

ANNUAL PUBLICATIONS

2 0 1 9



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

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Graduate School of Medical and Dental Sciences

Medical and Dental Sciences

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Oral Pathology

Professor
Tohru Ikeda

Junior Associate Professor
Kei Sakamoto

Assistant Professor
Kou Kayamori

Technical Staff
Miwako Hamagaki

Graduate Students
Maiko Tsuchiya
TEERAWONG CHANYANUCH
Akiyo Sanpei
NGUYEN PHAN THE HUY
Fukawa Hironori

(1) Research

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

(2) Education

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

(3) Clinical Services & Other Works

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

(4) Publications

[Original Articles]

1. Osada AH, Endo K, Kimura Y, Sakamoto K, Nakamura R, Sakamoto K, Ueki K, Yoshizawa K, Miyazawa K, Saitoh M. Addiction of mesenchymal phenotypes on the FGF/FGFR axis in oral squamous cell carcinoma cells. *PloS one*. 2019; 14(11); e0217451
2. Suzuki N, Kuribayashi A, Sakamoto K, Sakamoto J, Nakamura S, Watanabe H, Harada H, Kurabayashi T. Diagnostic abilities of 3T MRI for assessing mandibular invasion of squamous cell carcinoma in the oral cavity: comparison with 64-row multidetector CT. *Dentomaxillofacial Radiology*. 2019.01;
3. Wada Akane, Tsuchiya Maiko, Ozaki-Honda Yuu, Kayamori Kou, Sakamoto Kei, Yamaguchi Akira, Ikeda Tohru. A new osteoclastogenesis pathway induced by cancer cells targeting osteoclast precursor cells BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 2019.01; 509(1); 108-113
4. Takada Kaho, Kuroshima Takeshi, Shimamoto Hiroaki, Ohsako Toshimitsu, Kayamori Kou, Ikeda Tohru, Harada Hiroyuki. Metastasis of lower gingival squamous cell carcinoma to buccinator lymph node: case report and review of the literature *WORLD JOURNAL OF SURGICAL ONCOLOGY*. 2019.01; 17(1); 13
5. Ishida Shoko, Kayamori Kou, Sakamoto Kei, Yukimori Akane, Kugimoto Takuma, Harada Hiroyuki, Ikeda Tohru. Alpha-L-fucosidase-1 is a diagnostic marker that distinguishes mucoepidermoid carcinoma from squamous cell carcinoma *PATHOLOGY INTERNATIONAL*. 2019.02; 69(2); 76-85
6. Ishida Shoko, Kayamori Kou, Sakamoto Kei, Yukimori Akane, Kugimoto Takuma, Harada Hiroyuki, Ikeda Tohru. Alpha-L-fucosidase-1 is a diagnostic marker that distinguishes mucoepidermoid carcinoma from squamous cell carcinoma(和訳中) *Pathology International*. 2019.02; 69(2); 76-85
7. Higuchi Y, Tsushima F, Sumikura K, Sato Y, Harada H, Kayamori K, Ikeda T. Diagnosis and treatment of oral focal mucinosis: a case series. *Journal of medical case reports*. 2019.04; 13(1); 108
8. 石田 尚子, 栢森 高, 坂本 啓, 行森 茜, 釘本 琢磨, 原田 浩之, 池田 通. 粘表皮癌における FUCA1 の発現と病理組織診断への応用 (The expression of FUCA1 in mucoepidermoide carcinoma and application to histopathological diagnosis) *日本病理学会会誌*. 2019.04; 108(1); 325
9. Yoshitake H, Kayamori K, Wake S, Sugiyama K, Yoda T. Biomarker expression related to chondromatosis in the temporomandibular joint. *Cranio : the journal of craniomandibular practice*. 2019.06; 1-5
10. Komiya R, Wada T, Tsushima F, Sakamoto K, Ikeda T, Yamaguchi A, Harada H, Uo M. Quantitation and distribution of metallic elements in sequestra of medication-related osteonecrosis of jaw (MRONJ) using inductively coupled plasma atomic emission spectroscopy and synchrotron radiation X-ray fluorescence analysis. *Journal of bone and mineral metabolism*. 2019.07; 37(4); 676-684
11. Nakazato Keiichiro, Mogushi Kaoru, Kayamori Kou, Tsuchiya Maiko, Takahashi Ken-Ichiro, Sumino Jun, Michi Yasuyuki, Yoda Tetsuya, Uzawa Narikazu. Glucose metabolism changes during the development and progression of oral tongue squamous cell carcinomas *ONCOLOGY LETTERS*. 2019.08; 18(2); 1372-1380
12. Yamamura Kiyonobu, Ashida Hiroshi, Okano Tokuju, Kinoshita-Daitoku Ryo, Suzuki Shiho, Ohtani Kaori, Hamagaki Miwako, Ikeda Tohru, Suzuki Toshihiko. Inflammasome Activation Induced by Perfringolysin O of *Clostridium perfringens* and Its Involvement in the Progression of Gas Gangrene *FRONTIERS IN MICROBIOLOGY*. 2019.10; 10; 2406
13. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer science*. 2019.11;
14. Yokokawa M, Morita KI, Oikawa Y, Kayamori K, Sakamoto K, Ikeda T, Harada H. Co-expression of EGFR and MET has a synergistic effect on the prognosis of patients with oral squamous cell carcinoma *J Oral Pathol Med*. 2019.12;
15. Tsuchiya Maiko, Kayamori Kou, Wada Akane, Komaki Motohiro, Ohata Yae, Hamagaki Miwako, Sakamoto Kei, Ikeda Tohru. A Novel, Tumor-Induced Osteoclastogenesis Pathway Insensitive to Denosumab but Interfered by Cannabidiol *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES*. 2019.12; 20(24);

16. 坂本 啓, 池田 通. 舌扁平上皮癌における p16 発現の検討 日本口腔内科学会雑誌. 2019.12; 25(2); 103
17. Rokutanda, S., Yamada, S., Kawasaki, G., Kawano, T., Yanamoto, S., Fujita, S., Ikeda, T., Umeda, M.. Solitary neurofibroma of the maxillary sinus: Report of a case Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 24(201200); 237-240

[Conference Activities & Talks]

1. Tohru Ikeda. Functional bone substitutes for repairment of large bone defect and mechanism of bone destruction by oral squamous cell carcinoma. KPPIKG2019 2019.10.10 Jakarta
2. Tohru Ikeda. Histopathologica Diagnosis of Odontogenic Tumors. KPPIKG2019 2019.10.11 Jakarta
3. 池田 通. 人工骨移植に対する生体反応と骨代謝. 第 2 3 回日本顎顔面インプラント学会 2019.12.01 つくば市

Bacterial Pathogenesis

Professor
SUZUKI Toshihiko
Associate Professor
ASHIDA Hiroshi
Assistant Professor
SUZUKI Shiho
Research fellow of JSPS
TSUKAZAKI Masayuki
Graduate Student and JSPS fellow
OKANO Tokuju
Graduate Student
YAMAMURA Kiyonobu
Graduate Student
LEEWANANTHAWET Anongwee (Department of Periodontology)
Graduate Student
ABASS Adiza (Department of Molecular Virology)
Graduate Student
BOONYALEKA Kotchakorn
Research Co-investigator
KINOSHITA DAITOKU Ryo (Osaka University)
Research Co-investigator
TANAKA Mototsugu (PMDA)
Technical Assistant Staff
IIDA Tamako

(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. Nakamoto Nobuhiro, Sasaki Nobuo, Aoki Ryo, Miyamoto Kentaro, Suda Wataru, Teratani Toshiaki, Suzuki Takahiro, Koda Yuzo, Chu Po-Sung, Taniki Nobuhito, Yamaguchi Akihiro, Kanamori Mitsuhiko, Kamada Nobuhiko, Hattori Masahira, Ashida Hiroshi, Sakamoto Michiie, Atarashi Koji, Narushima Seiko, Yoshimura Akihiko, Honda Kenya, Sato Toshiro, Kanai Takanori. Gut pathobionts underlie intestinal barrier dysfunction and liver T helper 17 cell immune response in primary sclerosing cholangitis *NATURE MICROBIOLOGY*. 2019.03; 4(3); 492-503
2. Suzuki Shiho, Suzuki Toshihiko, Sasakawa Chihiro. GLMN-cIAP1/2 axis controls inflammasome activation in response to bacterial infection *Japanese journal of bacteriology*. 2019.03; 74(1); 112
3. Yamamura kiyonobu, Okano Tokuju, Iku Otani, Suzuki Toshihiko. Inflammasome activation induced by *Clostridium perfringens* *Japanese Journal of Bacteriology*. 2019.03; 74(1); 94
4. Ashida Hiroshi, Sasakawa Chihiro, Suzuki Toshihiko. The interplay analysis between microbiota and bacterial pathogens *Japanese Journal of Bacteriology*. 2019.03; 74(1); 24
5. Kinoshita Ryo, Kiga Kotaro, Otsubo Ryota, Ogura Yoshitoshi, Sanada Takahito, Okano Tokuju, Suzuki Toshihiko, Hayashi Tetsuya, Mimuro Hitomi. Analysis of persistent infection mechanisms by *Helicobacter pylori* small RNA *Japanese Journal of Bacteriology*. 2019.03; 74(1); 95
6. Ayumi Saeki, Kohsuke Tsuchiya, Takashi Suda, Takeshi Into, Akira Hasebe, Toshihiko Suzuki, Ken-ichiro Shibata. How does the mycoplasmal lipopeptide FSL-1 induce IL-1 β release by living macrophages? *Japanese Journal of Bacteriology*. 2019.03; 74(1); 85
7. Okano Tokuju, Suzuki Shiho, Shoji Mikio, Nakayama Koji, Suzuki Toshihiko. Hypoxia induces enhancement of inflammasome activation by *P. gingivalis* infection *Japanese Journal of Bacteriology*. 2019.03; 74(1); 91
8. Ryota Otsubo, Hitomi Mimuro, Hiroshi Ashida, Jun Hamazaki, Shigeo Murata, Chihiro Sasakawa. Shigella effector IpaH4.5 targets 19S regulatory particle subunit RPN13 in the 26S proteasome to dampen cytotoxic T lymphocyte activation. *Cell. Microbiol.* 2019.03; 21(3); e12974
9. Anongwee Leewananthawet, Shinichi Arakawa, Tokuju Okano, Ryo Daitoku Kinoshita, Hiroshi Ashida, Yuichi Izumi, Toshihiko Suzuki. Ozone ultrafine bubble water induces the cellular signaling involved in oxidative stress responses in human periodontal ligament fibroblasts *Science and Technology of Advanced Materials*. 2019.05; 20(1); 589-598
10. Yamamura Kiyonobu, Ashida Hiroshi, Okano Tokuju, Kinoshita-Daitoku Ryo, Suzuki Shiho, Ohtani Kaori, Hamagaki Miwako, Ikeda Tohru, Suzuki Toshihiko. Inflammasome Activation Induced by Perfringolysin O of *Clostridium perfringens* and Its Involvement in the Progression of Gas Gangrene *FRONTIERS IN MICROBIOLOGY*. 2019.10; 10; 2406

[Misc]

1. Okano Tokuju, Ashida Hiroshi, Suzuki Shiho, Suzuki Toshihiko. The induction of host inflammatory responses by *Porphyromonas gingivalis* *The Journal of the Stomatological Society, Japan*. 2019.07; 86(2); 47

[Conference Activities & Talks]

1. Okano Tokuju, Suzuki Shiho, Shoji Mikio, Nakayama Koji, Suzuki Toshihiko. Hypoxia induces enhancement of inflammasome activation by *P. gingivalis* infection. The 92th Annual Meeting of Japanese Society for Bacteriology 2019.04.23 Sapporo
2. Saeki Ayumu, Tsuchiya Kosuke, Suda Takashi, Into Takashi, Hasebe Akira, Suzuki Toshihiko, Shibata Ken-ichiro. How does the mycoplasmal lipopeptide FSL-1 induce IL-1 β release by living macrophages?. The 92th Annual Meeting of Japanese Society for Bacteriology 2019.04.23 Sapporo

3. Kinoshita Ryo, Kiga Kotaro, Otsubo Ryota, Ogura Yoshitoshi, Sanada Takahito, Okano Tokuju, Suzuki Toshihiko, Hayashi Tetsuya, Mimuro Hitomi. Analysis of persistent infection mechanisms by *Helicobacter pylori* small RNA. The 92th Annual Meeting of Japanese Society for Bacteriology 2019.04.23 Sapporo
4. Ashida Hiroshi, Sasakawa Chihiro, Suzuki Toshihiko. The interplay analysis between microbiota and bacterial pathogens. The 92th Annual Meeting of Japanese Society for Bacteriology 2019.04.23 Sapporo
5. Yamamura kiyonobu, Okano Tokuju, Iku Otani, Suzuki Toshihiko. Inflammasome activation induced by *Clostridium perfringens*. The 92th Annual Meeting of Japanese Society for Bacteriology 2019.04.23 Sapporo
6. Suzuki Shiho, Suzuki Toshihiko, Sasakawa Chihiro. GLMN-cIAP1/2 axis controls inflammasome activation in response to bacterial infection. The 92th Annual Meeting of Japanese Society for Bacteriology 2019.04.23 Sapporo
7. Okano Tokuju, Suzuki Toshihiko. Hypoxia induces enhancement of inflammasome activation by *P. gingivalis*. 7th International Cytokine and Interferon Society 2019.10.20 Vienna
8. Tokuju Okano, Miwa Sasai, Masahiro Yamamoto, Toshihiko Suzuki. *Aggregatibacter actinomycetemcomitans* induces activation of noncanonical inflammasome via lysosomal degradation. The 48th annual meeting of the Japanese Society for Immunology 2019.12.13 Hamamatsu

Molecular Immunology

Professor	Miyuki Azuma
Associate Professor	Shigenori Nagai
Assistant Professor	Tatsukuni Ohno(~ Mar.) Yohei Kawano(Apr. ~)
Adjunct instructor	Hiroshi Kiyono Takeshi Azuma Tatsukuni Ohno(Jul. ~)
Graduate Students(Doctor)	Emi Furusawa(Pediatric Dentistry)(~ Mar.) Xia Yulong(~ Sept.) Yang Yue Yoshihisa Kashima(Oral and Maxillofacial Surgery) Ao Xiang(Pulp Biology and Endodontics) Wongtim Keeratika Amrita Widyagarini Subagyo(Pediatric Dentistry) Droonpan Pissacha(Oct. ~)
Affiliated Researcher	Hidetake Tachinami(University of Toyama)(~ Mar.)

(1) Research

Research Subjects

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

(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. Kagami S, Kizukuri R, Nagai S, Aizawa M. Responses of immune cells to hydroxyapatite ceramics loaded with immunostimulators. Journal of the Society of Inorganic Materials, Japan. 2019; 26; 74-81

2. Ikeda E, Shiba T, Ikeda Y, Suda W, Nakasato A, Takeuchi Y, Azuma M, Hattori M, Izumi Y. Deep sequencing reveals specific bacterial signatures in the subgingival microbiota of healthy subjects. *Clinical oral investigations*. 2019.01; e-pub;
3. Mulati K, Hamanishi J, Matsumura N, Chamoto K, Mise N, Abiko K, Baba T, Yamaguchi K, Horikawa N, Murakami R, Taki M, Budiman K, Zeng X, Hosoe Y, Azuma M, Konishi I, Mandai M. VISTA expressed in tumour cells regulates T cell function. *Br J Cancer*. 2019.01; 120(1); 115-127
4. Copland A, Sparrow A, Hart P, Diogo GR, Paul M, Azuma M, Reljic R. *Bacillus calmette-guérin* induces PD-L1 expression on antigen-presenting cells via autocrine and paracrine interleukin-STAT3 circuits. *Sci Rep*. 2019.03; 9(1); 3655
5. Tachinami H, Nishii N, Xia Y, Kashima Y, Ohno T, Nagai S, Li L, Lau W, Tomihara K, Noguchi M, Azuma M. Differences of tumor-recruiting myeloid cells in murine squamous cell carcinoma influence the efficacy of immunotherapy combined with a TLR7 agonist and PD-L1 blockade. *Oral Oncology*. 2019.04; 91; 21-28
6. Yoshikawa S, Oh-Hora M, Hashimoto R, Nagao T, Peters L, Egawa M, Ohta T, Miyake K, Adachi T, Kawano Y, Yamanishi Y, Karasuyama H. Pivotal role of STIM2, but not STIM1, in IL-4 production by IL-3-stimulated murine basophils. *Science Signaling*. 2019.04; 12(576);
7. Vu CTB, Thammahong A, Yagita H, Azuma M, Hirankarn N, Ritprajak P, Leelahavanichkul A. Blockade of PD-1 attenuated post-sepsis aspergillosis via the activation of IFN- γ and the dampening of IL-10. *Shock*. 2019.07; 11;
8. Ikeda E, Shiba T, Ikeda Y, Suda W, Nakasato A, Takeuchi Y, Azuma M, Hattori M, Izumi Y. Japanese subgingival microbiota in health vs disease and their roles in predicted functions associated with periodontitis. *Odontology*. 2019.09;
9. Furusawa E, Ohno T, Nagai S, Noda T, Komiyama T, Kobayashi K, Hamamoto H, Miyashin M, Yokozeki H, Azuma M. Silencing of PD-L2/B7-DC by topical application of small interfering RNA inhibits elicitation of contact hypersensitivity. *J Invest Dermatol*. 2019.10; 139(10); 2164-2173
10. Xia Y, Ohno T, Nishii N, Bhingare A, Tachinami H, Kashima Y, Nagai S, Saito H, Nakae S, Azuma M. T cell antitumor responses overcoming pro-tumor effects by regulatory T cells in a colon carcinoma model. *Biochem Biophys Res Commun*. 2019.10; 518(2); 331-336
11. Kunishige T, Taniguchi H, Ohno T, Azuma M, Hori J. VISTA is crucial for corneal allograft survival and maintenance of immune privilege. *Invest Ophthalmol Vis Sci*. 2019.12; 60(15); 4958-4965

[Books etc]

1. Azuma M. Co-signal molecules in T cell activation:Immune regulation in health and disease. Springer, 2019.11 (ISBN : 978-981-32-9716-6)

[Misc]

1. Azuma M. Co-signal molecules in T-cell activation : Historical overview and perspective. *Adv Exp Med Biol.* 2019.11; 1189; 3-23
2. Nagai S, Azuma M. The CD28-B7 family of co-signaling molecules. *Adv Exp Med Biol.* 2019.11; 1189; 25-51

Advanced Biomaterials

Professor UO Motohiro
 Assistant Professor WADA Takahiro
 Graduate Student CHAIAMORNSUP Patcharanun
 Graduate Student KOYAMA Akihiro (Orthodontic Science)
 Graduate Student KINJO Rio (Sports Medicine and Dentistry)
 Graduate Student Saleh Sherif Adel Abdelfattah (Pulp Biology and Endodontics)

(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. Sayed M., Matsui N., Uo M., Nikaido T., Oikawa M., Burrow M.F., Tagami J.. Morphological and elemental analysis of silver penetration into sound/demineralized dentin after SDF application Dental Materials. 2019; 35; 1718-1727
2. Sai Kham Lyann, Tomohiro Takagaki, Tohru Nikaido, Takahiro Wada, Motohiro Uo, Masaomi Ikeda, Alireza Sadr, Junji Tagami. Efficacy of Various Surface Treatments on the Bonding Performance of Saliva Contaminated Lithium-Disilicate Ceramics The journal of adhesive dentistry. 2019.02; 21(1); 51-58
3. Dhaifallah Alqarni, Masatoshi Nakajima, Keiichi Hosaka, Kurumi Ide, Daiki Nagano, Takehiro Wada, Masaomi Ikeda, Teerapong Mamanee, Ornnicha Thanatvarakorn, Taweesak Prasansuttiporn, Richard Foxton, Junji Tagami. The repair bond strength to resin matrix in cured resin composites after water aging. Dent Mater J. 2019.03; 38(2); 233-240
4. Wakisaka Y, Kido D, Uehara H, Yuan Q, Feiten FE, Mukai S, Takakusagi S, Uemura Y, Yokoyama T, Wada T, Uo M, Sekizawa O, Uruga T, Iwasawa Y, Asakura K. Development of Surface Fluorescence X-ray

Absorption Fine Structure Spectroscopy using a Laue-Type Monochromator. Chemical record (New York, N.Y.). 2019.07; 19(7); 1157-1165

5. Komiya R, Wada T, Tsushima F, Sakamoto K, Ikeda T, Yamaguchi A, Harada H, Uo M. Quantitation and distribution of metallic elements in sequestra of medication-related osteonecrosis of jaw (MRONJ) using inductively coupled plasma atomic emission spectroscopy and synchrotron radiation X-ray fluorescence analysis. Journal of bone and mineral metabolism. 2019.07; 37(4); 676-684
6. Ayumi Ogawa, Takahiro Wada, Yoshiyuki Mori, Motohiro Uo. Time dependence of multi-ion absorption into human enamel from surfae pre-reacted glass-ionomer (S-PRG) filler eluate Dental Materials Journal. 2019.07; 38(5); 707-712
7. Upendar Kashaboina, Yuta Nishikawa, Yuki Wakisaka, Natee Sirisit, Shinichi Nagamatsu, Deling Bao, Hiroko Ariga-Miwa, Satoru Takakusagi, Yuta Inami, Fumiya Kuriyama, Arnoldus Lambertus Dipu, Hitoshi Ogiwara, Shoji Iguchi, Ichiro Yamanaka, Takahiro Wada, Kiyotaka Asakura. Metamorphosis-like Transformation During Activation of In/SiO₂ Catalyst for Non-Oxidative Coupling of Methane: In Situ X-ray Absorption Fine Structure Analysis Chemistry Letters. 2019.07; 48(9); 1145-1147
8. Shima Y., Koyama A., Uo M., Ono T.. Effectiveness of low binding frictional materials: Evaluation of the binding frictional resistance of improved superelastic nickel-titanium alloy wires with different bracket combinations APOS Trends in Orthodontics. 2019.07; 9(3); 156-164

[Conference Activities & Talks]

1. Kashaboina Upendar, Natee Sirisit, Hiroko Ariga-Miwa, Satoru Takakusagi, Yuta Nishikawa, Fumiya Kuriyama, Arnoldus lambertus Dipu, Hitoshi Ogiwara, Shoji Iguchi, Ichiro Yamanaka, Takahiro Wada, Kiyotaka Asakura. Operando EXAFS Analysis of In/SiO₂ Catalyst during NMC. IRCCS The 2nd International Symposium “New Future by Chemical Synthesis and Energy Materials” 2019.01.25 Kihada Hall, Uji Campus, Kyoto University, Uji Japan
2. Inokoshi M, Shimizubata M, Hatano K, Wada T, Uo M, Takahashi R, Minakuchi S. Application of S-PRG filler containing materials for geriatric dentistry. The 4th Bioactive Materials S-PRG Research Meeting 2019.03.22 Kyoto
3. Hatano K, Inokoshi M, Wada T, Uo M, Takahashi R, Minakuchi S. Ion release capacity of a novel S-PRG filler containing denture adhesive. The 73rd General Session of the Japanese Society for Dental Materials and Devices 2018 2019.04.21 Tokyo
4. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Ion release and acid buffering capacity of S-PRG containing cement. 97th General Session & Exhibition of the IADR 2019.06.21 Vancouver
5. Uo M.. Application of synchrotron X-ray radiation for the analyses of biomaterials and biological tissues. 4th International Conference on Innovations in Biomaterials, Biomanufacturing, and Biotechnologies (Bio-4) 2019.07.22 Marriott Downtown at CF Toronto Eaton Centre Hotel Toronto, Canada
6. Takashima Y, Wada T, Uo M, Minami F. Study on impact response of thermoplastics for face or mouth guards. The 4th International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-4) 2019.10.03 Sendai, Japan
7. Uo M, Wada T. Time dependent absorption of ions into human enamels from the multi-ion releasing glass fillers for dental composite resins. The 4th International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-4) 2019.10.03 Sendai, Japan
8. Hidekazu TAKAHASHI, Kazuyuki HANDA, Yashuhiro HOTTA, Naohiko IWASAKI, Patcharanun CHAIAMORNSUP, Yumi TSUCHIDA . Dimensional stability of dental model fabricated with vat photopolymerization . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
9. Shimizubata M, Inokoshi M, Hatano K, Wada T, Takahashi R, Uo M, Minakuchi S. Fluoride recharge and release capacity of a S-PRG filler containing glass ionomer cement. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki

10. Structure-Activity Relation of In/SiO₂ and In/ZSM-5 Studied by Simultaneous Measurement of QXAFS and Mass Spectroscopy. 2019.10.28

[Awards & Honors]

1. Brilliant Poster Awar, International Academy for Digital Dental Medicine, 2019.10

Oral Radiation Oncology

Professor
Assistant Professor

Clinical Fellow
Graduate Students

Masahiko MIURA
Atsushi KAIDA
Yusuke ONOZATO (April~)
Ryo NAKTANI (~March)
Nisha GOWRI MANILA (March)
Hisao HOMMA
Hitomi NOJIMA
Hiroaki SHIMONO
Esther NG FENG YING (Oct~)
Kohki TOHYAMA (April~)

(1) Outline

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

(2) Research

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

(3) Education

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

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

(6) Clinical Performances

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

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

1. Goto T, Homma H, Kaida A, Miura M. WEE1 inhibition enhances sensitivity to hypoxia/reoxygenation in HeLa cells. *J Radiat Res.* 2019.09; 60(5); 714-718
2. Hisao Homma, Hitomi Nojima, Atsusi Kaida, Masahiko Miura. Induction of endomitosis-like event in HeLa cells following CHK1 inhibitor treatment *Biochem Biophys Res Commun.* 2019.12; 520(2); 492-497

[Misc]

1. Masahiko Miura. Basics of Radiation Oncology Dental Radiology. 2019.09; 59(1); 1-7

[Conference Activities & Talks]

1. Kazuki Takahashi, Katarzyna A. Inoue, Yasuhiro Yoshimatsu, Atsushi Kaida, Kei Takahashi, Shimpei Kubota, Akinari Sugauchi, Toshihiro Uchihashi, Susumu Tanaka, Mikihiro Kogo, Masahiko Miura, Kohei Miyazono and Tetsuro Watabe. TGF- β -induced cell cycle arrest is associated with increased migration and metastasis of oral squamous carcinoma cells. AACR-JCA Joint Conference 2019.02.09 Maui, USA
2. Kazuki Takahashi, Katarzyna A. Inoue, Yasuhiro Yoshimatsu, Atsushi Kaida, Kei Takahashi, Shimpei Kubota, Akinari Sugauchi, Toshihiro Uchihashi, Susumu Tanaka, Mikihiro Kogo, Masahiko Miura, Kohei Miyazono and Tetsuro Watabe. Regulatory role of transforming growth factor- β signals in the migration and cell cycle of oral squamous carcinoma cells. Keystone Symposia; Cancer Metastasis: The role of metabolism, immunity and microenvironment 2019.03.17 Florence, Italy
3. Kazuki Takahashi, Katarzyna A. Inoue, Atsushi Kaida, Kei Takahashi, Shimpei Kubota, Akinari Sugauchi, Toshihiro Uchihashi, Susumu Tanaka, Mikihiro Kogo, Masahiko Miura, Kohei Miyazono, Tetsuro Watabe. TGF- β -induced cell cycle arrest is associated with increased migration and metastasis of oral squamous carcinoma cells. The 78th Annual Meeting of the Japanese Cancer Association 2019.09.28 kyoto
4. Masahiko MIURA. Development of hypoxic cell radiosensitizers: Myth and reality. The 62nd Annual Meeting of the Japanese Radiation Research Society 2019.11.16 kyoto

Oral and Maxillofacial Surgery

Professor Hiroyuki HARADA

Junior Associate Professor Yasuyuki MICHl, Fumihiko TSUSHIMA

Assistant Professor Hiroaki SHIMAMOTO, Hirofumi TOMIOKA,

Kae TANAKA, Hideaki HIRAI, Takeshi KUROSHIMA

Specially Appointed Assistant Professor

Yumi MOCHIZUKI, Takuma KUGIMOTO, Toshimitsu OHSAKO, Kouhei OKUYAMA

Graduate Student

Yoshihisa KASHIMA, Hitomi NOJIMA, Misaki YOKOKAWA,

Naoya KINOSHITA, Yuuki TAKAGAWA, Aoi KANEKO, Shintaro SAKAKITANI,

Yoshimitsu SATO, Misako TANAKA, Hiroaki SHIMONO, Kaho Takada, Shohei YANAGISAWA,

Takuya KOMIYAMA, Cuong TRAN MINH, Shunya HAYASHI, Yuta IKAMI, Junko TAKEI,

Phung TRAN XUAN, Rika NOJI

(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 and experimental studies on bone regeneration using β -TCP and/or platelet rich plasma.
- 5) 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, oral mucosal disease, temporomandibular joint 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, oral mucosal disease and temporomandibular joint 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. Suzuki N, Kuribayashi A, Sakamoto K, Sakamoto J, Nakamura S, Watanabe H, Harada H, Kurabayashi T. Diagnostic abilities of 3T MRI for assessing mandibular invasion of squamous cell carcinoma in the oral cavity: comparison with 64-row multidetector CT. *Dentomaxillofacial Radiology*. 2019.01;
2. Takada Kaho, Kuroshima Takeshi, Shimamoto Hiroaki, Ohsako Toshimitsu, Kayamori Kou, Ikeda Tohru, Harada Hiroyuki. Metastasis of lower gingival squamous cell carcinoma to buccinator lymph node: case report and review of the literature *WORLD JOURNAL OF SURGICAL ONCOLOGY*. 2019.01; 17(1); 13
3. Suzuki N, Kuribayashi A, Sakamoto K, Sakamoto J, Nakamura S, Watanabe H, Harada H, Kurabayashi T. Diagnostic abilities of 3T MRI for assessing mandibular invasion of squamous cell carcinoma in the oral cavity: comparison with 64-row multidetector CT *Dentomaxillofac Radiol*. 2019.01;
4. Fukuda S, Akiyama M, Harada H, Nakahama KI.. Effect of gap junction-mediated intercellular communication on TGF- β induced epithelial-to-mesenchymal transition. *Biochem Biophys Res Commun*.. 2019.01; 508(3); 928-933
5. Sato Kiyoshi, Shimamoto Hiroaki, Mochizuki Yumi, Hirai Hideaki, Tomioka Hirofumi, Shimizu Risa, Marukawa Eriko, Fukayama Haruhisa, Yoshimura Ryoichi, Ishida Hiroo, Harada Hiroyuki. Treatment of oral cancers during pregnancy: a case-based discussion *JOURNAL OF OTOLARYNGOLOGY-HEAD & NECK SURGERY*. 2019.02; 48(1); 9
6. Ishida S, Kayamori K, Sakamoto K, Yukimori A, Kugimoto T, Harada H, Ikeda T.. Alpha-L-fucosidase-1 is a diagnostic marker that distinguishes mucoepidermoid carcinoma from squamous cell carcinoma. *Pathol Int*.. 2019.02;
7. Yoshikazu F, Shinji Y, Shunsuke I, Masato S, Takuro N, Miyuki Y, masato F, Hiroyuki H, Takuya M, Yusuke S, Masaki T, Mika K.K, Yukinari K. A Monoclonal Antibody Against Pig Podoplanin *Monoclon. Antib. Immunodiagn. Immunother*.. 2019.02; 38(1); 30-36
8. Yoshikazu F, Shinji Y, Shunsuke I, Takuro N, Miyuki Y, Masato S, Hiroyuki H, Masato F, Mika K.K, Yukinari K. A monoclonal antibody for the immunohistochemical analysis of horse podoplanin *Biochem Biophys Rep*.. 2019.02; (18); 100616
9. Tachinami H, Nishii N, Xia Y, Kashima Y, Ohno T, Nagai S, Li L, Lau W, Tomihara K, Noguchi M, Azuma M. Differences of tumor-recruiting myeloid cells in murine squamous cell carcinoma influence the efficacy of immunotherapy combined with a TLR7 agonist and PD-L1 blockade. *Oral Oncology*. 2019.04; 91; 21-28
10. Furusawa Y, Yamada S, Itai S, Nakamura T, Takei J, Sano M, Harada H, Fukui M, Kaneko MK, Kato Y. Establishment of a monoclonal antibody PMab-233 for immunohistochemical analysis against Tasmanian devil podoplanin. *Biochem Biophys Rep*. 2019.04;
11. Kaneko MK, Furusawa Y, Sano M, Itai S, Takei J, Harada H, Fukui M, Yamada S, Kato Y. Epitope mapping of the anti-horse podoplanin monoclonal antibody PMab-202. *Monoclon Antib Immunodiagn Immunother*.. 2019.04; 37(5); 233-237
12. Furusawa Y, Kaneko MK, Nakamura T, Itai S, Fukui M, Harada H, Yamada S, Kato Y. Establishment of a monoclonal antibody PMab-231 for tiger podoplanin. *Monoclon Antib Immunodiagn Immunother*.. 2019.04; 38(2); 89-95
13. Okuyama K, Fukushima H, Naruse T, Yanamoto S, Tsuchihashi H, Umeda M.. CD44 Variant 6 Expression and Tumor Budding in the Medullary Invasion Front of Mandibular Gingival Squamous Cell Carcinoma Are Predictive Factors for Cervical Lymph Node Metastasis. *Pathology and Oncology Research*. 2019.04; 25(2); 603-609
14. Higuchi Y, Tsushima F, Sumikura K, Sato Y, Harada H, Kayamori K, Ikeda T.. Diagnosis and treatment of oral focal mucinosis: a case series. *Journal of Medical Case Reports*. 2019.04; 13(1)(108); Published online

15. Mochizuki Y., Harada H., Oyama J., Sakamoto K., Michi Y., Kuroshima T., Kugimoto T.. Metastatic gastric adenocarcinoma of the tongue with initial symptoms of glossodynia. *Curr Probl Cancer.* . 2019.05; 2019 May 23. pii: S0147-0272(18)30403-3.;
16. Takei J, Itai S, Furusawa Y, Yamada S, Nakamura T, Sano M, Harada H, Fukui M, Kaneko MK, Kato Y. Epitope mapping of anti-tiger podoplanin monoclonal antibody PMab-231. *Monoclon Antib Immunodiagn Immunother.*. 2019.06; 38(3); 129-132
17. Kato Y, Furusawa Y, Itai S, Takei J, Nakamura T, Sano M, Harada H, Yamada S, Kaneko MK. . Establishment of an Anticetacean Podoplanin Monoclonal Antibody PMab-237 for Immunohistochemical Analysis. *Monoclon Antib Immunodiagn Immunother.*. 2019.06; 38(3); 108-113
18. UESUGI Atsushi, TSUSHIMA Fumihiko, SHIMIZU Risa, NAKAGAWA Chisato, SATO Kiyoshi, SAKURAI Jinkyō, HARADA Hiroyuki. A case of secondary syphilis with inflammation of oral mucosa 2019.06; 25(1); 16-19
19. A case of neuroendocrine carcinoma arising in the floor of the mouth 2019.07; 65(7); 455-460
20. Komiya R, Wada T, Tsushima F, Sakamoto K, Ikeda T, Yamaguchi A, Harada H, Uo M. Quantitation and distribution of metallic elements in sequestra of medication-related osteonecrosis of jaw (MRONJ) using inductively coupled plasma atomic emission spectroscopy and synchrotron radiation X-ray fluorescence analysis *Journal of Bone and Mineral Metabolism.* 2019.07; 37(4); 676-684
21. Yoshikazu F, Shinji Y, Takuro N, Masato S, Yusuke S, Shunsuke I.. A monoclonal antibody for the immunohistochemical analysis of goat podoplanin Heliyon. 2019.07; 5(7); e02063
22. Takei J, Furusawa Y, Yamada S, Nakamura T, Sayama Y, Sano M, Konnai S, Kobayashi A, Harada H, Kaneko MK, Kato Y. PMab-247 Detects Bear Podoplanin in Immunohistochemical Analysis. *Monoclon Antib Immunodiagn Immunother.*. 2019.08; 38(4); 171-174
23. Nakazato K, Mogushi K, Kayamori K, Tsuchiya M, Takahashi KI, Sumino J, Michi Y, Yoda T, Uzawa N. Glucose metabolism changes during the development and progression of oral tongue squamous cell carcinomas. *Oncol Lett.* 2019.08; 8(2); 1372-1380
24. Okuyama K, Naruse T, Yutori H, Yanamoto S, Umeda M.. Oral surgery in patients with antiphospholipid syndrome. *Journal of Oral Science.* 2019.08; 61(3); 386-390
25. Atsushi Uesugi, Kaori Mochida, Hiroyuki Harada, Hideki Imai. Ossifying fibroma arising from the zygomatic arch: a case report *Journal of Stomatology Oral and Maxillofacial Surgery.* 2019.08;
26. Kato Y, Ohishi T, Yamada S, Itai S, Takei J, Sano M, Nakamura T, Harada H, Kawada M, Kaneko MK.. Anti-Human Epidermal Growth Factor Receptor 2 Monoclonal Antibody H2Mab-41-Exerts Antitumor Activity in a Mouse Xenograft Model of Colon Cancer *Monoclon. Antib. Immunodiagn. Immunother.*. 2019.08; 38(4); 157-161
27. Ohsako T, Shimamoto H, Tomioka H, Hirai H, Kuroshima T, Mochizuki Y, Kugimoto T, Tsushima F, Nakamura S, Kurabayashi T, Harada H.. Detection of extraoral primary cancers by positron emission tomography/computed tomography in patients with oral squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2019.09;
28. Kojima Y, Kawaoka Y, Sawada S, Hayashida S, Okuyama K, Yutori H, Kawakita A, Ishida S, Soutome S, Yanamoto S, Umeda M, Iwai H.. Clinical significance of periosteal reaction as a predictive factor for treatment outcome of medication-related osteonecrosis of the jaw. *Journal of Bone and Mineral Metabolism.* 2019.09; 37(5); 913-919
29. Xia Y, Ohno T, Nishii N, Bhingare A, Tachinami H, Kashima Y, Nagai S, Saito H, Nakae S, Azuma M. T cell antitumor responses overcoming pro-tumor effects by regulatory T cells in a colon carcinoma model. *Biochem Biophys Res Commun.* 2019.10; 518(2); 331-336
30. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M.. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer Science.*. 2019.11;

32. Homma H, Nojima H, Kaida A, Miura M. Induction of endomitosis-like event in HeLa cells following CHK1 inhibitor treatment *Biochem Biophys Res Commun.* . 2019.12;
33. Oikawa Y, Michi Y, Tsushima F, Tomioka H, Mochizuki Y, Kugimoto T, Osako T, Nojima H, Yokokawa M, Kashima Y, Harada H. Management of retropharyngeal lymph node metastasis in oral cancer. *Oral Oncology.* 2019.12; 99;
34. Shuhei Fukuda, Takeshi Kuroshima, Hirofumi Tomioka, Yu Oikawa, Hiroyuki Harada. The delayed appearance of occult cervical lymph node metastasis after long periods in patients with tongue squamous cell carcinoma: a report of three cases 2019.12; 31(4); 197-202

[Conference Activities & Talks]

1. A clinical study of T4 cases . 37th Japan Society for Oral Oncology 2019.01.24 Nagasaki
2. Hakoyama T, Yamada SI, Yokozeki M, Tanaka H, Hasegawa T, Okuyama K, Yamakawa N, Okura M, Yanamoto S, Komori T, Kirita T, Umeda M, Kurita H.. Clinical significance of the G8 screening tool in elderly patients with oral squamous cell carcinoma.. 37th Japan Society for Oral Oncology 2019.01.24 Nagasaki
3. Naoya Kinoshita, Yoshihiro Sasaki, Riku Kawasaki, Eriko Marukawa, Hiroyuki Harada, Kazunari Akiyoshi. Magnetic nanogel delivery of transcription factor to adipose-derived stem cell for muscle tissue regeneration. Kyoto Winter School 2019 "Quantifying Dynamics of Life" 2019.3.11-20 2019.03.11
4. Yuki Takagawa, Yasuyuki Gen, Tomoki Muramatsu, Hiroyuki Harada, Johji Inazawa. Exploring novel tumor suppressive microRNAs in OSCC. ISPCM ANNUAL MEETING 2019 2019.3.12 2019.03.12 Seoul Dongdaemun, Korea
5. Naoya Kinoshita, Yoshihiro Sasaki, Riku Kawasaki, Eriko Marukawa, Hiroyuki Harada, Kazunari Akiyoshi. Magnetic delivery of transcription factors to stem cells for muscle regeneration. Society For Biomaterials 2019 Annual Meeting and Exposition 2019.4.3-6 2019.04.03 Seattle
6. Okuyama K, Yanamoto S, Naruse T, Yutori H, Ishida S, Umeda M. Clinical significance on oral squamous cell carcinoma in adolescent and young adult patients. 43rd Japan Society for Head and Neck Cancer 2019.06.13 Kanazawa
7. Manila NG, Sakamoto J, Kurabayashi T, Harada H, Tahmasbi-Arashlow M, Nair MK. Odontogenic myxoma: A case report and literature review. 2019 Joint Conference of IADMFR/AAOMR 2019.08.26 Philadelphia, USA
8. Michi Y, Harada H, Hirai H, Mochizuki Y, Kuroshima T, Shimamoto H, Tomioka H. Okuyama K, Kugimoto T, Ohsako T, Kayamori K.. Diffuse large B-cell lymphoma with initial presentation in the upper and lower jaws. . 7th world congress of the international academy of oral oncology. 2019.9.1 2019.09.01 Rome Italy.
9. Takeshi KUROSHIMA, Yasuyuki MICH, Hiroaki SHIMAMOTO, Hirofumi TOMIOKA, Hideaki HIRAI, Takuma KUGIMOTO, Yumi MOCHIZUKI, Kae TANAKA and Hiroyuki HARADA. Contralateral cervical lymph node metastases in tongue squamous cell carcinoma. 7th world congress of the international academy of oral oncology. 2019.9.1 2019.09.01 Rome Italy.
10. UESUGI Atsushi, TSUSHIMA Fumihiko, HARADA Hiroyuki. Laugier-Hunziker-Baran Syndrome: A Case Report. 2019.09.20
11. Yoshihiro Sasaki, Ryosuke Mizuta, Naoya Kinoshita, Kazunari Akiyoshi . Intracellular delivery of biologics using magnetically-navigated nanocarrier. 第 57 回日本生物物理学会年会 2019.9.26 2019.09.26 宮崎
12. Okuyama K, Michi Y, Tomioka H, Shimamoto H, Kuroshima T, Shibata E, Yanamoto S, Umeda M, Yoda T, Harada H. Clinical study on oral squamous cell carcinomas in Adolescent and Young Adult (AYA) generation.. The 64th Congress of the Japanese Society of Oral and Maxillofacial Surgeons 2019.10.25 Sapporo
13. Yu Oikawa, Takuma Kugimoto, Yuriko Sato, Ken Omura. Management of dental extractions in patients undergoing anticoagulant therapy. The 64th Congress of the Japanese Society of Oral and Maxillofacial Surgeons 2019.10.25 Sapporo

14. Eri Shibata, Keiichi Morita, Kou Kayamori, Misaki Yokokawa, Erina Tonouchi, Yu Oikawa, Eri Anzai, Yosuke Harazono, Yasuyuki Michi, Tohru Ikeda, Hiroyuki Harada, Tetsuya Yoda. Analysis of correlation between Mammaglobin expression and ETV6 split in diagnosis of secretory carcinoma. The 64th Annual Meeting of the Japan Society of Human Genetics 2019.11.08 Nagasaki
15. UESUGI Atsushi, TSUSHIMA Fumihiko, OKUYAMA Kohei, SATO Yuriko, TOMIOKA Hirofumi, MICHII Yasuyuki, HARADA Hiroyuki. A case of pemphigoid associated with lower gingival carcinoma. 2019.12.14

[Awards & Honors]

1. Young Scientists Award, Cancer Science, 2019.09

Oral and Maxillofacial Radiology

Professor: Tohru KURABAYASHI

Associate Professor: Hiroshi WATANABE

Junior Associate Professor: Naoto OHBAYASHI, Norio YOSHINO

Assistant Professor: Shin NAKAMURA, Ami KURIBAYASHI, Junichiro SAKAMOTO

Hospital Staff: Yoshikazu NOMURA, Mamiko FUJIKURA

Graduate Student: Hiroko ISHII, Noriko SUZUKI, Tran Thi Xuan LAN, Sakurako ASAI,

Wamasing PEERAPONG, Miharuru TAGUCHI, Yumi TSUCHIDA

Natnisha PEERAPONG

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. Wamasing P, Watanabe H, Tsuchida Y, Ohbayashi N, Suzuki T, Kurabayashi T. The development of new image receptor-holding instruments with appropriate horizontal X-ray beam angulation for periapical radiographs Dentomaxillofacial Radiology. 2019.01; 48; 20180354

2. Suzuki N, Kuribayashi A, Sakamoto K, Sakamoto J, Nakamura S, Watanabe H, Harada H, Kurabayashi T. Diagnostic abilities of 3T MRI for assessing mandibular invasion of squamous cell carcinoma in the oral cavity: comparison with 64-row multidetector CT. *Dentomaxillofacial Radiology*. 2019.01;
3. Tsuchida Y, Takahashi H, Watanabe H, Oki M, Shiozawa M, Kurabayashi T, Suzuki T. Effects of number of metal restorations and mandibular position during computed tomography imaging on accuracy of maxillofacial models *J Prosthodont Res*. 2019.04; 63(2); 239-244
4. Tran LTX, Sakamoto J, Kuribayashi A, Watanabe H, Tomisato H, Kurabayashi T. Quantitative evaluation of artefact reduction from metallic dental materials in short tau inversion recovery imaging: efficacy of syngo WARP at 3.0 tesla. *Dentomaxillofacial Radiology*. 2019.07; 20190036
5. Kawabata I, Imai H, Kanno Z, Tetsumura A, Tsutsumi Y, Doi H, Ashida M, Kurabayashi T, Hanawa T, Yamamoto T, Ono T. Three-dimensional quantification of magnetic resonance imaging artifacts associated with shape factors *Dent Mater J*. 2019.07; 38; 638-645
6. Fujikura M, Nakamura S, Asai S, Kurabayashi T. Diagnostic ability of [¹⁸F] -fluorodeoxyglucose-positron emission tomography/computed tomography for retropharyngeal lymph node in patients with oral cancer *Nuclear Medicine Communications*. 2019.09; 40(10); 1036-1042
7. Yamada I, Miyasaka N, Kobayashi D, Wakana K, Oshima N, Wakabayashi A, Sakamoto J, Saida Y, Tateishi U, Eishi Y. Endometrial carcinoma: texture analysis of apparent diffusion coefficient maps and its correlation with histopathologic findings and prognosis. *Radiology: Imaging Cancer*. 2019.11; 1(2); e190054

