controlled trial. *Arthroscopy.* 2015.01; 31(1); 69-76
3. Kanayama T, Miyamoto H, Yokoyama A, Takahashi T, Shibuya Y. The influence of bite force strength on brain activity *J Biomed Grap Comput.* 2015.01; 5(1); 28-32
4. Shimoda M, Enomoto M, Horie M, Miyakawa S, Yagishita K.. Effects of hyperbaric oxygen on muscle fatigue after maximal intermittent plantar flexion exercise *J Strength Cond Res.* 2015.03; 17;
5. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Effect of Initial Graft Tension on Knee Stability and Graft Tension Pattern in Double-Bundle Anterior Cruciate Ligament Reconstruction. *Arthroscopy.* 2015.05; 31(9); 1756-1763
6. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Otabe K, Sekiya I.. Effect of posterolateral bundle graft fixation angles on clinical outcomes in double-bundle anterior cruciate ligament reconstruction: a randomized controlled trial. *Am J Sports Med.* 2015.05; 43(5); 1157-1164
7. Chowdhury RU, Churei H, Takahashi H, Shahrin S, Fukasawa S, Shrestha A, Negoro T, Ueno T. Suitable design of mouthguard for sports active person with spaced dentition *Dental Traumatology.* 2015.06; 31(3); 238-242

8. Hideyuki Koga, Takeshi Muneta, Kazuyoshi Yagishita, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Ichiro Sekiya. Evaluation of a behind-remnant approach for femoral tunnel creation in remnant-preserving double-bundle anterior cruciate ligament reconstruction - Comparison with a standard approach. *Knee*. 2015.06; 22(3); 249-255
9. Manabu Shimoda, Mitsuhiro Enomoto, Masaki Horie, Shumpei Miyakawa, Kazuyoshi Yagishita. Effects of hyperbaric oxygen on muscle fatigue after maximal intermittent plantar flexion exercise. *J Strength Cond Res*. 2015.06;
10. Koji Nakamaru, Junya Aizawa, Takayuki Koyama, Osamu Nitta. Reliability, Validity, and Responsiveness of the Japanese Version of the Patient-Specific Functional Scale in patients with neck pain *European Spine Journal*. 2015.09; 24(12); 2816-2820
11. YASUSHI KOJIMA, MITSUHIRO ENOMOTO, TAKUYA OYAIKU, KAZUYOSHI YAGISHITA. The effects of delayed recompression treatment over 7 days after the onset of symptoms in patients with mild decompression illness *The Japanese Journal of Hyperbaric and Undersea Medicine*. 2015.09; 50(3); 129-134
12. Shrestha A, Takahashi T, Kurokawa K, Churei H, Chowdhury NU, Chowdhury RU, Shahrin S, Toyoshima Y, Ueno T. Physical and oral injuries and awareness of mouthguard among martial arts athletes in Nepal *Int J Sports Dent*. 2015.10; 8(1); 45-57
13. Yuichi Nishikawa, Junya Aizawa, Naohiko Kanemura, Tetsuya Takahashi, Naohisa Hosomi, Hirofumi Maruyama, Hiroaki Kimura, Masayasu Matsumoto, Kiyomi Takayanagi. Immediate effect of passive and active stretching on hamstrings flexibility: a single-blinded randomized control trial *Journal of Physical Therapy Science* . 2015.11; 27; 3167-3170
14. Yoko Yamamoto, Yoshihiro Noguchi, Mitsuhiro Enomoto, Kazuyoshi Yagishita, Ken Kitamura. Otological complications associated with hyperbaric oxygen therapy. *Eur Arch Otorhinolaryngol*. 2015.12;
15. Kohei Yamakoshi, Kazuyoshi Yagishita, Hirotsugu Tsuchimochi, Tadakatsu Inagaki, Mikiyasu Shirai, David C Poole, Yutaka Kano. Microvascular oxygen partial pressure during hyperbaric oxygen in diabetic rat skeletal muscle. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*. 2015.12; 309(12); R1512-R1520

[Books etc]

1. Kei-ichi Ishigami, Toshiaki Ueno, Misao Kawara, Yoshinobu Maeda, Toshikazu Yasui. *Yousetsu Sports Dentistry*. Igaku Joho-Sha Ltd., 2015.01 (ISBN : 978-4-903553-53-5)

[Misc]

1. Mitsuhiro Enomoto. The future of bone marrow stromal cell transplantation for the treatment of spinal cord injury. *Neural Regen Res*. 2015.03; 10(3); 383-384

[Conference Activities & Talks]

1. OYAIKU Takuya, ENOMOTO Mitsuhiro, YAGISHITA Kazuyoshi. Acceleration of muscle volume reduction and recovery from hypoxia of injured skeletal muscle by hyperbaric oxygen.. *Undersea and Hyperbaric Medical Society Annual Scientific Meeting 2015* 2015.06.18 Montreal, Canada
2. Tomomasa Nakamura. Comparison of short-term results between 3 approaches for femoral tunnel creation in remnant-preserved double bundle anterior cruciate ligament reconstruction. 2015.06.19
3. Yoshinao Sato, Takumi Yamada, Takehiro Omi, Ryota Shimamura. Comparison of foot kinetics during gait initiation between young and elderly subjects. *9th World Congress of the International Society of Physical and Rehabilitation Medicine* 2015.06.21 Berlin
4. Takehiro Ohmi, Takumi Yamada, Yoshinao Sato. Correlation between joint reaction force and gait speed in Osteoarthritis of the knee.. *9th World Congress of the International Society of Physical and Rehabilitation Medicine* 2015.06.21 Berlin
5. Shrestha A, Churei H, Yoshida Y, Sumita Y, Taniguchi H, Ueno T. Fabrication of customized obturator type of mouthguard: a clinical approach. *7th TMDU International Summer Program (ISP2015)* 2015.08.30 Tokyo, Japan

6. Shrestha A, Takahashi T, Kurokawa K, Churei H, Chowdhury NU, Chowdhury RU, Shahrin S, Toyoshima Y, Ueno T. Oral injuries and mouthguard among martial arts athletes in Nepal. 103th FDI Annual World Dental Congress 2015.09.24 Bangkok, Thailand
7. Chowdhury RU, Churei H, Mizobuchi , Fukasawa S, Iwasaki N, Sharika S, Shrestha A, Uo M, Takahashi H, Ueno T. Effective design of custom-made mouthguard for athletes undergoing orthodontic treatment. 103th FDI Annual World Dental Congress 2015.09.24 Bangkok, Thailand
8. ENOMOTO Mitsuhiro,KABURAGI Hidetoshi,HIRAI Takashi,WAKABAYASHI Yoshiaki,YAGISHITA Kazuyoshi,YOKOTA Takanori,OKAWA Atsushi. A model of chronic pain from human prostate cancer cells implanted into the mouse tibia. The 45th annual meeting of the Society for Neuroscience 2015.10
9. OYAIZU Takuya, ENOMOTO Mitsuhiro,HORIE Masaki,OKAWA Atsushi, YAGISHITA Kazuyoshi. Hyperbaric and high-oxygen environment reduce swelling and maintain oxygen tension in skeletal muscle contusion injury.. 2015.10.22
10. Takahashi T, Kurokawa K, Mitsuyama A, Ueno T. Masseter muscle recruitment involved in voluntary arm movement using dumbbell. 63rd Annual Meeting of the Japanese Association for Dental Research 2015.10.30 Fukuoka, Japan