[Misc]

1. Yoshida M, Honda E, Ozawa E, Inoue-Arai SM, Ohmori H, Moriyama K, Ono T, Kurabayashi T, Yoshihara H, Nunthayanon K. Principles of the magnetic resonance imaging movie method for articulatory movement *Oral Radiol*. 2019.06; 35; 91-100
2. Tsuchimochi M, Kurabayashi T.. Role of imaging in drug-related osteonecrosis of the jaw: an up-to-date review. *Jpn Dent Sci Rev..* 2019.11; 55; 1-4

[Conference Activities & Talks]

1. Kurabayashi T. Odontogenic tumors and cysts: imaging characteristics.. The 41st Annual Dental Scientific Conference 2019.04.02 Ho Chi Minh city
2. Sakamoto J. Imaging diagnosis of temporomandibular joint diseases. The 41th annual scientific conference of dental reserch 2019.04.02 Ho Chi Minh city, Vietnam
3. Nakamura S. Normal anatomy of jaw bone on CBCT imaging. The 41th Dental Scientifio Conference 2019.04.02 Ho Chi Minh City
4. Watanabe H, Wamasing P, Deepho C, Sakamoto J, Kurabayashi T. Imaging of the bifid mandibular canal using MRI. 2019 Joint Conference of IADMFR/AAOMR 2019.08.24 Philadelphia, USA
5. Manila NG, Sakamoto J, Kurabayashi T, Harada H, Tahmasbi-Arashlow M, Nair MK. Odontogenic myxoma: A case report and literature review. 2019 Joint Conference of IADMFR/AAOMR 2019.08.26 Philadelphia, USA

Anesthesiology and Clinical Physiology

Professor

Haruhisa Fukayama

Associate Professor

Ryo Wakita

Junior Associate Professor

Keiko Abe (～ Sep) ,

Tomoka Matsumura (Feb ～)

Assistant Professors

Tomoyuki Miyamoto,

Tomoka Matsumura (～ Jan)

Yukiko Baba (Apr ～)

Hospital Staffs

Kotomi Uchinuma (Apr ～)

Hidetaka Murata (Apr ～)

Tunataka Abo

Takutoshi Inoue (Apr ～)

Kouichirou Ozawa (Apr ～)

Sayaka Asano (Apr ～)

Graduate Students

Chihiro Suzuki,

Kaeko Araki,

Takaya Itou,

Yuu Satou,

Keiko Abe (Apr ～)

Research Students

Keita Niimi (Apr ～),

Moegi Toyomaki (Apr ～),

Advanced Clinical Training

Feng Yu Pin (～ Jun)

Secretary

Natsu Sato

(1) Outline

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

(2) Research

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

(3) Education

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

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

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

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

(6) Clinical Performances

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

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

(7) Publications

[Original Articles]

1. Funayama H, Tashima I, Okada S, Ogawa T, Yagi H, Tada H, Wakita R, Asada Y, Endo Y. Effects of Zoledronate on Local and Systemic Production of IL-1 β , IL-18, and TNF- α in Mice and Augmentation by Lipopolysaccharide. Biological & pharmaceutical bulletin. 2019; 42(6); 929-936

2. Sato Kiyoshi, Shimamoto Hiroaki, Mochizuki Yumi, Hirai Hideaki, Tomioka Hirofumi, Shimizu Risa, Marukawa Eriko, Fukayama Haruhisa, Yoshimura Ryoichi, Ishida Hiroo, Harada Hiroyuki. Treatment of oral cancers during pregnancy: a case-based discussion JOURNAL OF OTOLARYNGOLOGY-HEAD & NECK SURGERY. 2019.02; 48(1); 9
3. Suzuki Chihiro, Ikeda Yumiko, Tateno Amane, Okubo Yoshiro, Fukayama Haruhisa, Suzuki Hidenori. Acute atomoxetine selectively modulates encoding of reward value in ventral medial prefrontal cortex JOURNAL OF NIPPON MEDICAL SCHOOL. 2019.04; 86(2); 98-107
4. Successful management for a child with ADHD using Dexmedetomidine after a maxillofacial reconstructive surgery 2019.09; 47(抄録号); 253
5. Hirotohi Iwasaki, Atsushi Sakai, Motoyo Maruyama, Takaya Ito, Atsuhiro Sakamoto, Hidenori Suzuki. Increased H19 Long Non-coding RNA Expression in Schwann Cells in Peripheral Neuropathic Pain. J Nippon Med Sch. 2019.09; 86(4); 215-221
6. Tomoka Matsumura, Shigeki Mitani, Haruhisa Fukayama. Sugammadex-induced anaphylaxis involving sudden onset of severe abdominal pain Journal of Clinical Anesthesia. 2019.11; 57C; 119-120
7. Sato Y, Ikoma T, Wakita R, Fukayama H. Interfacial interaction of anesthetic lidocaine and mesoporous silica nanoparticles in aqueous solutions and its release properties. Journal of materials chemistry. B. 2019.11; 7(44); 7026-7032
8. Ikeda Yumiko, Funayama Takuya, Tateno Amane, Fukayama Haruhisa, Okubo Yoshiro, Suzuki Hidenori. Bupropion increases activation in nucleus accumbens during anticipation of monetary reward PSYCHOPHARMACOLOGY. 2019.12; 236(12); 3655-3665

[Conference Activities & Talks]

1. Ito Takaya, Sakai Atsushi, Maruyama Motoyo, Miyagawa Yoshitaka, Okada Takashi, Fukayama Haruhisa, Suzuki Hidenori. Dorsal Root Ganglia Homeobox (DRGX) in primary sensory neurons is involved in neuropathic pain. 2019.10.12

Orofacial Pain Management

Professor Masahiko SHIMADA

Junior Associate Professor Akira NISHIYAMA

Assistant Professor Yoko YAMAZAKI

Hospital Staff Hiroko KIMURA, Hiroko IMURA, Hiroyuki ISHIYAMA, Maya SAKAMOTO,
Yuusuke HARADA, Keisuke MIYAZONO, Masako TOBE

Graduate Student Akitoshi HOSODA, Ngan Nguyen, Liang Shanshan,

KAY THWE YE MIN SOE, Masako TOBE, Ryoko KURISU, Keisuke MIYAZONO,
Graduate International Research Student Li Xinyue

(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 ptheripheral 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 ptheripheral 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. Ngan Gia Kieu Nguyen, Akira Nishiyama, Masahiko Shimada. A rat model for inducing temporomandibular anterior disc displacement experimentally *Journal of Oral Science*. 2019.12; 62(1); 70-74

[Misc]

1. Akiko Shimada, Shoichi Ishigaki, Yoshizo Matsuka, Osamu Komiyama, Tetsurou Torisu, Yuka Oono, Hitoshi Sato, Takuya Naganawa, Atsushi Mine, Yoko Yamazaki, Kazuo Okura, Yasushi Sakuma, Keiichi Sasaki. Effects of exercise therapy on painful temporomandibular disorders. *J Oral Rehabil*. 2019.05; 46(5); 475-481
2. Hiroyuki Ishiyama, Daichi Hasebe, Kazumichi Sato, Yuki Sakamoto, Akifumi Furuhashi, Eri Komori, Hidemichi Yuasa. The Efficacy of Device Designs (Mono-block or Bi-block) in Oral Appliance Therapy for Obstructive Sleep Apnea Patients: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2019.08; 16(17); 3182-3197
3. Yuki Sakamoto, Akifumi Furuhashi, Eri Komori, Hiroyuki Ishiyama, Daichi Hasebe, Kazumichi Sato, Hidemichi Yuasa. The Most Effective Amount of Forward Movement for Oral Appliances for Obstructive Sleep Apnea: A Systematic Review *Int J Environ Res Public Health*. 2019.09; 16(18); 3248-3259

Pediatric Dentistry

Associate Professor
Michiyo MIYASHIN

Junior Associate Professor
Satoko Kakino

Assistant Professor
Yoshiaki HASHIMOTO, Tomoki UEHARA, Kanae WADA

Adjunct Lecturer
Keiichi TAKEI, Mitsuko INOUE, Yoshiaki ONO, Masayo ONO,
Asuri jayawarudeina, Yuko MATSUMURA, Ryu MATSUBARA,
Makiko TAKASHI, Naoko UEHARA, Natsumi TSUCHIHASHI

Hospital project assistant professor
Atsushi OISHI

Hospital staff
Taki SEKIYA, Emi FURUSAWA(Apr. ∼), Kenichi MIURA(Apr. ∼),
Ayano INOUE (∼ Mar.), Yuko SEKI, Emi KANAI(Jan. ∼ Mar.),
Kaori KOHI(Apr. ∼)

Graduate Student
Erika KUBOTA, WIT Yee Wint(∼ Sep.), Emi FURUSAWA(∼ Mar.),
Shigeki NAGAHIRO, Rika KODAMA, Manami TAKENOSHITA,
Amrita Widyagarini Subagyo, Cho LI, Yujeong SHIN(Apr. ∼)

Research Student
Yui SEKIDO (∼ Mar.), Emi KANAI (Apr. ∼), Kaori KONUMA,
Haruka NAITO, Karen INOUE(Apr. ∼), Daishi SAITO(Apr. ∼)

Enrolled dentist
Tomoko KAWAMURA, Gaku SHIMADA, Kaori KOHI(∼ Mar.)

(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. Ijbara M, Wada K, Wada J, Jayawadena A, Miyashin M. The Application of Cellulose Acetate Replication Sheets in Enamel Wear investigations. *Dental Materials Journal*. 2019.02; 38(1); 86-95
2. Wint WY, Horiuchi N, Nozaki K, Nagai A, Yamashita K, Miyashin M. Plate-like hydroxyapatite synthesized from dodecanedioic acid enhances chondrogenic cell proliferation. *Bio-medical materials and engineering*. 2019.08; 30(4); 375-386
3. Furusawa E, Ohno T, Nagai S, Noda T, Komiyama T, Kobayashi K, Hamamoto H, Miyashin M, Yokozeki H, Azuma M. Silencing of PD-L2/B7-DC by topical application of small interfering RNA inhibits elicitation of contact hypersensitivity. *J Invest Dermatol*. 2019.10; 139(10); 2164-2173
4. Miura Kennichi, Miyashin Michiyo, Kanao Takako, Oishi Atsushi. Eruption disturbance caused by an odontoma that was partially attached to the crown of the adjacent maxillary first molar, and step lesion excavation for the tooth preservation: A case report *Clinical Case Report*. 2019.10; 7(12); 2462-2465
5. Kubota Erika, Takechi Masaki, Miyashin Michiyo, Iseki Sachiko. Functions of fibroblast growth factor signaling in osteoblast differentiation Congenital Anomalies. 2019.11; 59(6); A83-A84

[Conference Activities & Talks]

1. Wit Yee Wint , Horiuchi Naohiro, Wada Kanae, Yamashita Kimihiro, Miyashin Michiyo. Surface characterization of the glass coated hydroxyapatite synthesized by hydrothermal method. The 57th Annual Conference of the Japanese Society of Pediatric Dentistry 2019.06.10 Sapporo
2. Development of a stress monitoring system for pediatric dentistry: Analyses of child's emotional changes from physiological indicators. 2019.06.11

[Works]

1. Michiyo Miyashin : Natural root canal model of children, Educational Materials, 2013.04 - Now

Orthodontic Science

Professor	Takashi ONO
Associate Professor	
Junior Associate Professor	Yoshiro MATSUMOTO, Zusei KANNO, Jun HOSOMICHI
Assistant Professor	Kazuo SHIMAZAKI, Ippei WATARI, Ikuo YONEMITSU Yuji ISHIDA, Takayoshi ISHIDA, Risa USUMI
Project Assistant Professor	Chiho KATO (Apr-), Shuji OISHI (Apr-)
Dental Resident	Hidemasa OKIHARA, Shuji OISHI (-Mar) Yasunori ABE, Yuki KASAHARA (-Mar), Takuya OGAWA (Apr-) Asuka MANABE (Apr-)
Graduate Students	Iku SHIBATA (-Mar), Eri SAITO, Yuta NAKAI(-Mar) Kenzo WATAKABE (-Mar), Erusu NIN (-Mar), Huan TANG(-Mar) Edward CHO, Masamu INOUE (-Mar), Erika OZAWA(-Mar) Moe SATO (-Mar), Kasumi HATANNO (-Mar), Keiko FUKINO (-Mar) Shin-Sheng Yang, Lu ZHAO (-Sep) , Thi Kim Uyen DONG Yuta UCHIKAWA, Akihiro KOYAMA, Sun-min KIM Thura AUNG PHYO, Ryo KIMURA, Shahriar Mohd SHAMS, Haixin HONG Anindya Kamaratih GUNARSO, Kai LI Sasin SRITARA, Hideyuki ISHIDORI, Seiko ISHIHARA Aiko TAKADA, Yoshiyuki HAMADA Akiyo FUJITA, Narubhorn ONGPRAKOBKUL (-Jul) Wirongrong WONGKITIKAMJORN (-Jul), Ahmad F J M SH ALSULAILI Saranya SERIRUKCHUTARUNGSEE (Apr-), Yixin LOU (Apr-) Keita ISHIZUKA (Apr-), Mirei KEITOKU(Apr-), Rikima TAKANO (Apr-) Eri MISAWA (Apr-), Kitanon ANGKANAWARAPHAN (Jun-) Ruixin LI (Oct-), Chun Shuo HUANG (Oct-) Wenqian SUN (Oct-)
Graduate School Research Students	Takuya OGAWA (-Mar), Yukano FUKUSHIMA Misako KOKETSU (-Mar), Takahiro SHIMAMINE (-Mar) Katsuhiko SUZUKI (-Mar), Asuka MANABE (-Mar) Makiko OKUZAWA, Masako KAWADA, Shuko ARAI Yixin LOU (-Mar), Saranya SERIRUKCHUTARUNGSEE (-Mar) Aiko ISHIZAKI, Misa TAKAHASHI Ruixin LI (-Sep), Chun Shuo HUANG (Apr-Sep), Kazuki SAWAYA (Apr-) Chiyo SHIMIZU (Apr-), Naoaki MIKAMI (Apr-)

(1) Outline

Orthodontic Science is one of the dental sciences which propose to control the craniofacial growth and development in equilibrium with the whole body, and also deals with the prevention and/or treatment of malocclusion and related disorders, by which the alteration of maxillofacial function with aging could be kept to the most suitable condition.

(2) Research

Research Subjects

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

(3) Education

Subjects of Education:

Orthodontic Science, Pathophysiology for Malocclusion, Biology for Functional Adaptation

(4) Lectures & Courses

Orthodontic Science

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

Pathophysiology for Malocclusion

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

Biology for Functional Adaptation

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

(5) Clinical Services & Other Works

Clinical Services

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

Students in the graduate course not only pursue their scientific researches but also being educated in accordance with our curriculum for the post-graduated clinical program. In this program, we aim to bring up the leading persons of next generation who have highly specialized knowledge and skills of orthodontics as well as prominent minds of clinical researches.

(6) Clinical Performances

Highlights of Clinical Services

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

2) Comprehensive Orthodontic Treatments

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

(7) Publications

[Original Articles]

1. Oishi S, Ishida Y, Matumura T, Kita S, Sakaguchi-Kuma T, Imamura T, Ikeda Y, Kawabe A, Okuzawa M, Ono T. A cone-beam computed tomographic assessment of the proximity of the maxillary canine and posterior teeth to the maxillary sinus floor: Lessons from 4778 roots. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2019; In press;
2. Okihara H, Ono T. A patient with deeply and mesially impacted second molars on the bilateral sides treated with improved super-elastic nickel-titanium alloy wires. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2019; In press;
3. Tang H, Yonemitsu I, Ikeda Y, Watakabe K, Shibata S, Hosomichi J, Ono T. Effects of unilateral nasal obstruction on the characteristics of jaw-closing muscles in growing rats. *The Angle orthodontist*. 2019.01; 89(1); 102-110
4. Uchikawa Y, Hosomichi J, Suzuki JI, Yamaguchi H, Ishida Y, Hatano K, Usuni-Fujita R, Shimizu Y, Kaneko S, Uesugi S, Ono T.. Differential growth of craniofacial and tibial bones to sympathetic hyperactivity-related hypertension in rats. *Archives of Oral Biology*. 2019.01; 99; 73-81
5. Kokai S, Fukuyama E, Omura S, Kimizuka S, Yonemitsu I, Fujita K, Ono T. Long-term stability after multidisciplinary treatment involving maxillary distraction osteogenesis, and sagittal split ramus osteotomy for unilateral cleft lip and palate with severe occlusal collapse and gingival recession: A case report. *Korean Journal of Orthodontics*. 2019.01; 49(1); 59-69
6. Inoue M, Ono T, Kameo Y, Sasaki F, Ono T, Adachi T, Nakashima T. Forceful mastication activates osteocytes and builds a stout jawbone. *Scientific Reports*. 2019.03; 9(1);
7. Zhao L, Matsumoto Y, Ono T, Iseki S.. Effects of mechanical force application on the developing root apex in rat maxillary molars. *Arch Oral Biol*.. 2019.05; 101; 64-76
8. Yoshida M, Honda E, Ozawa E, Inoue-Arai SM, Ohmori H, Moriyama K, Ono T, Kurabayashi H, Yoshihara H, Nunthayanon Parakonthun K. Principles of the magneticresonance imaging movie method for articulatory movement. *Oral Radiology*. 2019.05; 35(2); 91-100
9. Shimazaki K, Kanno Z, Ono T. Alternative approach using miniscrew-anchored sliding jig to correct maxillary midline deviation in a patient with unilateral missing premolar. *APOS Trends in Orthodontics*. 2019.06; 9(2); 111-116
10. Asano T, Okamoto K, Nakai Y, Tsutsumi M, Muro R, Suematsu A, Hashimoto K, Okumura T, Ehata S, Nitta T, Takayanagi H. Soluble RANKL is physiologically dispensable but accelerates tumour metastasis to bone. *Nature Metabolism*. 2019.09; 1; 868-875
11. Kita S, Fujita K, Imai H, Aoyagi M, Shimazaki K, Yonemitsu I, Omura S, Ono T. Postoperative stability of conventional bimaxillary surgery compared with maxillary impaction surgery with mandibular autorotation for patients with skeletal class II retrognathia. *The British journal of oral & maxillofacial surgery*. 2019.11;

12. Ishida T, Manabe A, Yang SS, Watakabe K, Abe Y, Ono T. An orthodontic/orthognathic patient with obstructive sleep apnea treated with Le Fort I osteotomy advancement and alar cinch suture combined with a muco-musculo-periosteal V-Y closure to minimize nose deformity. *The Angle Orthodontist*. 2019.11; 89(6); 946-952
13. Imai H, Fujita K, Yamashita Y, Yajima Y, Takasu H, Takeda A, Honda K, Iwai T, Mitsudo K, Ono T, Omura S. Accuracy of mandible-independent maxillary repositioning using pre-bent locking plates: a pilot study. *The International Journal of Oral and Maxillofacial Surgery*. 2019.12; In press;

[Conference Activities & Talks]

1. Torikai K, Kijima T, Kaida E, Nagaoka R, Shimazaki K. Long-term treatment results of bilateral cleft lip and palate treated by all-in-one repair. 76th ACPA's(American Cleft Palate Craniofacial association) Annual Meeting 2019.04 Arizona, USA
2. Yonemitsu I, Lagou A, Denes BJ, Ono T, Kiliaridis S. Age- and functional related coronal changes of maxillary alveolar bone. 95th congress of the European Orthodontic Society 2019.06 Nice, France
3. Guo X, Watari I, Yonemitsu I, Ikeda Y, Ono T. Effect of functional lateral shift of the mandible on hyaluronic acid decomposition related to lubrication of temporomandibular joint in growing rats. 95th congress of the European Orthodontic Society 2019.06 Nice, France
4. Wongkitikamjorn W, Hosomichi J, Wada E, Maeda H, Satrawaha S, Hong H, Hayashi Y, Yoshida K, Ono T . Effect of Prenatal Intermittent Hypoxia on Muscle Development in Offspring . 2019 IADR/AADR/CADR General Session 2019.06 Vancouver, CANADA
5. Ongprakobkul N, Ishida Y, Hatano-sato K, Li K, Petdachai S, Hosomichi J, Mahatumarat K, Ono T . Effects of AMD3100 on Orthodontic Tooth Movement After Local/Systemic Administration. 2019 IADR/AADR/CADR General Session 2019.06 Vancouver, Canada
6. Sato M, Asano T, Hosomichi J, Nakata T, Ono T. Optogenetic manipulation of intracellular calcium by blue light-activated Ca²⁺ channel switch promotes osteogenic differentiation of MC3T3-E1 cells. 95th congress of the European Orthodontic Society 2019.06 Nice, France
7. Fukino K, Tsutsumi M, Nimura A, Sanudo J, Ono T, Akita K. Spatial distribution of the palatopharyngeus muscle in consideration to the role of the swallowing . 15th European Association of Clinical Anatomy 2019.06
8. Ohmori H, Kirimoto H, Ono T. Different response properties of the human periodontal-masseteric reflex between the canine and the first premolar. 95th congress of the European Orthodontic Society 2019.06 Nice, France
9. Watari I, Hsu J, Ren E, Beauboeuf R, Ono T. Does malocclusion alter the gustatory function? . 2019 IADR/AADR/CADR General Session 2019.06 Vancouver, Canada
10. Sritara Sasin, Tsutsumi Masahiro, Fukino Keiko, Ono Takashi, Akita Keiichi. Morphological analysis of the lateral pterygoid muscle inserting into the medial surface of the condylar process. The 6th Asian Academy congress for TMJ 2019.07 Tokyo

[Awards & Honors]

1. Ogawa T. Japanese Orthodontic Society, Young Researcher's Award, 2019.11
2. Kawada M. The 78th Annual Meeting of Japanese Orthodontic Society, Excellent Poster Award, 2019.11
3. Ishida T. The 78th Annual Meeting of Japanese Orthodontic Society, Excellent Poster Award, 2019.11
4. Kimura R. The 78th Annual Meeting of Japanese Orthodontic Society, Excellent Poster Award, 2019.11
5. Tanaka T. The 78th Annual Meeting of Japanese Orthodontic Society, Excellent Poster Award, 2019.11

Cariology and Operative Dentistry

Professor: Junji Tagami

Associate Professor: Masayuki Otsuki

Junior Associate Professor: Masatoshi Nakajima, Noriko Hiraish (January ~)

Assistant Professor: Takako Yoshikawa, Go Inoue, Keiichi Hosaka, Rena Takahashi, Naoko Mastui (~ March)

Hospital Staff: Takaaki Sato, Kento Sato, Takashi Hatayama (~ March), Nami Takashino, Ayako Nakamoto,

Daisuke Araoka (~ March), Akifumi Takahashi (~ March), Yusuke Kuno (April ~), Daiki Nagano (April ~), Shigeki Uchinuma (April ~),

Specially Appointed Assistant Professor: N. H. M. Khairul Matin, Hisaichi Nakagawa (April ~), Tomoko Tabata (April ~)

Staff Assistant: Shiori Ogi, Takako Nakagawa (~ December)

Graduate Student: Sae Akehashi (~ March), Nao Kominami (~ March), Yuna Kanamori (~ March),

Yukina Ochiai (~ March), Kurumi Ide (~ March), Yusuke Kuno (~ March), Yuki Ito (~ March),

Shigeki Uchinuma (~ March), Daiki Nagano (~ March), Yusuke Kakiuchi (~ March), Akira Nakane

(~ March), RIMA ZAKZOUK (~ September), HALABI SOMAYAH ABDULRAHMAN A,

RUMMANI GHASSAN MAHMOOD S, ALQAHTANI ALI AWAD M, ARAVETI SANDEEP

KUMAR (~ September), HOSEA LAL RIN MUANA (~ September),

SAI KHAM LYANN (~ September), AYE KO KO, Meiken Hayashi,

Shou Obayashi, Saori Muta, Kazuhide Yonekura, Satomi Matsunaga, Shin Rozan, HESHAM

HASSAN OSMAN MOHAMMED, Yukiko Tanno, AHMED MOHAMED ABDELRAHMAN

ABDOU, MAHMOUD MOHAMED SAYED AHMED, SOE YU PAING, SWE ZIN AUNG,

QUTAIBA Y A A ALSANDI, SAN SAN MAY PHYO AUNG, ALMASABI WALEED

ABDULQADER M, WIJETUNGA CHAMARI LASINDRA, ERICK LUZ MADRIGAL,

Motoi Takahashi, Kim Seunggun, Kyoko Ishikawa, Toyoaki Kobayashi, Miyuki Shimizu,

Mayu Hasegawa, Shun Kobayashi, Nanako Ueda, Misa Kashiwa, Saki Uchiyama, Yosuke Minato,

Yuta Baba, LEILA NASIRY KHANLAR, VICHEVA MARTINA GEORGIEVA, Citra Kusumasari,

Min Khant Ko Ko, Pa Pa Kay Khine, MULTUZA AYED ALI (April ~), WAHYUNI SUCI DWIANDHANY,

Mayuri Nshimaki, Ryuta Andou, Shiori Yamamoto, Ayaka Sato, Yorichika Shioya, Yusuke Koshimitsu,

Chin Akane, Yutaro Oda, SAEED, NOORULDEEN ALI, MURTUZA AYED ALI, TICHY ANTONIN,

Yutaro Motoyama (April ~), Ako YAamashita (April ~), Kiyoka Furusawa (April ~), Satoshi Akiya

(April ~), Yuko Ogawa (April ~), Aya Ishizaka (April ~ September), Seiki Nakano (April ~ June),

KITTISAK SANON (April ~), SOE KAY THWE NAING (October ~), QI FENG (April ~),

TAGHREED ABDULRAHMAN ALREFAIE (April ~), Research Student: Shinji Ogura, Mineo Kijima,

WEI DIANTONG, RIMA ZAKZOUK (October ~)

(1) Outline

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

At Cariology and Operative Dentistry, we believe that the ultimate goal of the oral health care programs is to

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

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

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

(2) Research

1) Evaluation of dentin bonding systems

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

2) Super Enamel and Super Dentin

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

3) Development of OCT for establishing its clinical application

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

4) Non-destructive test of adhesive restorations

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

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

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

6) Resin coating technique

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

7) Research on optical properties of the dental structure

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

8) Research on direct core build up materials

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

9) Study on dental erosion

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

10) Caries risk assessment

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

11) Adhesion of cariogenic bacteria to dentin surface

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

12) Biocompatibility of resin-based dental adhesives

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

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

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

14) Evaluation of caries removal methods

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

15) Development and evaluation of aesthetic dental materials

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

16) Clinical research

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

(3) Education

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

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

(6) Clinical Performances

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

(7) Publications

[Original Articles]

1. Sato T, Takagaki T, Baba Y, Vicheva M, Matsui N, Hiraishi N, Ikeda M, Nikaido T, Tagami J. Effects of Different Tooth Conditioners on the Bonding of Universal Self-etching Adhesive to Dentin. *J Adhes Dent.* 2019; 21(1); 77-85
2. Ayako Nakamoto, Takaaki Sato, Naoko Matsui, Masaomi Ikeda, Toru Nikaido, Michael F Burrow, Junji Tagami. Effect of fluoride mouthrinse and fluoride concentration on bonding of a one-step self-etch adhesive to bovine root dentin. *J Oral Sci.* 2019; 61(1); 125-132
3. Marwa M S Abbass, Sara Ahmed Mahmoud, Sara El Moshy, Dina Rady, Nermeen AbuBakr, Israa Ahmed Radwan, Attera Ahmed, Ahmed Abdou, Ayoub Al Jawaldeh. The prevalence of dental caries among Egyptian children and adolescences and its association with age, socioeconomic status, dietary habits and other risk factors. A cross-sectional study. *F1000Res.* 2019; 8; 8
4. Somayah Halabi, Naoko Matsui, Toru Nikaido, Michael F Burrow, Junji Tagami. Effect of Office Bleaching on Enamel Bonding Performance. *J Adhes Dent.* 2019; 21(2); 167-177
5. Hosea Lalrin Muana, Noriko Hiraishi, Masatoshi Nakajima, Kalyan Kong, Junji Tagami. Effect of the Dentin Chelating Agents Phytic Acid and EDTA on Degree of Conversion, Microhardness, and Bond Strength of Chemical-curing Self-adhesive Cements. *J Adhes Dent.* 2019; 21(4); 299-306
6. Seung-Hoon Han, Alireza Sadr, Yasushi Shimada, Junji Tagami, Sung-Ho Park. Internal adaptation of composite restorations with or without an intermediate layer: Effect of polymerization shrinkage parameters of the layer material. *J Dent.* 2019.01; 80; 41-48
7. Sai Kham Lyann, Tomohiro Takagaki, Tohru Nikaido, Takahiro Wada, Motohiro Uo, Masaomi Ikeda, Alireza Sadr, Junji Tagami. Efficacy of Various Surface Treatments on the Bonding Performance of Saliva Contaminated Lithium-Disilicate Ceramics The journal of adhesive dentistry. 2019.02; 21(1); 51-58
8. Shinagawa J, Inoue G, Nikaido T, Ikeda M, Burrow MF, Tagami J. Early bond strengths of 4-META/MMA-TBB resin cements to CAD/CAM resin composite Dent Mater J. 2019.02; 38(1); 28-32
9. Hayashi J, Espigares J, Takagaki T, Shimada Y, Tagami J, Numata T, Chan D, Sadr A. Real-time in-depth imaging of gap formation in bulk-fill resin composites. *Dental materials : official publication of the Academy of Dental Materials.* 2019.02;
10. Pavethynath Velusamy, Yasushi Shimada, Zuissei Kanno, Takashi Ono, Junji Tagami. Optical evaluation of enamel white spot lesions around orthodontic brackets using swept-source optical coherence tomography (SS-OCT): An in vitro study. *Dent Mater J.* 2019.02; 38(1); 22-27
11. Dhaifallah Alqarni, Masatoshi Nakajima, Keiichi Hosaka, Kurumi Ide, Daiki Nagano, Takehiro Wada, Masaomi Ikeda, Teerapong Mamane, Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Richard Foxton, Junji Tagami. The repair bond strength to resin matrix in cured resin composites after water aging. *Dent Mater J.* 2019.03; 38(2); 233-240
12. Amr Saad, Go Inoue, Toru Nikaido, Ahmed M A Abdou, Mahmoud Sayed, Michael F Burrow, Junji Tagami. Effect of dentin contamination with two hemostatic agents on bond strength of resin-modified glass ionomer cement with different conditioning. *Dent Mater J.* 2019.03; 38(2); 257-263
13. Okada M, Otsuki M, Tagami J. Effect of nonthermal atmospheric discharge on stain removal of tooth. *Dental Materials Journal.* 2019.03; 33(3); 396-402
14. Amr Saad, Toru Nikaido, Ahmed Abdou, Khairul Matin, Michael F Burrow, Junji Tagami. Inhibitory effect of zinc-containing desensitizer on bacterial biofilm formation and root dentin demineralization. *Dent Mater J.* 2019.03; 38(6); 940-946
15. Thwe Zin Ei, Yasushi Shimada, Ahmed Abdou, Alireza Sadr, Masahiro Yoshiyama, Yasunori Sumi, Junji Tagami. Three-dimensional assessment of proximal contact enamel using optical coherence tomography. *Dent Mater.* 2019.04; 35(4); e74-e82

16. Aung SSMP, Takagaki T, Lyann SK, Ikeda M, Inokoshi M, Sadr A, Nikaido T, Tagami J. Effects of alumina-blasting pressure on the bonding to super/ultra-translucent zirconia. *Dent Mater.* 2019.05; 35(5); 730-739
17. Keiichi Hosaka, Antonin Tichy, Masaomi Ikeda, Keiichi Nakagawa, Alireza Sadr, Junji Tagami, Masahiro Takahashi, Kento Sato, Yoshihiro Nishitani, Celso Afonso Klein-Junior, David H Pashley, Masatoshi Nakajima. Ultra-high-speed videography of resin-dentin interface failure dynamics under tensile load. *Dent Mater.* 2019.05; 35(7); e153-e161
18. Takako Yoshikawa, Makoto Arakawa, Junji Tagami. Effect of radiotherapy on resin composite adaptation to the cavity wall and elastic modulus of dentin *Asian Pacific Journal of Dentistry.* 2019.05; 19; 39-44
19. Ito Y, Otsuki M, Tagami J. Effect of pH conditioners on tooth bleaching. *Clinical and experimental dental research.* 2019.06; 5(3); 212-218
20. Mark Van Duker, Juri Hayashi, Daniel C Chan, Junji Tagami, Alireza Sadr. Effect of silver diamine fluoride and potassium iodide on bonding to demineralized dentin. *Am J Dent.* 2019.06; 32(3); 143-146
21. Kurumi Ide, Masatoshi Nakajima, Juri Hayashi, Keiichi Hosaka, Masaomi Ikeda, Yasushi Shimada, Richard M Foxton, Yasunori Sumi, Junji Tagami. Effect of light-curing time on light-cure/post-cure volumetric polymerization shrinkage and regional ultimate tensile strength at different depths of bulk-fill resin composites. *Dent Mater J.* 2019.07; 38(4); 621-629
22. Ochiai Y, Inoue G, Nikaido T, Ikeda M, Tagami J. Evaluation of experimental calcium-containing primer in adhesive system on micro-tensile bond strength and acid resistance. *Dental materials journal.* 2019.07; 38(4); 565-572
23. Rima Zakzuk Alshahni, Yasushi Shimada, Yuan Zhou, Masahiro Yoshiyama, Alireza Sadr, Yasunori Sumi, Junji Tagami. Cavity adaptation of composite restorations prepared at crown and root: Optical assessment using SS-OCT. *Dent Mater J.* 2019.07;
24. San San May Phy Aung, Tomohiro Takagaki, Aye Ko Ko, Somayah Halabi, Takaaki Sato, Masaomi Ikeda, Toru Nikaido, Michael F Burrow, Junji Tagami. Adhesion durability of dual-cure resin cements and acid-base resistant zone formation on human dentin. *Dent Mater.* 2019.07; 35(7); 945-952
25. Shigeki Uchinuma, Yasushi Shimada, Khairul Matin, Keiichi Hosaka, Masahiro Yoshiyama, Yasunori Sumi, Junji Tagami. Effects of UVB and UVC irradiation on cariogenic bacteria in vitro *Lasers in Medical Science.* 2019.07; 34(5); 981-989
26. Phan Bhongsatiern, Ploypailin Manovilas, Methaphon Songvejkasem, Siriporn Songsiripradubboon, Thipawan Tharapiwattananon, Paiboon Techalertpaisarn, Hidenori Hamba, Junji Tagami, Dowen Birkhed, Chutima Trairatvorakul. Adjunctive use of fluoride rinsing and brush-on gel increased incipient caries-like lesion remineralization compared with fluoride toothpaste alone in situ. *Acta Odontol. Scand.* 2019.08; 77(6); 419-425
27. Kyaw KY, Otsuki M, Hiraishi N, Segarra MS, Tagami J. Effect of application of desensitizers before bleaching on change of tooth shade. *Dental Materials Journal.* 2019.08; 38(5); 790-797
28. Ide Kurumi, Nakajima Masatoshi, Hayashi Juri, Hosaka Keiichi, Ikeda Masaomi, Shimada Yasushi, Foxton Richard M., Sumi Yasunori, Tagami Junji. Effect of light-curing time on light-cure/post-cure volumetric polymerization shrinkage and regional ultimate tensile strength at different depths of bulk-fill resin composites *Dental Materials Journal.* 2019.08; 38(4); 621-629
29. Takako Yoshikawa, Alireza Sadr, Junji Tagami. Effect of light curing method and thermal cycling on resin composite adaptation to the cavity wall *Asian Pacific Journal of Dentistry.* 2019.09; 19; 59-64
30. Nao Kominami, Yasushi Shimada, Keiichi Hosaka, Minh Nguyet Luong, Masahiro Yoshiyama, Alireza Sadr, Yasunori Sumi, Junji Tagami. The effect of flowable composite lining and dentin location on microtensile bond strength and internal fracture formation. *Dent Mater J.* 2019.10; 38(5); 798-805
31. Takashi Hatayama, Yukinori Kano, Asami Aida, Ayaka Chiba, Kento Sato, Naoko Seki, Keiichi Hosaka, Richard M Foxton, Junji Tagami, Masatoshi Nakajima. The combined effect of light-illuminating direction and enamel rod orientation on color adjustment at the enamel borders of composite restorations. *Clin Oral Investig.* 2019.10; 37(3); 474-483

32. Yusuke Kuno, Keiichi Hosaka, Masatoshi Nakajima, Masaomi Ikeda, Celso Afonso Klein Junior, Richard M Foxton, Junji Tagami. Incorporation of a hydrophilic amide monomer into a one-step self-etch adhesive to increase dentin bond strength: Effect of application time. *Dent Mater J.* 2019.12; 38(6); 892-899
33. Sae Akehashi, Rena Takahashi, Toru Nikaido, Michael F Burrow, Junji Tagami. Enhancement of dentin bond strength of resin cement using new resin coating materials. *Dent Mater Journal.* 2019.12; 38(6); 955-962
34. Antonin Tichy, Keiichi Hosaka, Pavel Bradna, Masaomi Ikeda, Ahmed Abdou, Masatoshi Nakajima, Junji Tagami. Subsequent application of bonding agents to a one-step self-etch adhesive - Its effect with/without previous light-curing. *Dent Mater.* 2019.12; 35(12); e299-e309
35. Yuna Kanamori, Rena Takahashi, Toru Nikaido, Elias P Bamidis, Michael F Burrow, Junji Tagami. The effect of curing mode of a high-power LED unit on bond strengths of dual-cure resin cements to dentin and CAD/CAM resin blocks. *Dent Mater J.* 2019.12; 38(6); 947-954

[Conference Activities & Talks]

1. Keiichi Hosaka. The Potentials and Limitations of Direct Composite Restorations -From Macroscopic and Microscopic Points of View-. Invited Lecture 2019.01.20 Thammasat University, Bangkok, Thailand
2. Junji TAGAMI. Lecture: Operative Dentistry. 2019.01.23 Okayama University, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Japan
3. Dr. Julian Conejo D.D.S/M.Sc., University of Pennsylvania. Special Seminar, Department of Cariology and Operative Dentistry, TMDU. 2019.02.06 Tokyo Medical and Dental University
4. Inokoshi M, Shimizubata M, Hatano K, Wada T, Uo M, Takahashi R, Minakuchi S. Application of S-PRG filler containing materials for geriatric dentistry. The 4th Bioactive Materials S-PRG Research Meeting 2019.03.22 Kyoto
5. Keiichi Hosaka. Direct Composite Restoration Promotes Our Oral Health. The 41st Annual Dental Scientific Conference 2019.04.01 University of Medicine and Pharmacy at Ho Chi Minh City
6. Junji Tagami. Update on Adhesion: Research and Clinical Applications. 6th Annual Academy of Biomimetic Dentistry Conference 2019.04.12 Hotel Omni Dallas at Park West
7. Hatano K, Inokoshi M, Wada T, Uo M, Takahashi R, Minakuchi S. Ion release capacity of a novel S-PRG filler containing denture adhesive. The 73rd General Session of the Japanese Society for Dental Materials and Devices 2018 2019.04.21 Tokyo
8. Keiichi Hosaka. Keys to Success in Direct Composite Restorative Challenges. 35th Annual American Academy of Cosmetic Dentistry Scientific Session 2019.04.26 San Diego, US
9. Keiichi Hosaka. Esthetic direct composite restoration. Joint Hands-on Program Peking University Hospital of Stomatology 2019.05.19 Beijing
10. Noriko Hiraishi, Fumiaki Hayashi, Toru Nikaido, Junji Tagami. Ions release from S-PRG filler for biomimetic nucleation of calcium phosphate studied by solid-state NMR. 97th General Session & Exhibition of the IADR/AADR 2019.06 Vancouver, Canada
11. Mayuri Nishimaki, Ayako Nakamoto, Noriko Hiraishi, Yukihiro Tamura, Toru Nikaido, Junji Tagami. S-PRG Filler Eluate for Dental pulp Cell and Dentin Cavity. The 150th Meeting of The Japanese Society of Conservative Dentistry 2019.06
12. Shiori Yamamoto, Noriko Hiraishi, Khairul Matin, Motoi Takahashi, Toru Nikaido, Junji Tagami. Evaluation of biofilm formation on root dentin after application of PRG barrier coat. The 150th Meeting of The Japanese Society of Conservative Dentistry 2019.06
13. Seunggun Kim, Noriko Hiraishi, Yukihiro Tamura, Toru Nikaido, Junji Tagami. Cytotoxicity of Silver Diamine Fluoride on Pulpal-like Cells and Glutathione Detoxification. The 150th Meeting of The Japanese Society of Conservative Dentistry 2019.06
14. Tumor-like hardening tissues around apical of lower incisors: a case report. 2019.06

15. OTSUKI Masayuki, HOSAKA Keiichi, HIRAISHI Noriko, TAGAMI Junji. Bleaching effect of a new bleaching material; Whiteessence Whitening Pro. 2019.06
16. Junji Tagami. The History and Development of Adhesive Dentistry. International Adhesive Dentistry Congress 2019 2019.06.16 University of Washington
17. Keiichi Hosaka. The Power of Direct Composite Restoration -from Crown & Bridge to Occlusal Reconstruction-. 2019 International Congress on Adhesive Dentistry 2019.06.17 University of Washington, Seattle, US
18. Masatoshi Nakajima.. Smear layer-deproteinization; Improving the dentin interface of self-etch adhesives. . International Congress on Adhesive Dentistry 2019 2019.06.17
19. Junji Tagami. Application of SS-OCT to research and clinic in cariology and operative dentistry. IADR Satellite Symposium Application of Optical Coherence Tomography to Dental Clinic and Research 2019.06.18 Vancouver Convention Centre West
20. E. Luz Madrigal, K. Hosaka, M. Nakajima, M. Ikeda, A. Abdou, A. Tichy, J.Tagami.. Influence of Tooth-storage in Chloramine-T Solution on Bovine Dentin TBS.. International Association for Dental Research. 2019.06.19 Vancouver Convention Center
21. Yuna Kanamori, Rena Takahashi, Toru Nikaido, Junji Tagami, Reinhard Hickel, Karl-Heinz Kunzelmann. Effect of Resin Coating Techniques on CAD/CAM Hybrid Ceramic Inlays. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
22. Ali Alghamdi, Tomohiro Takagaki, Ahmed Abdou, Toru Nikaido, Junji Tagami. Influence of Ambient-air Storage on the Bonding Performance of CRBs. 2019 IADR/AADR/CADR General Session 2019.06.20 Vancouver, BC, Canada
23. Erick Luz Madrigal, Keiichi Hosaka, Masatoshi Nakajima, Masaomi Ikeda, Ahmed Abdou, Antonin Tichy, Junji Tagami. Influence of Tooth-storage in Chloramine-T Solution on Bovine Dentin TBS.. 2019 IADR/AADR/CADR General Session 2019.06.20 Vancouver, BC, Canada
24. Disapong Youngcharoen, Tomohiro Takagaki, Akifumi Takahashi, Ahmed Abdou, Toru Nikaido, Junji Tagami. Effect of Different Cleaning Agent on Bonding Performance to Y-PSZ. IADR/AADR/CADR General Session 2019.06.20 Vancouver, BC, Canada
25. Martina Vicheva, Takaaki Sato, Tomohiro Takagaki, Yuuta Baba, Masaomi IKEDA, Toru NIKAIDO, Junji Tagami. Effect of Repair Systems on Dentin Bonding Performance. 97th General Session & Exhibition of the IADR in Vancouver, Canada 2019.06.20
26. Eric Luz Madrigal, K Hosaka, M Nakajima, J Tagami.. Influence of Tooth-storage in Chloramine-T Solution on Bovine Dentin TBS.. 97th IADR 2019.06.20
27. Wijetunga Chamari, Luong Minh, Otsuki Masayuki, Tagami Junji. Effect of pH on Tooth Bleaching Action in vitro. 2019 IADR/AADR/CADR General Session 2019.06.20 Vancouver, BC, Canada
28. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Ion release and acid buffering capacity of S-PRG containing cement. 97th General Session & Exhibition of the IADR 2019.06.21 Vancouver
29. Yutaro ODA, Rena TAKAHASHI, Shin ROZAN, Toru NIKAIDO, Junji TAGAMI. Influence of resin coating technique on bonding of self-adhesive resin cement to CAD/CAM resin block and dentin. The 150th Meeting of the Japanese Society of Conservative Dentistry 2019.06.27 Ishikawa, Japan
30. Keiichi Hosaka. The Power of Direct Composite Restoration. 20th NADTI Trade Exhibit 2019.09.25 Manilla, Phillipines
31. Yoshikawa T, Sadr A, Tagami J. Effect of various lights on polymerization behavior of light-cured resin composite. 2019.09.28 Nagoya
32. Keiichi Hosaka. Digital Dentistry Meets MI-based Adhesive Restorations. 2019.09.28 Nagoya, Aichi
33. Yamamoto M, Inokoshi M, Shimizubata M, Takagaki T, Yoshihara K, Minakuchi S. Degree of conversion of 4-META/MMA-TBB resin containing antibacterial agents. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki

34. Shimizubata M, Inokoshi M, Hatano K, Wada T, Takahashi R, Uo M, Minakuchi S. Fluoride recharge and release capacity of a S-PRG filler containing glass ionomer cement. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki
35. State of art in adhesive dentistry and future atrategies. KPPIKG 2019 Universitas Indonesia ,Faculty of Dentistry 、 the 18th Scientific Meeting & Refresher Course in Dentistry 2019.10.11
36. Optical coherent tomography , the applications to research and clinic. King Abdulaziz University ,the 5th international dental conference 2019.10.21 The Ritz Carlton Jeddah
37. Development of adhesive resin and its clinical applications . King abdulaziz University,the 5th international dental conference 2019.10.24 The Ritz Carlton Jeddah
38. Go Inoue. Super tooth concept regarding with the Acid-Base Resistant Zones. 3rd Mansoura International Dental Congress 2019.10.30 Mansoura, Egypt
39. OTSUKI Masayuki, HOSAKA Keiichi, HIRAISHI Noriko, TAGAMI Junji . Effect of light irradiation on in-office bleaching. 2019.11
40. Minimally Invasive Aesthetic Restoration with Innovative Materials. ConsAsia 2019 2019.11.09 COEX Convention Center
41. Citra KUSUMASARI, Masatoshi NAKAJIMA, Ahmed ABDYOU, Takashi HATAYAMA, Keiichi HOSAKA, Junji TAGAMI. . Effect of Papain Enzyme and NaOCl-based Gel on Sealing Performances of Self-etch Adhesives. ConsAsia 2019 2019.11.09 Seoul, Korea
42. Tichy A., Brabec M., Bradna P., Hosaka K., Nakajima M., Tagami J.. Competing Risk Model for Bond Strength Data Analysis. 4th Meeting of the International Association for Dental Research Asia-Pacific Region 2019.11.28 Brisben, Austiralia
43. Masayuki Otsuki, Yuki Ito, Keiichi Hosaka, Junji Tagami. Effect of pH conditioners on tooth bleaching. 2019.11.30
44. Seki N, Mizutani K, Hosaka K, Komada W, Kanazawa M, Komagamine Y, Moross J, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Essential Expertise for Clinical Dentistry (EECD), International Dental Clinical Education Course for Graduate School of Medical and Dental Sciences. The 84th annual meeting of the Stomatological Society 2019.12.07 Tokyo
45. Yuna Kanamori, Kanako Noritake, Sachi Umemori, Maiko Iwaki, Daisuke Kido, Shogo Takeuchi, Akitaka Hattori, Ken-ichi Tonami, Arata Ebihara, Masayuki Hideshima, Kouji Araki, Hiroshi Nitta. Introduction of objective clinical skills examination for TMDU's trainee residents. 2019.12.07

Fixed Prosthodontics

Professor
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Ruri TSUKAHARA
Tomoyuki MIHARA
Ko YANAKA
Syu YOSHIMATSU
Taisuke OZAKI
Yusuke YOKOSUKA
Huang Ling
Omni Ismarik Mohanmed Saleh
Deng Jia

(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. Kai Shibaguchi, Atsushi Tamura, Masahiko Terauchi, Mitsuaki Matsumura, Hiroyuki Miura, Nobuhiko Yui. Mannosylated polyrotaxanes for increasing cellular uptake efficiency in macrophages via receptor-mediated endocytosis. *Molecules*. 2019.01; 24(3); 439
2. Mina Takita, Satoshi Omori, Chiharu Shin, Ayaka Shirasaki, Reina Nemoto, Hiroyuki Miura. Effect of framework design on fracture strength of composite resin veneered polyetheretherketone (PEEK) crowns The Journal of the Japan Academy of Digital Dentistry. 2019.02; 8(3); 151-162

3. Rikitoku S, Otake S, Nozaki K, Yoshida K, Miura H. Influence of SiO₂ content of polyetheretherketone (PEEK) on flexural properties and tensile bond strength to resin cement. *Dental materials journal*. 2019.06; 38(3); 464-470
4. Wint WY, Horiuchi N, Nozaki K, Nagai A, Yamashita K, Miyashin M. Plate-like hydroxyapatite synthesized from dodecanedioic acid enhances chondrogenic cell proliferation. *Bio-medical materials and engineering*. 2019.08; 30(4); 375-386
5. Asano Rana, Otake Shiho, Nozaki Kosuke, Yoshida Keiichi, Miura Hiroyuki. Effect of elapsed time after air abrasion on bond strength of luting agent to CAD/CAM resin blocks *JOURNAL OF ORAL SCIENCE*. 2019.09; 61(3); 459-467
6. Chiharu Shin, Daizo Okada, Reiko Ogura, Ling Huang, Kunihiko Mizusawa, Keiichi Yoshida, and Hiroyuki Miura. . Stress distribution in crown and root dentin associated with different crown materials and thicknesses. *Asian Pacific Journal of Dentistry*. 2019.12; 19(2); 71-76
7. Hayashi K, Nozaki K, Tan Z, Fujita K, Nemoto R, Yamashita K, Miura H, Itaka K, Ohara S. Enhanced Antibacterial Property of Facet-Engineered TiO₂ Nanosheet in Presence and Absence of Ultraviolet Irradiation. *Materials (Basel, Switzerland)*. 2019.12; 13(1);

[Conference Activities & Talks]

1. Hayasi K, Nozaki K, Nemoto R, Yamashita K, Miura H. Redox and antibacterial ability of titania nanosheet with highly oriented crystal orientation. The 73 th General Session of the Japanese Society for Dental Materials and Devices (JSDMD) 2019.04.21 Tokyo
2. Inokoshi M, Nozaki K, Minakuchi S. Degradation of dental zirconia stored in artificial saliva. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.11 Sapporo
3. Nozaki K, Hayashi K, Kowaka Y, Mihara T, Nemoto R, Miura H, Ohara S. Enhanced antibacterial property of highly organized titania. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.11 Sapporo
4. Hayashi K, Nozaki K, Kowaka Y, Mihara T, Nemoto R, Ohara S, Miura H. Evaluation of ROS activity of antimicrobial titania nanosheet by higher order structure control. The 128th Annual Scientific Meeting of the Japan Prosthodontic Society 2019.05.11 Sapporo
5. Matsumura M, Nozaki K, Yanaka W, Matsumura M, Miura H. Surface roughness and mechanical property of composite resin block by controlling milling condition. The 128th Annual Scientific Meeting of the Japan Prosthodontic Society 2019.05.11 Sapporo
6. Ogura R, sato M, Shin C, Okada D, Katou H, Shiota M, Miura H. Clinical study of occlusal forces and occlusal sensitivity on oral implants. The 128th Annual Meeting of Japan Prosthodontic Society 2019.05.11 Sapporo
7. Shimizubata M, Inokoshi M, Hatano K, Nozaki K, Minakuchi S. Degree of conversion of an ion-releasing S-PRG filler containing denture base resin. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.12 Sapporo
8. Sukumoda E, Neomoto R, Omori S, Nozaki K, Miura H. Investigation of detachment risk with zirconia RBFPDs for periodontal disease . The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.12 Sapporo
9. Mizusawa K, Okada D, Shin C, Ogura R, Komada W, Miura H. The investigation of the stress distribution in the abutment teeth for connected crowns. The 128th Annual Meeting of Japan Prosthodontic Society 2019.05.12 Sapporo
10. Inokoshi M, Zhang F, Nozaki K, Shimizu H, Vleugels J, Van Meerbeek B, Minakuchi S. Translucency, flexural strength and aging behavior of highly translucent zirconia. 97th General Session & Exhibition of the IADR 2019.06.21 Vancouver
11. Yamamoto M, Inokoshi M, Shimizubata M, Takagaki T, Yoshihara K, Minakuchi S. Degree of conversion of 4-META/MMA-TBB resin containing antibacterial agents. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki

12. Thaw Di CT, Inokoshi M, Nozaki K, Minakuchi S. Influence of sintering conditions on translucency of highly translucent dental zirconia. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki
13. Miura H. Forefront of digital dentistry and the future. 2019.10.05
14. Noda M, Sukumoda E, Shin C, Nemoto R, Omori S, Takita M, Miura H. Investigation of color matching of CAD/CAM crown using multilayered block and natural tooth. The 10th Scientific Meeting of Japan Academy of Digital Dentistry 2019.10.06 Nara
15. Kosuke Nozaki, Kenichiro Hayashi, Zhenquan Tan, Kimihiro Yamashita, Hiroyuki Miura, Satoshi Ohara, and Keiji Itaka. Antibacterial effect of highly oriented TiO₂ nanosheet in dark conditions. The 4th International Symposium on Biomedical Engineering (ISBE2019) 2019.11.14
16. Kosuke Nozaki, Kenichiro Hayashi, Zhenquan Tan, Kimihiro Yamashita, Hiroyuki Miura, Satoshi Ohara, Keiji Itaka. Enhanced antibacterial property in dark condition by highly-oriented TiO₂ nanosheet.. 2019.11.26
17. Seki N, Mizutani K, Hosaka K, Komada W, Kanazawa M, Komagamine Y, Moross J, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Essential Expertise for Clinical Dentistry (EECD), International Dental Clinical Education Course for Graduate School of Medical and Dental Sciences. The 84th annual meeting of the Stomatological Society 2019.12.07 Tokyo
18. Nakai H, Inokoshi M, Nozaki K, Minakuchi S. Crystallographic analysis of additive manufactured zirconia. The 23rd scientific meeting of Japan Prosthodontic Society, Tokyo branch 2019.12.08 Tokyo
19. Matsumura M, Nozaki K, Yanaka W, Nemoto R, Takita M, Matsumura M, Miura H. Effect of machining condition on mechanical strength of composite resin for CAD/CAM crown. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2019.12.08
20. Shin C, Okada D, Takita M, Ogura R, Mizusawa K, Huang L, Saleh O, Miura H. The influence of different thicknesses and various crown materials on the stress distribution in the abutment teeth. The 23th Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2019.12.08 Tokyo
21. Nozaki K, Hayashi K, Kowaka Y, Mihara T, Nemoto R, Miura H. The redox activity of titania nanosheet under dark conditions. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2019.12.08
22. Sukumoda E, Nemoto R, Omori S, Nozaki K, Takita M, Miura H. Effect of bone loss on the force distribution around abutment teeth with zirconia RBFPD.. The 23th Annual Meeting of the Japan Prosthodontic Society Tokyo Branch 2019.12.08 Tokyo

[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

Pulp Biology and Endodontics

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Yoshiko IINO (March ~)

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Miharu SHIMIZU, Sonoko YABUMOTO, Nanami NIKAIDO, Sousuke IZAWA, Hiroko SOEDA

(1) Outline

The Department of Pulp Biology and Endodontics provides research, education and patient care 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 this tissue 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. Biology of dentin/pulp complex and dental pulp tissue regeneration
 - Analysis of M1 and M2 macrophage populations in engineered rat dental pulp tissue
 - Analysis of regeneration/remodeling of nerve fibers immunoreactive to substance P and calcitonin gene-related peptide in engineered rat coronal pulp tissue
 - Analysis of crosstalk between human dental pulp stem cells and endothelial cells via nuclear factor kappa B dependent pathways
 - Effect of cell culture condition on the osteogenic differentiation of human dental pulp-derived mesenchymal stem cells
 - Expression and function of transient receptor potential channels in dental pulp cells
2. Expression of pain-associated genes in the thalamus following experimental dental pulp inflammation in rats
3. Detection of human pulpal blood flow using transmitted-light plethysmography
4. Mechanisms of dental pulp inflammation
 - microRNA regulation of inflammatory responses in dental pulp
 - Role of hypoxia inducible factor 1 α in dental pulp inflammation
5. Laser-activated root canal irrigation (LAI)
 - Evaluation of efficacy- and safety-related properties of LAI
 - Cleaning effectiveness of LAI on complex root canal morphologies
6. Evaluation of newly developed endodontic sealers and pulp capping materials
 - Anti-inflammatory effects of mineral trioxide aggregate
 - Effect of an experimental sealer containing surface reaction type pre-reacted glassionomer (S-PRG) on osteoblastic cells
 - Development of new tricalcium silicate-based endodontic materials
 - Effect of heating on the physical properties of calcium silicate-based root canal sealers
7. Nickel-titanium rotary root canal instrumentation
 - Evaluation of cyclic fatigue resistance, bending properties and torque/force generation of reciprocating NiTi rotary instruments
 - Shaping ability of different root canal shaping techniques using NiTi files performed by undergraduate students.
 - Effect of different speeds of up-and-down motion on shaping ability of nickel-titanium rotary instruments
 - Force/torque generation and canal volume changes of NiTi rotary glide path preparation using HyFlex EDM Glide Path File compared with manual instrumentation with stainless steel K-file.
 - Effect of Optimum torque reverse motion on torque and force generation during root canal instrumentation with crown-down and single-length techniques
8. Endodontic diagnosis
 - Diagnosis of vertical root fracture: difference in the coronal-apical location of sinus tracts and buccal cortical bone defects between vertically root-fractured and non-root fractured teeth based on periradicular microsurgery
 - Ability of the SS-OCT system to detect crack formation and propagation following root-end resection, ultrasonic root-end cavity preparation and obturation
 - Cone-beam computed tomography analysis of root canal configuration in a Japanese population

(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 therapy,
- Nonsurgical root canal therapy,
- Root canal retreatment,
- Endodontic microsurgery,
- Internal tooth bleaching, and
- Post-endodontic restoration.

(5) Clinical Performances

The latest development of endodontics is remarkable as seen in root canal instrumentation with super-elastic Ni-Ti rotary files, diagnosis with 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. Tazawa K, Kawashima N, Kusano M, Ikeda H, Okiji T. LYVE-1 expressing macrophages co-express CD163 in rat normal dental pulp tissue. The Journal of Japan Endodontic Association. 2019.01; 40(1); 7-13
2. Hirai K, Furusho H, Kawashima N, Xu S, de Beer MC, Battaglini R, Van Dyke T, Stashenko P, Sasaki H. Serum amyloid A contributes to chronic apical periodontitis via TLR2 and TLR4. Journal of Dental Research. 2019.01; 98(1); 117-125
3. Maki K, Ebihara A, Kimura S, Nishijo M, Tokita D, Okiji T. Effect of different speeds of up-and-down motion on canal centering ability and vertical force and torque generation of nickel-titanium rotary instruments. Journal of Endodontics. 2019.01; 45(1); 68-72
4. Kaneko T, Zaw SYM, Sueyama Y, Katsube KI, Kaneko R, Nör JE, Okiji T. Inhibition of nuclear factor- κ B prevents the development of experimental periapical lesions. Journal of Endodontics. 2019.02; 45(2); 168-173
5. Matsumoto H, Sunakawa M, Suda H, Izumi Y. Analysis of factors related to needle-stick and sharps injuries at a dental specialty university hospital and possible prevention methods. Journal of Oral Science. 2019.03; 61(1); 164-170
6. Gu B, Kaneko T, Zaw SYM, Sone PP, Murano H, Sueyama Y, Zaw ZCT, Okiji T. Macrophage populations show an M1-to-M2 transition in an experimental model of coronal pulp tissue engineering with mesenchymal stem cells. International Endodontic Journal. 2019.04; 52(4); 504-514
7. Noda S, Kawashima N, Yamamoto M, Hashimoto K, Nara K, Sekiya I, Okiji T. Effect of cell culture density on dental pulp-derived mesenchymal stem cells with reference to osteogenic differentiation. Scientific reports. 2019.04; 9(1); 5430

8. Hongo T, Watanabe S, Yao K, Satake K, Okiji T. Evaluation of cleaning efficacy -related properties of root canal irrigant activation using a computer -controlled hot tippowered with a diode laser .Asian Pacific Journal of Dentistry. 2019.04;19;9-15
9. Tong F, Maki K, Kimura S, Nishijo M, Tokita D, Ebihara A, Okiji T. Assessment of mechanical properties of WaveOne Gold Primary reciprocating instruments . Dental Materials Journal. 2019.06;38(3); 490-495
10. Kaneko T, Sone PP, Zaw SYM, Sueyama Y, Zaw ZCT, Okada Y, Murano H, Gu B, Okiji T. In vivo fate of bone marrow mesenchymal stem cells implanted into rat pulpotomized molars. Stem Cell Research. 2019.07;38;
11. Ding J, Liu W, Sadr A, He Y, Ebihara A, Li Y. Detection of simulated periradicular lesions in porcine bone by optical coherence tomography. Journal of Endodontics. 2019.08; 45(8); 1024-1029
12. Htun PH, Ebihara A, Maki K, Kimura S, Nishijo M, Tokita D, Okiji T. Comparison of torque, force generation and canal shaping ability between manual and nickel-titanium glide path instruments in rotary and optimum glidepath motion. Odontology. 2019.09; ePub;
13. Maki K, Ebihara A, Nakatsukasa T, Kimura S, Okiji T. A comparative evaluation of the shaping ability of different nickel-titanium rotary root canal preparation techniques performed by undergraduate students. The Journal of Japan Endodontic Association. 2019.09;40(3);179-185
14. Hashimoto K, Kawashima N, Noda S, Yamamoto M, Nozaki K, Okiji T. Effect of heat application on the property of a bioactive glass-based endodontic sealer. The Journal of Japan Endodontic Association. 2019.09;40(3);167-173
15. Nara K, Kawashima N, Noda S, Fujii M, Hashimoto K, Tazawa K, Okiji T. Anti -inflammatory roles of microRNA 21 in lipopolysaccharide -stimulated human dental pulp cells. Journal of Cellular Physiology .2019. 11;234(11);21331-21341
16. Hongo T, Watanabe S, Kouno A, Yamauchi S, Hoshinara Y, Yao K, Satake K, Okiji T. Evaluation of apical pressure during root canal irrigant activation using a diode laser with an optothermal converter-coated tip. The Japanese Journal of Conservative Dentistry. 2019.12;62(6);304-310
17. Rashed B, Iino Y, Ebihara A, Okiji T. Evaluation of crack formation and propagation with ultrasonic root-end preparation and obturation using a digital microscope and optical coherence tomography .Scanning . 2019.12; 2019;5240430

[Misc]

1. Kouno A, Watanabe S, Okiji T. Treatment outcomes of 4 vital pulp therapies in mature molars. The Quintessence. 2019.01; 38(1); 220-221
2. Orikasa S, Kaneko T, Okiji T. The effect of long-term dressing with calcium hydroxide on the fracture susceptibility of teeth. The Nippon Dental Review. 2019.05; 79(5); 154-155
3. Okada Y, Kaneko T, Okiji T. Root canal shaping using nickel titanium, M -Wire, and Gold wire : a micro - computed tomographic comparative study of One Shape, ProTaper Next, and WaveOne Gold instruments in maxillary first molars. The Nippon Dental Review. 2019.09; 79(9); 154-155
4. Hosoya N, Takigawa T, Horie T, Maeda H, Yamamoto Y, Momoi Y, Yamamoto K, Okiji T. A review of the literature on the efficacy of mineral trioxide aggregate in conservative dentistry. Dental Material Journal. 2019.10;38(5);693-700

[Conference Activities & Talks]

1. Okiji T. Defense, repair and regeneration of the dentin/pulp complex: a biological basis for vital pulp therapy. The 20th Scientific Congress of the Asian Pacific Endodontic Confederation 2019.04.26 Istanbul, Turkey

2. Sherif Adel, Wada T, Okiji T, Uo M. Preparation of strontium cement as an alternative component of MTA cement. The 40th Annual Scientific Meeting of Japan Endodontic Association 2019.06.14 Tokyo
3. Nakatsukasa T, Maki K, Kimura S, Nishijo M, Ebihara A, Okiji T. Shaping ability and stress generation of a newly developed heat-treated NiTi rotary instrument. The 40th Annual Scientific Meeting of Japan Endodontic Association 2019.06.14 Tokyo
4. Murano H, Kaneko T, Sunakawa M, Zaw SYM, Sone PP, GUB, Zaw ZCT, Okada Y, Okiji T. Temporal changes in the expression of voltage-gated potassium channel-related genes in rat thalamus following experimental dental pulp injury. The 40th Annual Scientific Meeting of Japan Endodontic Association 2019.06.15 Tokyo
5. Yabumoto S, Watanabe S, Kouno A, Hongo T, Yao K, Satake K, Okiji T. Cone-beam computed tomography analysis of root canal configuration of maxillary premolars using a new classification system. The 40th Annual Scientific Meeting of Japan Endodontic Association 2019.06.15 Tokyo
6. Gu B, Kaneko T, Zaw SYM, Sone PP, Murano H, Sueyama Y, Zaw ZCT, Okada Y, Okiji T. Expression of antigen presenting cell-associated molecules in an experimental model of coronal pulp tissue engineering in rats: Effect of co-implantation of mesenchymal stem cells and endothelial cells. The 40th Annual Scientific Meeting of Japan Endodontic Association 2019.06.15 Tokyo
7. Iino Y, Izawa T, Yao K, Okiji T. Surgical endodontic treatment of radicular cyst associated with periapical osteoperiostitis in a maxillary molar: a case report. The 150th Meeting of the Japanese Society of Conservative Dentistry 2019.06.27 Kanazawa
8. Bayan R, Iino Y, Ebihara A, Okiji T. Evaluation of crack formation and propagation with ultrasonic root-end preparation and obturation using a digital microscope and optical coherence tomography. The 150th Meeting of the Japanese Society of Conservative Dentistry 2019.06.27 Kanazawa
9. Kasahara Y, Iino Y, Ebihara A, Sasaki Y, Okiji T. Evaluation of the association of the periapical index and clinical signs and symptoms with periapical bone defects detected with cone beam computed tomography. The 150th Meeting of the Japanese Society of Conservative Dentistry 2019.06.27 Kanazawa
10. Zaw SYM, Kaneko T, Zaw ZCT, Sone PP, Murano H, Gu B, Yamato O, Sueyama Y, Okiji T. Effects of nuclear factor kappa B inhibition on angiogenic factor expression in dental pulp stem cells co-cultured with endothelial cells. The 150th Meeting of the Japanese Society of Conservative Dentistry 2019.06.27 Kanazawa
11. Sone PP, Kaneko T, Zaw SYM, Gu B, Murano H, Zaw ZCT, Okada Y, Sueyama Y, Okiji T. Gene-expression analysis of nerve growth factor and reowth associated protein 43 in a rat experimental model of coronal pulp tissue engineering with mesenchymal stem cells. The 150th Meeting of the Japanese Society of Conservative Dentistry 2019.06.27 Kanazawa
12. Maki K, Ebihara A, Nakatsukasa T, Kimura S, Nishijo M, Miyara K, Okiji T. Shaping ability of nickel-titanium rotary instruments used by non-experienced operators in curved canals. The 150th Meeting of the Japanese Society of Conservative Dentistry 2019.06.28 Kanazawa
13. Hama Y, Minakuchi S, Sasaki K, Maeda T, Hamura A, Ichinohe T, Okiji T, Watabe T. The dental education consortium to promote healthy longevity-fifth report- Future prospects at the expiration of the five years project. 38th Japanese Dental Education Association Meeting 2019.07.19 Fukuoka
14. Aung S, Watanabe S, Kouno A, Hongo T, Yao K, Satake K, Okiji T. Cleaning potential beyond the ledge using Er:YAG Laser-activated irrigation A particle image velocimetry analysis. 10th Mandalay Dental Conference 2019.07.20 Mandalay, Myanmar
15. Nikaido N, Watanabe S, Kouno A, Hongo T, Yao K, Satake K, Okiji T. Cone-beam computed tomography analysis of root canal configuration of mandibular premolars. The 151st Meeting of the Japanese Society of Conservative Dentistry 2019.11.07 Fukuoka

16. Nakatsukasa T, Ebihara A, Maki K, Kimura S, Nishijo M, Okiji T. Effect of heat treatment on the mechanical properties of a newly developed heat-treated NiTi rotary instrument. The 151st Meeting of the Japanese Society of Conservative Dentistry 2019.11.07 Fukuoka
17. Zaw ZCT, Kaneko T, Zaw SYM, Sone PP, Murano H, Gu B, Okada Y, Sueyama Y, Okiji T. Effect of nuclear factor kappa B inhibition on angiogenic factor expression in rat dental pulp cells and bone marrow stem cells co-cultured with endothelial cells. The 151st Meeting of the Japanese Society of Conservative Dentistry 2019.11.07 Fukuoka
18. Kuramoto M, Kawashima N, Tazawa K, Nara K, Fujii M, Noda S, Hashimoto K, Okiji T. MTA suppresses inflammatory mediator synthesis from macrophages via calcineurin /NFAT signal. The 151th Meeting of Japanese Society of Conservative Dentistry 2019.11.08 Fukuoka
19. Fujii M, Kasashima N, Oriksa S, Noda S, Nara K, Hashimoto K, Tazawa K, Nagai S, Okiji T. HIF1a inhibits LPS-mediated induction of IL-6 synthesis via SOCS3-dependent CEBPb suppression in human dental pulp cells. The 21st KACD-JSCD Joint Scientific Meeting 2019.11.09 Seoul, Korea
20. Oriksa S, Kawashima N, Fujii M, Yamamoto M, Hashimoto K, Tazawa K, Okiji T. Hypoxic condition induces hypoxia-inducible factor 1 and upregulates Wnt / β -catenin transcriptional cofactors, Bcl9 and Bcl9l, in mouse dental papillae cells. The 21st KACD-JSCD Joint Scientific Meeting 2019.11.09 Seoul, Korea
21. Okiji T. Defense, repair and regeneration of the dental pulp. Special Lecture, Wuhan University School and Hospital of Stomatology 2019.11.29 Wuhan, China
22. Yamauchi S, Watanabe S, Okiji T. Effect of heating on the physical properties of calcium silicate based root canal sealers. The 84th Meeting of the Stomatological Society, Japan 2019.12.06 Tokyo
23. Hoshihara Y, Watanabe S, Kouno A, Hongo T, Yao K, Satake K, Okiji T. Er:YAG laser activated root canal irrigation: Efficacy in cleaning lateral canals. The 84th Meeting of the Stomatological Society, Japan 2019. 12.07 Tokyo
24. Kanamori Y, Noritake K, Umemori S, Iwaki M, Kido D, Takeuchi S, Hattori A, Tonami K, Ebihara A, Hideshima M, Araki K, Nitta H. Introduction of objective clinical skills examination for TMDU's trainee residents. The 84th Meeting of the Stomatological Society, Japan 2019.12.07 Tokyo

[Awards & Honors]

1. Tasawa K. Outstanding performance award of Balance unit workshop for young researchers, 2019.01
2. Yabumoto S. The 40th Annual Scientific Meeting of Japan Endodontic Association Excellence Presentation Award, 2019.06
3. Iino Y. The 150th Meeting of the Japanese Society of Conservative Dentistry, Accredited Specialists Excellent Case Presentation Award, 2019.06
4. Aung Nyen Pyae Sone. The 10th Mandalay Dental Conference Excellence Presentation Award, 2019.07
5. Oriksa S. The 21st KACD-JSCD Joint Scientific Meeting, Best Presentation Award, 2019.11

Removable Partial Prosthodontics

Professor - Noriyuki Wakabayashi

Associate professor - Kenji Fueki

Junior associate professor - Takeshi Ueno

Assistant professors

- Eiko Kohno, Junnichi Wada, Natsuko Murakami, Atsushi Takaichi, Yuki Arai, Yuka Inamochi

Specially Appointed Assistant Professors

- Kensuke Takakusaki, Toshiki Yamazaki

Hospital staff

- Hideaki Inagawa, Gen Nabeshima, Masahiro Hirasawa, Yasuo Nakajima, Keigo Isoshima, Shiro Hibi, Taihei Kasai, Daiki Hikita

Graduate students

- AMR GAMAL, Yurika Ishioka, Keiichiro Uchikura, Hirofumi Uchida, Wang Zuo, Hisami Okawara, Kim Eung Yeol, K Zin Myint Oo, Hiroki Saito, Kazuki Sakamoto, SAN WIN THANT, Yuka Shichiri, Tenhaku Tan, Gu Zheng, Zhao Qian, Tomiharu Nagayama, Yoko Hayashi, Hao Jialin, Hein Linn Htat, Hitomi Matsuno, Hla Htoot Wai Cho, Yu Huaxin, Abdullah Kamel, Hideaki Umi, QU WENRUI, Wu huaze, CUI XIAOWEI, Hirokazu Sato, Deng Fan, Yoko Mashimo

(1) Outline

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

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

(2) Research

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

(3) Education

School of Dentistry

Year 1

Introduction to Dentistry

Year 3

Tooth Carving

Introduction to Clinical Dentistry

Observation and assistance at clinic term I and II

Basic Occlusal Reconstruction

Introduction to Research article writing and Patent acquisition

Year 4

Research Project

Removable Partial Prosthodontics

Advanced knowledge and skill with occlusion

Experience learning of dental practice

Years 5 and 6

Case study

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

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

Year 2 Prosthodontics

Years 3 and 4 Practice for Dental Hygiene Care

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

Year 2 Removable Prosthodontics Technology

(4) Lectures & Courses

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

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

(5) Clinical Services & Other Works

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

(6) Clinical Performances

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

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

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

1. Tsutsumi-Arai C, Takakusaki K, Arai Y, Terada-Ito C, Takebe Y, Imamura T, Ide S, Tatehara S, Tokuyama-Toda R, Wakabayashi N, Satomura K. Grapefruit seed extract effectively inhibits the *Candida albicans* biofilms development on polymethyl methacrylate denture-base resin. *PloS one*. 2019; 14(5); e0217496
2. Hiroshi Matsuura, Sai Yu, Koichi Sawasaki, Junichiro Wada, Masayuki Hideshima. Development and practical evaluation of a Japanese utterance education support system using phonetic segments and fundamental frequencies *Journal of Japan e-Learning Association*. 2019; (19); 15-26
3. Natsuko Murakami. A removable partial denture supported by structurally compromised and endodontically treated abutments for a patient exhibiting high bite force *Ann Jpn Prosthodont Soc*. 2019.01; 11(1); 68-71
4. Ijbara M, Wada K, Wada J, Jayawadena A, Miyashin M. The Application of Cellulose Acetate Replication Sheets in Enamel Wear investigations. *Dental Materials Journal*. 2019.02; 38(1); 86-95
5. Malik Ismail Hudieb, Noriyuki Wakabayashi, Osama Abdullah Abu-Hammad, Shohei Kasugai. Biomechanical Effect of an Exposed Dental Implant's First Thread: A Three-Dimensional Finite Element Analysis Study. *Med. Sci. Monit.*. 2019.05; 25; 3933-3940
6. Seki Erina, Kajima Yuka, Takaichi Atsushi, Kittikundecha Nuttaphon, Cho Hla Htoot Wai, Htat Hein Linn, Doi Hisashi, Hanawa Takao, Wakabayashi Noriyuki. Effect of heat treatment on the microstructure and fatigue strength of CoCrMo alloys fabricated by selective laser melting *MATERIALS LETTERS*. 2019.06; 245; 53-56
7. Yamazaki T, Murakami N, Suzuki S, Handa K, Yatabe M, Takahashi H, Wakabayashi N. Influence of block-out on retentive force of thermoplastic resin clasps: an in vitro experimental and finite element analysis. *Journal of prosthodontic research*. 2019.07; 63(3); 303-308
8. Keigo Isoshima, Takeshi Ueno, Yuki Arai, Hiroki Saito, Peng Chen, Yusuke Tsutsumi, Takao Hanawa, Noriyuki Wakabayashi. The change of surface charge by lithium ion coating enhances protein adsorption on titanium. *J Mech Behav Biomed Mater*. 2019.08; 100; 103393
9. Chiaki Tsutsumi-Arai, Yuki Arai, Chika Terada-Ito, Yusuke Takebe, Shinji Ide, Hirochika Umeki, Seiko Tatehara, Reiko Tokuyama-Toda, Noriyuki Wakabayashi, Kazuhito Satomura. Effectiveness of 405-nm blue LED light for degradation of *Candida* biofilms formed on PMMA denture base resin. *Lasers Med Sci*. 2019.09; 34(7); 1457-1464
10. Kittikundecha N, Kajima Y, Takaichi A, Wai Cho HH, Htat HL, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Fatigue properties of removable partial denture clasps fabricated by selective laser melting followed by heat treatment. *Journal of the mechanical behavior of biomedical materials*. 2019.10; 98; 79-89
11. Natsuko Murakami, Noriyuki Wakabayshi. Fulcrum line Prosthetic treatment 100. 2019.10; 98-99
12. Natsuko Murakami, Noriyuki Wakabayshi. Connector type Prosthetic treatment 100. 2019.10; 100-101
13. Yamada Masahiro, Watanabe Jun, Ueno Takeshi, Ogawa Takahiro, Egusa Hiroshi. Cytoprotective Preconditioning of Osteoblast-Like Cells with N-Acetyl-L-Cysteine for Bone Regeneration in Cell Therapy *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES*. 2019.10; 20(20);

14. Kenji Fueki, Eiko Yoshida-Kohno, Yuka Inamochi, Noriyuki Wakabayashi. The association between mucosal pain and subjective masticatory function in patients with partial removable dental prostheses. *J Oral Rehabil.* 2019.12; 46(12); 1095-1099
15. Wada J, Hideshima M, Uchikura K, Shichiri Y, Inukai S, Matsuura H, Wakabayashi N. Influence of the Covering Area of Major Connectors of Mandibular Dentures on the Accuracy of Speech Production: A Pilot Study *Folia Phoniatrica et Logopaedica.* 2019.12; 18; 1-10

[Misc]

1. Sanda M, Fueki K, Baric PR, Baba K. Comparison of immediate and conventional loading protocols with respect to marginal bone loss around implants supporting mandibular overdentures: A systematic review and meta-analysis *Japanese Dental Science Review.* 2019.01; 55(1); 20-25
2. Yuka Kajima, Atsushi Takaichi, Noriyuki Wakabayashi. Application of selective laser melting in manufacturing of dental prostheses *The Journal of the Japanese Society for Dental Materials and Devices.* 2019.10; 38(3); 161-164

[Conference Activities & Talks]

1. Uchikura K, Murakami N, Handa K, Takahashi H, Wakabayashi N. Influence of the fit of the rest on fracture resistance of tooth-colored CAD-CAM materials with the rest seat. The 128 Annual Meeting of Japan Prosthodontic Society 2019.05.10 Sapporo
2. Yuka Inamochi, Kenji Fueki, Nobuo Usui, Noriyuki Wakabayashi. The mechanism of adaptive change during tongue movement in a new oral environment: An fMRI study. The 128th Annual Meeting of Japan Prosthodontic Society 2019.05.11 Sapporo convention center
3. Watanabe C, Wada J, Nagayama T, Uchida H, Mizutani K, Wakabayashi N. The effect of alveolar bone density around abutment teeth of removable partial denture on diabetic patients -A retrospective cohort study-. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.12 Sapporo
4. Effectiveness of grapefruits seed extracts for the removal of Candida biofilms formed on polymethyl methacrylate denture-base resin.. 2019.05.12
5. Junichiro Wada, Yoichiro Ogino, Masahiro Wada. Save periodontally weakened teeth with prosthodontic interventions! -The prosthetic strategy to maximally utilize prosthodontic treatment options-. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.12 Sapporo
6. Effectiveness of 405-nm LED light for the removal of Candida biofilms formed on polymethyl methacrylate denture-base resin.. 2019.05.12
7. Kajima Y, Takaichi A, Oishi T, Kittikundecha N, Tsutsumi Y, Hanawa T, Wakabayashi N. Enhanced mechanical properties and corrosion resistance of SLM-processed CoCrMo alloys. 97th General Session of the IADR 2019.06.20 Vancouver
8. Yuka Inamochi, Kenji Fueki, Nobuo Usui, Noriyuki Wakabayashi. Adaptive brain activity changes during tongue movement with palatal coverage. IADR 97th General Session & Exhibition 2019.06.21 Vancouver convention center
9. Yuki Arai, Chiaki Tsutsumi-Arai, Kensuke Takakusaki, Noriyuki Wakabayashi, Kazuhito Satomura. Degradation Of Candida Biofilms On PMMA By 405-nm LED Light. 2019.06.21
10. Chie Watanabe, Junichiro Wada, Tomiharu Nagayama, Hirofumi Uchida, Koji Mizutani, Noriyuki Wakabayashi. The Effect of Removable Partial Denture Placement for Diabetic Patients. 97th General Session & Exhibition of the IADR 2019.06.22 Vancouver, BC, Canada
11. Takaichi A, Kittikundecha N, Kajima Y, Takahashi H, Hanawa T, Wakabayashi N. Enhanced Fatigue Strength of SLMed Co-Cr-Mo clasp by Post-heat Treatment Clasp . 97th General Session & Exhibition of the IADR 2019.06.22 Vancouver
12. Tomiharu Nagayama, Junichiro Wada, Chie Watanabe, Hirofumi Uchida, Koji Mizutani, Noriyuki Wakabayashi. . Influence Of RPD Placement On Mobility Of Periodontally Weakened Teeth. 97th General Session & Exhibition of the IADR 2019.06.22 Vancouver, BC, Canada

13. Junichiro Wada. How should removable partial dentures play a role against increasing elders with periodontitis?. 5th Prosthodontics 2019.09.08 Tokyo
14. Uchikura K, Murakami N, Yamazaki T, Nagata K, Ona M, Iwasaki N, Takahashi H, Wakabayashi N. Fracture behavior of tooth-colored CAD/CAM materials with the rest seat - Influence of misfit-. The 74th General Session of the Japanese Society for Dental Materials and Devices 2019.10.05 Nagasaki University Bunkyo Campus
15. Yuka Inamochi, Kenji Fueki, Nobuo Usui, Noriyuki Wakabayashi . The mechanism of adaptive change during tongue movement in a new oral environment: An fMRI study. The 31th Annual Meeting of Japanese Society for Mastication Science and Health Promotion 2019.10.05 Tokyo medical and dental university
16. Cho Hla Htoot Wai, Kajima Yuka, Takaichi Atsushi, Nuttaphon Kittikundecha, Htat Hein Linn, Hanawa Takao, Wakabayashi Noriyuki. Effect of cooling conditions after heat treatment on the micro-structure and mechanical properties of cobalt-chromium-molybdenum alloy prepared by selective laser melting. The 74th General Session of the Japanese Society for Dental Materials and Devices 2019.10.05 Nagasaki
17. Hao Jialin, Murakami Natsuko, Yamazaki Toshiki, Iwasaki Naohiko, Yatabe Masaru, Takahashi Hidekazu, Wakabayashi Noriyuki. Fatigue resistance of machinable polyester for dentures. 第 74 回日本歯科理工学会学術講演会 2019.10.06 長崎大学文京キャンパス
18. Zuo Wang, Eiko Kohno, Kenji Fueki, Yuka Inamochi, Takeshi Ueno, Noriyuki Wakabayashi. The effect of flipped classroom on learning outcomes: randomized controlled trial in prosthodontic class. The 84th Annual Meeting of the stomatological society, Japan 2019.12.06 Tokyo medical and dental university
19. Nagayama T, Wada J, Watanabe C, Uchida H, Wakabayashi N. Short-term effect of removable partial denture placement on periodontally weakened abutment teeth with poor prognosis. Tokyo branch meeting of Japan Prosthodontic Society, 2019 2019.12.08 Tokyo
20. H. Saito, T. Ueno, K. Isoshima, Y. Toyoshima, P. Chen, T. Hanawa, N. Wakabayashi. The change of surface charge by lithium ion coating increases osteoblastic cell activity on titanium . 8th International Conference on Mechanics of Biomaterials and Tissues 2019.12.15 Waikoloa beach, HI, USA
21. Atsushi Takaichi, Yuka Kajima, Tatsuya Oishi, Nuttaphon Kittikundecha, Hein Linn Htat, Yusuke Tsutsumi, Takao Hanawa, Noriyuki Wakabayashi. Influence of heat treatment on the mechanical and corrosion properties of CoCrMo alloys fabricated by selective laser melting. 8th International Conference on Mechanics of Biomaterials and Tissues 2019.12.15 Waikoloa
22. Yuka Kajima, Atsushi Takaichi, Nuttaphon Kittikundecha, Hein Linn Htat, Takao Hanawa, Noriyuki Wakabayashi, Takayuki Yoneyama. Effect of various heat treatments on the microstructure, texture and mechanical anisotropy of CoCrMo alloys produced by selective laser melting. 8th international conference on mechanics of biomaterials and tissues 2019.12.17 Waikoloa

[Awards & Honors]

1. Best poster award, Japanese Society for Mastication Science and Health Promotion, 2019.10

Plastic and Reconstructive Surgery

Professor(Chairman):Mori Hiroki
Professor:Tanaka Kentaro
Assistant Professor (Hospital Staff):Uemura Noriko
Project Assistant Professor (Hospital Staff) :Inoue Makiko
Graduate Student:Homma Tsutomu,Suesada Nobuko,Hamanaga Mayuko,Ogawa Kazuya

(1) Research

Plastic and Reconstructive Surgery :
MORI Hiroki

1. Pre and post operative breast or facial contour evaluation using 3D camera
2. Sensory recovery in the nipple-sparing or skin-sparing mastectomy
3. Development of classification and algorithm in blepharoptosis and blepharospasm surgery
4. Elucidation of the role of TRP channel and the midline in the interaction between keratinocyte and peripheral nervous system
5. Blood circulation study of the surgical flap using indocyanine green angiography and multi slice CT

Functional Reconstruction :
TANAKA Kentaro

1. Development of functional and aesthetic reconstruction following cancer ablation in head and neck
2. Does the improvement of capillary patency rate contribute to the preservation of transferred fatty tissue volume ?
3. Evaluation of blood supply to various flaps using ICG fluorescence angiography
4. Development of ambulatory functional reconstruction for refractory ulcer especially in CLI patients
5. Development of functional and aesthetic reconstruction for facial paralysis

(2) Education

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

(3) Clinical Performances

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

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

1. Higashino T, Okazaki M, Mori H, Yamaguchi K, Akita K. Reply: Microanatomy of Sensory Nerves in the Upper Eyelid. A Cadaveric Anatomical Study. *Plast. Reconstr. Surg.* 2019.02; 143(2); e437-e438
2. Usami S, Kawahara S. Flexor Tendon Entrapment Caused by Intratendinous Tumor-Like Chronic Proliferative Tenosynovitis. *J Hand Microsurg.* 2019.04; 11(1); 50-53
3. Usami S, Inami K. Combination Therapy Involving Ear Cartilage Transfer and Suture-Button Suspension Arthroplasty for Symptomatic Thumb Carpometacarpal Joint Arthritis. *J Wrist Surg.* 2019.04; 8(2); 157-160
4. Namiki T, Hisieh M, Iwamoto Y, Ugajin T, Tanaka K, Mori H, Miura k, Yokozeki H. Subcutaneous ossifying fibromyxoid tumor of the scalp: a potential importance of CT, MRI, and PET/CT on the diagnosis. *International journal of dermatology.* 2019.06; 58(6); e121-e123
5. Usami S, Kawahara S, Inami K. Additional advancement after elevation of a neurovascular advancement flap with interposition of an artificial nerve conduit. *J Plast Reconstr Aesthet Surg.* 2019.08; 72(8); 1418-1433
6. Usami S, Kawahara S, Inami K, Hirase Y. Use of a vascularized dorsal sensory branch of an ulnar nerve flap for repairing a proper digital nerve with coverage of a volar soft tissue defect: Report of two cases. *Microsurgery.* 2019.10; 39(7); 647-650

[Conference Activities & Talks]

1. Tanaka K, Suesada N, Homma T, Mori H. Vascular Anastomosis in the Temporal Region: Comparison between Head & Neck and Skull Base Surgery. 10th Congress of World Society for Reconstructive Microsurgery 2019.06.14 Bologna, Italy
2. Usami S, Inami K. Sensate ulnar parametacarpal perforator flap for finger resurfacing. 10th congress of World Society for Reconstructive Microsurgery 2019.06.14 Bologna, Italy
3. Mori H, Uemura N, Tanaka K, Inoue M, Homma T, Koga H. Cephalic view of breast helps to assess the patient's satisfaction. Plastic Surgery The Meeting 2019 2019.09.20 San Diego, USA

Head and Neck Surgery

Professor: Takahiro Asagkage

Junior associate professor: Yosuke Ariizumi, Kazuchika Ohno

Assistant professor: Akihisa Tasaki

Senior Resident: Hiroaki Kawabe, Nobuaki Koide, Ryosuke Takahashi, Ymiko Tateishi

Student: Masaharu Kishikawa

(1) Outline

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

(2) Research

Surgical approaches to the skull base and deep area of the face.

Surgical anatomy of the skull base.

Establishment of the standard neck dissection.

Treatment of pediatric head and neck tumors.

Chemoradiotherapy for head and neck cancers.

Clinical application of navigation system and 3D entity model surgery for skull base surgery.

Diagnosis and treatment for superficial squamous cell carcinoma of head and neck region.

Human papilloma virus infection and head and neck cancer.

Polymorphisms in alcohol metabolism genes and Head and Neck Cancers.

(3) Education

Education: Undergraduate Course

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

Education :Graduate Course

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

(4) Publications

[Original Articles]

1. Fusa Ogata, Tadanobu Nagaya, Yasuhiro Maruoka, Joshua Akhigbe, Adam Meares, Melissa Y Lucero, Andrius Satraitis, Daiki Fujimura, Ryuhei Okada, Fuyuki Inagaki, Peter L Choyke, Marcin Ptaszek,

- Hisataka Kobayashi. Activatable Near-Infrared Fluorescence Imaging Using PEGylated Bacteriochlorin-Based Chlorin and BODIPY-Dyads as Probes for Detecting Cancer. *Bioconjug. Chem.* 2019.01; 30(1); 169-183
2. Okada R, Ito T, Nomura F, Kirimura S, Cho Y, Sekine M, Tateishi Y, Ariizumi Y, Asakage T. The quantitative analysis of the human papillomavirus DNA load in submandibular gland lesions with droplet digital polymerase chain reaction. *Acta oto-laryngologica.* 2019.02; 1-6
 3. Yurika Kimura, Seiji Kishimoto, Takuro Sumi, Mio Uchiyama, Keiko Ohno, Hitome Kobayashi, Makoto Kano. Improving the Quality of Life of Patients With Severe Dysphagia by Surgically Closing the Larynx. *Ann. Otol. Rhinol. Laryngol.* 2019.02; 128(2); 96-103
 4. Nomura Fuminori, Ariizumi Yosuke, Kiyokawa Yusuke, Tasaki Akihisa, Tateishi Yumiko, Koide Nobuaki, Kawabe Hiroaki, Sugawara Takashi, Tanaka Kentaro, Asakage Takahiro. 顎関節に生じた色素性絨毛結節性滑膜炎 (Pigmented villonodular synovitis occurring in the temporomandibular joint) *Auris· Nasus· Larynx.* 2019.08; 46(4); 609-617
 5. Ryuhei Okada, Yasuhiro Maruoka, Aki Furusawa, Fuyuki Inagaki, Tadanobu Nagaya, Daiki Fujimura, Peter L Choyke, Hisataka Kobayashi. The Effect of Antibody Fragments on CD25 Targeted Regulatory T Cell Near-Infrared Photoimmunotherapy. *Bioconjug. Chem.* 2019.10; 30(10); 2624-2633
 6. Yu A Nakamura, Shuhei Okuyama, Aki Furusawa, Tadanobu Nagaya, Daiki Fujimura, Ryuhei Okada, Yasuhiro Maruoka, Philip C Eclarinal, Peter L Choyke, Hisataka Kobayashi. Near-infrared photoimmunotherapy through bone. *Cancer Sci.* 2019.12; 110(12); 3689-3694
 7. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. *Am J Otolaryngol.* 35(3); 402-404

[Conference Activities & Talks]

1. Asakage T, et al. Head and Neck Sarcoma in AYA generation.. 6th Asian Society for Head and Neck Oncology 2019.03 Seoul, Korea
2. Masahiro Kishikawa, Jun Inoue, Takahiro Asakage, Johji Inazawa. Therapeutic potential of the topical treatment of miR-634 ointment for skin cancer. The 3rd international Symposium of International Society of Precision Cancer Medicine 2019.03.12 Seoul
3. Ariizumi Y, Asakage T. Endoscopic endonasal approach in salvage surgery after radiotherapy for sinonasal malignancies.. Asian Society of Head & Neck Oncology 2019.03.28
4. Okada R, Maruoka Y, Furusawa A, Inagaki F, Fujimura D, Choyke PL, Kobayashi H. The Effect of Antibody Fragments on CD25-Targeted Regulatory T Cell Near Infrared Photoimmunotherapy (NIR-PIT) in Mouse Models. 2019 World Molecular Imaging Congress 2019.09 Montreal, Canada
5. 岸川正大, 井上純, 朝蔭孝宏, 稲澤譲治, 他. Development of miRNA-formulation using miR-634 for anaplastic thyroid cancer therapy. 第78回日本癌学会学術総会 2019.09.28 京都
6. Asakage T. An experience of 100 case of skull base surgery.. The 107th Annual congress and international symposium of the Taiwan society of otorhinolaryngology head and neck surgery 2019.11 Kaohsiun
7. Asakage T. Present status of endoscopic surgery for malignant sinonasal tumors in Japan.. 15th Japan-Taiwan Conference on Otolaryngology-Head and Neck Surgery. 2019.12 Fukuoka
8. Asakage T. Moderator Symposium 3 Skull base. 15th Japan-Taiwan Conference on Otolaryngology-Head and Neck Surgery. 2019.12 福岡

Radiation Therapeutics and Oncology

Professor Ryoichi Yoshimura

Lecturers Kazuma Toda

Research Associates Keiko Nakagawa(∼ Mar.), Mio Kojima(∼ Mar.)
Hirofumi Kuwabara(Oct. ∼)

Hospital Staff members Kazuma Sasamura(∼ Mar.),
Hirofumi Kuwabara(Apr. ∼ Sep.)

Resident Daigoro Matsubara (∼ Mar.), Meika Koide(Apr. ∼)

Graduate Students

Yoshinao Takada, Takuya Nagano, Hiroshi Hirota, Masahiro Yoshida

(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 695 patients, including 181 head and neck cancer patients, 160 urological cancer patients, 63 breast cancer patients, 77 lung cancer patients, and 44 esophageal cancer patients, were treated at our hospital in

2017.

(6) Clinical Performances

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

(7) Publications

[Original Articles]

1. Kuwabara Hirofumi, Toriihara Akira, Yuasa-Nakagawa Keiko, Toda Kazuma, Tateishi Ukihide, Yoshimura Ryoichi. Prognostic value of metabolic tumor burden calculated using dual-time-point 18F-fluorodeoxyglucose positron emission tomography/CT in patients with oropharyngeal or hypopharyngeal cancer HEAD AND NECK-JOURNAL FOR THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK. 2019.01; 41(1); 103-109
2. Sato Kiyoshi, Shimamoto Hiroaki, Mochizuki Yumi, Hirai Hideaki, Tomioka Hirofumi, Shimizu Risa, Marukawa Eriko, Fukayama Haruhisa, Yoshimura Ryoichi, Ishida Hiroo, Harada Hiroyuki. Treatment of oral cancers during pregnancy: a case-based discussion JOURNAL OF OTOLARYNGOLOGY-HEAD & NECK SURGERY. 2019.02; 48(1); 9
3. Nagano Takuya, Yoshimura Ryo-ichi, Kojima Mio, Nakagawa Keiko, Toda Kazuma. Outcomes of radiotherapy in advanced external auditory canal cancer JOURNAL OF RADIATION RESEARCH. 2019.05; 60(3); 380-386
4. Yoshida S, Takahara T, Arita Y, Ishii C, Uchida Y, Nakagawa K, Toda K, Sakamoto T, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Yoshimura R, Fujii Y. Progressive Site-Directed Therapy for Castration-Resistant Prostate Cancer: Localization of the Progressive Site as a Prognostic Factor. International journal of radiation oncology, biology, physics. 2019.06;
5. Sasamura K, Matsubara D, Kojima M, Yuasa-Nakagawa K, Toda K, Miura K, Yoshimura R. Intensity Modulated Radiation Therapy for Syringomatous Carcinoma of the Face: A Case Report. Advances in radiation oncology. 2019.07; 4(3); 473-477
6. Toda K., Sasamura K., Tateishi U., Yoshimura R. I.. Time Dependency of Textural Features Obtained by Dual-Time-Point TOF-PET/CT in Head and Neck Squamous Cell Cancer. INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS. 2019.09; 105(1); S203-S204

[Conference Activities & Talks]

1. Ryo-ichi Yoshimura. Low-dose-rate brachytherapy for oral cancer. Annual Meeting of Japanese Society of Oral Oncology 2019.01.24 Nagasaki
2. Ryo-ichi Yoshimura. PET-CT Simulation for Radiotherapy. 2019.02.15
3. Kazuma Toda, Kazuma Sasamura, Ukihide Tateishi, Ryo-ichi Yoshimura. Time Dependency of Textural Features Obtained by Dual-Time-Point TOF-PET/CT in Head and Neck Squamous Cell Cancer.. 61st annual meeting of American Society for Radiation Oncology 2019.09.16

Maxillofacial Anatomy

Professor Shunichi SHIBATA
Assistant Professor Shun-ichi SHIKANO (Until March)
Graduate Student Masato Takahashi (Until March)
Graduate Student Maki Hasegawa
Graduate Student Angamma Randilini
Lecturer Rei Sato
Lecturer Kumiko Sugimoto

(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) Hyaluronan synthesis in tooth germ.
- 6) Studies on regeneration of jaw bone.
- 7) 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. Tang H, Yonemitsu I, Ikeda Y, Watakabe K, Shibata S, Hosomichi J, Ono T. Effects of unilateral nasal obstruction on the characteristics of jaw-closing muscles in growing rats. *The Angle orthodontist*. 2019.01; 89(1); 102-110
2. Takahashi M, Fujikawa K, Angammana R, Shibata S. An in situ hybridization study of MMP-2, -9, -13, -14, TIMP-1, and -2 mRNA in fetal mouse mandibular condylar cartilage as compared with limb bud cartilage. *Gene expression patterns : GEP*. 2019.02; 32; 1-11
3. Shibata S, Takahashi M, Fujikawa K. Histochemical and ultrastructural study of developing gonial bone with reference to initial ossification of the malleus and reduction of Meckel's cartilage in Mice *Anatomical record (Hoboken, N.J. : 2007)*. 2019.06;
4. Shibata S, Amano H, Nagayama M, Takahashi M, Watanabe M, Tanaka M. Immunohistochemical and ultrastructural evaluation of matrix components in mandibular condylar cartilage in comparison with growth plate cartilage in cartilage calcification insufficient rats. *Anatomical science international*. 2019.06;
5. Horigome Y, Ida-Yonemochi H, Waguri S, Shibata S, Endo N, Komatsu M. Loss of autophagy in chondrocytes causes severe growth retardation *AUTOPHAGY*. 2019.06; 1-11
6. Takeuchi A, Nagayama M, Tanaka M, Watanabe M, Amamo H, Shibata S, Kitai N. Morphological and molecular biology study of cranial base synchondrosis in cartilage calcification deficient rat 2019.06; 46(1); 27-39
7. Suzuki D, Kim JH, Shibata S, Abe H, Murakami G, Rodríguez-Vázquez JF. Flap valve of the heart foramen ovale revisited: macroscopic and histologic observations of human near-term fetuses. *Annals of anatomy = Anatomischer Anzeiger : official organ of the Anatomische Gesellschaft*. 2019.07; 224; 8-16
8. Jin ZW, Cho KH, Shibata S, Yamamoto M, Murakami G, Rodríguez-Vázquez JF. Nervus terminalis and nerves to the vomeronasal organ: a study using human fetal specimens *Anatomy & Cell Biology*. 2019.09; 52(3); 278-285
9. Suzuki D, Kim JH, Shibata S, Abe H, Murakami G, Rodríguez-Vázquez JF. Topographical anatomy of the greater omentum and transverse mesocolon : a study using human fetuses *Anatomy & Cell Biology*. 2019.12; 52(4); 443-454
10. Kim JH, Shibata S, Abe H, Murakami G, Rodríguez-Vázquez JF. Topographical variations of the incisive canal and nasopalatine duct in human fetuses *Anatomy & Cell Biology*. 2019.12; 52(4); 426-435

[Conference Activities & Talks]

1. アンガンマナ ランディリニ, 柴田俊一. Expression of leucine rich proteoglycans (SLRPs) in developing mouse molar tooth germ. 第 61 回歯科基礎医学会学術大会 2019.10.12 東京歯科大学
2. Angammana R, Shibata S. Expression, localization, and synthesis of small leucine-rich proteoglycans (SLRPs) in developing mouse molar tooth germ. 第 84 回口腔病学会学術大会 2019.12.06

Cognitive Neurobiology

Assistant Professor:

Nobuo Usui

Adjunct Lecturer:

Narumi Katsuyama

Hisayuki Ojima

Akiko Yamashita

Rui Watanabe

Eriko Kikuchi(Tachi)

Yoko Kono

Kazuo Toda

Masamichi Shinoda

Masahiro Kondo

Kumiko Sugimoto

(1) Outline

The neuronal mechanisms underlying higher brain function, such as judgement, decision making, and language, are largely unknown. Our goal is to elucidate the neuronal mechanisms by using various techniques in neuroscience including functional MRI, psychophysical experiments, and animal experiments.

(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) 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. Unit of "Practice of Physiology"

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. Sugiyama, Y., Oishi, T., Yamashita, A., Murata, Y., Yamamoto, T., Takashima, U., Isa, T., Higo, N. Neuronal and microglial localization of secreted phosphoprotein 1 (osteopontin) in intact and damaged motor cortex of macaques. *Brain Research*. 2019.02; 1714; 52-64
2. Rui Watanabe, Narumi Katsuyama, Nobuo Usui, Masato Taira. Effects of pseudoexperience on the understanding of hemiplegic movements in physical therapists: An fMRI study. *NeuroImage. Clinical*. 2019.04; 23; 101845
3. Kim Yuri, Usui Nobuo, Miyazaki Atsushi, Haji Tomoki, Matsumoto Kenji, Taira Masato, Nakamura Katsuki, Katsuyama Narumi. Cortical Regions Encoding Hardness Perception Modulated by Visual Information Identified by Functional Magnetic Resonance Imaging With Multivoxel Pattern Analysis *FRONTIERS IN SYSTEMS NEUROSCIENCE*. 2019.10; 13; 52

[Conference Activities & Talks]

1. Yuka Inamochi, Kenji Fueki, Nobuo Usui, Noriyuki Wakabayashi. The mechanism of adaptive change during tongue movement in a new oral environment: An fMRI study. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.11 Sapporo
2. R Watanabe, Y Kim, Y Kikuchi.. The effect of visual perspective on a better understanding of difficulties in hemiplegic movements.. *OHBM* 2019.06 Roma
3. Yuka Inamochi, Kenji Fueki, Nobuo Usui, Noriyuki Wakabayashi. Adaptive brain activity changes during tongue movement with palatal coverage. The 97th General Session & Exhibition of the IADR 2019.06.21 Vancouver, Canada

Molecular Craniofacial Embryology

Staffs and Students

Professor

Sachiko ISEKI

Associate Professor

Masa-Aki IKEDA

Tenure Track Assistant Professor

Masaki TAKECHI

Part-time lecturers

Shumpei YAMADA

Youichirou NINOMIYA

Toshiko FURUTERA

Shigeru Okuhara

Graduate Students

Erika KUBOTA

RAJENDRAN Arun kumar

Takahiko YAMADA

Shohei YANAGISAWA

VU HOANG Tri

Manami TAKENOSHITA

Rika TAKEUCHI

NAMANGKALAKUL Worachat

Research students

Yukiko HOSHINO

(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 the mechanism of their stemness
- 4) Regulation of gene expression in cell growth and differentiation
- 5) Modulating endochondral ossification of mesenchymal stem cells for bone regeneration

(2) Publications

[Original Articles]

1. Arun Kumar Rajendan, Yoshinori Arisaka, Sachiko Iseki, Nobuhiko Yui. Sulfonated polyrotaxane surfaces with basic fibroblast growth factor alters the osteogenic potential of human mesenchymal stem cells in short-term culture ACS Biomaterials Science and Engineering. 2019.02; 5(11); 5652-5659
2. Zhao L, Matsumoto Y, Ono T, Iseki S.. Effects of mechanical force application on the developing root apex in rat maxillary molars. Arch Oral Biol.. 2019.05; 101; 64-76
3. Cobourne MT, Iseki S, Birjandi AA, Adel Al-Lami H, Thauvin-Robinet C, Xavier GM, Liu KJ.. How to make a tongue: Cellular and molecular regulation of muscle and connective tissue formation during mammalian tongue development. Semin. Cell Dev. Biol.. 2019.07; 91; 45-54

[Conference Activities & Talks]

1. Saadat K ASM, Arman K, Ikeda MA. ARID3A Regulates the Tumor Suppressor Tap73 in Osteosarcoma. 2nd ZEUGMA International Congress on Multidisciplinary Studies 2019.01.18 Gaziantep Turkey
2. Saadat K ASM, Arman K, Ikeda MA. ARID3A Directly Regulates Autophagy Related Gene Becln1 in Osteosarcoma. 2nd ZEUGMA International Congress on Multidisciplinary Studies 2019.01.18 Gaziantep Turkey
3. Öğr. Üyesi. Saadat K ASM. Saadat, Arman K, Ikeda MA. ARID3A Regulates the Tumor Suppressor Tap73 in Osteosarcoma. 2nd ZEUGMA International Congress on Multidisciplinary Studies 2019.01.20 Gaziantep Turkey
4. Saadat K ASM, Ikeda MA. Gene-Silencing Efficiency Determination of ARID3B in Osteosarcoma Cell Lines by siRNA and shRNA. III. International Eurasia Multidisciplinary Studies Congress 2019.04.04 Gaziantep, Turkey
5. Saadat K ASM, Ikeda MA. Gene-Silencing Efficiency Determination of ARID3B in Osteosarcoma Cell Lines by siRNA and shRNA. 6th International Multidisciplinary Studies Congress 2019.04.26 Gaziantep, Turkey
6. Takechi M, Furutera T, Kitazawa T, Kurihara H, Rijli FM, Kuratani S, Iseki S.. Similarities and differences of tympanic membrane development in mammals and diapsids. . International Congress of Vertebrate Morphology 12 2019.07.21 Prague, Czech Republic
7. Hoang TV, Takechi M, Shimizu M, Kitazawa T, Higashiyama H, Iwase A, Kurihara H, Iseki S. Dlx5-augmentation in neural crest cells induces ectopic calvarial cartilages. 第 59 回日本先天異常学会学術集会 2019.07.28 愛知学院大学 名城公園キャンパス
8. Takechi M. Evolutionary developmental biology (Evo-Devo) of the middle ear in amniotes. 第 6 回生物音響学会年次研究発表会（シンポジウム講演） 2019.11.22
9. Khandakar A.S.M. Saadat, Widya Lestari, Teng Ma, Endrawan Pratama, Sachiko Iseki, Kiyoshi Ohtani, Masa-Aki Ikeda. ARID3B modulates E2F target gene expression and cell proliferation.. 2019 年度生命科学学会合同年次大会 2019.12.04 福岡

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama

Junior Associate Professor Hiroshi Fujita, Yasuki Ishizaki, Masao Saito

Research Student : Hong Ding Liu

: Syun Nishihara

: Hiroki Kuwahara

: Syuhei Fukuda

: Hirohito Miki

: SUN WEIMING

(1) Outline

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

(2) Research

Research Subjects

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

(3) Education

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

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

(4) Lectures & Courses

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

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

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

1. Hirayama J, Alifu Y, Hamabe R, Yamaguchi S, Tomita J, Maruyama Y, Asaoka Y, Nakahama KI, Tamaru T, Takamatsu K, Takamatsu N, Hattori A, Nishina S, Azuma N, Kawahara A, Kume K, Nishina H. The clock components Period2, Cryptochrome1a, and Cryptochrome2a function in establishing light-dependent behavioral rhythms and/or total activity levels in zebrafish. *Scientific reports*. 2019.01; 9(1); 196
2. Nagaoka N, Yoshida T, Cao K, Iwasaki Y, Nakahama KI, Morita I, Ohno-Matsui K. Visual arrestin modulates gene expression in the retinal pigment epithelium: Implications for homeostasis in the retina. *Biochemistry and biophysics reports*. 2019.12; 20; 100680

[Conference Activities & Talks]

1. Impact of GPR68 on cAMP signaling in osteoblasts. 2019.06.25 Okinawa
2. VD3/cAMP-mediated transcriptional regulation of osteopontin in osteoblasts. MBSJ 2019 2019.12.06 Fukuoka
3. The Role of G-protein coupled receptor 110 (GPR110) in osteoclast differentiation. . MBSJ 2019 2019.12.06 Fukuoka

Maxillofacial Surgery

Professor: Tetsuya YODA

Associate Professor: Eriko MARUKAWA

Junior Associate Professor: Keiiti MORITA

Assistant Professor: Hiroyuki YOSHITAKE, Kouichi NAKAKUKI, Namiaki TAKAHARA, Nobuyoshi TOMOMATSU

Special Assistant Professor: Yasuhiro KURASAWA, Tsubasa KIHARA, Yosuke HARAZONO,

Atsushi KIMURA, Eri ANZAI, Masahiko TERAUCHI

Hospital Staff: Takeshi OKAMURA, Reiko HOSHI, Keiitirou NAKAZATO, Takahiko YAMADA,

Erina NAKAMURA, Tomomi SAKUMA

Graduate Student: Hiroshi KATOU, Katuya HYODOU, Daisuke YAMAMOTO, Eri SHIBATA, Hiroki MASUDA,

(April)Yuu AKAIKE, Kouhi SYU, Noboru MARUTA, Shintarou YAMAZAKI

Social Graduate Student: (April)Takahiko YAMADA, Mari SHIBATA

Student: Tizuko KOMURO, Takahiro KIKUCHI, Soichi ROKUSHIMA, Junya KUMAGAI, Ichirou YOKOMIZO,

Yuuko KATSUKI, Chika MIURA, (April)Mako KUBOTA

Part-time Lecturer: Hiroyuki WAKE, Masashi YAMASHIRO, Jin SATO, Hideo MIYACHI, Akiko KOBAYASHI,

Fumiaki SATO, Tetsuo SUZUKI, Yutaka SATO, Takashi MISHIMAGI, Kazuto KUROHARA,

Katuya AIKOU, Yosio OOOYAMA, Itaru SONODA, Shigehiro ABE, Chieko MICHIKAWA,

Ryosuke NAGAOKA, Toshiyuki YAMADA, Erina TONOUCHI

(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 injures 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 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.

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

1. Masahiko Terauchi, Mari Shibata, Akane Wada, Yasuyuki Michi, Satoshi Yamaguchi, Tetsuya Yoda. Second primary squamous cell carcinoma in an oral cavity free flap: a case report and review of the literature Oral and Maxillofacial Surgery Cases. 2019;
2. Hyodo K, Arisaka Y, Yamaguchi S, Yoda T, Yui N. Stimulation of Microvascular Networks on Sulfonated Polyrotaxane Surfaces with Immobilized Vascular Endothelial Growth Factor. Macromolecular bioscience. 2019.01; e1800346
3. Kai Shibaguchi, Atsushi Tamura, Masahiko Terauchi, Mitsuaki Matsumura, Hiroyuki Miura, Nobuhiko Yui. Mannosylated polyrotaxanes for increasing cellular uptake efficiency in macrophages via receptor-mediated endocytosis. Molecules. 2019.01; 24(3); 439
4. Yusoo Kim, Mikihiro Hayashi, Takehito Ono, Tetsuya Yoda, Hiroshi Takayanagi, Tomoki Nakashima. Suppression of hematopoietic cell kinase ameliorates the bone destruction associated with inflammation Modern Rheumatology. 2019.01;
5. Sone E, Noshiro D, Ikebuchi Y, Nakagawa M, Khan M, Tamura Y, Ikeda M, Oki M, Murali R, Fujimori T, Yoda T, Honma M, Suzuki H, Ando T, Aoki K. The induction of RANKL molecule clustering could stimulate early osteoblast differentiation. Biochemical and biophysical research communications. 2019.02; 509(2); 435-440
6. Oshibe N, Marukawa E, Yoda T, Harada H. Degradation and interaction with bone of magnesium alloy WE43 implants: A long-term follow-up in vivo rat tibia study. Journal of biomaterials applications. 2019.02; 885328218822050
7. Sato Kiyoshi, Shimamoto Hiroaki, Mochizuki Yumi, Hirai Hideaki, Tomioka Hirofumi, Shimizu Risa, Marukawa Eriko, Fukayama Haruhisa, Yoshimura Ryoichi, Ishida Hiroo, Harada Hiroyuki. Treatment of oral cancers during pregnancy: a case-based discussion JOURNAL OF OTOLARYNGOLOGY-HEAD & NECK SURGERY. 2019.02; 48(1); 9
8. A case of nodal marginal zone lymphoma in the submandibular region 2019.02; 65(2); 83-86
9. Masahiko Terauchi, Satoshi Akiya, Junya Kumagai, Yoshio Ohyama, Satoshi Yamaguchi. An Analysis of Dentigerous Cysts Developed around a Mandibular Third Molar by Panoramic Radiographs. Dent J (Basel). 2019.02; 7(1);
10. Minegishi S, Ohtani S, Noritake K, Funakoshi T, Ishii N, Utsuno H, Sakuma A, Saitoh H, Yamaguchi S, Marukawa E, Harada H, Uemura K, Sakurada K. Preparation of dentin standard samples for age estimation based on increased aspartic acid racemization rate by heating. Legal Medicine. 2019.03; 38; 25-31
11. Yoshitake Hiroyuki. Development and clinical application of a new mouth-opening exercise device that induces a protrusive sliding movement of the mandibular condyle and increases the hinge mobility of the temporomandibular joint Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2019.03; 31(2); 131-134

12. Fukushima Y, Kitamura T, Ikami E, Yumoto M, Sano Y, Sato T, Yoda T. A case of burning mouth syndrome leading to suicide 10 days after self-cutting of tongue. *Psychogeriatrics : the official journal of the Japanese Psychogeriatric Society*. 2019.04;
13. Fukushima Y, Sano Y, Isozaki Y, Endo M, Tomoda T, Kitamura T, Sato T, Kamijo Y, Haga Y, Yoda T. A pilot clinical evaluation of oral mucosal dryness in dehydrated patients using a moisture-checking device. *Clinical and experimental dental research*. 2019.04; 5(2); 116-120
14. Naoki Hayashi — Tsuyoshi Sato — Megumi Yumoto — Shoichiro Kokabu — Yosuke Fukushima — Yumiko Kawata — Takeshi Kajihara — Yumi Mizuno — Yosuke Mizuno — Tetsuji Kawakami ,Tadaaki Kirita , Tadayoshi Hayata , Masaki Noda , Tetsuya Yoda. Cyclic stretch induces decorin expression via yes-associated protein in tenocytes: A possible mechanism for hyperplasia in masticatory muscle tendon-aponeurosis hyperplasia *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology*. 2019.05; 31; 175-179
15. Tomomatsu N, Kurohara K, Nakakuki K, Yoshitake H, Kanemaru T, Yamaguchi S, Yoda T. Influence of the anatomical form of the posterior maxilla on the reliability of superior maxillary repositioning by Le Fort I osteotomy *Int J Oral Maxillofac Surg*.. 2019.05; 48(5); 612-619
16. Masahiko Terauchi, Mari Shibata, Akane Wada, Yasuyuki Michi,*, Satoshi Yamaguchi, Tetsuya Yoda . Second primary squamous cell carcinoma in an oral cavity free flap: A case report and review of the literature *Oral and Maxillofacial Surgery Cases* . 2019.05; 5;
17. Samira Bernardino Ramos do Prado, Tânia Misuzu Shiga, Yosuke Harazono, Victor A Hogan, Avraham Raz, Nicholas C Carpita, João Paulo Fabi. Migration and proliferation of cancer cells in culture are differentially affected by molecular size of modified citrus pectin. *Carbohydr Polym*. 2019.05; 211; 141-151
18. Yoshitake H, Kayamori K, Wake S, Sugiyama K, Yoda T. Biomarker expression related to chondromatosis in the temporomandibular joint. *Cranio : the journal of craniomandibular practice*. 2019.06; 1-5
19. Kurohara K, Tomomatsu N, Nakakuki K, Arai N, Yoda T. Skeletal stability after maxillary step osteotomy compared with original Le Fort I osteotomy during one-year of follow-up. *Scientific reports*. 2019.07; 9(1); 9742
20. Nakazato Keiichiro, Mogushi Kaoru, Kayamori Kou, Tsuchiya Maiko, Takahashi Ken-Ichiro, Sumino Jun, Michi Yasuyuki, Yoda Tetsuya, Uzawa Narikazu. Glucose metabolism changes during the development and progression of oral tongue squamous cell carcinomas *ONCOLOGY LETTERS*. 2019.08; 18(2); 1372-1380
21. Masahiko Terauchi, Atsushi Tamura, Asato Tonegawa, Satoshi Yamaguchi, Tetsuya Yoda, Nobuhiko Yui. Polyelectrolyte complexes between polycarboxylates and BMP-2 for enhancing osteogenic differentiation: effect of chemical structure of polycarboxylates *Polymers*. 2019.08; 11(8); 1327
22. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer science*. 2019.11;
23. Takahara N, Kimura A, Tomomatsu N, Nakakuki K, Yoda T. Does the amount of mandibular setback during bimaxillary surgery correlate with the degree of surgical relapse? *Oral surgery, oral medicine, oral pathology and oral radiology*. 2019.11;
24. Takahiro Abe, Tomoya Sato, Tetsuya Yoda, Kazuto Hoshi. The period circadian clock 2 gene responds to glucocorticoids and regulates osteogenic capacity *Regenerative Therapy*. 2019.12; 11; 199-206
25. Yokokawa M, Morita KI, Oikawa Y, Kayamori K, Sakamoto K, Ikeda T, Harada H. Co-expression of EGFR and MET has a synergistic effect on the prognosis of patients with oral squamous cell carcinoma *J Oral Pathol Med*. 2019.12; 235-242
26. Abe Takahiro, Sato Tomoya, Yoda Tetsuya, Hoshi Kazuto. The period circadian clock 2 gene responds to glucocorticoids and regulates osteogenic capacity(和訳中) *Regenerative Therapy*. 2019.12; 11; 199-206

[Books etc]

1. Joe Iwanaga, R.Shane Tubbs, Jingo Kusakawa, Shin, Daniel E., Solomon, Charles S., Tomaszewska, Iwona M., He, Puhon, Soichiro Ibaragi, Katsuichiro Maruo, Tomaszewska, Iwona M., Tatsuo Okui, Yosuke Harazono, Norie Yoshioka, Shogo Kikuta, Koichi Watanabe, Ramdhan, Rebecca C., Tsuyoshi Tanaka, Yasuhiko Kamura, Masayoshi Uezono. Anatomical Variations in Clinical Dentistry . 2019 (ISBN : 978-3-319-97961-8)
2. TCH Management and Rehabilitation Training Methods for TMD. 2019.06

[Misc]

1. Yoda T. Masticatory muscle tendon-aponeurosis hyperplasia accompanied by limited mouth opening J Korean Assoc Oral Maxillofac Surg . 2019.08; 45; 174-179

[Conference Activities & Talks]

1. Eri ANZAI, Takayuki YAMADA, Ryousuke NAGAOKA, Namiaki TAKAHARA, Keiichi MORITA, Tetsuya YODA. Prediction of the need for orthognathic surgery at age 5 in patients with unilateral cleft lip and palate. The 43rd annual meeting of japanese cleft palate assosiation 2019.05.30
2. Chieko Michikawa, Pedro A. Torres-Saavedra, Natalie L. Silver, Paul M. Harari, Merrill S. Kies, David I. Rosenthal, Quynh-Thu Le, Richard C. Jordan, Dzifa Y. Duose, Saradhi Mallampati, Sanchit Trivedi, Rajyalakshmi Luthra, Ignacio I. Wistuba, Olivier Lichtarge, Robert L. Foote, Upendra Parvathaneni, D. Neil Hayes, Curtis R. Pickering, Jeffrey N. Myers. Evolutionary action score of TP53 analysis in pathologically high-risk HPV-negative head and neck cancer from a phase II clinical trial. Clinical Science Symposium, American Society of Clinical Oncology (ASCO) 2019.05.31 Chicago
3. Yoda T. A new New disease Disease named Named Masticatory Muscle Tendon-Aponeurosis Hyperplasia and outline Outline of Oral Surgery in Tokyo Medical and Dental University . 3rd Culture and Art Festival 2019.07.06 Seoul
4. Chieko Michikawa, Pedro A. Torres-Saavedra, Natalie L. Silver, Paul M. Harari, Merrill S. Kies, David I. Rosenthal, Quynh-Thu Le, Richard C. Jordan, Dzifa Y. Duose, Saradhi Mallampati, Sanchit Trivedi, Rajyalakshmi Luthra, Ignacio I. Wistuba, Olivier Lichtarge, Robert L. Foote, Upendra Parvathaneni, D. Neil Hayes, Curtis R. Pickering, Jeffrey N. Myers. Evolutionary action score of TP53 analysis in pathologically high-risk HPV-negative head and neck cancer from a phase II clinical trial. NRG Oncology July 2019 Semiannual Meeting 2019.07.18 Philadelphia
5. Masahiko Terauchi, Atsushi Tamura Satoshi Yamaguchi, Tetsuya Yoda, Nobuhiko Yui. Bone regeneration with bone morphogenetic protein-2amplified by supramolecular sulfonated polyrotaxane. 日韓若手アワードシンポジウム 2019.11.25 筑波
6. Masahiko Terauchi, Eriko Marukawa, Shintaro Yamazaki, Zhu Hongfei, Narumi Oshibe, Aoi Kaneko, Tranminh Cuomng, Tetsuya Yoda. Comparative evaluation of the various bone substitutes for bone regeneration at peri-implant defects in dogs.. 8th International Conference on Mechanics of Biomaterials and Tissues 2019.12.15 Hawaii
7. Shintaro Yamazaki, Eriko Marukawa, Masahiko Terauchi, Zhu Hongfei, Narumi Oshibe, Aoi Kaneko, Tranminh Cuomng, Tetsuya Yoda. The effectiveness of various bone substitutes for the alveolar ridge preservation after tooth extraction in canine models. 8th International conference on Mechanics of biomaterials and tissues 2019.12.15 Hawaii, USA

Maxillofacial Orthognathics

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Yosuke ITO, Yuko YASUDA, Ryo MARUOKA

(1) Research

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

(2) Education

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

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

(3) Clinical Performances

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

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

1. Ahiko N, Baba Y, Tsuji M, Horikawa R, Moriyama K. Investigation of maxillofacial morphology and oral characteristics with Turner syndrome and early mixed dentition. *Congenital Anomalies*. 2019.01; 59(1); 11-17
2. Funahashi K, Shiba T, Watanabe T, Muramoto K, Takeuchi Y, Ogawa T, Izumi Y, Sekizaki T, Nakagawa I, Moriyama K. Functional dysbiosis within dental plaque microbiota in cleft lip and palate patients. *Progress in Orthodontics*. 2019.03; 20(1); 11
3. Wu Y, Kadota-Watanabe C, Ogawa T, Moriyama K. Combination of estrogen deficiency and excessive mechanical stress aggravates temporomandibular joint osteoarthritis in vivo. *Archives of Oral Biology*. 2019.03; 102(2019); 39-46
4. Hiratsuka T, Uezono M, Takakuda K, Kikuchi M, Oshima S, Sato T, Suzuki S, Moriyama K. Enhanced bone formation onto the bone surface using a hydroxyapatite/collagen bone-like nanocomposite. *Journal of biomedical materials research. Part B, Applied biomaterials*. 2019.04;
5. Yoshida M, Honda E, Ozawa E, Inoue-Arai SM, Ohmori H, Moriyama K, Ono T, Kurabayashi T, Yoshihara H, Nunthayanon Parakonthun K. Principles of the magnetic resonance imaging movie method for articulatory movement. *Oral Radiology*. 2019.05; 35(2); 91-100
6. Kamimoto H, Kobayashi Y, Moriyama K. Relaxin 2 carried by magnetically directed liposomes accelerates rat midpalatal suture expansion and subsequent new bone formation. *Bone Reports*. 2019.06; 10; 100202

7. Yoshizawa H, Miyamoto JJ, Hanakawa T, Shitara H, Honda M, Moriyama K. Reciprocal cortical activation patterns during incisal and molar biting correlated with bite force levels: an fMRI study. *Scientific Reports*. 2019.06; 9(1); 8419
8. Matsuno S, Tsuji M, Hikita R, Matsumoto T, Baba Y, Moriyama K. Clinical study of dentocraniofacial characteristics in patients with Williams syndrome. *Congenital Anomalies*. 2019.09; 59(5); 162-168
9. Tsuji M, Suzuki H, Suzuki S, Moriyama K. Three-dimensional evaluation of morphology and position of impacted supernumerary teeth in cases of cleidocranial dysplasia. *Congenital Anomalies*. 2019.10;
10. Nakagawa Kang J, Unnai Yasuda Y, Ogawa T, Sato M, Yamagata Z, Fujiwara T, Moriyama K. Association between Maternal Smoking during Pregnancy and Missing Teeth in Adolescents. *International Journal of Environmental Research and Public Health*. 2019.11; 16(22); 4536

[Conference Activities & Talks]

1. Moriyama K. Surgical and non-surgical orthodontic treatment for patients with Class III malocclusion. 32nd Annual Meeting of Egyptian Orthodontic Society Joint Meeting with Asociation Mexicana De Orthodoncia 2019.01.25 Cairo, Egypt
2. Moriyama K. Soft Tissue Considerations in Treatment of Dentoskeletal Discrepancy Cases. 32nd Annual Meeting of Egyptian Orthodontic Society Joint Meeting with Asociation Mexicana De Orthodoncia 2019.01.25 Cairo, Egypt
3. Iwanami-Kadowaki K, Uchikoshi T, Uezono M, Kikuchi M, Moriyama K. HAp/Col-EPD-coating represent suitable substrates for cell adhesion and cell proliferation . The 31st Research DAY 2019.02.13 Bangkok, Thailand
4. Ogawa T. Considering the Evidence of Treatment for Cleft Lip and / or Palate Through Multidisciplinary Approach in Adulthood. The 43rd Annual Meeting of Japanese Cleft Palate Association 2019.05.30 Niigata
5. Uezono M, Ogawa T, Unnai-Yasuda Y, Araki M, Baba Y, Hiratsuka T, Moriyama K. Relationship between missing of lateral incisor and alveolar cleft morphology in UCLA patients. The 43rd Annual Meeting of Japanese Cleft Palate Association 2019.05.30 Niigata
6. Araki M, Higashihori N, Unnai-Yasuda Y, Arimura M, Kamimoto H, Matsumoto H, Ogawa T, Morita K, Yoda T, Moriyama K. A surgical orthodontic treatment case of CLP whose occlusion had not been managed until adulthood. The 43rd Annual Meeting of Japanese Cleft Palate Association 2019.05.30 Niigata
7. Arimura M, Araki Y, Unnai-Yasuda Y, Higashihori N, Ogawa T, Moriyama K. A survey of CLP patients without orthodontic management until permanent dentition stage. The 43rd Annual Meeting of Japanese Cleft Palate Association 2019.05.30 Niigata
8. Akiyama S, Higashihori N, Hikita R, Ito Y, Kadota C, Takahashi Y, Matsumoto T, Moriyama K. Three-Dimensional Analysis of Nasal morphology in Patients with Facial Asymmetry Undergoing Two-jaw Surgery. The 29th Annual Meeting of the Japanese Society for Jaw Deformities 2019.06.08 Tokyo
9. Akiyama S, Higashihori N, Hikita R, Ogasawara T, Kinoshita R, Tominaga C, Matsumoto T, Moriyama K. Changes of hard / soft tissue position affect respiratory function during sleep in mandibular retrognathia patients. The 29th Annual Meeting of the Japanese Society for Jaw Deformities 2019.06.08 Tokyo
10. Matsumoto T, Ogasawara T, Kinoshita R, Tominaga C, Kadota C, Higashihori N, Moriyama K. Questionnaire study on subjective evaluation of maxillofacial morphology and function in patients with facial deformity. The 29th Annual Meeting of the Japanese Society for Jaw Deformities 2019.06.08 Tokyo
11. Ekprachayakoon I, Miyamoto JJ, Inoue-Arai MS, Takada J, Moriyama K. New application of dynamic magnetic resonance imaging for the assessment of deglutitive tongue movement. 95th European Orthodontic Society Congress 2019.06.17 Nice, France
12. Higashihori N, Yahiro K, Phyo Thiha, Kano S, Moriyama K. Histone Methyltransferase SETDB1 is Crucial for Craniofacial Development. 97th General Session & Exhibition of International Association for Dental Research 2019.06.19 Vancouver, Canada

13. Yoshizawa H, Miyamoto J, Hanakawa T, Shitara H, Honda M, Moriyama K. Correlations Between Brain and Masticatory-muscle Activities During Molar- and Incisal-biting. 97th General Session & Exhibition of International Association for Dental Research 2019.06.19 Vancouver, Canada
14. Iwanami-Kadowaki K, Uchikoshi T, Uezono M, Kikuchi M, Moriyama K. HAp/Col-EPD-coating Improve Adhesive Strength and Provide Good Cell Proliferation. 97th General Session & Exhibition of International Association for Dental Research 2019.06.19 Vancouver, Canada
15. Kang Nakagawa J, Yasuda Y, Ogawa T, Sato M, Yamagata Z, Fujiwara T, Moriyama K. Association between Maternal Smoking During Pregnancy and Missing Teeth. 97th General Session & Exhibition of International Association for Dental Research 2019.06.19 Vancouver, Canada
16. Tsuji M, Shoji A, Hirabayashi K, Kobayashi Y, Moriyama K. Analysis of dentocraniofacial morphology in patients with achondroplasia. The 59th Annual Meeting of the Japanese Teratology Society-The 13th World Congress of International Cleft Lip and Palate oundation CLEFT 2019 ICPF 2019.07.26 Aichi
17. Moriyama K. Clinical and biological considerations of maxillary transverse deficiency. 2019 International Orthodontic Conference(CIOC&COS 2019) 2019.09.23 Nanjin, China
18. Ogawa T. Current status of postgraduate orthodontic education at the Department of Maxillofacial Orthognathics in TMDU. 2019 International Orthodontic Conference(CIOC&COS 2019) 2019.09.23 Nanjin, China
19. Moriyama K. Therapeutic effect of nanogel-based delivery of soluble FGFR2 with S252W mutation on craniosynostosis in apert syndrome model mice. 2019 Tokyo Medical and Dental University-Taipei Medical University Joint Symposium on Medical Innovation 2019.10.05 Taipei, Taiwan
20. Iwanami-Kadowaki K, Uchikoshi T, Uezono M, Kikuchi M, Moriyama K. Cell culture tests of hydrox-yapatite/collagen bone-like nanocomposite coated on Ti by modified electrophoretic deposition method . 13th Pacific Rim Conference on Ceramic and Glass Technology 2019.10.27 Ginowan City, Okinawa
21. Hla-Myint T, Tsuji M, Ohbayashi N, Suzuki S, Moriyama K. Observation of tongue movement during deglutition by integration of ultrasound video image and lateral cephalogram. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
22. Uezono M, Takakuda K, Moriyama K. Evaluation on bone bonding properties of a novel orthodontic anchorage device targeting cortical bone. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
23. Matsumoto H, Arakawa T, Mitsubayashi K, Moriyama K. Evaluation on bone bonding properties of a novel orthodontic anchorage device targeting cortical bone. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
24. Arimura M, Araki M, Unnai(Yasuda) Y, Tumurkhuu T, Ganburged G, Bazar A, Ogawa T, Moriyama K. School-based epidemiological study of dental anomalies in Mongolian adolescents. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
25. Niki Y, Kobayashi Y, Moriyama K. The expression pattern of the transcription factor Tead1 in the developing mouse molar tooth. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
26. Kaisaka Y, Uezono M, Inoue M, Takakuda K, Moriyama K. Bone formation induced by prototype models of a novel orthodontic anchorage device targeting cortical bone. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
27. Uezono M, Takakuda K, Moriyama K. Evaluation on microdamage caused by a newly developed orthodontic miniscrew using synthetic cortical bone. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
28. Uezono M, Takakuda K, Hiratsuka T, Moriyama K. Evaluation on bonding strength of a newly developed orthodontic miniscrew using synthetic cortical bone. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki

29. Uezono M, Takakuda K, Hiratsuka T, Ogasawara T, Inoue M, Kaisaka Y, Moriyama K. Evaluation on bone bonding properties of a newly developed orthodontic miniscrews using mini swine. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
30. Yokouchi R, Ogura K, Shoji A, Nakajima S, Tsuji M, Matsumoto T, Moriyama K. Analysis of craniofacial and upper airway morphology in Treacher Collins syndrome patients. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
31. Inoue A, Shoji A, Ogura K, Kanou S, Sagawa Y, Kobayashi Y, Tsuji M, Matsumoto T, Moriyama K. Morphological analysis of mandibular antegonial notch in Treacher Collins syndrome patients. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
32. Kadota C, Ogawa T, Kang J, Yoda T, Moriyama K. A Class II open bite case with functional disharmony treated by surgical orthodontic treatment. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
33. Hirabayashi K, Tsuji M, Moriyama K. Craniofacial characteristics of a patient with cartilage-hair hypoplasia. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
34. Ogasawara T, Matsumoto T, Igarashi N, Phyo T, Hayakawa D, Baba Y, Moriyama K. A case of class II malocclusion with dental anomaly patterns. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
35. Badrakhukhuu N, Araki M, Yasuda Y, Ogawa T, Tumurkhuu T, Ganburged G, Bazar A, Fujiwara T, Moriyama K. Association between malocclusion and academic performance among Mongolian adolescents. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
36. Minswe NM, Kobayashi Y, Kamimoto H, Moriyama K. Aberrant activation of Wnt/ β -catenin signaling in the coronal sutures of an Apert syndrome mouse model. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
37. Nakano H, Tachiki C, Sato T, Tsuji M, Mano M, Minoura Y, Ogawa K, Nomura Y, Soya T, Koshio Y, Miyazawa K, Shimizu N, Moriyama K. A statistical and clinical investigation on fenestration, traction and orthodontic treatment of impacted teeth. The 78th Annual Meeting of the Japanese Orthodontic Society 2019.11.20 Nagasaki
38. Ogawa T. Oculofaciocardiodental syndrome: abnormal root formation in rare inherited disorder. 4th Meeting of the International Association for Dental Research Asia Pacific Region 2019 2019.11.28 Brisbane, Australia
39. Uezono M. Effect of pilot-hole size on stress generation of cortical bone. 4th Meeting of the International Association for Dental Research Asia Pacific Region 2019 2019.11.28 Brisbane, Australia
40. Moriyama K. Surgical Orthodontic Treatment for Mandibular Prognathism with Facial Asymmetry. 2019 TAO Annual Meeting in Taichung 2019.12.07 Taichung, Taiwan

Maxillofacial Prosthetics

2019 April

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(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.

1. Research for prosthetic diagnosis in patients with a maxillofacial defect
2. Research for functional rehabilitation of patients with a maxillofacial defect
3. Research for masticatory function in patients with a maxillofacial defect
4. Research for speech evaluation in patients with a maxillofacial defect
5. Research for development of new materials for facial prosthesis

(3) Publications

[Original Articles]

1. Elbashti ME, Sumita YI, Kelimu S, Aswehlee AM, Awuti S, Hattori M, Taniguchi H. Application of digital technologies in maxillofacial prosthetic literature: A 10-year observation of prosthodontic journals. *International Journal of Prosthodontics*. 2019.01; 32(1); 45-50
2. Kosaka M, Sumita YI, Taniguchi H, Suzuki T, Sasaki K. Evaluation of salivary cortisol levels in relation to dento-maxillary prosthesis adjustment. *Journal of Prosthodontic Research*. 2019.01; 63(1); 73-77
3. Kelimu S, Hattori M, Awuti S, Elbashti ME, Sumita YI, Taniguchi H. Color change of airborne particle-abraded acrylic resin surfaces: A palatography method. *Journal of Prosthodontic Dentistry*. 2019.04; 121(4); 671-675
4. Hattori M. A case of post-maxillectomy prosthodontic rehabilitation with spontaneous closure of perforation *Ann Jpn Prosthodont Soc*. 2019.04; 11(2); 147-150
5. Elbashti ME, Hattori M, Patzelt SBM, Aswehlee AM, Sumita YI, Taniguchi H. Precision and trueness of computerized optical impressions in maxillectomy defects: an in vitro 3D comparison. *International Journal of Prosthodontics*. 2019.05; 32(3); 289-292
6. Aswehlee AM, Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Geometric evaluation of the effect of prosthetic rehabilitation on facial asymmetry in mandibulectomy patients. *International Journal of Prosthodontics*. 2019.05; 32(3); 293-296
7. Yeerken Y, Otomaru T, Sumita YI. Three assessments of food-mixing ability and their association with food-comminuting and perceived chewing ability in maxillectomy patients. *Maxillofacial Prosthetics*. 2019.06; 42(1); 39-44
8. Watanabe M, Otomaru T, Li N, Hideshima M, Taniguchi H, Sumita YI. Fabrication of the oral appliance and 2-year clinical follow up in a maxillectomy patients with obstructive sleep apnea: A case report 2019.06; 42(1); 45-50
9. Elbashti ME, Sumita YI, Hattori M, Aswehlee A, Taniguchi H. Digitized speech characteristics in patients with maxillectomy defects. *Journal of Prosthodontics*. 2019.07; 28(6); 649-655
10. Suzuki A, Hoshiai T, Nakata H, Otomaru T, Oki M, Taniguchi H, Kasugai K, Kuroda S. Modal analysis of two different types of fixed implant-supported prostheses embedded in edentulous maxillae. *Journal of Prosthodontic Research*. 2019.07; 63(3); 327-333
11. Elbashti ME, Sumita YI, Aswehlee AM, Seelaus R. Smartphone application as a low-cost alternative for digitizing facial defects: is it accurate enough for clinical application? *International Journal of Prosthodontics*. 2019.11; 32(6); 541-543

12. Kamiyanagi A, Sumita YI, Otomaru T, Hattori M, Murase M, Haraguchi M, Watanabe M, Taniguchi H. Clinical Survey about Immediate Surgical Obturator at the Clinic for Maxillofacial Prosthetics Tokyo Medical and Dental University. *Journal of Prosthodontic Research*. 2019.12; accepted;
13. Matsumoto Y, Sakaguchi Y, Haraguchi M, Sumita YI, Otomaru T, Adachi T, Taniguchi H. Oral hygiene management by dental hygienists for a patient with blindness and bilateral forearm amputation because of severe extensive burns: A case report 2019.12; 42(2); 91-96
14. Sumita YI, Kamarudin KH, Hattori M, Kamiyanagi A, Namba T, Ino S. Obturators to facilitate speech and swallowing in a maxillectomy patient with dementia and cerebral infarction *International Journal of Maxillofacial Prosthetics*. 2019.12; 1(1); 33-35

[Misc]

1. Shioiri S, Murakami K, Hata M, Miyamae S, Nakabayashi S, Ohyama T, Haraguchi M, Hattori M, Nakajima J, Minagi Y, Fujiwara S, Ono T. Is a maxillary prosthesis more useful than surgical reconstruction for functional recovery of patients with maxillary defects? *Maxillofacial Prosthetics*. 2019.06; 42(1); 18-23
2. Murakami K, Shioiri S, Hata M, Miyamae S, Nakabayashi S, Ohyama T, Haraguchi M, Hattori M, Nakajima J, Minagi Y, Fujiwara S, Ono T. Is implant therapy effective for functional recovery of patients with maxillary defect? *Maxillofacial Prosthetics*. 2019.06; 42(1); 24-32
3. Hata M, Miyamae S, Shioiri S, Murakami K, Nakabayashi S, Ohyama T, Haraguchi M, Hattori M, Nakajima J, Minagi Y, Fujiwara S, Ono T. Is implant therapy effective for functional recovery of patients with mandibular defects? *Maxillofacial Prosthetics*. 2019.06; 42(1); 33-38

[Conference Activities & Talks]

1. Kamiyanagi A, Sumita YI, Habara Y, Inohara K, Ino S. Pilot Study on relationship between hand manipulation ability and handling ability of denture in elderly people. *Tsukuba Biomedical Engineering Collaboration Forum 2019* 2019.01.25 Ibaraki (Japan)
2. Sumita YI. Education for Maxillofacial prosthetics in Tokyo Medical and Dental University. *ICP workshop* 2019.03.05 Tokyo (Japan)
3. Sumita YI. Radiotherapy prosthesis in Tokyo Medical and Dental University. *ICP workshop* 2019.03.05 Tokyo (Japan)
4. Sumita YI. Immediate surgical obturator in Tokyo Medical and Dental University. *ICP workshop* 2019.03.05 Tokyo (Japan)
5. Hattori M, Elbashti ME, Sumita YI, Taniguchi H. Dental Treatment of Frontal tooth Injury on a Saxophone Player. *Rehabilitation & Music* 2019.04.24 Beetsterzwaag (Netherlands)
6. Hattori M, Gao Y, Zhang M, Sumita YI, Taniguchi H. Three dimensional measurement of the oral surface while blowing an musical instrument. *The 128th Annual Meeting of the Japan Prosthodontic Society* 2019.05.12 Hokkaido (Japan)
7. Zhang M, Hattori M, Sumita YI. The possibility of data acquisition of maxillectomy defect using intraoral scanner. *The 128th Annual Meeting of the Japan Prosthodontic Society* 2019.05.12 Hokkaido (Japan)
8. Otomaru T, Hattori M, Murase M, Haraguchi M, Sumita YI. Prosthetic treatment in a left cleft lip and palate patient with fistula; A case report. *The 43rd Annual Meeting of Japanese Cleft Palate Association* 2019.05.30 Niigata (Japan)
9. Haraguchi M, Sumita YI, Hattori M, Otomaru T, Murase M, Kanazaki A. Prosthodontic treatment for patients with cleft lip and palate in the last 5 years in our clinic. *The 43rd Annual Meeting of Japanese Cleft Palate Association* 2019.05.30 Niigata (Japan)
10. Hattori M, Zhang M, Sumita YI. Use of a voice analysis with several test sentences for the adjustment of a speech aid prosthesis. *The 43rd Annual Meeting of Japanese Cleft Palate Association* 2019.05.30 Niigata (Japan)

11. Sumita YI, Hattori M, Zhang M . The use of ingressive voice for the speech analysis in a cleft lip and palate patient. The 43rd Annual Meeting of Japanese Cleft Palate Association 2019.05.30 Niigata (Japan)
12. Zhang M, Hattori M, Sumita YI, Taniguchi H. Observation of dental arch in cleft lip and palate patients using three-dimensional assessment. The 43rd Annual Meeting of Japanese Cleft Palate Association 2019.05.30 Niigata (Japan)
13. Haraguchi M, Michi Y, Shibata M, Ohyama Y, Sumita YI, Harada H. A prospective study of masticatory function and satisfaction in segmental mandibulectomy patients - for 3 years after surgery -. The 43th Annual Meeting of Japan Society for Head and Neck Cancer 2019.06.14 Ishikawa (Japan)
14. Sumita YI, Hattori M, Wiebke SH, Gao Y, Zhang M, Elbashti ME . A four-dimensional scanning approach to obtain surface data of the face. 7th Biennial Congress of the Advanced Digital Technology in Head & Neck Reconstruction 2019.06.20 Tokyo (Japan)
15. Hattori M, Stadler S, Kohal R, Vach K, Elbashti E, Sumita YI. Application of various intraoral scanners for digitizing a nose. 7th Biennial Congress of the Advanced Digital Technology in Head & Neck Reconstruction 2019.06.20 Tokyo (Japan)
16. Elbashti ME, Aswehlee A, Kelimu S, Hattori M, Sumita YI. An image is an image until you have three-dimensional glasses: A potential approach for visualization . 2019.06.20 Tokyo (Japan)
17. Yeerken Y, Otomaru T, Zhang M, Sumita YI. Investigation of perceived chewing ability in maxillectomy patients with and without perforation. 2019.06.28 Miyagi (Japan)
18. Hattori M, Zhang M, Gao Y, Wang Y, Elbashti ME, Sumita YI. Digital impression using three intraoral scanners on maxillectomy model simulating trismus condition. The 36th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2019.06.28 Miyagi (Japan)
19. Liu R, Hattori M, Zhang M, Sumita YI. Application of an occlusal ramp for mandibulectomy patients and its effect on mastication. The 36th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2019.06.28 Miyagi (Japan)
20. Kelimu S, Hattori M, Elbashti ME, Sumita YI. Clinical application of a new palatography method using abrasive paper. The 36th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2019.06.28 Miyagi (Japan)
21. Murase M, Tani H, Sumita YI. A case report of a glossectomy patient treated by a palatal augmentation prosthesis. The 36th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2019.06.28 Miyagi (Japan)
22. Sumita YI, Hattori M. Education of Maxillofacial prosthetics in TMDU. Lecture in Seoul national university 2019.08.26 Seoul (South Korea)
23. Hattori M, Sumita YI. Clinical works of Maxillofacial prosthetics in TMDU. Lecture in Seoul national university 2019.08.26 Seoul (South Korea)
24. Gao Y, Awuti S, Hattori M, Wang Y, Sumita YI. Volume analysis of the piezographic impression using digital technology. The 5th Annual Meeting of the International Academy for Digital Dental Medicine 2019.10.05 Nara (Japan)
25. Awuti S, Kelimu S, Hattori M, Sumita YI. Morphological difference of the denture space for patients taken with and without instruction. The 66th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2019.10.26 Florida (USA)
26. Fujita H, Otomaru T, Takahashi T, Iwasaki N, Sumita YI. Effect of direct retainer types on residual teeth in maxillectomy patients: an in vitro study. The 66th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2019.10.26 Florida (USA)
27. Tani H, Murase M, Sumita YI. Factors affecting the resting metabolic rate (RMR) in patients treated oral cancer. The 66th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2019.10.26 Florida (USA)

28. Yu H, Wang Y, Hattori M, Sumita YI. Maxillofacial Prosthetic rehabilitation on a patient with a congenital palatal incompetence. The 66th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2019.10.26 Florida (USA)
29. Otomaru T. Implant Overdenture Treatment for Patients after Surgical Resection of Maxillofacial Tumors. 3rd Mansoura International Dental Congress 2019.10.31 Mansoura (Egypt)

Cell Biology

Professor : Takao Nakata
Junior Associate Professor : Tomohiro Ishii
Assistant Professor : Toshifumi Asano
Assistant Professor : Hironori Inaba
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 are activated locally within the cells and we observe the cell phenotypes by time-lapse microscope using these techniques. We can understand molecular mechanisms of cell signaling in spatio-temporal fashion and also can manipulate cellular conditions using these switches.

(3) Education

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

In new curriculum, lecture provide students information on fine structure and hints or laboratory work. This helps the students to sketch the tissue in their laboratory work. The aim of our lecture is to provide fundamental knowledge of human tissues and organ to understand clinical lectures. In laboratory work we adopt classical sketch of tissues because we believe it shows the ability of students to search the representative 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 and cell cycle because we avoid to teach the same contents that they have learned in the 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. Bernd Bufe, Yannick Teuchert, Andreas Schmid, Martina Pyrski, Anabel Pérez-Gómez, Janina Eisenbeis, Thomas Timm, Tomohiro Ishii, Günter Lochnit, Markus Bischoff, Peter Mombaerts, Trese Leinders-Zufall,

Frank Zufall. Bacterial MgrB peptide activates chemoreceptor Fpr3 in mouse accessory olfactory system and drives avoidance behaviour. Nat Commun. 2019.10; 10(1); 4889

[Conference Activities & Talks]

1. Takanori Miyamoto, Toshifumi Asano, Takao Nakata. Study of activity dependent neuromuscular junction formation. The 124th Annual Meeting of the Japanese Association of Anatomists 2019.03.27 Nippon Dental University of Life Dentistry at Niigata
2. Moe Sato, Toshifumi Asano, Jun Hosomichi, Takashi Ono, Takao Nakata. Control of osteoblast differentiation using optogenetic tool BACCS. The 124th Annual Meeting of the Japanese Association of Anatomists 2019.03.29 Nippon Dental University of Life Dentistry at Niigata
3. Takao Nakata. Optogenetic study of cell polarity - a simple assay. The 9th Federation of Asian and Oceanian Physiological Societies Congress (FAOPS2019) 2019.03.31 Kobe Convention Center
4. Hironori Inaba, Takao Nakata.. Analyses on the intracellular Ca²⁺ signaling regulated by RhoA using optogenetics. Joint Annual Meeting of 71st JSCB & 19th PSSJ 2019.06.25 Kobe Convention Center

Medical Biochemistry

Professor Yutaka Hata

Assistant Professor Hiroaki Iwasa

Assistant Professor Kyoko Arimoto-Matsuzaki

Assistant Professor Junichi Maruyama

Other two staffs

(1) Research

- 1) The biological and chemical approach to study the Hippo pathway that controls cell proliferation, cell differentiation, and cell death.
- 2) Versatile roles of the tumor suppressor 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) Development of mouse models mimicking human progeria syndromes
- 6) Study of health life span in *Caenorhabditis elegans*

(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. Ito M, Hara H, Takeda N, Naito AT, Nomura S, Kondo M, Hata Y, Uchiyama M, Morita H, Komuro I. Characterization of a small molecule that promotes cell cycle activation of human induced pluripotent stem cell-derived cardiomyocytes. *Journal of molecular and cellular cardiology*. 2019.01; 128; 90-95
2. Wenzhe Qiu, Arimoto-Matsuzaki Kyoko, Kitamura Masami, Hata Yutaka. Human keratinocyte HaCaT cells form aggregates containing Ras-GAP SH3 domain-binding proteins in the cytoplasm in response to a low dose of teniposide(和訳中) *Journal of Medical and Dental Sciences*. 2019.06; 66(2); 23-30
3. ダイル, 松崎 京子, 畑 裕, 平岡 優一, 山本 浩平. Characterization of Hutchinson-Gilford Progeria syndrome mouse as a model to study sarcopenia(和訳中) *日本生化学会大会プログラム・講演要旨集*. 2019.09; 92 回; [1P-291]
4. 丸山 順一, 相村 春彦, 畑 裕. Doublecortin-like kinase 1 は DNA 損傷修復機構を抑制し染色体不安定化を誘導する (Doublecortin-like kinase 1 compromises DNA repair and induces chromosomal instability) *日本癌学会総会記事*. 2019.09; 78 回; P-3210
5. 江欣 亮, 丸山 順一, 畑 裕. Heat shock-mediated regulation of transcriptional co-activator YAP1(和訳中) *日本生化学会大会プログラム・講演要旨集*. 2019.09; 92 回; [1P-173]

[Books etc]

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

[Misc]

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

[Conference Activities & Talks]

1. Yutaka Hata. New tricks that regulate YAP and TAZ. *Telluride Science Research Center Workshop* 2019.06.12 Telluride, Collardo, USA

Joint Surgery and Sports Medicine

Hideyuki Koga
Hiroki Katagiri, Kazumasa Miyatake

Department of Cartilage Regeneration
Kunikazu Tsuji
Yusuke Nakagawa

Masaki Amemiya, Naoko Araya, Hiroaki Onuma, JaeSung An,
Kazumasa Kawata, Masaaki Isono, Aritoshi Yoshihara, Tang Guo,
Yusuke Amano, Zhu Ling, Qu Zhen, Yang Yang, Li Nan

Miyoko Ojima, Miho Okada, Masayo Tsukamoto

(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. Genetic approach to secondary hip osteoarthritis

(2) Lectures & Courses

We are working with the Orthopaedic and Spinal Surgery as a Department of Orthopaedic Surgery of University Hospital. The doctors start to have education of orthopedic surgery as a member of the department from the staffs of the department of Orthopaedic Surgery according to the orthopaedic education and training program after completing the two-year fundamental education and training program as a junior resident. They experience a lot of traumatic patients and deepen their basic orthopaedic skills for two-year junior orthopaedic training in one of the branch hospitals every year. They expand their skills and obtain orthopaedic specialty educations in the advanced two-year education and training program. After completing a six-year educational program of the orthopaedic surgery, they are recommended to apply to the orthopedic specialist form the Japanese Orthopaedic Association. They usually apply to enter the graduate school program after 4 or 5 years of clinical experience. We encourage not only orthopedic doctors but doctors of other specialty, veterinarian doctors and physical therapists, etc to work with us.

(3) Clinical Services & Other Works

Treatment for sports injuries

Prevention, conservative treatment and rehabilitation for sports injuries

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

Surgical treatment for knee multiple ligament injuries

Surgical treatment for meniscal injuries to restore meniscal function

Regenerative medicine for unrepairable meniscus and cartilage injuries

Treatment for osteoarthritis (OA)

Conservative approaches to early OA

Joint-sparing surgeries such as osteotomies for moderate OA

Total arthroplasties for severe OA

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

(4) Clinical Performances

Sports injuries

We have been performing double-bundle ACL reconstruction since 1994 as a pioneer, and reported good clinical outcomes regarding knee stability, ratio of return to sports and patients' satisfaction. As for meniscal surgeries, we have been trying to repair as much as possible to restore meniscal function. In addition, we have developed a novel surgical procedure to restore meniscal function for patients with post-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. Tomomasa Nakamura, Hideyuki Koga, Koji Otabe, Masafumi Horie, Toshifumi Watanabe, Kazuyoshi Yagishita, Ichiro Sekiya, Takeshi Muneta. Comparison of three approaches for femoral tunnel during double-bundle anterior cruciate ligament reconstruction: A case controlled study. J Orthop Sci. 2019.01; 24(1); 147-152
2. Inomata Kei, Tsuji Kunilazu, Onuma Hiroaki, Hoshino Takashi, Udo Mio, Akiyama Masako, Nakagawa Yusuke, Katagiri Hiroki, Miyatake Kazumasa, Sekiya Ichiro, Muneta Takeshi, Koga Hideyuki. Time course analyses of structural changes in the infrapatellar fat pad and synovial membrane during inflammation-induced persistent pain development in rat knee joint BMC Musculoskelet Disord. 2019.01; 20(8);

3. Mai Katakura, Masafumi Horie, Toshifumi Watanabe, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Kenta Katagiri, Hiroko Ueki, Stefano Zaffagnini, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Effect of meniscus repair on pivot-shift during anterior cruciate ligament reconstruction: Objective evaluation using triaxial accelerometer. *Knee*. 2019.01; 26(1); 124-131
4. Watanabe Toshifumi, Aoki Akino, Hoshi Kenji, Muneta Takeshi, Sekiya Ichiro, Koga Hideyuki. Anterior Tibial Post Impingement during Stair Climbing: A Kinematic Analysis and Clinical Outcome *J Arthroplasty*. 2019.02; 34(2); 379-384
5. Yusuke Nakagawa, Amir H Lebaschi, Susumu Wada, Samuel J E Green, Dean Wang, Zoe M Album, Camilla B Carballo, Xiang-Hua Deng, Scott A Rodeo. Duration of postoperative immobilization affects MMP activity at the healing graft-bone interface: Evaluation in a mouse ACL reconstruction model. *J. Orthop. Res.*. 2019.02; 37(2); 325-334
6. Hiroki Katagiri, Mendes LF, Luyten FP.. Reduction of BMP6-induced bone formation by calcium-phosphate in wild-type compared to nude mice. *J Tissue Eng Regen Med*. . 2019.02; 2019(13); 846-856
7. Nobutake Ozeki, Hideyuki Koga, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Tomoyuki Saito, Takeshi Muneta, Ichiro Sekiya. Biomechanical analysis of the centralization procedure for extruded lateral menisci with posterior root deficiency in a porcine model. *J Orthop Sci.*. 2019.03; S0949-2658(19); 30064-30068
8. Naritomi Mana, Mizuno Mitsuru, Katano Hisako, Ozeki Nobutake, Otabe Koji, Komori Keiichiro, Fujii Shizuka, Ichinose Shizuko, Tsuji Kunikazu, Koga Hideyuki, Muneta Takeshi, Sekiya Ichiro.. Petaloid recombinant peptide enhances in vitro cartilage formation by synovial mesenchymal stem cells. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society*. 2019.06; 37(6); 1350-1357
9. Kaori Nakamura, Kunikazu Tsuji, Mitsuru Mizuno, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Initial cell plating density affects properties of human primary synovial mesenchymal stem cells. *J. Orthop. Res.*. 2019.06; 37(6); 1358-1367
10. Ryota Fujisawa, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Cryopreservation in 95% serum with 5% DMSO maintains colony formation and chondrogenic abilities in human synovial mesenchymal stem cells. *BMC Musculoskelet Disord*. 2019.07; 20(1); 316
11. Susumu Wada, Amir H Lebaschi, Yusuke Nakagawa, Camila B Carballo, Tyler J Uppstrom, Guang-Ting Cong, Zoe M Album, Arielle J Hall, Liang Ying, Xiang-Hua Deng, Scott A Rodeo. Postoperative Tendon Loading With Treadmill Running Delays Tendon-to-Bone Healing: Immunohistochemical Evaluation in a Murine Rotator Cuff Repair Model. *J. Orthop. Res.*. 2019.07; 37(7); 1628-1637
12. Hiroko Ueki, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Takashi Hoshino, Ichiro Sekiya, Hideyuki Koga. Contribution of Additional Anterolateral Structure Augmentation to Controlling Pivot Shift in Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*. 2019.07; 47(9); 2093-2101
13. Shimpei Kondo, Yusuke Nakagawa, Mitsuru Mizuno, Kenta Katagiri, Kunikazu Tsuji, Shinji Kiuchi, Hideo Ono, Takeshi Muneta, Hideyuki Koga, Ichiro Sekiya. Transplantation of Aggregates of Autologous Synovial Mesenchymal Stem Cells for Treatment of Cartilage Defects in the Femoral Condyle and the Femoral Groove in Microminipigs. *Am J Sports Med*. 2019.08; 47(10); 2338-2347
14. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Kazuyoshi Yagishita, Toshitaka Yoshii, Atsushi Okawa. Supine versus lateral position for accurate positioning of acetabular cup in total hip arthroplasty using the modified Watson-Jones approach: A randomized single-blind controlled trial. *Orthop Traumatol Surg Res*. 2019.09; 105(5); 915-922
15. Yusuke Nakagawa, Lisa A Fortier, Jeremy J Mao, Chang Hun Lee, Margaret B Goodale, Matthew F Koff, Tyler J Uppstrom, Brett Croen, Susumu Wada, Camila B Carballo, Hollis G Potter, Scott A Rodeo. Long-term Evaluation of Meniscal Tissue Formation in 3-dimensional-Printed Scaffolds With Sequential Release of Connective Tissue Growth Factor and TGF- β 3 in an Ovine Model. *Am J Sports Med*. 2019.09; 47(11); 2596-2607

16. Kazuyoshi Yagishita, Mitsuhiro Enomoto, Yuji Takazawa, Jun Fukuda, Hideyuki Koga. Effects of hyperbaric oxygen therapy on recovery acceleration in Japanese professional or semi-professional rugby players with grade 2 medial collateral ligament injury of the knee: A comparative non-randomized study. *Undersea Hyperb Med.* 2019.09; 46(5); 647-654
17. Yusuke Nakagawa, Toshifumi Watanabe, Yusuke Amano, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Benefit of subcutaneous patient controlled analgesia after total knee arthroplasty. *Asia Pac J Sports Med Arthrosc Rehabil Technol.* 2019.10; 18; 18-22
18. Akinobu Hyodo, Nobutake Ozeki, Yuji Kohno, So Suzuki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Makoto Tomita, Yusuke Nakagawa, Hideyuki Koga, Shinji Kiuchi, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Ichiro Sekiya. Projected Cartilage Area Ratio Determined by 3-Dimensional MRI Analysis: Validation of a Novel Technique to Evaluate Articular Cartilage. *JB JS Open Access.* 2019.10; 4(4); e0010
19. Mitsuru Mizuno, Hisako Katano, Yuri Shimozaiki, Sho Sanami, Nobutake Ozeki, Hideyuki Koga, Ichiro Sekiya. Time-lapse image analysis for whole colony growth curves and daily distribution of the cell number per colony during the expansion of mesenchymal stem cells. *Sci Rep.* 2019.11; 9(1); 16835
20. Tomomasa Nakamura, Monica A Linde, Brandon D Marshall, Hideyuki Koga, Takeshi Muneta, Patrick Smolinski, Freddie H Fu. Arthroscopic centralization restores residual knee laxity in ACL-reconstructed knee with a lateral meniscus defect. *Knee Surg Sports Traumatol Arthrosc.* 2019.11; 27(11); 3699-3704
21. Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Tsuyoshi Yamada, Shuta Ushio, Hiroaki Onuma, Keigo Hirai, Yutaka Kobayashi, Kurando Utagawa, Jun Hashimoto, Atsuyuki Kawabata, Kenichiro Sakai, Tsuyoshi Kato, Shigenori Kawabata, Atsushi Okawa. Is Modified K-line a Powerful Tool of Surgical Decision Making for Patients With Cervical Spondylotic Myelopathy? *Clin Spine Surg.* 2019.11; 32(9); 351-356
22. Ichiro Sekiya, Hideyuki Koga, Koji Otabe, Yusuke Nakagawa, Hisako Katano, Nobutake Ozeki, Mitsuru Mizuno, Masafumi Horie, Yuji Kohno, Kenta Katagiri, Naoto Watanabe, Takeshi Muneta. Additional Use of Synovial Mesenchymal Stem Cell Transplantation Following Surgical Repair of a Complex Degenerative Tear of the Medial Meniscus of the Knee: A Case Report. *Cell Transplant.* 2019.11; 28(11); 1445-1454
23. Naoto Watanabe, Mitsuru Mizuno, Junpei Matsuda, Naoko Nakamura, Koji Otabe, Hisako Katano, Nobutake Ozeki, Yuji Kohno, Tsuyoshi Kimura, Kunikazu Tsuji, Hideyuki Koga, Akio Kishida, Ichiro Sekiya. Comparison of High-Hydrostatic-Pressure Decellularized Versus Freeze-Thawed Porcine Menisci. *J. Orthop. Res..* 2019.11; 37(11); 2466-2475
24. Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Ichiro Sekiya, Hideyuki Koga. The effect of a longitudinal tear of the medial meniscus on medial meniscal extrusion in anterior cruciate ligament injury patients. *Knee.* 2019.12; 26(6); 1292-1298
25. Mai Katakura, Hideyuki Koga, Tomomasa Nakamura, Daisuke Araki, Kanto Nagai, Kyohei Nishida, Ryosuke Kuroda, Takeshi Muneta. Biomechanical Effects of Additional Anterolateral Structure Reconstruction With Different Femoral Attachment Sites on Anterior Cruciate Ligament Reconstruction. *Am J Sports Med.* 2019.12; 47(14); 3373-3380
26. Daisuke Araki, Takehiko Matsushita, Yuichi Hoshino, Kanto Nagai, Kyohei Nishida, Hideyuki Koga, Tomomasa Nakamura, Mai Katakura, Takeshi Muneta, Ryosuke Kuroda. The Anterolateral Structure of the Knee Does Not Affect Anterior and Dynamic Rotatory Stability in Anterior Cruciate Ligament Injury: Quantitative Evaluation With the Electromagnetic Measurement System. *Am J Sports Med.* 2019.12; 47(14); 3381-3388
27. Claire D Eliasberg, Susumu Wada, Camila B Carballo, Yusuke Nakagawa, Daniel A Nemirov, Reyna Bhandari, Miguel Otero, Xiang-Hua Deng, Scott A Rodeo. Identification of Inflammatory Mediators in Tendinopathy Using a Murine Subacromial Impingement Model. *J. Orthop. Res..* 2019.12; 37(12); 2575-2582

[Conference Activities & Talks]

1. Hideyuki Koga. Root tears: Treatment with meniscal centralization . 4th The Meniscus 2019.01.31 Bologna, Italy
2. Hiroaki Onuma, Kunikazu Tsuji, Takashi Hoshino, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Inflammation of infrapatellar fat pad with fibrosis and angiogenesis induced by monoiodoacetic acid persists knee pain.. Orthopaedic Research Society 2019.02.02 Austin, USA
3. Nakagawa Y, Carballo C, Zhang Y, Selvaggio E, Lebaschi A, Wada S, Otero M, Delco M, Fortier L, Rodeo S.. Mitochondria dysfunction in tenocytes from human tendinopathy patients.. Orthopaedic Research Society 2019.02.02 Austin, USA
4. Nakagawa Y, Deng X, Carballo C, Zhang X, Wada S, Album Z, Ying L, Rodeo S.. Establishment of a New Post-Traumatic Osteoarthritis Model in Mice Induced by Non-Invasive ACL Rupture.. Orthopaedic Research Society 2019.02.02 Austin, USA
5. Masaki Amemiya, Kunikazu Tsuji, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Comprehensive analysis of the difference between synovium derived mesenchymal stem cells and synovial fluid derived mesenchymal stem cells. Orthopaedic Research Society 2019.02.02 Austin, USA
6. Naoko Araya, Kazumasa Miyatake, Kunikazu Tsuji, Takashi Hoshino, Hiroaki Onuma, Saisei An, Ichiro Sekiya, Hideyuki Koga. Pure platelet-rich plasma is most effective for the treatment of arthritis. Orthopaedic Research Society 2019.02.02 Austin, USA
7. Hiroko Ueki, Hiroki Katagiri, Yusuke Nakagawa, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Takashi Hoshino, Mai Katakura, Ichiro Sekiya, Hideyuki Koga. Contribution of Additional Anterolateral Structure Augmentation to Controlling Pivot Shift in Anterior Cruciate Ligament Reconstruction.. Orthopaedic Research Society 2019.02.02 Austin, USA
8. Kazumasa Kawata, Hiroki Katagiri, Kunikazu Tsuji, Kazumasa Miyatake, Yusuke Nakagawa, Ichiro Sekiya, Hideyuki Koga. The enhancement of mesenchymal stem cells and chondrocytes proliferation by exosomes derived from human synovial mesenchymal stem cells . Orthopaedic Research Society 2019.02.02 Austin, USA
9. Hideyuki Koga. Meniscal centralization. Arthrex Japan Knee Faculty Forum 2019.02.28 Singapore
10. Hideyuki Koga. Medial meniscus root repair feat. centralization. Arthrex Japan Knee Faculty Forum 2019.02.28 Singapore
11. Hiroaki Onuma, Hirai T, Yoshii T, Inose H, Yuasa M, Kawabata A, Okawa A. Influence of Segmental Fusion on Postoperative Outcomes of Bone Grafted and Non-bone grafted Double-door Laminoplasty for Treatment of Cervical Spondylotic Myelopathy. 2019 10th Annual Meeting of Cervical Spine Research Society Asia Pacific Section 2019.03.14 Yokohama
12. Mai Katakura, Yasuyuki Jujo, Okugura Kazuaki, Yukinori Mori, Keisuke Hayashi, Hideyuki Koga, Masato Takao. All-inside Arthroscopic Lateral Ankle Ligament Repair with Accelerated Rehabilitation Achieved Earlier Return to Sports Compared to Open Procedures. 2019 ISAKOS 2019.05.12 Cancun, Mexico
13. Hideyuki Koga. Arthroscopic centralization for extruded meniscus. 11th JOSKAS 2019.06.13
14. Hideyuki Koga. Arthroscopic centralization. 11th JOSKAS 2019.06.13
15. Yusuke Nakagawa, Toshihumi Watanabe, Kenta Katagiri, So Suzuki, Hyodo Akinobu, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta, Atsushi Okawa, Hideyuki Koga. Investigation of factors influencing patient satisfaction after total knee arthroplasty. 11th JOSKAS 2019.06.13
16. Yusuke Nakagawa, Mai Katakura, Weiding Cui, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga. Improving outcomes after ACL reconstruction: Secondary restraint meniscus . 11th JOSKAS 2019.06.13
17. Yusuke Nakagawa, Toshiyuki Ohara, Kei Inomata, Aritoshi Yoshihara, Kanehiro Hiyama, Hiroko Ueki, Takashi Hoshino, Tsuyoshi Nagase, Takashi Ogiuchi, Takeshi Muneta, Hideyuki Koga. TMDU MAKs study. 11th JOSKAS 2019.06.13

18. Onuma Hiroaki. Influence of Segmental Fusion on Postoperative Outcomes of Bone Grafted and Non-Bone Grafted Double-Door Laminoplasty, the Modified Kirita-Miyazaki Method, for Treatment of Cervical Spondylotic Myelopathy. The International Combined Orthopaedic Research Societies (ICORS) Meeting 2019.06.20 Montreal, Canada
19. Hideyuki Koga. Patellar tendinopathy -Does surgery work?. 11th IOC advanced team physical course 2019.07.01 Tokyo
20. Hideyuki Koga. ACL injury mechanisms and its prevention. Taiwan Academy of Sports Medicine & TMDU seminar 2019.10.30 Tokyo, Japan
21. Hideyuki Koga. Centralization & Meniscus root repair. 12th Murup Hospital Live Surgery 2019.11.23 Busan, Korea
22. Hideyuki Koga. Knee joint preservation surgery; Minimum correction HTO + Centralization of medial meniscus. 1st Knee Surgery Symposium 2019.11.24 Seoul, Korea

Biostructural Science

Associate Professor: Makoto TABATA

Technician: Makoto SUGIURA

Graduate Student: Momoko SAKAGUCHI

(1) Outline

Section of biostructural science is the inheritor of the laboratory of Oral Anatomy II, then we focus understanding of the mechanism of tooth development, tooth cell differentiations, and tooth evolution using methods of histology, cell biology, and molecular biology. We also teach three courses of histology for the second grade of dental student, and attend to the preparation works of gross anatomy.

(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)Research of Tooth Germ Developmen
- 2)Research of Ameloblast Differentiation & Function
- 3)Research of Fish Scales & Teeth
- 4)Space Experiments using Fish
- 5)Comparative Morphology of the Tooth

(3) Lectures & Courses

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

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

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

(4) Publications

[Original Articles]

1. Mika Ikegame, Atsuhiko Hattori, Makoto J Tabata, Kei-Ichiro Kitamura, Yoshiaki Tabuchi, Yukihiro Furusawa, Yusuke Maruyama, Tatsuki Yamamoto, Toshio Sekiguchi, Risa Matsuoka, Taizo Hanmoto,

Takahiro Ikari, Masato Endo, Katsunori Omori, Masaki Nakano, Sayaka Yashima, Sadakazu Ejiri, Toshiki Taya, Hiroshi Nakashima, Nobuaki Shimizu, Masahisa Nakamura, Takashi Kondo, Kazuichi Hayakawa, Ichiro Takasaki, Atsushi Kaminishi, Ryosuke Akatsuka, Yuichi Sasayama, Takumi Nishiuchi, Masayuki Nara, Hachiro Iseki, Vishwajit S Chowdhury, Shigehito Wada, Kenichi Ijiri, Toshio Takeuchi, Tohru Suzuki, Hironori Ando, Kouhei Matsuda, Masanori Somei, Hiroyuki Mishima, Yuko Mikuni-Takagaki, Hisayuki Funahashi, Akihisa Takahashi, Yoshinari Watanabe, Masahiro Maeda, Hideaki Uchida, Akio Hayashi, Akira Kambegawa, Azusa Seki, Sachiko Yano, Toru Shimazu, Hiromi Suzuki, Jun Hirayama, Nobuo Suzuki. Melatonin is a potential drug for the prevention of bone loss during space flight. *J. Pineal Res.* 2019.07; e12594

[Conference Activities & Talks]

1. Hiroshi Takase, Makoto Sugiura-Nakazato. Recycling of Uranyl acetate solution. 2019.11.28 SAITAMA HALL

Pharmacology

Staffs and Students

Assistant Professor Yukihiro TAMURA

Researchers

Tomoki UEHARA (Pediatric Dentistry)

Yuki ARAI (Removable Prosthodontics)

Noriko HIRAISHI (Cariology and Operative Dentistry)

Graduate Students

Kenya YONEDA (Regenerative Dental Medicine)

Eri SONE (Maxillofacial Surgery)

Michiko OZAWA

Shigeki NAGAHIRO (Pediatric Dentistry)

Keo Preksa (Orthodontic Science)

C.Supachatwong (Regenerative Dental Medicine)

Jason Hou (Regenerative Dental Medicine)

Meng Sikun (Regenerative Dental Medicine)

Lecturers

Yoshihiro WAKI

Etsuko TAKAHASHI

Kenichi NAGANO

Eiichi MURASE

Hirofumi SETO

Toshimi SATO

Genki KATO

Kiichi NONAKA

Fumie SATO

(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) 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. Sone E, Noshiro D, Ikebuchi Y, Nakagawa M, Khan M, Tamura Y, Ikeda M, Oki M, Murali R, Fujimori T, Yoda T, Honma M, Suzuki H, Ando T, Aoki K. The induction of RANKL molecule clustering could stimulate early osteoblast differentiation. *Biochemical and biophysical research communications*. 2019.02; 509(2); 435-440
2. Touyama K, Khan M, Aoki K, Matsuda M, Hiura F, Takakura N, Matsubara T, Harada Y, Hirohashi Y, Tamura Y, Gao J, Mori K, Kokabu S, Yasuda H, Fujita Y, Watanabe K, Takahashi Y, Maki K, Jimi E. Bif-1/Endophilin B1/SH3GLB1 regulates bone homeostasis. *Journal of cellular biochemistry*. 2019.06;

Connective Tissue Regeneration

Associate Professor Tamayuki SHINOMURA

(1) Outline

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

(2) Research

Currently, we are engaged in the following research subject.

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

(3) Education

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

(4) Lectures & Courses

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

(5) Publications

[Original Articles]

1. Miyazaki Y, Horie A, Tani H, Ueda M, Okunomiya A, Suginami K, Kondoh E, Baba T, Konishi I, Shinomura T, Sato Y. Versican V1 in human endometrial epithelial cells promotes BeWo spheroid adhesion in vitro. *Reproduction*. 2019.01; 157(1); 53-64
2. Giang Thi Hien Nham, Xiang Zhang, Yoshinori Asou, Tamayuki Shinomura. Expression of type II collagen and aggrecan genes is regulated through distinct epigenetic modifications of their multiple enhancer elements. *Gene*. 2019.07; 704; 134-141

[Conference Activities & Talks]

1. 張響、ジャン ニャン、篠村多摩之. II 型コラーゲンの遺伝子発現を制御するエンハンサー特異的転写因子の同定. 第 3 2 回日本軟骨代謝学会 2019.03.01 大阪
2. 小池宏、西田佳弘、篠村多摩之、大河原美静、大野欽司、卓麗聖、木全弘治、石黒直樹. KIAA1199 活性の抑制を介して炎症性関節炎を抑制する薬剤開発. 第 3 2 回日本軟骨代謝学会 2019.03.01 大阪
3. Tamayuki Shinomura. Expression of type II collagen and aggrecan genes is regulated through the distinct epigenetic modification of multiple enhancer elements. Gordon Research Conference; Cartilage Biology and Pathology 2019.03.21 Galveston, TX, USA

Biochemistry

Professor Testuro Watabe
Associate Professor Miki Yokoyama
Junior Associate Professor Yasuhiro Yoshimatsu
Assistant Professor Katarzyna Anna Podyma-Inoue, Miho Kobayashi
Technical staff Megumi Naito, Kazue Terasawa
Part-time Lecturer Akira Asari
Graduate student Kazuki Takahashi, Nagoya Takahashi, Shiori Kimuro,
Rina Takayama, Hitomi Takahashi, Ikumi Wakabashi

(1) Outline

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

(2) Research

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

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

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

Tumor angiogenesis and lymphangiogenesis are key features of tumor progression and metastasis. While multiple signaling pathways have been implicated in the formation of blood and lymphatic vessels, the molecular mechanisms underlying these processes have not yet fully elucidated. Recent findings revealed that members of the transforming growth factor- 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. In addition, we elucidated the molecular mechanism for anti-angiogenesis by vasohibin-1 (VASH1). We are conducting basic research aimed at suppressing tumor progression through the functional analysis of VASH1.

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

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

(4) Unraveling of the physiological role of VASH1 as a deetyrosination enzyme

VASH1, which is induced expression by VEGF stimulation in endothelial cells, was re-identified as an enzyme of deetyrosination. Deetyrosination is one of the post-translational modification of microtubules. It is known that deetyrosinated microtubules play a key role for several physiological phenomena, such as chromosome partition in mitosis or functional beating of heart. We are conducting basic research aimed at molecularly elucidating of role as a deetyrosination enzyme in physiological function of VASH1.

(5) Elucidation of the role of LAMP-1/2 proteins in the lysosomal intracellular degradation system

Lysosomes are intracellular organelles, containing various hydrolytic enzymes, essential for maintaining cell homeostasis such as acquisition of energy and nutrients, biological defense, removal of unnecessary substances. In recent years it has also been found that lysosomes sense the state of energy acquisition of cells and decide whether the cells proliferate or gain nutrition. Lysosomal dysfunction clinically results in progressive and severe effects, especially notable in the nervous system, bone, connective tissue.

Lysosome-associated membrane protein-1/2 is the abundant membrane - spanning glycoprotein present in lysosomal membranes. Most of the proteins of LAMP-1 and LAMP-2 are present on the luminal side of lysosomes, both of which are composed of two homologous domains. However, LAMP-2 deficient mice exhibit a more severe phenotype than LAMP-1 deficient mice and Danone disease develops in humans due to abnormalities of LAMP-2. Accumulation of autophagosome-like vesicles was observed in myocytes of Danone disease, suggesting that LAMP-2 is associated with autophagy. Since LAMP-1 and LAMP-2 are considered to be similar proteins, the reason why they are functionally different remained mystery. We first discovered that the mode of multimerization is different between LAMP-1 and LAMP-2. We reported the crystal structure analysis of the domains of LAMP-1 and LAMP-2 and based on the findings we analyzed the mode of multimerization at the atomic level by site-specific crosslinking reaction utilizing introduction of non-natural amino acid. Then we are generating LAMP-2 with mutation in multimerization. By using the LAMP-2 mutants, we are now investigating the functional aspect of lysosomal membrane during intracellular degradation.

(6) HSPGs, Exosomes and EMT

Metastasis is the cause of the death in a majority of human cancers. Tumor-derived, small extracellular vesicles (exosomes) are suggested to play important roles in different steps of metastatic cascade. Tumor-derived exosomes has been shown to participate in tumor progression by mediating epithelial-to-mesenchymal transition (EMT), stimulating the invasion, migration, angiogenesis. Heparan sulfate proteoglycans (HSPGs) are strategically localized on the cell surface and serves as receptors for a number of extracellular ligands. HSPG-dependent signals regulate tumor proliferation, angiogenesis and metastasis. HSPGs have been also implicated in the formation/uptake of tumor-derived exosomes, but the detailed mechanisms still remain to be characterized. We are working on the characterization of exosomal cargo and identification of the molecules responsible for exosome-recipient cell interactions as well as pathways involved in the internalization of exosomes focusing on the role of HSPGs in those events.

(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.

For the graduate students, in order to demonstrate various research examples, we lectured on the structure and function of proteoglycans and the structure and role of extracellular matrix.

(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. K. Iwasaki, K. Akazawa, M. Nagata, M. Komaki, I. Honda, C. Morioka, N. Yokoyama, H. Ayame, K. Yamaki, Y. Tanaka, T. Kimura, A. Kishida, T. Watabe, I. Morita. The fate of transplanted periodontal ligament stem cells in surgically created periodontal defects in rats *Int J Mol Sci.* 2019.01; 20(1); 192
2. Hayato Okamoto, Yasuhiro Yoshimatsu, Taishi Tomizawa, Akiko Kunita, Rina Takayama, Teppei Morikawa, Daisuke Komura, Kazuki Takahashi, Tsukasa Oshima, Moegi Sato, Mao Komai, Katarzyna A Podyma-Inoue, Hiroaki Uchida, Hirofumi Hamada, Katsuhito Fujiu, Shumpei Ishikawa, Masashi Fukayama, Takeshi Fukuhara and Tetsuro Watabe. Interleukin-13 receptor $\alpha 2$ is a novel marker and potential therapeutic target for human melanoma. *Sci Rep.* 2019.02; 9(1); 1281
3. Ren E, Watari I, Jui-Chin H, Mizumachi-Kubono M, Podyma-Inoue KA, Narukawa M, Misaka T, Watabe T, Ono T. Unilateral nasal obstruction alters sweet taste preference and sweet taste receptors in rat circumvallate papillae. *Acta histochemica.* 2019.02; 121(2); 135-142
4. Akatsu Y, Takahashi N, Yoshimatsu Y, Kimuro S, Muramatsu T, Katsura A, Maishi N, Suzuki HI, Inazawa J, Hida K, Miyazono K, Watabe T. Fibroblast growth factor signals regulate transforming growth factor- β -induced endothelial-to-myofibroblast transition of tumor endothelial cells via Elk1. *Mol. Oncol.* 2019.08; 13(8); 1706-1724
5. Miki Hara-Yokoyama, Hidetake Kurihara, Shozo Ichinose, Hironori Matsuda, Shizuko Ichinose, Masaru Kurosawa, Norihiro Tada, Chihiro Iwahara, Kazue Terasawa, Katarzyna A. Podyma-Inoue, Koichi Furukawa and Kazuhisa Iwabuchi. KIF11 as a potential marker of spermatogenesis within mouse seminiferous tubule cross-sections. *Journal Histochem Cytochem.* 2019.08; 22155419871027
6. Iwasaki K, Nagata M, Akazawa K, Watabe T, Morita I. Changes in characteristics of periodontal ligament stem cells in spheroid culture. *Journal of periodontal research.* 2019.08; 54(4); 364-373
7. Iwasaki K, Komaki M, Akazawa K, Nagata M, Yokoyama N, Watabe T, Morita I. Spontaneous differentiation of periodontal ligament stem cells into myofibroblast during ex vivo expansion. *Journal of cellular physiology.* 2019.11; 234(11); 20377-20391
8. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer science.* 2019.11;
9. Kato Y, Arakawa S, Terasawa K, Inokuchi JI, Iwata T, Shimizu S, Watabe T, Hara-Yokoyama M. The ceramide analogue N-(1-hydroxy-3-morpholino-1-phenylpropan-2-yl)decanamide induces large lipid droplet accumulation and highlights the effect of LAMP-2 deficiency on lipid droplet degradation. *Bioorganic & medicinal chemistry letters.* 2019.12; 126891

[Conference Activities & Talks]

1. Daisuke Yamamoto, Kou Kayamori, Kei Sakamoto, Maiko Tsuchiya, Tohru Ikeda, Hiroyuki Harada, Tetsuya Yoda, Tetsuro Watabe, Miki Yokoyama. Change in localization of claudin-1 at the invasion tip of squamous cell carcinoma of the tongue. The 37th Japanese Society of Oral Tumors 2019.01.24 Nagasaki
2. Miho Kobayashi, Yasuhiro Suzuki, Yasufumi Sato. The anti-angiogenic mechanism through the post-translational modification of microtubules by vasohibin-1, negative feedback regulator of angiogenesis. The 48th Annual Scientific Meeting of the Japanese Society for Circulation Research 2019.02.08 Toyama
3. Kazuki Takahashi, Katarzyna A. Inoue, Yasuhiro Yoshimatsu, Atsushi Kaida, Kei Takahashi, Shimpei Kubota, Akinari Sugauchi, Toshihiro Uchihashi, Susumu Tanaka, Mikihiro Kogo, Masahiko Miura, Kohei Miyazono and Tetsuro Watabe. TGF- β -induced cell cycle arrest is associated with increased migration and metastasis of oral squamous carcinoma cells. AACR-JCA Joint Conference 2019.02.09
4. Tetsuro Watabe. Roles of TGF- β signals during the EndMT which promotes cancer progression.. 2019.02.16 Sendai

5. Miho Kobayashi, Yasuhiro Suzuki, Masanori Nakayama, Yasufumi Sato. The function of post-translational modification of microtubules by vasohibin-1. The 14th Vasohibin meeting 2019.02.17 Sendai
6. Miho Kobayashi, Yasuhiro Suzuki, Masanori Nakayama, Yasufumi Sato. The function and role of vasohibin-1 via the post-translational modification of microtubules. Vascular biology meeting 2019.03.03 Tokyo
7. Katarzyna A. Inoue, Kazuki Takahashi, Yasuhiro Yoshimatsu, Akinari Sugauchi, Kei Takahashi, Shimpei I. Kubota, Toshihiro Uchihashi, Atsushi Kaida, Susumu Tanaka, Masahiko Miura, Mikihiro Kogo, Kohei Miyazono and Tetsuro Watabe. Highly motile oral squamous carcinoma cells responding to TGF- β are under cell cycle arrest. Keystone Symposia; Cancer Metastasis: The role of metabolism, immunity and microenvironment 2019.03.17 Florence, Italy
8. Daisuke Yamamoto, Satoshi Yamaguchi, Tetsuro Watabe, Tetsuya Yoda, Miki Yokoyama. Relationship between Claudine-1 expression and clinicopathological findings in tongue squamous cell carcinoma. The 73rd Annual Meeting of Japanese Stomatological Society 2019.04.20 Kawagoe
9. Kato.Y, Terasawa.K, Watabe.T, Aoki.A, Iwata.T, Yokoyama.M. Role of LAMP-2 assembly in Autolysosome formation. 2019.05.24
10. Yohei Hama, Shunsuke Minakuchi, Keiichi Sasaki, Takeyasu Maeda, Akira Hamura, Tatsuya Ichinohe, Takashi Okiji, Tetsuro Watabe. The Dental Education Consortium to promote healthy longevity -Fifth report- Future prospects at the expiration of the five years project . 38th Japanese Dental Education Association Meeting 2019.07.19 Hakata
11. Katarzyna A. Inoue, Kazuki Takahashi, Yasuhiro Yoshimatsu, Akinari Sugauchi, Kei Takahashi, Shimpei I. Kubota, Toshihiro Uchihashi, Atsushi Kaida, Susumu Tanaka, Masahiko Miura, Mikihiro Kogo, Kohei Miyazono and Tetsuro Watabe. Role of TGF- β in a progression of oral cancer. Research PlaNet 2019 2019.07.20
12. Miho Kobayashi, Ikumi Wakabayashi, Yasuhiro Suzuki, Masanori Nakayama, Tetsuro Watabe, Yasufumi Sato. The molecular mechanism of the inhibiting angiogenesis by vascular and lymphatic vessel regulator vasohibin-1. The 1st New Lymphology Research Conference 2019.08.10 Tokyo
13. Tetsuro Watabe. TGF- β -induced cell cycle arrest is associated with increased migration and metastasis of oral squamous carcinoma cells.. TGF- β Signaling Meeting 2019.08.24 Leiden, The Netherlands
14. Tetsuro Watabe. Roles of TGF- β family signals during the formation and maintenance of vascular systems.. Joint Vascular Biology Meeting 2019.09.20 Sydney, Australia
15. Kazuki Takahashi, Katarzyna A. Inoue, Atsushi Kaida, Kei Takahashi, Shimpei Kubota, Akinari Sugauchi, Toshihiro Uchihashi, Susumu Tanaka, Mikihiro Kogo, Masahiko Miura, Kohei Miyazono, Tetsuro Watabe. TGF- β -induced cell cycle arrest is associated with increased migration and metastasis of oral squamous carcinoma cells. The 78th annual meeting of the Japanese Cancer Association 2019.09.28 Kyoto
16. Katarzyna Inoue, Rina Takayama, Kazuki Takahashi, Tetsuro Watabe. Characterization of exosomes secreted from oral squamous carcinoma cells during epithelial to mesenchymal transition. Proteoglycans 2019 2019.10.01 Kanazawa, Japan
17. Tetsuro Watabe. TGF- β ; and TNF- α cooperate to induce mesenchymal transition of endothelial cells via activation of Activin signals. 2019.12.03
18. Miho Kobayashi, Yasuhiro Suzuki, Ikumi Wakabayashi, Tetsuro Watabe, Yasufumi Sato . Vasohibin-1 induced post-translational modification of microtubules mediates VEGF-signaling in angiogenesis. The 43rd Annual Meeting of the Molecular Biology Society of Japan (MBSJ2020) 2019.12.03 Fukuoka
19. Rina Takayama, Hayato Okamoto, Yasuhiro Yoshimatsu, Taishi Tomizawa, Akiko Kunita, Kazuki Takahashi, Katarzyna Inoue, Masashi Fukayama, Takeshi Fukuhara and Tetsuro Watabe. Role of IL13R α 2 in the progression of malignant melanoma. The 27th Annual Meeting of the Japanese Vascular Biology and Medicine Organization (Cardiovascular and Metabolic week 2019 (CVMW2019)) 2019.12.14 Kobe
20. Shiori Kimuro, Yasuhiro Yoshimatsu, Akihiko Inagawa, Kentaro Maeda and Tetsuro Watabe. TNF- α enhances TGF- β -induced endothelial-to-mesenchymal transition via TGF- β signal augmentation. The 27th Annual Meeting of the Japanese Vascular Biology and Medicine Organization (Cardiovascular and Metabolic week 2019 (CVMW2019)) 2019.12.14 Kobe

21. Miho Kobayashi, Ikumi Wakabayashi, Yasuhiro Suzuki, Masanori Nakayama, Tetsuro Watabe, Yasufumi Sato. The molecular mechanism of vasohibin-1-induced anti-angiogenesis. (CVMW2019)The 27th Annual Meeting of the Japanese Vascular Biology and Medicine Organization 2019.12.15 Kobe

Cell Signaling

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

(1) Research

Research Subjects

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

(2) Education

Purpose of Education

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

(3) Publications

[Original Articles]

1. Mikihiro Hayashi, Tomoki Nakashima, Noriko Yoshimura, Kazuo Okamoto, Sakae Tanaka, Hiroshi Takayanagi.. Autoregulation of Osteocyte Sema3A Orchestrates Estrogen Action and Counteracts Bone Aging. *Cell Metab.* 2019.03; 29(3); 627-637.e5
2. Inoue M, Ono T, Kameo Y, Sasaki F, Ono T, Adachi T, Nakashima T. Forceful mastication activates osteocytes and builds a stout jawbone. *Scientific reports.* 2019.03; 9(1); 4404
3. Mikihiro Hayashi, Tomoki Nakashima, Noriko Yoshimura, Kazuo Okamoto, Sakae Tanaka, Hiroshi Takayanagi.. Osteocyte Sema3A orchestrates estrogen action and counteracts bone aging. *Cell Metabolism.* 2019.03; 29; 627-637
4. Jing-Yi Xue, Zheng Wang, Satoshi Shinagawa, Hirofumi Ohashi, Nao Otomo, Nursel H Elcioglu, Tomoki Nakashima, Gen Nishimura, Shiro Ikegawa, Long Guo. TNFRSF11A-Associated Dysosteosclerosis: A

Report of the Second Case and Characterization of the Phenotypic Spectrum. *J. Bone Miner. Res.* 2019.10; 34(10); 1873-1879

[Conference Activities & Talks]

1. Mikihiro Hayashi, Yusoon Kim, Takehito Ono, Hiroshi Takayanagi, Tomoki Nakashima. Suppression of hematopoietic cell kinase ameliorates the bone destruction associated with inflammation. The 5th Annual Meeting of Japanese Society of Osteoimmunology 2019.06.25
2. Wengqiang, Tin, Kazuo Okamoto, Asuka Terashima, Takehito Ono, Hiroshi Takayanagi. Establishment of injury-induced heterotopic ossification model mouse. The 5th Annual Meeting of Japanese Society of Osteoimmunology 2019.06.25
3. Takehito Ono, Masamu Inoue, Fumiyuki Sasaki, Tomoki Nakashima. Forceful mastication activates osteocytes and builds a stout jawbone. The 5th Annual Meeting of Japanese Society of Osteoimmunology 2019.06.25

Periodontology

From January.2019

【Professor】 Takanori Iwata(Feb～)

【Associate Professor】 Akira Aoki(Feb～)

【Junior Associate Professor】 Yasuo Takeuchi, Tatsuya Akizuki

【Assistant Professor】 Koji Mizutani, Sayaka Katagiri, Yuichi Ikeda

【Project Assistant Professor】 Yuuka Tsumanuma(Apr～)

【Specially appointed Assistant Professor】 Takahiko Shiba(～Aug), Shogo Maekawa

【Clinical Fellow】 Takanori Matsuura(～May), Takeaki Sudo, Wataru Ono(～ Mar),

Toru Takagi, Risako Tanimoto, Shunsuke Fukuba(Sep), Kohei Takeda(Oct ～),

Hideyuki Takamatsu(Jun ～), Norihiko Ashigaki(Jun ～), Makoto Hirai(Jun ～),

Yujin Ohsugi(Sep ～)

【Graduate Students】 Shinta Suzuki(～ Mar), Naoki Sasaki(～ Mar), Nay Aung(～ Mar),

Anongwee Leewananthawe (～ Sep), Prima Buranasin (～ Sep), Yosuke Tsuchiya,

Munehiro Okada, Chihiro Kano, Yuji Kato, Rie Kawamura, Keitesu Kure(～ Mar),

Yutaro Kitanaka, Kohei Nohara, Kazuki Watanabe, Keiji Komatsu, Ryo Satou,

Daiki Tanaka, Takashi Nemoto, Hiromi Kominato, Natsumi Saito, Ryo Mikami,

Tsuyoshi Shimohira(Apr～), Shunsuke Takeuchi(Apr～), Masahiro Hatasa(Apr～)

【Adult graduate student】

Kaori Fujiwara, Naho Suzuki(～ Mar), Akiko Kobayashi, Miho Ogawa

【Graduate Research Student】

Yukako Kusunoki(～ Jun), Shogo Takeuchi(～ Mar), Takae Shimoda(～ Mar),

Yuto Mukaiyama(～ Mar), Naoaki Yoshida(～ Mar), Yoshiyuki Iwabuchi(～ Mar),

Aya Suzuki, Shotaro Mori, Takeshi Iida, Tomoaki Kariya, Ayako Kawada, Mai Kitamura,

Yuri Ito(Apr～), Aiko Fujino(Apr～), Kazuki Miyata(Apr～), Miki Dobashi(Apr～)

【Clinical Professor】 Hiroaki Kobayashi, Shigenari Kikuchi, Hiroaki Tsutioka

【Adjunct Lecturer】 36

【Registered dentist】 34

【Assistant Administrative Staff】 Tomomi Anai

(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) Inflammatory and immunological factors in periodontal diseases
- 2) Periodontopathic bacteria and their pathogenicity

- 3) Influence of periodontal disease on general health
- 4) Analyses of growth factors and bio materials in periodontal regeneration
- 5) Clinical applications of laser in periodontics

(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. Takeda K, Mizutani K, Matsuura T, Kido D, Mikami R, Noda M, Buranasin P, Sasaki Y, Izumi Y. Correction: Periodontal regenerative effect of enamel matrix derivative in diabetes. PloS one. 2019; 14(6); e0218798
2. Sjöqvist S, Ishikawa T, Shimura D, Kasai Y, Imafuku A, Bou-Ghannam S, Iwata T, Kanai N. Exosomes derived from clinical-grade oral mucosal epithelial cell sheets promote wound healing. Journal of extra-cellular vesicles. 2019; 8(1); 1565264
3. Khemwong T, Kobayashi H, Ikeda Y, Matsuura T, Sudo T, Kano C, Mikami R, Izumi Y. Fretibacterium sp. human oral taxon 360 is a novel biomarker for periodontitis screening in the Japanese population. PloS one. 2019; 14(6); e0218266
4. Ohtsu A, Takeuchi Y, Katagiri S, Suda W, Maekawa S, Shiba T, Komazaki R, Udagawa S, Sasaki N, Hattori M, Izumi Y. Influence of *Porphyromonas gingivalis* in gut microbiota of streptozotocin-induced diabetic mice. Oral diseases. 2019.01; 25(3); 868-880
5. Ohsugi Y, Aoki A, Mizutani K, Katagiri S, Komaki M, Noda M, Takagi T, Kakizaki S, Meinzer W, Izumi Y. Evaluation of bone healing following Er:YAG laser ablation in rat calvaria compared with bur drilling. Journal of Biophotonics. 2019.03; 12(3); e201800245
6. Ikeda E, Shiba T, Ikeda Y, Suda W, Nakasato A, Takeuchi Y, Azuma M, Hattori M, Izumi Y. Deep sequencing reveals specific bacterial signatures in the subgingival microbiota of healthy subjects. Clinical oral investigations. 2019.03; 23(3); 1489-1493
7. Funahashi K, Shiba T, Watanabe T, Muramoto K, Takeuchi Y, Ogawa T, Izumi Y, Sekizaki T, Nakagawa I, Moriyama K. Functional dysbiosis within dental plaque microbiota in cleft lip and palate patients. Progress in Orthodontics. 2019.03; 20(1); 11
8. Kure K, Sato H, Suzuki J, Itai A, Aoyama N, Izumi Y. A novel IkB kinase inhibitor attenuates ligature-induced periodontal disease in mice. J. Periodont. Res.. 2019.04; 54(2); 164-173
9. Tanaka K, Takahashi H, Eguchi Y, Katagiri S, Ohsugi Y, Watanabe K, Iwata T, Anzai K. 肥満者と糖尿病患者の骨格筋に及ぼす canagliflozin と運動の効果 (The effects of canagliflozin and exercise training on skeletal muscle in obesity and diabetes) 糖尿病. 2019.04; 62(Suppl.1); S-370
10. Aung N, Aoki A, Takeuchi Y, Hiratsuka K, Katagiri S, Kong S, Shujaa Addin A, Meinzer W, Sumi Y, Izumi Y. The effects of ultraviolet light-emitting diodes with different wavelengths on periodontopathic bacteria *In Vitro*. Photobiomodulation, photomedicine, and laser surgery. 2019.05; 37(5); 288-297

11. Kaibuchi N, Iwata T, Onizuka S, Yano K, Tsumanuma Y, Yamato M, Okano T, Ando T. Allogeneic multipotent mesenchymal stromal cell sheet transplantation promotes healthy healing of wounds caused by zoledronate and dexamethasone in canine mandibular bones. *Regenerative therapy*. 2019.06; 10; 77-83
12. Toda K, Mizutani K, Minami I, Ye M, Arakawa T, Mitsubayashi K, Ogawa Y, Araki K, Shinada K. Effects of oral health instructions on glycemic control and oral health status of periodontitis patients with type 2 diabetes mellitus: A preliminary observation *Journal of Dental Sciences*. 2019.06; 14(2); 171-177
13. Sebastian S, Kasai Y, Shimura D, Ishikawa T, Ali N, Iwata T, Kanai N. Oral keratinocyte-derived exosomes regulate proliferation of fibroblasts and epithelial cells. *Biochem. Biophys. Res. Commun.*. 2019.06; 514(3); 706-712
14. Onizuka S, Iwata T. Application of Periodontal Ligament-Derived Multipotent Mesenchymal Stromal Cell Sheets for Periodontal Regeneration. *Int J Mol Sci*. 2019.06; 20(11);
15. Kobayashi T, Suda T, Mizutani K, Aoyama N, Koyanagi T, Hayakumo S, Ikeda Y, Izumi Y. Clarification of Quantitative Intraoral Circumstances with the Community Periodontal Index of Treatment Needs Data using Covariance Structure Analysis *Journal of Clinical and Diagnostic Research*. 2019.06; 13(6); ZC41-ZC44
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21. Lin T, Taniguchi Y, Aoki A, Chang YC. . Clinical evaluation of multiple peri-implant bony defect management by Er:YAG laser-assisted bone regenerative therapy. *Er:YAG laser-assisted bone regenerative therapy*. 2019.07; 2019 Dec;14(4); 430-432
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25. Aoyama N, Kure K, Minabe M, Izumi Y. Increased Heart Failure Prevalence in Patients with a High Antibody Level Against Periodontal Pathogen *International Heart Journal*. 2019.09; 60(5); 1142-1146
26. Maekawa S, Onizuka S, Katagiri S, Hatasa M, Ohsugi Y, Sasaki N, Watanabe K, Ohtsu A, Komazaki R, Ogura K, Miyoshi-Akiyama T, Iwata T, Nitta H, Izumi Y. RNA sequencing for ligature induced periodontitis in mice revealed important role of S100A8 and S100A9 for periodontal destruction *Scientific Reports*. 2019.10; 9(1); 14663

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[Books etc]

1. Unfailing Periodontal Regenerative Therapy. Ishiyaku Publishers, Inc., 2019.03 (ISBN : 978-4-263-44546-4)
2. Aoki A. Minimally invasive flapless periodontal surgery. Tokyo Medical and Dental University Alumni Meeting News, 2019.12

[Misc]

1. Aoki A. Minimally invasive flapless periodontal surgery Tokyo Medical and Dental University Almni Meeting News. 2019; 194; 46-47
2. Aoki A, Mizutani K, Taniguchi Y, Izumi Y. A new approach in periodontal therapy using Er:YAG laser: Theory and practice of Er-LCPT & Er-LBRT - Characteristics of Er:YAG laser and development of new therapy for periodontal pockets *The Nippon Dental Review*. 2019.01; 79(1); 89-101
3. Mizutani K, Aoki A, Taniguchi Y, Izumi Y. A new approach in periodontal therapy using Er:YAG laser: Theory and practice of Er-LCPT & Er-LBRT - Evidence of Er:YAG Laser therapy on periodontitis and peri-implantitis 1 *The Nippon Dental Review*. 2019.02; 79(2); 95-105
4. Mizutani K, Taniguchi Y, Izumi Y, Aoki A. A new approach in periodontal therapy using Er:YAG laser: Theory and practice of Er-LCPT & Er-LBRT - Evidence of Er:YAG Laser therapy on periodontitis and peri-implantitis 2 *The Nippon Dental Review*. 2019.03; 79(3); 115-125
5. Tsubokawa M, Tsukui A, Kakizaki S, Aoki A. Easy and low-costing 3D print by Mac for everyone - Simulation of laser irradiation using 3D printer *The Nippon Dental Review*. 2019.04; 133(4); 798-803
6. Aoki A, Mizutani K, Taniguchi Y, Komaki M, Iwata T, Izumi Y. A new approach in periodontal therapy using Er:YAG laser: Theory and practice of Er-LCPT & Er-LBRT - Practice of Er:LCPT technique: application in severe periodontal pockets and peri-implantitis *The Nippon Dental Review*. 2019.04; 79(4); 117-130
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8. Iwasaki K, Washio K, Meinzer W, Tsumanuma Y, Yano K, Ishikawa I. Application of cell-sheet engineering for new formation of cementum around dental implants. *Heliyon*. 2019.06; 5(6); e01991
9. Aoki A. Find the medical frontline desired by doctors - The latest periodontal therapy "Bio-regeneration method" *Ken*. 2019.06; 48(3); 35-38
10. Taniguchi Y, Mizutani K, Iwata T, Izumi Y, Aoki A. A new approach in periodontal therapy using Er:YAG laser: Theory and practice of Er-LCPT & Er-LBRT - Application of Er-LBRT (Er:YAG laser-assisted bone regenerative therapy) on alveolar ridge preservation in peri-implantitis *The Nippon Dental Review*. 2019.07; 79(7); 137-145

11. Taniguchi Y, Mizutani K, Iwata T, Izumi Y, Aoki A. A new approach in periodontal therapy using Er:YAG laser: Theory and practice of Er-LCPT & Er-LBRT - Application of Er-LBRT (Er:YAG laser-assisted bone regenerative therapy) on alveolar ridge augmentation in peri-implantitis The Nippon Dental Review. 2019.08; 79(8); 99-106
12. Taniguchi Y, Mizutani K, Takagi T, Iwata T, Izumi Y, Aoki A. A new approach in periodontal therapy using Er:YAG laser: Theory and practice of Er-LCPT & Er-LBRT - Application of Er-LBRT (Er:YAG laser-assisted bone regenerative therapy) on regenerative therapy in peri-implantitis The Nippon Dental Review. 2019.09; 79(9); 101-111
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14. Gholami L, Asefi S, Hooshyarsard A, Sculean A, Romanos GE, Aoki A, Fekrazad R. Photobiomodulation in Periodontology and Implant Dentistry: Part I Photobiomodulation, photomedicine, and laser surgery. 2019.11; 37(12); 739-765
15. Gholami L, Asefi S, Hooshyarsard A, Sculean A, Romanos GE, Aoki A, Fekrazad R. Photobiomodulation in Periodontology and Implant Dentistry: Part II. Photobiomodulation, photomedicine, and laser surgery. 2019.11; 37(12); 766-783

[Conference Activities & Talks]

1. Aoki A, Tsubokawa M, Kakizaki S. Application of OCT in Periodontal Examination. The 1st Review Committee in 2018 fiscal year for developing periodontal examination technique using OCT 2019.01.14 Tokyo
2. Suzuki W, Uchida Y, Yonekawa J, Satake A, Makino Y, Kurobe M, Mizutani K, Mizutani Y, Ichimiya H, Watanabe J, Kanashiro M, Ichimiya S. Impact of Severe Aortic Stenosis on Mitral Annulus Geometry: A 3-dimensional Transesophageal Echocardiography Study. The 83rd Annual Scientific Meeting of the Japanese Circulation Society 2019.03 Yokohama
3. Aoki A, Tsubokawa M, Kakizaki S. Application of OCT in Periodontal Examination. 2018 2nd Developing Periodontal Examination Technique using OCT Review Board 2019.03.11 Tokyo
4. Aoki A. Basics of periodontal therapy- from the main points to the latest treatments. Academic Meeting of Nishitama Dental Association 2019.03.14 Nishitama Dental Association, Oume-shi, Tokyo
5. Iwata T. Reconstruction of periodontal tissue by homologous periodontal ligament-derived mesenchymal stem cell sheet. The 18th Congress of the Japanese Society for Regenerative Medicine 2019.03.23 Kobe
6. Iwata T. Cell therapy and near-future diagnostic techniques for periodontal tissue regeneration. MID-G 2019.03.24 Tokyo
7. Ohsugi Y, Aoki A, Mizutani K, Katagiri S, Komaki M, Noda M, Takagi T, Kakizaki S, Kitanaka Y, Lin T, Meinzer W, Izumi Y. Comprehensive Analysis of Gene Expression Related to Healing After Bone Ablation with Er:YAG Laser. 2019.04.04 Dallas, Texas, US
8. Iwata T. Periodontal regeneration with periodontal ligament derived multipotent mesenchymal stromal cell sheets. The 41st Asia-Pacific Dental Congress 2019.05.10 Seoul
9. Watanabe C, Wada J, Nagayama T, Uchida H, Mizutani K, Wakabayashi N. The effect of alveolar bone density around abutment teeth of removable partial denture on diabetic patients -A retrospective cohort study-. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.12 Sapporo
10. Ex Vivo Evaluation of Gingival Ablation With Various Laser Systems and ElectroscaPel. 2019.05.24
11. Kato Y, Terasawa K, Watabe T, Aoki A, Iwata T, Yokoyama M. Role of LAMP-2 assembly in Autolysosome formation. 2019.05.24 Yokohama
12. Maruyama N, Shiba T, Takeuchi Y. A case of perio-orthodontic treatment for generalized severe chronic periodontitis patient. The 62th Spring Meeting of The Japanese Society of Periodontology 2019.05.25

13. Harada Y, Sunaga M, Takeuchi Y, Mizutani K, Akizuki T, Katagiri S, Ikeda Y, Aoki A, Iwata T, Kinoshita A. Standardization of examiners using a dental model for pocket probing training -Adequacy of evaluation with the model and standard accuracy rate of skilled examiners. The 62nd Spring Meeting of the Japanese Society of Periodontology 2019.05.25 Yokohama
14. Aoki A, Tsubokawa M, Kakizaki S. Application of OCT in Periodontal; Examination. The 1st Review Committee in 2019 fiscal year for developing periodontal examination technique using OCT 2019.05.28 Tokyo
15. Aoki A. Clinical part for making the best use of periodontal ligament - Application of Er:YAG laser in minimally invasive flapless periodontal surgery. The 37th Annual Meeting of the Japanese Academy of Clinical Periodontology 2019.06.01
16. Iwata T. Cell treatment of periodontal disease. Doctor-led clinical trial has begun!. Press conference 2019.06.06 Tokyo
17. Aoki A. Birth of Photoperiodontics. Stomatological Society and Faculty of Dentistry Joint Meeting 2019.06.13 Tokyo Medical and Dental University
18. Takeda K, Mizutani K, Matsuura T, Kido D, Mikami R, Noda M, Buranasin P, Sasaki Y, Izumi Y, Iwata T. Periodontal regenerative effect of enamel matrix derivative in diabetes. IADR/AADR/CADR General Session & Exhibition 2019.06.20
19. Watanabe C, Wada J, Nagayama T, Uchida H, Mizutani K, Wakabayashi N. The Effect of Removable Partial Denture Placement for Diabetic Patients. 97th General Session & Exhibition of the IADR 2019.06.22 Vancouver, BC, Canada
20. Nagayama T, Wada J, Watanabe C, Uchida H, Mizutani K, Wakabayashi N. Influence Of RPD Placement On Mobility Of Periodontally Weakened Teeth. 97th General Session & Exhibition of the IADR 2019.06.22 Vancouver, BC, Canada
21. Evaluation of antimicrobial performance of sports Mouse Guard material subjected to Pickash processing. 2019.06.23 Kagoshima
22. Komatsu K, Shiba T, Watanabe T, Koyanagi T, Nemoto T, Sato H, Maekawa S, Katagiri S, Takeuchi Y, Iwata T. Comparison of microbial network structure and functional composition between periodontitis and peri-implantitis using 16S rRNA and metagenomics sequencing. The 150th meeting of the Japanese society of conservative dentistry 2019.06.28 Kanazawa
23. ShimizuS, Saito T, Hamuro K, Matsumura Y, Ikeda E, Ikeda Y, Kohda N. The effects of continuous administration of Lactobacillus pentosus strain B240 on the production, constituents and properties of unstimulated saliva in healthy adults.- Randomized, double-blind, placebo-controlled parallel-group comparative study . 2019.06.28 Ishikawa
24. Aoki A. WFLD and Photoperiodontics. Japan Laser in Dentistry 10th Dental Laser Educational Lecture 2019.06.29 Tokyo
25. Kobayashi T, Torii D, Iwata T, Izumi Y, Nasu M, Tsutsui T. Analysis of gene expression profiles based on the difference of multipotency in clones from human dental pulp cells.. The 92th Annual Meeting (Tokyo 2019), Japanese Tissue Culture Association 2019.07.06 Tokyo
26. Iwata T. Regeneration of periodontal tissue by homologous periodontal ligament-derived mesenchymal stem cell sheet. The 1st Cell Sheet Engineering Innovation Forum 2019.07.19 Tokyo
27. Aoki A, Mizutani K, Taniguchi Y. Periodontal Er;YAG Super Concept - Painless Well Healing Fast Healing -. 56th CDE Lecture 2019.07.21 Tokyo Medical and Dental University
28. Aoki A. Photoperiodontics and Er:YAG Laser. The 22nd Annual Meeting of Clinical Society of Er:YAG Laser 2019.08.04 Hotel Granvia Kyoto, Kyoto
29. Aoki A, Tsubokawa M, Kakizaki S. Application of OCT in periodontal examination. The 2nd Review Committee in 2019 fiscal year for developing periodontal examination technique using OCT 2019.09.17 Tokyo

30. Yamaguchi Y, Aoki A, Suzuki S, Iwata T, Ohshima M. Highly expressed genes in ex vivo peri-implantitis model. The 92nd Annual meeting of the Japanese Biochemical Society 2019.09.18 Yokohama
31. Aoki A, Takeuchi Y, Kitanaka Y, Hiratsuka K, Iwata T. Application of antimicrobial photodynamic therapy in periodontal therapy. PhotoDynamic Medicine 2019 (PDM2019) 2019.09.19 Tokyo
32. Lin TC , Taniguchi Y , Aoki A, Lin PY, Chen CJ, Chen CC. Clinical Evaluation of Peri-implantitis Therapy Treated by Er:YAG Laser and Bone Graft without Membrane Coverage Technique: A Case Series. ITI Section - Taiwan Scientific Meeting 2019.09.21 Taipei, Taiwan
33. Tournadre C, Gritsch K, Takagi T, Shiba T, Mizutani K , Aoki A, Grosogeat B. Cleaning potential of five different methods for peri-implantitis treatment: an in-vitro study. EAO' s 28th annual scientific meeting 2019.09.26 Lisbon, Portugal
34. Ex Vivo Evaluation of Gingival Ablation With Various Laser Systems. 2019.10.05
35. 青木 章. 歯周治療におけるレーザーの応用. レーザー治療教育セミナー 2019.10.17 北京
36. Ohsugi Y. Evaluation of new bone formation and gene expression after bone ablation with Er:YAG laser and bur drilling. The 62th Annual meeting of Japanese Society of Periodontology 2019.10.25 Kitakyushu
37. Tsubokawa M, Kakizaki S, Ohsugi Y, Kitanaka Y, Mizutani K, Kaku Y, Iwata T, Aoki A. Detection and quantitative analysis of dental plaque using Optical Coherence Tomography (OCT). 62nd Autumn Meeting of the Japanese Society of Periodontology 2019.10.25 Kitakyushu
38. 青木 章. インプラント周囲炎治療と Er:YAG レーザーの応用. 2019 年中日口腔医学学術講演会 2019.10.25 北京
39. Nohara K, Matsuura T, Akizuki T, Addin A S, Fukuba S, Okada M, Mori S, Sato R, Takeuchi S, Izumi Y, Iwata T. Effects of experimental periodontitis on regenerated periodontal tissue by bone grafts . The 62st Autumn Meeting of Japanese Society of Periodontology 2019.10.25 Kitakyusyu
40. Mikami R, Mizutani K, Matsuura T, Kido D, Sasaki Y, Iwata T. The impact of diabetes on periodontal parameters in Japanese hemodialysis patients: A cross-sectional study. 105th Annual Meeting of the American Academy of Periodontology 2019.11.03 Chicago, IL
41. Ohsugi Y, Katagiri S, Mizutani K, Takagi T, Kakizaki S, Kitanaka Y, Watanabe K, Niimi H, Meinzer W, Hirota T, Iwata T, Aoki A. Comprehensive gene expression analysis in rat calvarial bone after ablation with Er:YAG laser and the effects of Er:YAG laser on osteocytes. The 105th Annual meeting American Academy of Periodontology 2019.11.03 Chicago, IL
42. Kido D, Mizutani K, Izumi Y, Nitta H. Insulin resistance improvement with periodontal treatment in type - 2 diabetic patients with localized, severe chronic periodontitis. 105th Annual meeting of American Academy of Periodontology 2019.11.03 Chicago, IL
43. Aoki A. History, effect, and prospect of laser therapy in periodontology. 19th Annual Meeting of the Japan Association for Oral laser Light Applications 2019.11.04 Tokyo
44. Aoki A. Laser applications in Periodontics. Basic laser certification course (BLCC). The first Asian Pacific Division of World Federation for Laser Dentistry Conference 2019 (WFLD-APD 2019) 2019.11.08 Beijing
45. Aoki A. Laser uses in Advance Periodontics and Implantology. The first Asian Pacific Division of World Federation for Laser Dentistry Conference 2019 (WFLD-APD 2019) 2019.11.08 Beijing
46. Ohsugi Y, Katagiri S, Mizutani K, Takagi T, Kakizaki S, Kitanaka Y, Watanabe K, Niimi H, Hatasa M, Shimohira T, Meinzer W, Hirota T, Iwata T, Aoki A. Microarray analysis of comprehensive gene expression in rat calvarial bone after Er:YAG laser ablation. The first asian pacific division of the World Federation for Laser Dentistry 2019.11.10 Beijing
47. Aoki A. Er:YAG laser-assisted comprehensive periodontal pocket therapy (Er-LCPT). 2019 Taiwan Academy of Periodontology (TAP) annual meeting and global symposium on "Challenges and solutions of periodontal and peri-implant diseases" 2019.11.22 Taipei
48. Lin T, Aoki A, Lin P PY, Yu-Chao Chang YC, Chun-Cheng Chen CC.. Periodontal and peri-implant disease management by Er:YAG Laser.. 2019 Taiwan Academy of Periodontology (TAP) annual meeting and global symposium 2019.11.22 Taipei

49. Seki N, Mizutani K, Hosaka K, Komada W, Kanazawa M, Komagamine Y, Moross J, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Essential Expertise for Clinical Dentistry (EECD), International Dental Clinical Education Course for Graduate School of Medical and Dental Sciences. The 84th annual meeting of the Stomatological Society 2019.12.07 Tokyo
50. Yuna Kanamori, Kanako Noritake, Sachi Umemori, Maiko Iwaki, Daisuke Kido, Shogo Takeuchi, Akitaka Hattori, Ken-ichi Tonami, Arata Ebihara, Masayuki Hideshima, Kouji Araki, Hiroshi Nitta. Introduction of objective clinical skills examination for TMDU's trainee residents. 2019.12.07
51. Aoki A. Periodontal Er:YAG laser operation - Less pain, well healing, fast healing . Tokyo Medical and Dental University Alumni Association: CDE workshop course 2019.12.08 Tokyo

[Awards & Honors]

1. Dr. Eugene M. Seidner Student Scholarship First Prize (Ohsugi Y), ALD, Academy of Laser Dentistry, 2019.04

[Others]

1. Healthy capsule! Genki time, 2019.06
"Periodontal disease" is said to affect 80% of people over 40 years old. Because there is no noticeable subjective symptom, it may be too late when you notice it. If you leave it alone, not only your teeth will fall out, but there is also a risk of life-threatening problems such as myocardial infarction and cerebral infarction. This time, I elucidate the fear of periodontal disease which creeps up quietly. We introduce periodontal disease prevention method that we can do at home.
2. Periodontal disease treatment without wisdom, 2019.07
Research to treat periodontal disease using unnecessary teeth such as "wisdom wisdom" that will be thrown away after removal is progressing. The idea of cultivating healthy stem cells at the base of teeth into a sheet and pasting them on the lesion to restore the work of bones and gums that support the teeth is attracting attention as a new method for regenerative medicine that effectively uses biomaterials.
3. Removed teeth for regenerative medicine, 2019.07
Research to treat periodontal disease using unnecessary teeth such as "wisdom wisdom" that is thrown away after removal. The idea of cultivating healthy stem cells at the base of teeth into a sheet and pasting them on the lesion to restore the work of bones and gums that support the teeth is attracting attention as a new method for regenerative medicine that effectively uses biomaterials.
4. Tissue regeneration with cell sheet, 2019.07
Research to treat periodontal disease using unnecessary teeth such as "wisdom wisdom" that is thrown away after removal. The idea of cultivating healthy stem cells at the base of teeth into a sheet and pasting them on the lesion to restore the work of bones and gums that support the teeth is attracting attention as a new method for regenerative medicine that effectively uses biomaterials.
5. Wisdom tooth periodontal treatment, 2019.07
Research to treat periodontal disease using unnecessary teeth such as "wisdom wisdom" that will be thrown away after removal is progressing. The idea of cultivating healthy stem cells at the base of teeth into a sheet and pasting them on the lesion to restore the work of bones and gums that support the teeth is attracting attention as a new method for regenerative medicine that effectively uses biomaterials.

Inorganic Biomaterials

Professor Masakazu Kawashita
Associate Prof. Taishi Yokoi

(1) Outline

In this department, we are conducting research on biomaterials (especially ceramic biomaterials) that contribute to the treatment of cancer and bone diseases. Specifically, various material synthesis methods such as the sol-gel method are used to synthesize cancer therapeutic materials (particularly fine particles) and bone filling materials, and evaluate their chemical, physical, and biological properties. By doing so, we aim to obtain knowledge that will lead to clinical application.

(2) Research

1. Development of Biomaterials for Intra-arterial Treatment of Cancer

Radioactive microspheres 20-30 μ m in diameter are useful for the radiotherapy of cancers, especially for tumors located deep inside the body. Also, ferromagnetic microspheres 20-30 μ m in diameter are useful as thermoseeds for inducing hyperthermia in deep-seated cancers under alternating magnetic field. In this department, we try to develop novel biomaterials for minimally invasive treatment of cancer by using various synthetic techniques.

2. Development of Bioactive Materials for Bone Repair

It has been found from 1970 that some ceramics can bond to living bone without fibrous tissues. They are called "bioactive" ceramics and clinically used as important bone substitutes. However, in a clinical field, novel bioactive materials showing excellent bone-bonding ability are required. In this laboratory, we try to develop novel bioactive materials by using various synthetic techniques.

3. Study on Osteoconductive Mechanism of Hydroxyapatite

Hydroxyapatite (HAp) is widely used as an artificial bone or a coating material for metallic biomaterials because it bonds to living bone (shows osteoconductivity). However, the details of the expression mechanism of its osteoconductivity have not been clarified yet. In this department, we are focusing on the initial adsorption of serum proteins such as albumin, fibronectin (Fn) and laminin (Ln) on HAp and hypothesize that some serum protein which specifically adsorbs on HAp causes the osteoconductivity of HAp.

4. Study on Organically Modified Octacalcium Phosphates

Octacalcium phosphate (OCP) is a precursor phase of hydroxyapatite (HAp) in bones and teeth, and has a high affinity for the hard tissues. OCP has been studied as bioabsorbable artificial bones. OCP has a layered structure, and various organic molecules can be incorporated into the OCP interlayers. We develop functional bone-repairing materials and ceramic materials that achieve both diagnosis and therapy utilizing the unique property of OCP.

(3) Lectures & Courses

Students aim to be able to comprehensively and comprehensively understand the structure, physical properties, chemical properties, reactions with biomolecules and cells, etc. of ceramic biomaterials. Their final goal is to

learn cutting-edge science and technology related to ceramic biomaterials and to acquire the ability to propose and design ceramic biomaterials that are useful for medical treatment.

(4) Publications

[Original Articles]

1. Masanobu Kamitakahara, Shohei Takahashi, Taishi Yokoi, Chihiro Inoue and Koji Ioku. Adhesion behavior of microorganisms isolated from soil on hydroxyapatite and other materials *Applied Biochemistry and Biotechnology*. 2019; 187; 984-993
2. Taishi Yokoi, Tomoyo Goto, Satoshi Kitaoka. Formation of hydroxyapatite crystals from octacalcium phosphate with incorporated succinate ion under hydrothermal conditions *Chemistry Letters*. 2019; 48; 855-858
3. Chigama H, Kanetaka H, Furuya M, Yokota K, Kawashita M. Evaluation of apatite-forming ability and antibacterial activity of raw silk fabrics doped with metal ions *Materials Transactions*. 2019.05; 60(5); 808-814
4. Miyazaki T, Akaike J, Kawashita M, Lim HN. In vitro apatite mineralization and heat generation of magnetite-reduced graphene oxide nanocomposites for hyperthermia treatment *Materials Science and Engineering: C*. 2019.06; 99; 68-72
5. Miyazaki T, Iwanaga A, Shirosaki Y, Kawashita M. In situ synthesis of magnetic iron oxide nanoparticles in chitosan hydrogels as a reaction field: Effect of cross-linking density *Colloids and Surfaces B: Biointerfaces*. 2019.07; 179; 334-339
6. Shibata M, Ogawa T, Kawashita M. Synthesis of iron nitride nanoparticles from magnetite nanoparticles of different sizes for application to magnetic hyperthermia *Ceramics International*. 2019.08; 45(17); 23707-23714
7. Taishi Yokoi. The development of novel calcium phosphate-polymer composite biomaterials with macro- to nano-level controlled hierarchical structures *Journal of the Ceramic Society of Japan*. 2019.10; 127(10); 715-721
8. Sota Terasaka, Hideaki Matsubara, Takashi Shirato, Masanobu Kamitakahara, Taishi Yokoi, Norio Yamaguchi, Byung-Nam Kim. Experimental and computational study on sintering of ceramic coating layers with complex porous structures *Journal of the American Ceramic Society*. 2019.12;
9. Emi Kawai, Hideki Kakisawa, Atsushi Kubo, Norio Yamaguchi, Taishi Yokoi, Takashi Akatsu, Satoshi Kitaoka, Yoshitaka Umeno. Crack initiation criteria in EBC under thermal stress *Coatings*. 2019.12;

[Books etc]

1. M. Kawashita. *Material Chemistry of Ceramics*. Springer Singapore, 2019 (ISBN : 978-981-13-9934-3)

Global Health Promotion

Professor: Takeo Fujiwara, MD, MPH, PhD

Junior Associate Professor: Ayako Morita, PhD

Assistant Professor: Yukako Tani, PhD; Yusuke Matsuyama, PhD; Nobutoshi Nawa, MD, MPH, PhD (Department of Medical Research Fellow of Japan Society for the Promotion of Science: Aya Isumi, PhD)

Project Assistant Professor: Satomi Doi, PhD

Specially Appointed Assistant Professor: Yu Funakoshi (Institute of Education) , MD

(1) Outline

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

(2) Research

The main focus of the department is as follows:

1. Social epidemiology (impact of social inequality, social capital, social network, and social support on health)
2. Life-course epidemiology (impact of child poverty and adverse childhood experiences on health) and international comparison study
3. Prevention on child abuse and neglect
4. Mental health (antenatal and postnatal mental health, mental health after a disaster, and child mental health)
5. Nutritional epidemiology (childhood nutrition from prenatal to early school-years and the food environment)
6. Environmental health (the physical environment and climate change)
7. Occupational health (harassment and work-place social capital)

(3) Lectures & Courses

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

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

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

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

(4) Publications

[Original Articles]

1. Ogawa K, Morisaki N, Kobayashi M, Jwa SC, Tani Y, Sago H, Horikawa R, Fujiwara T. Reply to Shakira et al.: Validation of a food frequency questionnaire for Japanese pregnant women in mid to late pregnancy. *European journal of clinical nutrition*. 2019.01; 73(1); 155-156
2. Nawa N, Fujiwara T. Association between social capital and second dose of measles vaccination in Japan: Results from the A-CHILD study. *Vaccine*. 2019.01;
3. Matsuyama Y, Jürges H, Listl S. The Causal Effect of Education on Tooth Loss: Evidence From United Kingdom Schooling Reforms. *American journal of epidemiology*. 2019.01; 188(1); 87-95
4. Fujiwara T, Shobugawa Y, Matsumoto K, Kawachi I. Association of early social environment with the onset of pediatric Kawasaki disease. *Annals of Epidemiology*. 2019.01; 29; 74-80
5. Amemiya A, Fujiwara T. Association of Low Family Income With Lung Function Among Children and Adolescents: Results of the J-SHINE Study. *Journal of epidemiology*. 2019.02; 29(2); 50-56
6. Inoue Y, Stickley A, Yazawa A, Aida J, Kawachi I, Kondo K, Fujiwara T. Adverse childhood experiences, exposure to a natural disaster, and posttraumatic stress disorder among survivors of the 2011 Great East Japan earthquake and tsunami. *Epidemiology and Psychiatric Sciences*. 2019.02; 28(1); 45-53
7. Saito J, Kondo N, Saito M, Takagi D, Tani Y, Haseda M, Tabuchi T, Kondo K. Exploring 2.5-Year Trajectories of Functional Decline in Older Adults by Applying a Growth Mixture Model and Frequency of Outings as a Predictor: A 2010-2013 JAGES Longitudinal Study. *J Epidemiol*. 2019.02; 29(2); 65-72
8. Amemiya A, Kondo N, Saito J, Saito M, Takagi D, Haseda M, Tani Y, Kondo K. Socioeconomic status and improvement in functional ability among older adults in Japan: a longitudinal study. *BMC Public Health*. 2019.02; 19(1); 209
9. Miki T, Fujiwara T, Yagi J, Homma H, Mashiko H, Nagao K, Okuyama M. Impact of Parenting Style on Clinically Significant Behavioral Problems Among Children Aged 4-11 Years Old After Disaster: A Follow-Up Study of the Great East Japan Earthquake. *Frontiers in Psychiatry*. 2019.02; 10(45);
10. Sato R, Fujiwara T, Kino S, Nawa N, Kawachi I. Pet Ownership and Children's Emotional Expression: Propensity Score-Matched Analysis of Longitudinal Data from Japan. *International journal of environmental research and public health*. 2019.03; 16(5);
11. Tani Y, Suzuki N, Fujiwara T, Hanazato M, Kondo K. Neighborhood Food Environment and Dementia Incidence: the Japan Gerontological Evaluation Study Cohort Survey. *Am J Prev Med*. 2019.03; 56(3); 383-392
12. Morita A, O'Caoimh R, Murayama H, Molloy DW, Inoue S, Shobugawa Y, Fujiwara T. Validity of the Japanese Version of the Quick Mild Cognitive Impairment Screen. *International journal of environmental research and public health*. 2019.03; 16(6);
13. Doi S, Fujiwara T, Isumi A. Development of the Intimate Partner Violence During Pregnancy Instrument (IPVPI). *Frontiers in Public Health*. 2019.03; 7(43);
14. Fujiwara T, Weisman O, Ochi M, Shirai K, Matsumoto K, Noguchi E, Feldman R. Genetic and Peripheral Markers of the Oxytocin System and Parental Care Jointly Support the Cross-Generational Transmission of Bonding across Three Generations. *Psychoneuroendocrinology*. 2019.04; 102; 172-181

15. Morishita S, Yoshii T, Okawa A, Fushimi K, Fujiwara T. Perioperative complications of anterior decompression with fusion versus laminoplasty for the treatment of cervical ossification of the posterior longitudinal ligament: propensity score matching analysis using a nation-wide inpatient database. *The Spine Journal*. 2019.04; 19(4); 610-616
16. Amemiya A, Saito J, Saito M, Takagi D, Haseda M, Tani Y, Kondo K, Kondo N. Social Capital and the Improvement in Functional Ability among Older People in Japan: A Multilevel Survival Analysis Using JAGES Data. *Int J Environ Res Public Health*. 2019.04; 16(8);
17. Shobugawa Y, Murayama H, Fujiwara T, Inoue S. Cohort profile of the NEIGE study in Tokamachi city, Japan. *JOURNAL OF EPIDEMIOLOGY*. 2019.05;
18. Doi S, Fujiwara T, Isumi A, Ochi M. Pathway of the Association Between Child Poverty and Low Self-Esteem: Results From a Population-Based Study of Adolescents in Japan. *Frontiers in Psychology*. 2019.05; 10(937);
19. Matsuyama Y, Tsakos G, Listl S, Aida J, Watt R G. Impact of Dental Diseases on Quality-Adjusted Life Expectancy in US Adults. *J. Dent. Res.*. 2019.05; 98(5); 510-516
20. Doi S, Fujiwara T. Combined effect of adverse childhood experiences and young age on self-harm ideation among postpartum women in Japan. *JOURNAL OF AFFECTIVE DISORDERS*. 2019.06; 253; 410-418
21. Honda Y, Fujiwara T*, Yagi J, Homma H, Mashiko H, Nagao K, Okuyama M, Ono-Kihara M, Kihara M. Long-Term Impact of Parental Post-Traumatic Stress Disorder Symptoms on Mental Health of Their Offspring After the Great East Japan Earthquake. *Frontiers in Psychiatry*. 2019.07; 10(496);
22. Honda Y, Fujiwara T, Ichiro K. Higher child-raising costs due to maternal social isolation: Large population-based study in Japan. *SOCIAL SCIENCE & MEDICINE*. 2019.07; 233; 71-77
23. Morita A, Matsuyama Y, Isumi A, Doi S, Ochi M, Fujiwara T. Association between grandparent coresidence, socioeconomic status and dental caries among early school-aged children in Japan: A population-based prospective study. *Scientific reports*. 2019.08; 9(1); 11345
24. Amemiya A, Fujiwara T*, Shirai K, Kondo K, Oksanen T, Pentti J, Vahtera J. Association between adverse childhood experiences and adult diseases in older adults: A comparative cross-sectional study in Japan and Finland. *BMJ Open*. 2019.08; 9(8); e024609
25. Morishita S, Yoshii T, Okawa A, Fushimi K, Fujiwara T. Comparison of Perioperative Complications Between Anterior Decompression With Fusion and Laminoplasty for Cervical Spondylotic Myelopathy: Propensity Score Matching Analysis Using Japanese Diagnosis Procedure Combination Database. *Clinical Spine Surgery*. 2019.08;
26. Morita A, Ochi M, Isumi A, Fujiwara T. Association between grandparent coresidence and weight change among first-grade Japanese children. *Pediatric Obesity*. 2019.08; 14(8); e12524
27. Watanabe M, Hikichi H, Fujiwara T, Honda Y, Yagi J, Homma H, Mashiko H, Nagao K, Okuyama M, Kawachi I. Disaster-related trauma and blood pressure among young children: a follow-up study after Great East Japan earthquake. *HYPERTENSION RESEARCH*. 2019.08; 42(8); 1215-1222
28. Nagamine Y, Kondo N, Yokobayashi K, Ota A, Miyaguni Y, Sasaki Y, Tani Y, Kondo K. Socioeconomic Disparity in the Prevalence of Objectively Evaluated Diabetes Among Older Japanese Adults: JAGES Cross-Sectional Data in 2010 *Journal of Epidemiology*. 2019.08; 29(7-8); 295-301
29. Saito T, Oksanen T, Shirai K, Fujiwara T, Pentti J, Vahtera J. Combined effect of marriage and education on mortality: A cross-national study of older Japanese and Finnish men and women. *Journal of epidemiology*. 2019.09;
30. Park S, Greene MC, Melby MK, Fujiwara T, Surkan PJ. Postpartum Depressive Symptoms as a Mediator Between Intimate Partner Violence During Pregnancy and Maternal-Infant Bonding in Japan. *Journal of interpersonal violence*. 2019.09; 886260519875561
31. Amagasa S, Inoue S, Murayama H, Fujiwara T, Kikuchi H, Fukushima N, Machida M, Chastin S, Owen N, Shobugawa Y. Associations of sedentary and physically-active behaviors with cognitive-function decline in community-dwelling older adults: compositional data analysis from the NEIGE study. *Journal of epidemiology*. 2019.10;

32. Nagamine Y, Fujiwara T, Tani Y, Murayama H, Tabuchi T, Kondo K, Kawachi I. Gender difference in the association between subjective socioeconomic mobility across life course and mortality at older ages: Results from the JAGES longitudinal study. *Journal of epidemiology*. 2019.10;
33. Koyama Y, Fujiwara T. Impact of Alcohol Outlet Density on Reported Cases of Child Maltreatment in Japan: Fixed Effects Analysis FRONTIERS IN PUBLIC HEALTH. 2019.10; 7; 265
34. Murayama H, Amagasa S, Inoue S, Fujiwara T, Shobugawa Y. Sekentei and objectively-measured physical activity among older Japanese people: a cross-sectional analysis from the NEIGE study BMC PUBLIC HEALTH. 2019.10; 19(1); 1331
35. Momosaki R, Wakabayashi H, Maeda K, Shamoto H, Nishioka S, Kojima K, Tani Y, Suzuki N, Hanazato M, Kondo K. Association between Food Store Availability and the Incidence of Functional Disability among Community-Dwelling Older Adults: Results from the Japanese Gerontological Evaluation Cohort Study. *Nutrients*. 2019.10; 11(10);
36. Ikeda T, Tsuboya T, Aida J, Matsuyama Y, Koyama S, Sugiyama K, Kondo K, Osaka K. Income and education are associated with transitions in health status among community-dwelling older people in Japan: the JAGES cohort study. *Family practice*. 2019.11; 36(6); 713-722
37. Nakagawa Kang J, Unnai Yasuda Y, Ogawa T, Sato M, Yamagata Z, Fujiwara T, Moriyama K. Association between Maternal Smoking during Pregnancy and Missing Teeth in Adolescents. *International Journal of Environmental Research and Public Health*. 2019.11; 16(22); 4536
38. Baba S, Ehab ES, Shirai K, Fujiwara T, Yamaoka Y, Iso H. Factors associated with family member's spanking of 3.5-year-old children in Japan. *Journal of epidemiology*. 2019.11;
39. Nishizawa T, Morita A, Fujiwara T, Kondo K. Association between Childhood Socioeconomic Status and Subjective Memory Complaints Among Older Adults: Results from the Japan Gerontological Evaluation Study 2010. *INTERNATIONAL PSYCHOGERIATRICS*. 2019.12; 1699-1707
40. Tani Y, Fujiwara T, Doi S, Isumi A. Home Cooking and Child Obesity in Japan: Results from the A-CHILD Study NUTRIENTS. 2019.12; 11(12);

[Conference Activities & Talks]

1. Sachi Umemori et al.. Association between second-hand smoking and dental caries in children, results from the A-CHILD study. The 29th Annual scientific meeting of the Japan Epidemiological Association 2019.01.31 Tokyo
2. Igarashi A, Aida J, Sairenchi T, Tsuboya T, Sugiyama K, Koyama S, Matsuyama Y, Sato Y, Osaka K, Ota H. Does Cigarette Smoking Increase Traffic Accident Death During 20 Years Follow-up in Japan? The Ibaraki Prefectural Health Study(和訳中). *Journal of Epidemiology* 2019.06.01
3. Kang J, Yasuda Y, Ogawa T, Sato M, Yamagata Z, Fujiwara T, Moriyama K. Association between Maternal Smoking during Pregnancy and Missing Teeth. 97th International Association of Dental Research (IADR) Conference 2019.06.20 Vancouver, BC, Canada
4. Nawa N, Yamaguchi K, Kawakami C, Nakagawa M, Fujiwara T, Akita K. Differences in effects of inter-professional education workshops by students' discipline and gender among medical and dental students. The Association for Medical Education in Europe (AMEE) Conference 2019 2019.08.27 Vienna, Austria
5. 藤原 武男. 整形外科における疫学研究の進め方. 第68回 東日本整形災害外科学会 2019.09.06 東京
6. Kusama T, Aida J, Sugiyama K, Matsuyama Y, Koyama S, Sato Y, Yamamoto T, Igarashi A, Tsuboya T, Osaka K. 東日本大震災と津波の避難者に関して仮設住宅居住は社会参加と健康に差異を生じさせるのか 横断研究 (Does the Type of Temporary Housing Make a Difference in Social Participation and Health for Evacuees of the Great East Japan Earthquake and Tsunami? A Cross-Sectional Study). *Journal of Epidemiology* 2019.10.01
7. Kanade Ito, Aya Isumi, Satomi Doi, Manami Ochi, Takeo Fujiwara. The association between eating vegetables at start of meal and dental caries among Japanese children. 12th European Public Health Conference 2019.11.20 Marseille, France
8. Doi S, Fujiwara T. Combined effect of adverse childhood experiences and young age on self-harm ideation after birth. 12th European Public Health Conference 2019.11.22 Marseille, France

Environmental Parasitology

Professor : Shiroh IWANAGA
 Lecturer : Takashi KUMAGAI
 Assistant Professor : Naoaki SINZAWA, Sora Enya
 PhD Course Students :
 Kofi Dadzie KWOFIE (D4)
 Michael Amoa-BOSOMPEM (D3)
 Sho ARIMOTO (D3)
 Daniel Addo-GYAN(D2)
 Rie KUBOTA (D1)
 Master Course Students:
 Tsubasa NISHI (M2)
 Taishi HIRAYAMA(M2)
 Takeshi SEKINE(M1)

(1) Outline

Parasitic infectious diseases including Malaria and some neglected tropical diseases have been still been prevalent over the world and the countermeasures against them are urgent issues in the global public health. The scientific research plays an important role in not only understanding the biology of the parasites, but also in developing the effective vaccines and new drugs.

Our laboratory carries molecular biological studies out on malaria and schistosome parasites. In particular, we are interested in transcriptional and epigenetic regulation of gene expression in malaria parasites, *P. falciparum*, and the communication between schistosome parasites using the extracellular vesicles including small RNAs. We are also interested in the drug resistance of malaria parasites and are thus attempt to identify the drug resistance gene by Plasmodium artificial chromosome, which is developed by us. In addition, we performed the epidemiological studies about Opisthorchis and Schistosomiasis to develop the new diagnostic tools.

(2) Research

The following studies have been carried out in our laboratory with molecular genetic, cell biological, and biochemical techniques:

- (1) Elucidation of molecular mechanism of transcriptional regulation of Malaria parasite, *P. falciparum*. (the functional analysis of AP2 transcriptional factors)
- (2) Identification of drug resistance genes of Malaria parasite using the artificial chromosome technology.
- (3) Investigation of cell-cell communication of schistosome parasites with extracellular vehicle containing small RNA.
- (4) Host immune response during parasite infection: Th2 response to helminth infection.
- (5) Epidemiological survey of Opisthorchis infection and Schistosomiasis in SE Asian areas using new diagnostic tools based on LAMP method.

(3) Education

Main objective of the parasitology course for undergraduate students is to provide them the basic knowledge of pathogenicity, treatment and diagnosis of parasitic diseases. We also lecture about the global action against parasitic diseases and basic biology of parasites. In the parasitology course for graduate students, they carry out the advanced molecular biology study about the parasites, in particular malaria and *Schistosoma* parasites, using genetic engineering, cellular biological, genome editing technologies. Furthermore, they have to join the weekly seminar, which are “seminar for the selected papers” and “the study session about the advanced molecular biology”.

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

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

1. Matsushima Y, Mizukoshi F, Sakon N, Doan YH, Ueki Y, Ogawa Y, Motoya T, Tsukagoshi H, Nakamura N, Shigemoto N, Yoshitomi H, Okamoto-Nakagawa R, Suzuki R, Tsutsui R, Terasoma F, Takahashi T, Sadamasu K, Shimizu H, Okabe N, Nagasawa K, Aso J, Ishii H, Kuroda M, Ryo A, Katayama K, Kimura H. Evolutionary Analysis of the < i> VP1< /i> and RNA-Dependent RNA Polymerase Regions of Human Norovirus GII.P17-GII.17 in 2013-2017. *Frontiers in microbiology*. 2019; 10; 2189
2. Amoa-Bosompem Michael, Kobayashi Daisuke, Murota Katsunori, Faizah Astri Nur, Itokawa Kentaro, Ohashi Mitsuko, Dadzie Samuel, Bonney Kofi J., Sasaki Toshinori, Isawa Haruhiko, Sawabe Kyoko, Iwanaga Shiroh. COMPARING THE COMPETENCE OF GHANAIAN AND VIETNAMESE AEDES MOSQUITOES AS VECTORS OF THE DENGUE VIRUS AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE. 2019; 101; 56
3. Djameh Georgina I., Tetteh Thelma, Uto Takuhiro, Ayertey Frederick, Amoa-Bosompem Michael, Azerigyik Faustus I., Kwofei Kofi D., Ohta Tomoe, Ayi Irene, Iwanaga Shiro, Ohta Nobuo, Shoyama Yukihiro, Ohashi Mitsuko. PHENOTYPIC CHARACTERIZATION OF TRYPANOSOMES CELLS TREATED WITH TETRACYCLIC IRIDOID, ML F52 SUPPRESSION OF FLAGELLA ATTACHMENT PROTEINS AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE. 2019; 101; 568
4. Yoshiki Fujii, Yen Hai Doan, Yoshiyuki Suzuki, Toyoko Nakagomi, Osamu Nakagomi, Kazuhiko Katayama. Study of Complete Genome Sequences of Rotavirus A Epidemics and Evolution in Japan in 2012-2014. *Front Microbiol*. 2019.01; 10; 38
5. Tian-Cheng Li, Huimin Bai, Sayaka Yoshizaki, Yasushi Ami, Yuriko Suzaki, Yen Hai Doan, Kazuaki Takahashi, Shunji Mishiro, Naokazu Takeda, Takaji Wakita. Genotype 5 Hepatitis E Virus Produced by a Reverse Genetics System Has the Potential for Zoonotic Infection. *Hepatol Commun*. 2019.01; 3(1); 160-172
6. Ohta T, Tilkanont T, Ayertey F, Nakagawa M, Tung NH, Bolah P, Blagogee H Jnr, Appiah AA, Ocloo A, Ohashi M, Tanoue K, Yamaguchi Y, Ohta N, Yamaoka S, Iwanaga S, Uto T, Shoyama Y. Establishment of a quantitative and qualitative analysis and isolation method for tetracyclic iridoids from *Morinda lucida* Bentham leaves. *Journal of pharmaceutical and biomedical analysis*. 2019.02; 164; 475-480

7. Yoshiyuki Suzuki, Yen Hai Doan, Hirokazu Kimura, Hiroto Shinomiya, Komei Shirabe, Kazuhiko Katayama. Predicting Directions of Changes in Genotype Proportions Between Norovirus Seasons in Japan. *Front Microbiol.* 2019.02; 10; 116
8. Kwofie KD, Sato K, Sanjoba C, Hino A, Shimogawara R, Amoa-Bosompem M, Ayi I, Boakye DA, Anang AK, Chang KS, Ohashi M, Kim HS, Ohta N, Matsumoto Y, Iwanaga S. Oral activity of the antimalarial endoperoxide 6-(1,2,6,7-tetraoxaspiro[7.11] nonadec-4-yl)hexan-1-ol (N-251) against *Leishmania donovani* complex. *PLoS neglected tropical diseases.* 2019.03; 13(3); e0007235
9. Funakoshi Y, Ito K, Morino S, Kinoshita K, Morikawa Y, Kono T, Doan YH, Shimizu H, Hanaoka N, Konagaya M, Fujimoto T, Suzuki A, Chiba T, Akiba T, Tomaru Y, Watanabe K, Shimizu N, Horikoshi Y. Enterovirus D68 respiratory infection in a children's hospital in Japan in 2015. *Pediatrics international : official journal of the Japan Pediatric Society.* 2019.05;
10. Alpha Fardah Athiyyah, Takako Utsumi, Rury Mega Wahyuni, Zayyin Dinana, Laura Navika Yamani, Soetjipto, Subijanto Marto Sudarmo, Reza Gunadi Ranuh, Andy Darma, Juniastuti, Dadik Raharjo, Chieko Matsui, Lin Deng, Takayuki Abe, Yen Hai Doan, Yoshiki Fujii, Hiroyuki Shimizu, Kazuhiko Katayama, Maria Inge Lusida, Ikuo Shoji. Molecular Epidemiology and Clinical Features of Rotavirus Infection Among Pediatric Patients in East Java, Indonesia During 2015-2018: Dynamic Changes in Rotavirus Genotypes From Equine-Like G3 to Typical Human G1/G3. *Front Microbiol.* 2019.05; 10; 940
11. Yoshiki Fujii, Yen Hai Doan, Rury Mega Wahyuni, Maria Inge Lusida, Takako Utsumi, Ikuo Shoji, Kazuhiko Katayama. Improvement of Rotavirus Genotyping Method by Using the Semi-Nested Multiplex-PCR With New Primer Set. *Front Microbiol.* 2019.05; 10; 647
12. Susan Afua Damanka, Sabina Kwofie, Francis Ekow Dennis, Belinda Larteley Lartey, Chantal Ama Agbemabiese, Yen Hai Doan, Theophilus Korku Adiku, Kazuhiko Katayama, Christabel Chika Enweronu-Laryea, George Enyimah Armah. Whole genome characterization and evolutionary analysis of OP354-like P[8] Rotavirus A strains isolated from Ghanaian children with diarrhoea. *PLoS ONE.* 2019.06; 14(6); e0218348
13. Yamamoto K, Takahashi K, Ato M, Iwanaga S, Ohta N. Antimalarial activity of vitamin D3 (VD3) does not result from VD3-induced antimicrobial agents including nitric oxide or cathelicidin. *Experimental parasitology.* 2019.06; 201; 67-77
14. Yuda M, Kaneko I, Iwanaga S, Murata Y, Kato T. Female-specific gene regulation in malaria parasites by an AP2-family transcription factor. *Molecular microbiology.* 2019.06;
15. Risako Katsuta, Fujiko Sunaga, Toru Oi, Yen Hai Doan, Satoko Tsuzuku, Yoshihisa Suzuki, Kaori Sano, Yukie Katayama, Tsutomu Omatsu, Mami Oba, Tetsuya Furuya, Yoshinao Ouchi, Junsuke Shirai, Tetsuya Mizutani, Tomoichiro Oka, Makoto Nagai. First identification of Sapoviruses in wild boar. *Virus Res..* 2019.08; 271; 197680
16. Bando H, Pradipta A, Iwanaga S, Okamoto T, Okuzaki D, Tanaka S, Vega-Rodríguez J, Lee Y, Ma JS, Sakaguchi N, Soga A, Fukumoto S, Sasai M, Matsuura Y, Yuda M, Jacobs-Lorena M, Yamamoto M. CXCR4 regulates *Plasmodium* development in mouse and human hepatocytes. *The Journal of experimental medicine.* 2019.08; 216(8); 1733-1748

Forensic Medicine

Professor
Koichi UEMURA

Associate Professor
Toshihiko AKI

Junior Associate Professor
Kana UNUMA

Assistant Professor
Takeshi FUNAKOSHI

Specially Appointed Assistant Professor
Kanao NORITAKE
Naho HIRAYAMA
Ryo WATANABE

Graduate Student
Midori NAGAI
Tomomi SANO
Momoka OHTA
Masumi MIZOBE
Moeka NOMURA
Tatsuhiko MURATA

(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. Kana Unuma, Toshihiko Aki, Ayaka Yamashita, Ayaka Yoshikawa, Koichi Uemura. Hydrogen sulfide donor NaHS causes bronchitis with enhanced respiratory secretion in rats. *J Toxicol Sci.* 2019; 44(2); 107-112
2. Toshihiko Aki, Kana Unuma, Kanako Noritake, Naho Hirayama, Takeshi Funakoshi, Koichi Uemura. Formation of high molecular weight p62 by CORM-3. *PLoS ONE.* 2019; 14(1); e0210474
3. Kana Unuma, Yohsuke Makino, Yoshiyuki Sasaki, Hirotarō Iwase, Koichi Uemura.. Presepsin: A potential superior diagnostic biomarker for the postmortem differentiation of sepsis based on the Sepsis-3 criteria *Forensic Science International.* 2019; 299; 17-20
4. Takeshi Funakoshi, Mako Furukawa, Toshihiko Aki, Koichi Uemura. Repeated exposure of cocaine alters mitochondrial dynamics in mouse neuroblastoma Neuro2a. *Neurotoxicology.* 2019; 75; 70-77
5. Kana Unuma, Ayaka Yoshikawa, Toshihiko Aki, Koichi Uemura. Increased circulating peroxiredoxin-4 in sepsis model rats involves secretion from hepatocytes and is mitigated by GYY4137. *J Toxicol Pathol.* 2019; 32(4); 305-310

Health Care Management and Planning

Professor Kazuo KAWAHARA
Assistant Professor Makiko SUGAWA
Graduate Student

Daisuke KUMAZAWA
Masao MURATA
Hisashi OMOTE
Masataka YANO
Hayato TAKAYAMA
Ritsuki NEGISHI
Katsunori OHYAMA
Toshio OHKA
Kiyoyuki TOMITA
Takeshi MATSUI
Hisayuki HASEGAWA
Haruka HANADA

(1) Outline

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

(2) Research

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

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

ensuring safety, and securing a stable supply. To achieve a stable supply of blood products, we also conduct epidemiological studies to review guidelines on collecting blood.

3) 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.

4) 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.

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

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

7) 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) Education

Through the MMA course, we provide education on the characteristics and issues of Japanese medical policy. In addition, the Graduate School of Policy Science provides lectures on analysis of the current state of the Japanese medical environment and solutions for medical problems. The dates and times of the lectures are as follows.

1)Lecture and Conference 18:00-19:30 Monday

2)Special Lecture as occasion demands 19 : 30-21 : 00 Monday

3)Seminar as occasion demands (Presentation and Conference) 21:00-22:30 Monday

(4) Lectures & Courses

Students are expected to learn how to analyze health and welfare policies adopted domestically and overseas using objective indicators as well as the ability to theoretically and systematically discuss what they think would be the optimal solution.

(5) Publications

[Conference Activities & Talks]

1. Shutaro SUGITA. Barbiturates Adversely Affect A Patient's Prognosis On Acute Drug Intoxication.. WPA 2019.08.21

Research Development

Faculty Staff
Professor
Kozo TAKASE

Graduate Students
Doctor course
Yasumasa OOSHIRO
Hideki TERUYA
Masakazu HARAMO
Kazushige ENDOH

Master course (Master of Medical Administration)
Mai INOUE
Shuichi INOSE
Fumiaki UEMICHI
Natuko HIGUCHI
Tetsuya MURAKAMI
Koji MORISHITA
Keiko YOSHIDA

(1) Outline

Department of Research Development was established in 2000.
This department has been managing the course of Master of Medical Administration.

(2) 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) Patient satisfaction and patient experience
- 10) Development of medical engineering apparatus

(3) 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) Health Promotion Policy program (General Medicine, Risk Management in Medicine) with Hitotsubashi University

(4) **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.

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

Kozo TAKASE

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

Committee member of Tokyo District Court

Chief Editorial Board of Japanese Society for Clinical Pathway

(6) **Publications**

[Original Articles]

1. Higashide Yuji, Izugami Satoko, Takase Kozo. Influence of Nurses' Work Environment on Their Self-Evaluation of Nursing Work Journal of Medical and Dental Sciences. 2019.06; 66(2); 31-42
2. Yasumasa Oshiro, Kozo Takase. Behavioral and oral characteristics of patients in a general dental clinic in Japan –Focus on cancellation without notice– Journal of Medical and Dental Sciences. 2019.09; 66(3); 43-90

Health Policy and Informatics

Professor: Kiyohide FUSHIMI

Graduate Student : Tetu OHNUMA, Akira HOMMA, Tomomitsu CHIKAWA, Mariko KODAN, Kyoko HIRANO, Mihoko OTA, Ken KAWASAKI, Natsuko KANAZAWA, Shunsuke EDAKUBO, Yoshiteru YANO, Senri WATANABE, Risa SUZUKI, Akihito UDA, Yuka SATO, Sayomi Tsukada, Kyunghee Lee, Takuaki Tani
Graduate Research Student: Masahiro INOUE

(1) Research

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

(2) Education

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

(3) Publications

[Original Articles]

1. Endo A, Shiraishi A, Otomo Y, Fushimi K, Murata K. Volume-outcome relationship on survival and cost benefits in severe burn injury: a retrospective analysis of a Japanese nationwide administrative database. *Journal of intensive care*. 2019; 7; 7
2. Hideyuki Mouri, Taisuke Jo, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Continuous Neuromuscular Blockade and Mortality in Subjects With Exacerbation of Idiopathic Interstitial Pneumonias. *Respir Care*. 2019.01; 64(1); 34-39
3. Megumi Koizumi, Miho Ishimaru, Hiroki Matsui, Kiyohide Fushimi, Tatsuya Yamasoba, Hideo Yasunaga. Tranexamic acid and post-tonsillectomy hemorrhage: propensity score and instrumental variable analyses. *Eur Arch Otorhinolaryngol*. 2019.01; 276(1); 249-254
4. Norihiko Inoue, Kiyohide Fushimi. Adjunctive Corticosteroids decreased the risk of mortality of non-HIV Pneumocystis Pneumonia. *Int. J. Infect. Dis.*. 2019.02; 79; 109-115

5. Enomoto M, Endo A, Yatsushige H, Fushimi K, Otomo Y. Clinical Effects of Early Edoxaban Use in Acute Ischemic Stroke Patients Treated by Endovascular Reperfusion Therapy. *Stroke*. 2019.02; STROKEAHA118023815
6. Hiroyuki Ohbe, Shunsuke Isogai, Mikio Nakajima, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Physician-manned prehospital emergency care in tertiary emergency centers in Japan. *Acute Med Surg*. 2019.02; 6(2); 165-172
7. Daisuke Takada, Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. Previously-initiated hemodialysis as prognostic factor for in-hospital mortality in pneumonia patients with stage 5 chronic kidney disease: Retrospective database study of Japanese hospitals. *PLoS ONE*. 2019.02; 14(2); e0213105
8. Koshi Ota, Yusuke Sasabuchi, Hiroki Matsui, Taisuke Jo, Kiyohide Fushimi, Hideo Yasunaga. Age distribution and seasonality in acute eosinophilic pneumonia: analysis using a national inpatient database. *BMC Pulm Med*. 2019.02; 19(1); 38
9. Yamaoka Y, Fujiwara T, Fujino Y, Matsuda S, Fushimi K. Incidence and age distribution of hospitalized presumptive and possible abusive head trauma of children under 12 months old in Japan. *JOURNAL OF EPIDEMIOLOGY*. 2019.02;
10. Takeshi Oichi, Yasushi Oshima, Hiroki Matsui, Kiyohide Fushimi, Sakae Tanaka, Hideo Yasunaga. Can Elective Spine Surgery Be Performed Safely Among Nonagenarians?: Analysis of a National Inpatient Database in Japan. *Spine*. 2019.03; 44(5); E273-E281
11. Michimasa Fujiogi, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Jun Fujishiro. Outcomes following laparoscopic versus open surgery for pediatric inguinal hernia repair: Analysis using a national inpatient database in Japan. *J. Pediatr. Surg.*. 2019.03; 54(3); 577-581
12. Yoshihisa Hiraishi, Taisuke Jo, Nobuaki Michihata, Wakae Hasegawa, Yukiyo Sakamoto, Hirokazu Urushiyama, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase, Hideo Yasunaga, Yasuhiro Yamauchi. Hospital Volume and Mortality following Diagnostic Bronchoscopy in Lung Cancer Patients: Data from a National Inpatient Database in Japan. *Respiration*. 2019.03; 97(3); 264-272
13. Daisuke Shigemi, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Safety of Laparoscopic Surgery for Benign Diseases during Pregnancy: A Nationwide Retrospective Cohort Study. *J Minim Invasive Gynecol*. 2019.03; 26(3); 501-506
14. Daisuke Shinjo, Kimikazu Matsumoto, Keita Terashima, Tetsuya Takimoto, Tetsu Ohnuma, Takashi Noguchi, Kiyohide Fushimi. Volume effect in paediatric brain tumour resection surgery: analysis of data from the Japanese national inpatient database. *Eur. J. Cancer*. 2019.03; 109; 111-119
15. Shingo Morishita, Toshitaka Yoshii, Atsushi Okawa, Kiyohide Fushimi, Takeo Fujiwara. Perioperative complications of anterior decompression with fusion versus laminoplasty for the treatment of cervical ossification of the posterior longitudinal ligament: propensity score matching analysis using a nation-wide inpatient database. *Spine J*. 2019.04; 19(4); 610-616
16. Hiroji Shinkawa, Hideo Yasunaga, Kiyoshi Hasegawa, Hiroki Matsui, Nobuaki Michihata, Kiyohide Fushimi, Norihiro Kokudo. Mortality and morbidity after pancreatoduodenectomy in patients undergoing hemodialysis: Analysis using a national inpatient database. *Surgery*. 2019.04; 165(4); 747-750
17. Jung-Ho Shin, Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. Effects of preoperative oral management by dentists on postoperative outcomes following esophagectomy: Multilevel propensity score matching and weighting analyses using the Japanese inpatient database. *Medicine (Baltimore)*. 2019.04; 98(17); e15376
18. Yusuke Okubo, Itaru Hayakawa, Hiroki Nariai, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Recent practice patterns in diagnostic procedures anticonvulsants, and antibiotics for children hospitalized with febrile seizure. *Seizure*. 2019.04; 67; 52-56
19. A Tsuchiya, H Yasunaga, Y Tsutsumi, T Kawahara, H Matsui, K Fushimi. Nationwide observational study of mortality from complicated intra-abdominal infections and the role of bacterial cultures. *Br J Surg*. 2019.04; 106(5); 606-615

20. Yoshihisa Miyamoto, Masao Iwagami, Shotaro Aso, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Yoshifumi Hamasaki, Masaomi Nangaku, Kent Doi. Temporal change in characteristics and outcomes of acute kidney injury on renal replacement therapy in intensive care units: analysis of a nationwide administrative database in Japan, 2007-2016. *Crit Care*. 2019.05; 23(1); 172
21. Daisuke Shinjo, Hisateru Tachimori, Keiko Maruyama-Sakurai, Tetsu Ohnuma, Kenji Fujimori, Kiyohide Fushimi. Risk factors for early unplanned readmission in patients with bipolar disorder: A retrospective observational study. *Gen Hosp Psychiatry*. 2019.05; 58; 51-58
22. Daisuke Shigemi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Laparoscopic Compared With Open Surgery for Severe Pelvic Inflammatory Disease and Tubo-Ovarian Abscess. *Obstet Gynecol*. 2019.06; 133(6); 1224-1230
23. Daisuke Shigemi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Therapeutic Impact of Initial Treatment for Chlamydia trachomatis Among Patients With Pelvic Inflammatory Disease: A Retrospective Cohort Study Using a National Inpatient Database in Japan. *Clin. Infect. Dis.*. 2019.07; 69(2); 316-322
24. Mikio Nakajima, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Yoshihiro Yamaguchi, Hideo Yasunaga. Disaster-related carbon monoxide poisoning after the Great East Japan Earthquake, 2011: a nationwide observational study. *Acute Med Surg*. 2019.07; 6(3); 294-300
25. Shunsuke Araki, Shinichi Tomioka, Makoto Otani, Shutaro Suga, Shun Ichikawa, Shinya Matsuda, Kiyohide Fushimi, Koichi Kusuhara, Akira Shirahata. Incidence and In-Hospital Mortality of Neonatal Disseminated Intravascular Coagulation in Japan: An Observational Study of a Nationwide Hospital Claims Database. *J. UOEH*. 2019.07; 41(3); 295-302
26. Hiroyuki Ohbe, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Early Enteral Nutrition in Patients Undergoing Sustained Neuromuscular Blockade: A Propensity-Matched Analysis Using a Nationwide Inpatient Database. *Crit. Care Med.*. 2019.08; 47(8); 1072-1080
27. Michimasa Fujiogi, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Jun Fujishiro. Early Outcomes of Laparoscopic Versus Open Surgery for Urachal Remnant Resection in Children: A Retrospective Analysis Using a Nationwide Inpatient Database in Japan. *J Laparoendosc Adv Surg Tech A*. 2019.08; 29(8); 1067-1072
28. Kojiro Morita, Hiroki Matsui, Nobuaki Michihata, Kiyohide Fushimi, Hideo Yasunaga. Association of Early Systemic Corticosteroid Therapy with Mortality in Patients with Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis: A Retrospective Cohort Study Using a Nationwide Claims Database. *Am J Clin Dermatol*. 2019.08; 20(4); 579-592
29. Megumi Koizumi, Miho Ishimaru, Hiroki Matsui, Kiyohide Fushimi, Tatsuya Yamasoba, Hideo Yasunaga. Outcomes of endoscopic sinus surgery for sinusitis-induced intracranial abscess in patients undergoing neurosurgery. *Neurosurg Focus*. 2019.08; 47(2); E12
30. Ryo Iketani, Shinobu Imai, Hiromasa Horiguchi, Daisuke Furushima, Kiyohide Fushimi, Hiroshi Yamada. Comparison of the association of risperidone and quetiapine with deteriorating performance in walking and dressing in subjects with Parkinson's disease: a retrospective cohort study using administrative claims data. *Int Clin Psychopharmacol*. 2019.09; 34(5); 234-240
31. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Kiyohide Fushimi, Hideo Yasunaga. In-hospital Takotsubo syndrome versus in-hospital acute myocardial infarction among patients admitted for non-cardiac diseases: a nationwide inpatient database study. *Heart Vessels*. 2019.09; 34(9); 1479-1490
32. Seiko Mizuno, Susumu Kunisawa, Noriko Sasaki, Kiyohide Fushimi, Yuichi Imanaka. Correction: Effects of night-time and weekend admissions on in-hospital mortality in acute myocardial infarction patients in Japan. *PLoS ONE*. 2019.09; 14(9); e0222125
33. Iwanari Kawamura, Mikio Nakajima, Takeshi Kitamura, Richard H Kaszynski, Rintaro Hojo, Hiroyuki Ohbe, Yusuke Sasabuchi, Hiroki Matsui, Kiyohide Fushimi, Seiji Fukamizu, Hideo Yasunaga. Patient characteristics and in-hospital complications of subcutaneous implantable cardioverter-defibrillator for Brugada syndrome in Japan. *J Arrhythm*. 2019.09; 35(6); 842-847

34. Seiko Bun, Susumu Kunisawa, Noriko Sasaki, Kiyohide Fushimi, Kimikazu Matsumoto, Akimasa Yamatani, Yuichi Imanaka. Analysis of concordance with antiemetic guidelines in pediatric, adolescent, and young adult patients with cancer using a large-scale administrative database. *Cancer Med.* 2019.10; 8(14); 6243-6249
35. Tetsuya Ishimaru, Michimasa Fujiogi, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hiroshi Kawashima, Jun Fujishiro, Hideo Yasunaga. Impact of congenital heart disease on outcomes after primary repair of esophageal atresia: a retrospective observational study using a nationwide database in Japan. *Pediatr. Surg. Int.* 2019.10; 35(10); 1077-1083
36. Mandai S, Sato H, Iimori S, Naito S, Tanaka H, Ando F, Susa K, Isobe K, Mori T, Nomura N, Sohara E, Okado T, Uchida S, Fushimi K, Rai T. Nationwide in-hospital mortality following major fractures among hemodialysis patients and the general population: An observational cohort study. *Bone.* 2019.10; 130; 115122
37. Shinobu Imai, Hayato Yamana, Norihiko Inoue, Manabu Akazawa, Hiromasa Horiguchi, Kiyohide Fushimi, Kiyoshi Migita, Hiroshi Yatsushashi, Masaya Sugiyama, Masashi Mizokami. Validity of administrative database detection of previously resolved hepatitis B virus in Japan. *J. Med. Virol.* 2019.11; 91(11); 1944-1948
38. Ikuyo Tsutsumi, Susumu Kunisawa, Chikashi Yoshida, Masanori Seki, Takuya Komeno, Kiyohide Fushimi, Satoshi Morita, Yuichi Imanaka. Impact of oral voriconazole during chemotherapy for acute myeloid leukemia and myelodysplastic syndrome: a Japanese nationwide retrospective cohort study. *Int. J. Clin. Oncol.* 2019.11; 24(11); 1449-1458
39. Takahiro Kinoshita, Hiroyuki Ohbe, Hiroki Matsui, Kiyohide Fushimi, Hiroshi Ogura, Hideo Yasunaga. Effect of tranexamic acid on mortality in patients with haemoptysis: a nationwide study. *Crit Care.* 2019.11; 23(1); 347
40. Hiroyuki Ohbe, Shunsuke Isogai, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Treatment with Antithrombin or Thrombomodulin and Mortality from Heatstroke-Induced Disseminated Intravascular Coagulation: A Nationwide Observational Study. *Semin. Thromb. Hemost.* 2019.11; 45(8); 760-766
41. Hiroyuki Ohbe, Shunsuke Isogai, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Extracorporeal membrane oxygenation improves outcomes of accidental hypothermia without vital signs: A nationwide observational study. *Resuscitation.* 2019.11; 144; 27-32
42. Yoshihisa Miyamoto, Masao Iwagami, Shotaro Aso, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Yoshifumi Hamasaki, Masaomi Nangaku, Kent Doi. Association between intravenous contrast media exposure and non-recovery from dialysis-requiring septic acute kidney injury: a nationwide observational study. *Intensive Care Med.* 2019.11; 45(11); 1570-1579
43. Morioka N, Moriwaki M, Tomio J, Kashiwagi M, Fushimi K, Ogata Y. Structure and process of dementia care and patient outcomes after hip surgery in elderly people with dementia: A retrospective observational study in Japan. *International journal of nursing studies.* 2019.11; 102; 103470
44. Tetsuji Minami, Mph, Hayato Yamana, Mph Ph D, Daisuke Shigemi, Mph, Hiroki Matsui Mph, Kiyohide Fushimi, Ph D, Hideo Yasunaga, Ph D. Artificial colloids versus human albumin for the treatment of ovarian hyperstimulation syndrome: A retrospective cohort study. *Int J Reprod Biomed (Yazd).* 2019.11; 17(10); 709-716
45. Ryosuke Kumazawa, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Association between Angiotensin-Converting Enzyme Inhibitors and Post-Stroke Aspiration Pneumonia. *J Stroke Cerebrovasc Dis.* 2019.12; 28(12); 104444
46. Fusao Ikawa, Nobuaki Michihata, Yasuhiko Akiyama, Koji Iihara, Fumihiko Matano, Akio Morita, Yoko Kato, Koji Iida, Kaoru Kurisu, Kiyohide Fushimi, Hideo Yasunaga. Treatment Risk for Elderly Patients with Unruptured Cerebral Aneurysm from a Nationwide Database in Japan. *World Neurosurg.* 2019.12; 132; e89-e98
47. Kazuaki Uda, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Intensive In-Hospital Rehabilitation After Hip Fracture Surgery and Activities of Daily Living in Patients With Dementia: Retrospective Analysis of a Nationwide Inpatient Database. *Arch Phys Med Rehabil.* 2019.12; 100(12); 2301-2307

48. Hideki Endo, Kiyohide Fushimi, Yasuhiro Otomo. Volume-outcome relationship in severe operative trauma surgery: A retrospective cohort study using a Japanese nationwide administrative database. *Surgery*. 2019.12; 166(6); 1105-1110
49. Tadahiro Goto, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hiroyuki Hayashi, Hideo Yasunaga. Machine Learning-Based Prediction Models for 30-Day Readmission after Hospitalization for Chronic Obstructive Pulmonary Disease. *COPD*. 2019.12; 16(5-6); 338-343
50. Yoshiteru Yano, Nobuo Sakata, Kiyohide Fushimi. Establishing a hospital transfusion management system promotes appropriate clinical use of human albumin in Japan: a nationwide retrospective study. *BMC Health Serv Res*. 2019.12; 19(1); 999
51. Mikio Nakajima, Morita Kojiro, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Yasuhiko Kaita, Hideaki Goto, Yoshihiro Yamaguchi, Hideo Yasunaga. Effect of high-dose vitamin C therapy on severe burn patients: a nationwide cohort study. *Crit Care*. 2019.12; 23(1); 407

[Conference Activities & Talks]

1. Shimizu, S., Fushimi, K. Influence of Outpatient Shift of Examination and Diagnostic Imaging on the Hospital Bundled Payment System: A Retrospective Cohort Study. 2019 IHEA 2019.07.13 Basel, Switzerland
2. Shinjo, D., Inoue, N., Fushimi, K. Association between hospital volume and mortality of Congenital Diaphragmatic Hernia repair surgery in Japan. 3rd jENS 2019.09.17 Maastricht, Holland; The Netherlands
3. Mutsuko Moriwaki, Mikayo Toba, Chihiri Takahashi, Yoshibumi Aiso, Yoshiri Hadanoo, Yoko Nukui, Satoshi Obayashi, Kiyohide Fushimi. Development of a Technique to Monitor the Implementation of De-escalation of Antibacterial Agent. International Forum on QUALITY & SAFETY in HEALTHCARE 2019.09.18 Taipei
4. TOBA, M. MORIWAKI, M. OBAYASHI, S. FUSHIMI, K. Prevention versus post-cesarean section venous thromboembolism intermediate risk cases in acute care hospitals implementation status and its outcomes in Japan. International Forum on QUALITY & SAFETY in HEALTHCARE 2019.09.18 Taipei
5. Daisuke Shinjo, Norihiko Inoue, Tetsuya Isayama, Yushi Itoh, Kiyohide Fushimi. VARIATIONS IN DURATION OF MECHANICAL VENTILATION IN VERY LOW BIRTH WEIGHT INFANTS IN JAPAN. ISPOR Europe 2019 2019.11.02 Copenhagen, Denmark

Life Sciences and Bioethics

Masayuki Yoshida
Yusuke Ebana
Hiroko Kohbata
Mizuko Osaka

(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. Kameyama Noriko, Maruyama Chizuko, Kitagawa Fuyuha, Nishii Kazunobu, Uenomachi Kaori, Katayama Yayoi, Koga Hiromi, Chikamoto Naoko, Kuwata Yuko, Torigoe Junko, Arimoto Masako, Tokumaru Toshiaki, Ikewaki Katsunori, Nohara Atsushi, Otsubo Yoshihiko, Yanagi Koji, Yoshida Masayuki, Harada-Shiba Mariko. Dietary Intake during 56 Weeks of a Low-Fat Diet for Lomitapide Treatment in Japanese Patients with Homozygous Familial Hypercholesterolemia JOURNAL OF ATHEROSCLEROSIS AND THROMBOSIS. 2019; 26(1); 72-83
2. Kamijo Y, Ishii H, Yamamoto T, Kobayashi K, Asano H, Miake S, Kanda E, Urata H, Yoshida M. Potential Impact on Lipoprotein Subfractions in Type 2 Diabetes. Clinical medicine insights. Endocrinology and diabetes. 2019; 12; 1179551419866811
3. Nohara Atsushi, Otsubo Yoshihiko, Yanagi Koji, Yoshida Masayuki, Ikewaki Katsunori, Harada-Shiba Mariko, Jurecka Agnieszka. Safety and Efficacy of Lomitapide in Japanese Patients with Homozygous Familial Hypercholesterolemia (HoFH): Results from the AEGR-733-301 Long-Term Extension Study JOURNAL OF ATHEROSCLEROSIS AND THROMBOSIS. 2019; 26(4); 368-377
4. Kameyama Noriko, Maruyama Chizuko, Kitagawa Fuyuha, Nishii Kazunobu, Uenomachi Kaori, Katayama Yayoi, Koga Hiromi, Chikamoto Naoko, Kuwata Yuko, Torigoe Junko, Arimoto Masako, Tokumaru Toshiaki, Ikewaki Katsunori, Nohara Atsushi, Otsubo Yoshihiko, Yanagi Koji, Yoshida Masayuki, Harada-Shiba Mariko. ホモ接合型家族性高コレステロール血症の日本人患者におけるロミタピド治療に対する 56 週間の低脂肪食摂取 (Dietary Intake during 56 Weeks of a Low-Fat Diet for Lomitapide Treatment in Japanese

- Patients with Homozygous Familial Hypercholesterolemia) *Journal of Atherosclerosis and Thrombosis*. 2019.01; 26(1); 72-83
5. Noriaki Yamada, Yoshihiro Asano, Masashi Fujita, Satoru Yamazaki, Atsushi Inanobe, Norio Matsuura, Hatasu Kobayashi, Seiko Ohno, Yusuke Ebana, Osamu Tsukamoto, Saki Ishino, Ayako Takuwa, Hidetaka Kioka, Toru Yamashita, Norio Hashimoto, Dimitar P Zankov, Akio Shimizu, Masanori Asakura, Hiroshi Asanuma, Hisakazu Kato, Yuya Nishida, Yohei Miyashita, Haruki Shinomiya, Nobu Naiki, Kenshi Hayashi, Takeru Makiyama, Hisakazu Ogita, Katsuyuki Miura, Hirotsugu Ueshima, Issei Komuro, Masakazu Yamagishi, Minoru Horie, Koichi Kawakami, Tetsushi Furukawa, Akio Koizumi, Yoshihisa Kurachi, Yasushi Sakata, Tetsuo Minamino, Masafumi Kitakaze, Seiji Takashima. Mutant KCNJ3 and KCNJ5 Potassium Channels as Novel Molecular Targets in Bradyarrhythmias and Atrial Fibrillation. *Circulation*. 2019.02;
 6. Takahashi Kenta, Oshima Noriko, Nakamura Reiko, Iwahara Yuki, Wakana Kimio, Yoshida Masayuki, Miyasaka Naoyuki. Detection of hereditary gynecologic cancer by screening and risk assessment using questionnaires in gynecological outpatient clinic(和訳中) *日本産科婦人科学会雑誌*. 2019.02; 71(臨増); S-196
 7. Yusuke Ebana, Tetsushi Furukawa. Networking analysis on superior vena cava arrhythmogenicity in atrial fibrillation. *Int J Cardiol Heart Vasc*. 2019.03; 22; 150-153
 8. Hirayama Atsushi, Yamashita Shizuya, Ruzza Andrea, Inomata Hyoe, Cyrille Marcoli, Hamer Andrew, Yoshida Masayuki, Kiyosue Arihiro, Teramoto Tamio. 日本人患者集団における evolocumab の OSLER 非盲検延長試験の 5 年間の最終報告 (Final 5-Year Report of the OSLER Open-Label Extension Studies of Evolocumab in the Japanese Patient Population) *日本循環器学会学術集会抄録集*. 2019.03; 83 回; LBCT2-4
 9. Nohara Atsushi, Otsubo Yoshihiko, Yanagi Koji, Yoshida Masayuki, Ikewaki Katsunori, Harada-Shiba Mariko, Jurecka Agnieszka. ホモ接合型家族性高コレステロール血症 (HoFH) の日本人患者におけるロミタピドの安全性と有効性 AEGR-733-301 長期延長試験の結果 (Safety and Efficacy of Lomitapide in Japanese Patients with Homozygous Familial Hypercholesterolemia(HoFH): Results from the AEGR-733-301 Long-Term Extension Study) *Journal of Atherosclerosis and Thrombosis*. 2019.04; 26(4); 368-377
 10. Hirayama Atsushi, Yamashita Shizuya, Ruzza Andrea, Inomata Hyoe, Cyrille Marcoli, Hamer Andrew W., Yoshida Masayuki, Kiyosue Arihiro, Teramoto Tamio. 日本人患者におけるエボロクマブによる長期治療 OSLER 非盲検延長試験の最終報告 (Long-Term Treatment With Evolocumab Among Japanese Patients: Final Report of the OSLER Open-Label Extension Studies) *Circulation Journal*. 2019.04; 83(5); 971-977
 11. Hirayama Atsushi, Yamashita Shizuya, Ruzza Andrea, Inomata Hyoe, Cyrille Marcoli, Lu Chen, Hamer Andrew W., Yoshida Masayuki, Kiyosue Arihiro, Teramoto Tamio. Long-Term Treatment With Evolocumab Among Japanese Patients - Final Report of the OSLER Open-Label Extension Studies *CIRCULATION JOURNAL*. 2019.05; 83(5); 971-977
 12. Dewan Syed Masudur Rahman, Shiraishi Orie, Deushi Michiyo, Tani Mariko, Osaka Mizuko, Yoshida Masayuki. C5a による好中球 β 2 インテグリン活性化は PKC δ の膜移行に関与する (C5a-induced β 2 integrin activation in neutrophils involves membrane translocation of PKC δ) *日本動脈硬化学会総会プログラム・抄録集*. 2019.07; 51 回; 2-P
 13. Takahashi Kenta, Oshima Noriko, Nakamura Reiko, Iwahara Yuki, Wakana Kimio, Yoshida Masayuki, Miyasaka Naoyuki. Detection of hereditary gynecologic cancer by screening and risk assessment using questionnaires in gynecological outpatient clinic(和訳中) *The Journal of Obstetrics and Gynaecology Research*. 2019.08; 45(8); 1682
 14. Yusuke Ebana, Yihan Sun, Xiaoxi Yang, Taiju Watanabe, Satoru Makita, Kouichi Ozaki, Toshihiro Tanaka, Hirokuni Arai, Tetsushi Furukawa. Pathway analysis with genome-wide association study (GWAS) data detected the association of atrial fibrillation with the mTOR signaling pathway. *Int J Cardiol Heart Vasc*. 2019.09; 24; 100383
 15. Yoshida H, Tada H, Ito K, Kishimoto Y, Yanai H, Okamura T, Ikewaki K, Inagaki K, Shoji T, Bujo H, Miida T, Yoshida M, Kuzuya M, Yamashita S. Reference Intervals of Serum Non-Cholesterol Sterols by Gender in Healthy Japanese Individuals. *Journal of atherosclerosis and thrombosis*. 2019.09;
 16. Nishi H., Inoue R., Osaka M., Inoue T., Yoshida M., Nangaku M.. Neutrophil interferon-induced, double-stranded RNA-activated protein kinase (EIF2AK2) mediates vascular adhesion and transmigration in non-viral inflammatory disease *EUROPEAN JOURNAL OF IMMUNOLOGY*. 2019.10; 49; 582

[Conference Activities & Talks]

1. Yusuke Ebana. "Specified clinical trials" and "clinical trials" defined in Clinical Trials Act No.16 of April 14, 2017. 2019.05.11 Tokyo
2. Syed Masudur Rahman Dewan, Mizuko Osaka, Masayuki Yoshida. C5a induces PKC α dependent β 2 integrin activation in neutrophil-like differentiated HL-60.. 第四回 J-ISCP 年次学術集会 国際心血管薬物療法学会日本部会 2019.06.08
3. Mizuko Osaka. Mechanism of vascular inflammation in LDLR null mice by PAD4-induced citrullination. The 51st Annual Scientific Meeting of the Japan Atherosclerosis Society 2019.07.16
4. Yusuke Ebana. Educational Training Lecture "Research Ethics for Principle investigator". The 21st Annual Meeting of Japan Osteoporosis Society 2019.10.11
5. Yusuke Ebana. Educational Lecture "Genetic Basis of Inherited Arrhythmia Syndrome". The 12th Asia Pacific Heart Rhythm Society Scientific Session 2019.10.24
6. Yusuke Ebana. Educational Lecture Genetic Testing 101, "Whom Should Be Tested?". The 12th Asia Pacific Heart Rhythm Society Scientific Session 2019.10.24
7. Genetic test for the suspected patients of inborn errors of immunity. 2019.11.07

Forensic Dentistry

Professor Koichi SAKURADA
Assistant Professor Hajime UTSUNO
Graduate Student Saki MINEGISHI
Graduate Student Jun OHTA
Graduate Student Chihiro TANAKA

(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. Saitoh H, Moriya T, Takeyama M, Yusa K, Sakuma A, Chiba F, Torimitsu S, Ishii N, Sakurada K, Iino M, Iwase H, Tokanai F. Estimation of birth year by radiocarbon dating of tooth enamel: Approach to obtaining enamel powder. *Journal of forensic and legal medicine*. 2019.01; 62; 97-102
2. Minegishi S, Ohtani S, Noritake K, Funakoshi T, Ishii N, Utsuno H, Sakuma A, Saitoh H, Yamaguchi S, Marukawa E, Harada H, Uemura K, Sakurada K. Preparation of dentin standard samples for age estimation based on increased aspartic acid racemization rate by heating. *Legal Medicine*. 2019.03; 38; 25-31
3. Hiroaki Ichioka, Koichi Sakurada, Hisako Saitoh, Maki Ohtani, Wataru Kumagaya, Hiroshi Ikegaya. The education effectiveness of postmortem dental chart recording practice for dentists *Forensic Dental Science*. 2019.03; 11(1); 10-14
4. Jun Ohta, Nanaka Noda, Koichi Sakurada. Comparison of Catalytic and Immunological Amylase Tests for Identifying of Saliva from Degraded Samples. *J. Forensic Sci.*. 2019.05; 64(3); 873-877
5. Jun Ohta, Koichi Sakurada. Oral gram-positive bacterial DNA-based identification of saliva from highly degraded samples. *Forensic Sci Int Genet*. 2019.09; 42; 103-112

[Books etc]

1. Takehiko Takatori, Masataka Nagao, Koichi Sakurada, etc.. *New Essentials of Forensic Medicine* 6th Edition. Ishiyaku Publishers Inc., 2019.03 (ISBN : 978-4-263-73189-5)

[Misc]

1. UTSUNO HAJIME. Victim identification in large-scale disasters using dental findings IATSS RESEARCH. 2019.07; 43(2); 90-96
2. Komuro T, Tsutsumi H, Izawa H, Katsumura S, Saitoh H, Sakurada K, Sato K, Furukawa A. Social contribution of forensic odontology in Japan. *The Japanese dental science review*. 2019.11; 55(1); 121-125

[Conference Activities & Talks]

1. Chihiro Tanaka, Hajime Utsuno, Yousuke Makino, Namiko Ishii, Saki Minegishi, Jun Ohta, Hisako Saitoh, Hiroto Iwase, Koichi Sakurada. Study of the shape of pyriform aperture and the line of nasolabial sulcus in Japanese. *The 103rd Congress of the Japanese Society of Legal Medicine* 2019.06.13 Sendai city
2. Midori Nagai, Koichi Sakurada, Kazuhiko Imaizumi, Yoshinori Ogawa, Jyouji Noritake, Ayumi Komatsu, Rina Kaseda, Motohiro Uo, Koichi Uemura. Study on post mortem time of bone using bovine femur. *The 103rd Congress of the Japanese Society of Legal Medicine* 2019.06.13 Sendai city
3. Tomoko Akutsu, Isao Yokota, Ken Watanabe, Koichi Sakurada.. Development of a Multiplex RT-PCR Assay and Its Statistical Evaluation for the Forensic Identification of Vaginal Fluid.. *The 28th International Congress of International Society for Forensic Genetics*. 2019.09.12 The Czech Republic, Prague Congress Center
4. Koichi Sakurada, Saki Minegishi, Hajime Utsuno, Jun Ohta, Chihiro Tanaka, Hikoto Ohta. Study on brain activity of PAM analogs Examination of AChE activity measurement system using MATP + . *The 88th Kanto District Meeting of the Japanese Society of Legal Medicine* 2019.10.12 Shinjyuku-ku

5. Hjime Utsuno, Chihiro Tanaka, Yosuke Makino, Hisako Saitoh, Saki Minegishi, Jun Ohta, Hirotaro Iwase, Koichi Sakurada. Study on estimation method of nasal wing shape around piriform aperture of maxilla. The 88th Kanto District Meeting of the Japanese Society of Legal Medicine 2019.10.12 Shinjyuku-ku
6. Saki Minegishi, Jun Ohta, Chihiro Tanaka, Hajime Utsuno, Namiko Ishii, Hisako Saitoh, Koichi Sakurada.. Examination of preparation of standard sample using enzyme in age estimation of dentin racemization method. 13th Annual Meeting of Japanese Society of Forensic Dental Science 2019.11.03 Hiroshima Prefectural Dental Association Hall

[Social Contribution]

1. Personal identification using dental findings and others (54 cases), 2019.01.01 - 2019.12.31
2. Appearance in court (1 case) (Koichi Sakurada), 2019.01.01 - 2019.12.31
3. 2018Personal Identification training program (Second, Tokyo metropolitan) (Koichi Sakurada) , Tokyo Dental association, Japan Dental Association Building, 2019.02.25
4. 2019Personal Identification training program (First) (Koichi Sakurada) , Tokyo Dental Association, Japan Dental Association Building, 2019.11.16

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. Kyaw Htin, IGARASHI Isao, KAWABUCHI Koichi. Effect of Belief and Knowledge on Betel Quid Chewing Behavior in Myanmar: Variation across Socioeconomic Status 口腔病学会雑誌. 2019.11; 86(3); 53-70

Dental Education Development

Professor: Ikuko MORIO
 Assistant Professor Naoko SEKI
 Graduate Student: Mio NAITO
 Graduate Student: Ai OSATO
 Graduate Student: Shin-ru LIAO
 Graduate Student: Kittichai SIREERAT

(1) Research

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

(2) Education

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

(3) Clinical Services & Other Works

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

1. Essential Expertise for Clinical Dentistry 5 (Seminar/Hands-on), Tokyo, Japan (TMDU). August 19-29.
2. International Faculty Development Course 2019 : Essential Expertise for Clinical Dentistry for Dental Professionals (Seminar/Hands-on), Tokyo, Japan. November 14-19.
3. International Dental Program 2019, Tokyo, Japan. August 25- September 1.

(4) Publications

[Original Articles]

1. Morio I. White Paper on Japanese Dental Education 2017 (2015-2017) Chapter 15 Quality assurance of dental education overseas Journal of Japanese Dental Education Association. 2019.03; suppl.; 174-176
2. Morio I. White Paper on Japanese Dental Education 2017 (2015-2017) Chapter 17 International Exchange Journal of Japanese Dental Education Association. 2019.03; suppl.; 188-197
3. Morio I. White Paper on Japanese Dental Education 2017 (2015-2017) Dental education-related international associations Journal of Japanese Dental Education Association. 2019.03; suppl.; 215-216
4. Morio I. Globalization of Dental Education The Journal of International College of Dentists Japan Section. 2019.07; 50(1); 49 -51

5. Mizutani K, Noritake K, Tsuruta J, Seki N, Kondo K, Katagiri S, Takeuchi Y, Akizuki T, Shiroyama H, Aoki A, Izumi Y, Iwata T, Arakawa S, Araki K. Clinical and educational effects of a new interprofessional program for dental students and dental hygiene students in practical clinical training Journal of the Japanese Society of Periodontology. 2019.09; 61(3); 148-156

[Conference Activities & Talks]

1. Morio I. Globalization of Dental Education. 49th Annual Session of the International College of Dentists, Japan Section 2019.03.10 Tokyo, JAPAN
2. Seki N, Moross J, Osato A, Sunaga M, Shinada K, Morio I, Kinoshita A. Development of clinical simulation teaching materials in English for dental hygienist education -the second report-. 38th Annual Meeting of the Japanese Dental Education Association 2019.07.19 Fukuoka
3. Moross J, Seki N, Sunaga M, Osato A, Kinoshita A, Morio I. Importance of preparatory courses for international exchange programs. 4th Meeting of the International Association for Dental Research Asia Pacific Region 2019.11.29 Brisbane, Australia
4. Seki N, Moross J, Sunaga M, Osato A, Kinoshita A, Morio I. e-Learning to supplement learning deficits for decision-making in English. 4th Meeting of the International Association for Dental Research Asia Pacific Region 2019.11.30 Brisbane, Australia
5. Seki N, Mizutani K, Hosaka K, Komada W, Kanazawa M, Komagamine Y, Moross J, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Essential Expertise for Clinical Dentistry (EECD), International Dental Clinical Education Course for Graduate School of Medical and Dental Sciences. The 84th annual meeting of the Stomatological Society 2019.12.07 Tokyo

Oral Health Promotion

Professor	Yoko Kawaguchi
Assistant Professor	Takashi Zaitso
Assistant Professor	Akiko Oshiro
Office administrator	Yuko Onishi (till March) Nami Kokuryu(from April)
Registered Resident	Hiromi Nishiyama
Graduate Student	Toshiya Kanazawa(till March) Takashi Tanemura Jin Aoki Zar Chi Kyaw Myint Nguyen Thi Nhat Vy Tomoya Saito Srinarupat Jarassri Chou Jan(till September) Yuko Inoue(from 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. Relationship between oral health and general health
3. Diagnosis and treatment system construction of oral malodor
4. Oral health care system
5. International oral health
6. Tele-dental system
7. Oral health promotion

(2) Lectures & Courses

1) Graduate School Education, 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 School 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 fifth and sixth 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, Akiko Oshiro, Yoko Kawaguchi. Relationship between Medical and Dental Health Expenditures of Industrial Workers Journal of Oral Health and Community Dentistry. 2019; 13(2); 54-58
2. Anish Harshad Kothari, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Application of a Visual Oral Health Literacy Instrument in Elementary Schoolchildren Primary Care Epidemiology and Global Health. 2019.01; 1; 19-29
3. Sachiko Takehara, Jorge L. Zeredo, Yasuhiro Kumei, Kensuke Kagiya, Kazumasa Fukasawa, Akiko Oshiro, Masayuki Ueno, Noriko Kojimahara, Shunsuke Minakuchi, Yoko Kawaguchi. Characterization of oral microbiota in marmosets: Feasibility of using the marmoset as a human oral disease model. PLoS ONE. 2019.02; 14(2); e0207560
4. Kaung Myat Thwin, Wa Than Lin, Zar Chi Kyaw Myint, Takashi Zaitzu, Akiko Oshiro, Masayuki Ueno, Yoko Kawaguchi. Oral Health Status and Oral Health Services Utilization of Myanmar Residents in Japan Myanmar Health Sciences Research Journal, . 2019.04; 31(1);
5. Ei Ei Aung, Akiko Oshiro, Takashi Zaitzu and Yoko Kawaguchi. Relationship of Halitosis Concern with Oral Health Behaviors and Knowledge Among Myanmar People science repository. 2019.10; 1(1);
6. Ei Ei Aung, Takashi Zaitzu, Akiko Oshiro and Yoko Kawaguchi. Oral Malodor Knowledge Among Myanmar Dental Students and Young Dentists science repository. 2019.10; 1(1);
7. Zar Chi Kyaw Myint, Takashi Zaitzu, Akiko Oshiro, Masayuki Ueno, Ko Ko Soe, Yoko Kawaguchi. Risk Indicators of Dental Caries and Gingivitis among 10-11-year-old Students in Yangon, Myanmar International Dental Journal . 2019.10;

[Conference Activities & Talks]

1. Takashi Zaitzu. Using “Implementation Intentions” to Promote Oral Health Behavior: Results of a Workplace Intervention. International Symposium on Life-course Oral Health Promotion 2019.04.05 Tokyo Medical and Dental University, Tokyo, Japan
2. Nguyen Thi Nhat Vy, Zaitzu Takashi, Oshiro Akiko, Kawaguchi Yoko. 12歳のベトナム人集団における主観的な口腔衛生に関する認識と口腔衛生状況の関係性 (Relationship between self-perceived oral health and oral health status among 12-year-olds in Vietnam). 第68回日本口腔衛生学会・総会 2019.05.24 ピアザ淡海, 滋賀

3. Srinarupat Jarassri, Zaitsu Takashi, Oshiro Aikiko, Kawaguchi Yoko. タイ人集団における口腔衛生状況と口腔衛生に関する行動 (Oral health status and oral health behaviors of Thai population). 第 68 回日本口腔衛生学会・総会 2019.05.24 ピアザ淡海, 滋賀
4. Zar Chi Kyaw Myint, Zaitsu Takashi, Oshiro Akiko, Kawaguchi Yoko. ミャンマーの中学生における口腔衛生に関する知識と関連因子 (Oral health literacy and its related factors among middle school students in Myanmar). 第 68 回日本口腔衛生学会・総会 2019.05.24 ピアザ淡海, 滋賀
5. Aung Ei Ei, Oshiro Akiko, Zaitsu Takashi, Kawaguchi Yoko. ミャンマー人における口臭に対する懸念と口腔衛生の行動および知識との関連性 (Relationship of halitosis concern with oral health behaviors and knowledge among Myanmar people). 第 68 回日本口腔衛生学会・総会 2019.05.24 ピアザ淡海, 滋賀
6. Takashi Zaitsu, Tomoya Saito, Akiko Oshiro, Yoko Kawaguchi. Using implementation intention to promote oral health behavior and oral health status. The 97th IADR/APR General Session & Exhibition 2019.06.20 Vancouver, BC, Canada
7. Takashi Zaitsu. The importance of oral health management for Japanese Antarctic Research Expedition Team.. 南極医学医療ワークショップ 2019 2019.07.20 国立極地研究所、立川市
8. Zar Chi Kyaw Myint, Takashi Zaitsu, Akiko Oshiro, Yoko Kawaguchi. ORAL HEALTH EDUCATION WITH A PEER GROUP APPROACH MODEL. The 10th Asian Conference of Oral Health Promotion for School Children 2019.09.20 The Wembley - A St Giles Hotel, Penang, Malaysia
9. Haslina Rani, Takashi Zaitsu, Yoko Kawaguchi. FACTORS RELATED TO HALITOSIS AMONG HIGH SCHOOL STUDENTS. The 10th Asian Conference of Oral Health Promotion for School Children 2019.09.20 The Wembley - A St Giles Hotel, Penang, Malaysia
10. Naoko Yamamuro, Aiko Suzuki, Kazuhiko Kubo, Izumi Yokoyama, Nakako Ogawa, Satoru Kabe, Hidekazu Hagiwara, Kazuhiko Kaneda, Taizo Minegishi, Yoko Kawaguchi, Yasushi Yamazaki, Yukimichi Komori, Shoji Sawada, Hiroshi Suzuki, Yoshimi Naganuma, Hideyo Suetaka. RESEARCH ON SCHOOL DENTAL HEALTH IN THE TOKYO METROPOLITAN AREA. The 10th Asian Conference of Oral Health Promotion for School Children 2019.09.20 The Wembley - A St Giles Hotel, Penang, Malaysia
11. Takashi Zaitsu. The importance of oral health management for Japanese Antarctic Research Expedition Team. The 10th Conference of the Korean Society Polar Medicine 2019.10.19 Seoul, Republic of Korea
12. Zar Chi Kyaw Myint, Zaitsu Takashi, Oshiro Akiko, Ko Ko Soe, Kawaguchi Yoko. Effectiveness of Oral Health Education for Myanmar Middle school students.. 4th Meeting of the International Association for Dental Research Asia-Pacific Region 2019.11.29 Brisbane Conventional Center, Australia.
13. Seki N, Mizutani K, Hosaka K, Komada W, Kanazawa M, Komagamine Y, Moross J, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Essential Expertise for Clinical Dentistry (EECD), International Dental Clinical Education Course for Graduate School of Medical and Dental Sciences. The 84th annual meeting of the Stomatological Society 2019.12.07 Tokyo

[Social Contribution]

1. International Seminar Public Health Dentistry between Japan and Thailand, Department of Oral Health Promotion Graduate School of Medical and Dental Sciences Tokyo Medical and Dental University, 2019.08.27

Sports Medicine and Dentistry

[Associate Professor] Toshiaki Ueno
[Assistant Professor] Hiroshi Churei
[Clinical fellow] Kairi Hayashi
[Graduate Student] Nana Kamiya-Shiota, Phyu Sin Tun, Rio Kinjo, Thet Khaing Aung, Yuumi Takahashi, Misaki Suzaka, Keishi Fujimoto
[Research Student] Kaito Togawa
[Part-time Instructor] Goshi Kondo, Yukio Sasaki, Ryo Sato, Takuto Yamanaka, Sachiko Fujino, Yuriko Yoshida, Gen Tanabe, Takefumi Negoro, Kazushi Watanabe
[Part-time Resident] Takaaki Fukuda, Chie Ichihara, Yoko Ohara, Akira Nagai
[Research fellow] Ruman Uddin Chowdhury

(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-Gaisetu
- 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 facilities>

Department of Sports Medicine/Dentistry: Mouthguard training facility certified by Japanese Academy of Sports Dentistry(JASD)

Clinic of Sports Dentistry in University Hospital: Medical Check-up Facility certified Japan Paralympic Committee

< Certified specialists>

Toshiaki Ueno (1.JSPO Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3.Mouthguard technical instructor certified by JASD, 4.Dental specialist certified by Japanese Academy of Maxillofacial Prosthetics, 5.Dental Material Senior Advisor certified by Japanese Society of Dental Materials and Devices), 4.Dental specialist certified by Japanese Academy of Dental Traumatology, 7.JPSA Sports Dentist certified by Japanese Para-Sports Association

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

Kairi Hayashi (1.JSPO Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3. MG technical instructor certified by JASD)

Sachiko Fujino (1.JSPO Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3.MG technical instructor certified by JASD)

Yuriko Yoshida (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Gen Tanabe (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Nana Kamiya-Shiota (1.JSPO Sports Dentist certified by Japan Sports Association, 2. MG technical instructor certified by JASD)

Misaki Suzaka(1. Sports dental hygienist certified by JASD)

(7) Publications

[Conference Activities & Talks]

1. Ueno T. Sports dentistry and mouthguard. GAMEX 2019-Gyeonggi International Dental Academic Meeting 2019.08.31 Seoul, Korea
2. Kazuhiro HIKITA, Takeo MAIDA, Yumiko ENAMI, Masahiro IJIMA, Tun Sin PHYU, Hiroshi CHUREI, Toshiaki UENO, Hidekazu TAKAHASHI. Manufacturing of sports mouthguard by digital technology . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
3. Phyu Sin TUN, Hiroshi CHUREI, Gen TANABE, Thet Khaing AUNG, Shingo KAMIJO, Meiko OKI, Hidekazu TAKAHASHI, Kazuhiro HIKITA, Toshiaki UENO. Shock-absorbing capability of rubber-like and rigid 3D printing materials compared to commercial mouthguard materials . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
4. Togawa K, Aung TK, Takahashi Y, Suzaka M, Tanabe G, Hayashi K, Churei H, Ueno T. Application of custom-designed faceguard to prevent eye injury for professional futsal player: a case report. World Congress on Dentistry and Oral Health 2019 2019.11.21 Kuala Lumpur, Malaysia
5. Hayashi K, Chowdhury RU, Chowdhury NU, Togawa K, Toyoshima Y, Churei H, Ueno T. Survey on thickness changes and deformations of custom-made mouthguards after 2 years of use by Bangladesh field hockey players. World Congress on Dentistry and Oral Health 2019 2019.11.21 Kuala Lumpur, Malaysia

[Awards & Honors]

1. Best Poster Award (Hayashi K), World Congress on Dentistry and Oral Health 2019, 2019.11

Educational System in Dentistry

Professor Kouji ARAKI
 Associate Professor Jun TSURUTA
 Junior Associate Professor(non-full time) Kouji IIDA
 Hiroki KATAOKA
 Graduate Student Akitaka HATTORI, Kanako TODA (～ 2019.3)
 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. Toda K, Mizutani K, Minami I, Ye M, Arakawa T, Mitsubayashi K, Ogawa Y, Araki K, Shinada K. Effects of oral health instructions on glycemic control and oral health status of periodontitis patients with type 2 diabetes mellitus: A preliminary observation. *Journal of Dental Sciences*. 2019.06; 14(2); 171-177

[Conference Activities & Talks]

1. Sachi Umemori et al.. Association between second-hand smoking and dental caries in children, results from the A-CHILD study. The 29th Annual scientific meeting of the Japan Epidemiological Association 2019.01.31 Tokyo
2. Kanako Noritake, Jun Tsuruta, Mina Nakagawa, Kumiko Yamaguchi, Tomoe Miyoshi, Kouji Araki.. The effect of a program that medical students learn from dental students in dental student clinic.. The 51st annual meeting of Japan Society of Medical Education 2019.07.26 Kyoto
3. Sachi Umemori, Kenichi Tonami, Hiroshi Nitta, Araki Kouji. The Analysis of Unprofessional behavior in the class in Faculty of Dentistry, TMDU. The 51st Annual Meeting of tha Japan Society for Medical Education 2019.07.27 Kyoto
4. Jun Tsuruta,Kanako Noritake, Kouji Araki. IMPROVEMENT OF IPE PROGRAM FOR DENTAL STUDENTS TEACHING MEDICAL STUDENTS AT THE DENTAL STUDENT' S CLINIC. 2019 Sounth East Asia Assciation for Dental Edcuation, Malaysia, 2019.08.06 QL
5. Akitaka Hattori ,Jun Turuta,Yasuyuki Kimura , Masayuki Hideshima, Kouji Araki. Study on the correlation between artificial tooth cutting and VR simulator. Japan Association for Simulation-based Education in Healthcare Professionals 2019.09.21 Tokyo
6. Akitaka Hattori ,Jun Turuta,Yasuyuki Kimura , Masayuki Hideshima, Kouji Araki. Study on the correlation between artificial tooth cutting and VR simulator. The Stomatological Society,Japan 2019.12.06 Tokyo
7. Yuna Kanamori, Kanako Noritake, Sachi Umemori, Maiko Iwaki, Daisuke Kido, Shogo Takeuchi, Akitaka Hattori, Ken-ichi Tonami, Arata Ebihara, Masayuki Hideshima, Kouji Araki, Hiroshi Nitta. Introduction of objective clinical skills examination for TMDU's trainee residents. 2019.12.07

[Social Contribution]

1. The Journal of Dental Education,peer reviewer, 2015.08.01 - Now
2. European Journal of Dental Education,peer reviewer, 2017.09.01 - Now

Educational Media Development

Professor KINOSHITA Atsuhiko
 Assistant Professor SUNAGA Masayo
 Graduate Student CAO Ridan(∼ March)
 Graduate Student AKIYAMA Kyoko
 Graduate Student HARADA Yusuke
 Graduate Student TAKENOUCHI Akane
 Graduate Student URAKAWA Ayaka(April ∼)
 Graduate Research Student YANG Shengsen(October ∼)

(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 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.

(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-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. Akane Takenouchi, Masayo Sunaga, Yuki Ohara, Takashi Matsukubo, Atsuhiko Kinoshita. Development and evaluation of an English learning system using smartphones in Japanese dental hygiene education Journal of Medical and Dental Sciences. 2019.09; 66; 51-58

[Conference Activities & Talks]

1. Akane Takenouchi, Yukiko Satoh, Hiroe Arai, Yumiko Kakegawa, Etsuyo Otani, Atsuhiko Kinoshita, Takashi Matsukubo. Effects of ultrasonic toothbrushes with different frequencies on oral hygiene. IADR General Session & Exhibition, 19-22 June 2019.06.22 Vancouver, Canada
2. Atsuhiko Kinoshita, Masayo Sunaga. Dental Education with ICT. - Introduction of TMDU SimPrac - IT Simulation 1, Educational Session. International Faculty Development Course(IFDC) 2019 2019.11.18 Tokyo Medical and Dental University (TMDU), Bunkyo-ku, Tokyo
3. Atsuhiko Kinoshita, Masayo Sunaga. Dental Education with ICT. Hands-on. IT Simulation 2, Educational Session. International Faculty Development Course(IFDC) 2019 2019.11.19 Tokyo Medical and Dental University (TMDU), Bunkyo-ku, Tokyo
4. Janelle MOROSS, Naoko SEKI, Masayo SUNAGA, Ai OSATO, Atsuhiko KINOSHITA, Ikuko MORIO. Importance of preparatory courses for international exchange programs. 4th Meeting of the International Association for Dental Research Asia Pacific Region 2019, 28-30 November 2019.11.29 Brisbane, Australia
5. Naoko SEKI, Janelle MOROSS, Masayo SUNAGA, Ai OSATO, Atsuhiko KINOSHITA, Ikuko MORIO. e-Learning to supplement learning deficits for decision-making in English. 4th Meeting of the International Association for Dental Research Asia Pacific Region 2019, 28-30 November 2019.11.30 Brisbane, Australia

Department of Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD
 Junior Associate Professor: Kaoruko Seino, PhD
 JSPS Research Fellow: Md. Mosiur Rahman, PhD
 Research Fellow: AL-SOBAIHI Saber, RN, MPH, PhD;
 Isaac Maro, MD, MPH, PhD;
 Graduate Student:
 Hoang Thuy Linh Nguyen, MD, MPH; Ahmad Shekib Arab, MD;
 Yuri Tashiro, MPharm, MPH; Deogratius Bintabara MD, MSc;
 TJ Robionson Moncatar, RN, MPH;
 Kathryn Lizbeth Lucena Siongco, RN, RM;
 Tran Dai Tri Han, MD, MPH; Hue Man Vo, MD;
 HASAN S M Mahmudul Hasan, DMD;
 Shayo Festo Kasmir, MD; Alemi Sharifullah, MD;
 Romnalin Thonglor, MPH;
 Ayano Miyashita, MSc; Kouki Akahoshi, MD;
 Yasushi Sakuramoto MD, MPH, MPA;
 Rueda Saleh Alojaimy, RN

(1) Outline

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

(2) Research

Major Research Topics:

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

(3) Education

PhD programs

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

conducted in English, thus facilitating the acquisition of international communication skills.

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

Master Programs

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

(4) Lectures & Courses

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

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

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

(5) Publications

[Original Articles]

1. Ngyen HTL, Nakamura K, Seino K, Al-Sobaihi S. Impact of parent–adolescent bonding on school bullying and mental health in Vietnamese cultural setting: evidence from the global school-based health survey. *BMC Psychology*. 2019.03; 7; 16
2. Watanabe N, Nakamura K, Nguyen HTL, Seino K, Van VT. Assessment of the validity of a physical activity questionnaire for Vietnamese children using an accelerometer. *International Journal of Physical Therapy & Rehabilitation*. 2019.03; 5; 149
3. Bintabara D, Nakamura K, Ntwenya J, Seino K, Mpondo BCT.. Adherence to standards of first-visit antenatal care among providers: a stratified analysis of Tanzanian facility-based survey for improving quality of antenatal care. *Plos ONE*. 2019.05; 14(5); e0216520
4. Miyashita A, Hiraki A, Nakamura K, Takano T, Seino K, Al-Sobaihi S, Heng NM, Pichenda K. . Geographical patterns of tuberculosis notification rates and their associations with sociodemographic characteristics in communes in Phnom Penh, Cambodia. *Journal of Tuberculosis Research*. 2019.05; 7; 118-129
5. Arab AS, Nakamura K, Seino K, Hemat S, Mashal MO, Tashiro Y. Lipid and diabetic profiles of school teachers in Afghanistan facing food insecurity and their association with knowledge relating to healthy lifestyle. *Food and Nutrition Sciences*, 2019, 10, 678-693. 2019.06; 10; 678-693
6. Alemi Sharifullah, Nakamura Keiko, Seino Kaoruko. アフガニスタンの女性が受ける産後ケアの地方と都市の不平等性 (Rural-Urban Disparities in Receiving Antenatal Care among Women in Afghanistan) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 266

7. Rueda Alojaimy, Nakamura Keiko, Seino Kaoruko. サウジアラビア王国における看護従事者の人口統計学的特徴と認識 (Demographic Characteristics and Perceptions of Nurses Working in Saudi Arabia) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 599
8. Thonglor Romnalin, Tejavaddhana Phudit, Nakamura Keiko, Seino Kaoruko. タイ国北部の都市部一次健康ケア施設の健康管理者の展望 (Health manager perspectives of an urban Primary Health Care in northern Thailand) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 599
9. Shayo Festo, Nakamura Keiko, Seino Kaoruko. タンザニアの結核治療施設は糖尿病治療の提供準備ができているのか (Are Tanzanian tuberculosis facilities ready to provide management of diabetes?) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 265
10. Hasan S.M. Mahmudul, Nakamura Keiko, Seino Kaoruko, Rahman Md Mosiur. バングラデシュの2型糖尿病患者の歯周炎に対する身体活動の影響 (Effects of Physical Activity on Periodontitis in type 2 diabetes in Bangladesh) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 597
11. Siongco Kathryn Lizbeth Lucena, Nakamura Keiko, Moncatar T.J. Robinson, Canila Carmelita, Lorenzo Fely Marilyn, Seino Kaoruko, Takano Takehito. フィリピンの高齢者における健康施設の利用方法の予測因子 (Predictors of type of health facility use among elderly in the Philippines) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 598
12. Siongco Kathryn Lizbeth Lucena, Nakamura Keiko, Robinson Moncatar T.J., Canila Carmelita, Lorenzo Fely Marilyn, Seino Kaoruko, Takano Takehito. フィリピンの高齢者における健康施設の利用方法の予測因子 (Predictors of type of health facility use among elderly in the Philippines) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 191
13. Miyashita Ayano, Al-Sobaihi Saber, Nakamura Keiko, Seino Kaoruko, Hiraki Aya. プノンペンの地方自治体における就労業種と TB 感染の関係性の検証 (Validation of occupational participation in TB in communes, Phnom Penh) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 265
14. Tran Dai Tri Han, Nakamura Keiko, Vo Thi Hue Man, Seino Kaoruko, Vo Van Thang, Takano Takehito. ベトナム中央部の高齢者の手段的日常生活動作の分析 (Instrumental activities of daily living of the elderly in the central Viet Nam) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 263
15. Vo Thi Hue Man, Nakamura Keiko, Tran Dai Tri Han, Vo Van Thang, Seino Kaoruko, Takano Takehito. ベトナム人高齢者における認知機能障害と転倒恐怖感の関係性 (Cognitive impairment and fear of falling among older Vietnamese adults) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 597
16. Moncatar T.J. Robinson, Nakamura Keiko, Siongco Kathryn Lizbeth Lucena, Seino Kaoruko, Canila Carmelita, Lorenzo Fely Marilyn, Takano Takehito, Rahman Md Mosiur. 独居のフィリピン人高齢者の住宅は NCD および施設の利用に影響を及ぼすのか (Does the residence of Filipino elderly living alone affect NCD and facility use?) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 598
17. Deogratijs Bintabara, Nakamura Keiko, Seino Kaoruko. 誰も見捨てるな 一定数のアフリカ人女性はヘルスケアへのアクセスが困難である (Leave no one behind: some African women face difficulty in accessing healthcare) 日本公衆衛生学会総会抄録集. 2019.10; 78 回; 192
18. Moncatar, T.R., Nakamura, K., Rahman, M. and Seino, K. . Health status and health facility utilization of community-dwelling elderly living alone in the Philippines: A nationwide cross-sectional study. Health. 2019.11; 11; 1554-1572
19. Tashiro, Y., Nakamura, K., Seino, K. et al.. The impact of a school-based tooth-brushing program on dental caries: a cross-sectional study. Environ Health Prev Med . 2019.12; 24; 83
20. Tashiro Yuri, Nakamura Keiko, Seino Kaoruko, Ochi Shiro, Ishii Hiroshi, Hasegawa Masaru, Kawauchi Yoshimichi, Chiba Mitsuyuki. The impact of a school-based tooth-brushing program on dental caries: a cross-sectional study(和訳中) Environmental Health and Preventive Medicine. 2019.12; 24; 1 of 9-9 of 9

[Misc]

1. Nakamura K. SDGs framework to promote public health activities and actions in communities 2019.07; 83(7); 496-498
2. Nakamura K. Featuring a Sustainable City Trends in the Sciences. 2019.10; 24(10); 66-70

[Conference Activities & Talks]

1. Nakamura K. Interprofessional training for delivering quality services for older people in the Philippines and Viet Nam. 2019.02.21 Manila
2. 中村桂子. 持続可能な開発目標（SDGs）の達成 にむけた元気な健康都市づくりの展開. 第15回健康都市連合日本支部大会 2019.07.30 香川県高松市
3. Nakamura K.. Community mHealth Integrated Care (ComHIC) to manage hypertension/diabetes in Tanzania' s overburdened health system. Multistakeholders Research Meeting 2019.08.09
4. Nakamura K.. Workforce Development to Improve Quality Health and Social Care Services for Older Adults in ASEAN Countries.. 7th International Health Literacy Conference 2019.11.11 Ho Chi Minh

Rehabilitation Medicine

Professor	Atsushi Okawa
Assistant Professor	Tomoko SAKAI
Associate Professor	Tetsuya JINNO
Assistant Professor	Dai UKEGAWA
Assistant Professor	Chisato HOSHINO
Assistant Professor	Reiko YAMAGUCHI(-Sep.)

Graduate Student	Kazuko KATSUKI
	Shunsuke OHJI
	Ryo ONUMA
	Yuji TAKAHASHI
	Kenji HIROHATA
	Tomoko KAWASAKI
	Keigo NANJO

(1) Research

Research Subjects

- 1) Rehabilitation for total joint arthroplasty
- 2) Motion and gait analysis of healthy and disabled subjects
- 3) Biomechanical research for prevention of sports injury
- 4) Patient safety in rehabilitation medicine
- 5) Osteoporosis of children (individuals) with severe motor and intellectual disabilities

(2) Lectures & Courses

Purpose of Education:

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

(3) Publications

[Original Articles]

1. Tomoko Sakai, Tetsuya Jinno, Chisato Hoshino, Atsushi Okawa. Cancellation criteria of acute rehabilitation :rehabilitation risk management. Progress in Rehabilitation Medicine. 2019; 4;
2. Kimura Y, Yamada M, Ishiyama D, Nishio N, Kunieda Y, Koyama S, Sato A, Otobe Y, Ohji S, Suzuki M, Ogawa H, Ito D, Ichikawa T, Hamanaka K, Tanaka N, Muroh Y. Impact of unilateral spatial neglect

with or without other cognitive impairments on independent gait recovery in stroke survivors. *Journal of rehabilitation medicine*. 2019.01; 51(1); 26-31

3. Yamada M, Kimura Y, Ishiyama D, Nishio N, Otobe Y, Tanaka T, Ohji S, Koyama S, Sato A, Suzuki M, Ogawa H, Ichikawa T, Ito D, Arai H. Synergistic effect of bodyweight resistance exercise and protein supplementation on skeletal muscle in sarcopenic or dynapenic older adults. *Geriatrics & gerontology international*. 2019.03;
4. Ohji S, Kimura Y, Otobe Y, Nishio N, Ito D, Taguchi R, Ogawa H, Yamada M. Measurement of self-propulsion distance of wheelchair using cycle computer excluding assistance distance by touch switch: A pilot study. *The journal of spinal cord medicine*. 2019.04; 1-5
5. Kimura Y, Yamada M, Ohji S, Ishiyama D, Nishio N, Otobe Y, Koyama S, Suzuki M, Ichikawa T, Ito D, Maehori N, Nagae H. Presence of sarcopenic obesity and evaluation of the associated muscle quality in Japanese older men with prostate cancer undergoing androgen deprivation therapy. *Journal of geriatric oncology*. 2019.04;
6. Chisato Hoshino, Daisuke Koga, Gaku Koyano, Yuki Yamauchi, Tomoko Sakai, Atsushi Okawa A, Tetsuya Jinno. Femoral nerve palsy following primary total hip arthroplasty with the direct anterior approach. *PLoS one*. 2019.05; 14(5);
7. Junya Aizawa, Shunsuke Ohji, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Kazuyoshi Yagishita. Relationship between asymmetrical jump-landing impact and quadriceps strength after unilateral anterior cruciate ligament reconstruction *Physical Medicine and Rehabilitation Research*. 2019.07; 4; 1-6
8. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Kazuyoshi Yagishita. Correlations between vertical ground reaction force, sagittal joint angles, and the muscle co-contraction index during single-leg jump-landing *Asian journal of sports medicine*. 2019.07; 10(3);
9. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Kazuyoshi Yagishita, Toshitaka Yoshii, Atsushi Okawa. Supine versus lateral position for accurate positioning of acetabular cup in total hip arthroplasty using the modified Watson-Jones approach: A randomized single-blind controlled trial. *Orthop Traumatol Surg Res*. 2019.09; 105(5); 915-922
10. Takashi Ikeda, Yuki Matsunaga, Masanori Kanbara, Arinori Kamono, Tadashi Masuda, Minoru Watanabe, Ryosuke Nakanishi, Tetsuya Jinno. Effect of exercise therapy combined with branched-chain amino acid supplementation on muscle strength in elderly women after total hip arthroplasty: a randomized controlled trial. *Asia Pac J Clin Nutr*. 2019.12; 28(4); 720-726

[Conference Activities & Talks]

1. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Atsushi Okawa. Accuracy of cup positioning of supine vs. lateral position in total hip arthroplasty using anterolateral approach: A prospective, randomized, controlled trial. *American Academy of Orthopaedic Surgeons 2019* 2019.03
2. Tomoko Sakai, Chisato Hoshino, Dai Ukegawa, Atsushi Okawa. The effect of daily multidisciplinary round to early mobilization in ICU. *13th International Society of Physical and Rehabilitation Medicine World Congress 2019*.06
3. Naoki Yamamoto, Tomoko Sakai, Dai Ukegawa, Chisato Hoshino, Jinno Tetsuya, Atsushi Okawa. Earlier mobility with T-cane after total knee arthroplasty influences long-term mobility. *13th International Society of Physical and Rehabilitation Medicine World Congress 2019*.06

Gerodontology and Oral Rehabilitation

Professor

MINAKUCHI Shunsuke

Associate Professor

TOHARA Haruka

Junior Associate Professor

SEKITA Toshiaki, KOBAYASHI Ken-ichi, KUBOTA Kazumasa

Assistant Professor

INOKOSHI Masanao, KANAZAWA Manabu, KOMAGAMINE Yuriko, MOTOMURA Kazuo,
NAKAGAWA Kazuharu, NAKANE Ayako, SATO Yusuke, OKUBO Mai, HAMA Yohei

Project Assistant Professor

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Dental Resident

ARAKIDA Toshio, UEDA Kaori, BABA Yuya, MIYAYASU Anna, YAMAGUCHI Kohei,
YOSHIMI Kanako, ASAMI Mari

Graduate Student

VO LAM THUY, KHAING MYAT THU, KAGIFUKU Yuko, KYOSAKA Yuka, KUROSAWA Yukiko,
SHIMADA Ryo, SHIMIZU Haruki, SHIMIZUBATA Makoto, DOKE Midori, MIURA Akemi,
YOSHIDA Saori, YOSHINAKA Shin, SOEDA Yumika, CHANTARAMANI Ariya, TUN MIN BO,
NEGORO Masatoshi, HASEGAWA Shohei, HADA Tamaki, HATANO Keita, HARA Yoshiko, ISHII Miki,
UEHARA Yoko, OTAKE Ryosuke, ONUMA Hiraku, OKUMURA Takuma, OBANA Michiyo,
KAKU Jakuen, KATHENG AWUTSADAPORN, SAI TUN NAING, SHIROBE Maki,
TAKAGI Daisuke, TAKANO Satoru, THAW DI CHO TOO, NOMOTO Akiko, MATSUBARA Chiaki,
YAMAMOTO Mao, KATADA Haruko, KAWASHIMA Mina, SHIMIZU Kento, TAMAI Tomoe,
TONPRASONG WATCHARAPONG, NAKAI Hiroto, NAGASAWA Yuki, YANAGIHARA Yuiko,
YAMAGUCHI Kohei, YOSHIKAWA Akira, LIU HENGYI, WATANABE Masataka

Staff

TERADA Mito, FUKUSHIMA Rie

(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
- 18) Development of novel restorative materials for root caries
- 19) Development of novel aesthetic, strong and ageing resistant highly translucent zirconia
- 20) Ultrastructural analysis of zirconia-veneering ceramic interface

(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. Tomoka Matsumura, Chihiro Suzuki, Kazumasa Kubota, Shunsuke Minakuchi, Fukayama Haruhisa. Difficult nasal intubation using Airway Scope for a child with large tumor. *Anesthesia Progress*. 2019.01; 65(5); 251-254
2. Komagamine Y, Kanazawa M, Sato Y, Iwaki M, Jo A, Minakuchi S. Masticatory performance of different impression methods for complete denture fabrication: a randomized controlled trial. *Journal of dentistry*. 2019.01;
3. Sachiko Takehara, Jorge L. Zeredo, Yasuhiro Kumei, Kensuke Kagiya, Kazumasa Fukasawa, Akiko Oshiro, Masayuki Ueno, Noriko Kojimahara, Shunsuke Minakuchi, Yoko Kawaguchi. Characterization of oral microbiota in marmosets: Feasibility of using the marmoset as a human oral disease model. *PLoS ONE*. 2019.02; 14(2); e0207560
4. Yojiro Umezaki, Trang T H Tu, Akira Toriihara, Yusuke Sato, Toru Naito, Akira Toyofuku. Change of Cerebral Blood Flow After a Successful Pharmacological Treatment of Phantom Bite Syndrome: A Case Report. *Clin Neuropharmacol*. 2019.02;
5. Taniguchi H, Matsuo K, Nakagawa K, Furuya J, Kanazawa M, Minakuchi S. Decline in tongue pressure during perioperative period in cancer patients without oral feeding. *Clin Nutr ESPEN*. 2019.02; 29; 183-188
6. Yamaguchi K, Tohara H, Hara K, Nakane A, Yoshimi K, Nakagawa K, Minakuchi S. Factors associated with masseter muscle quality assessed from ultrasonography in community-dwelling elderly individuals: A crosssectional study. *Archives of Gerontology and Geriatrics*. 2019.02; 12(82); 128-132

7. Hara Koji, Tohara Haruka, Kenichiro Kobayashi, Yamaguchi Kohei, Ariya Chantaramanee, Yoshimi Kanako, Nakane Ayako, Minakuchi Shunsuke. Association between tongue muscle strength and masticatory muscle strength Journal of Oral Rehabilitation. 2019.02; 46(2); 134-139
8. Nakagawa K, Matsuo K. Assessment of oral function and proper diet level for frail elderly individuals in nursing homes using chewing training food. J Nutr Health Aging. 2019.03; 23(5); 483-489
9. Namiki C, Hara K, Tohara H, Kobayashi K, Chantaramanee A, Nakagawa K, Saitou T, Yamaguchi K, Yoshimi K, Nakane A, Minakuchi S. Tongue pressure Resistance training improves tongue and suprahyoid muscle functions simultaneously. Clinical Interventions in Aging. 2019.03; 14; 601-608
10. Chizuru Namiki, Koji Hara, Haruka Tohara, Kenichiro Kobayashi, Ariya Chantaramanee, Kazuharu Nakagawa, Takayuki Saitou, Kohei Yamaguchi, Kanako Yoshimi, Ayako Nakane, Shunsuke Minakuchi. Tongue-pressure resistance training improves tongue and suprahyoid muscle functions simultaneously. Clinical Interventions in Aging. 2019.03; 14; 601-608
11. Ariya Chantaramanee, Haruka Tohara, Kazuharu Nakagawa, Koji Hara, Ayako Nakane, Kohei Yamaguchi, Kanako Yoshimi, Furuya Junichi, Shunsuke Minakuchi. Association between echo intensity of the tongue and its thickness and function in elderly subjects. Journal of Oral Rehabilitation.. 2019.03; 634-639
12. Hiroko Mori, Mariko Naito, Ayako Nakane, Haruka Tohara. Caregivers' Perspectives on the Slight Recovery of Oral Intake of Home-Dwelling Patients Living With a Percutaneous Endoscopic Gastrostomy Tube: A Qualitative Study Using Focus Group Interviews. Nutrition in Clinical Research. 2019.04; 34(2); 272-279
13. Saori Yoshida, Haruka Tohara, Kazuharu Nakagawa, Koji Hara, Kohei Yamaguchi, Ayako Nakane, Kanako Yoshimi, Chantaramanee Ariya, Yukiko Kurosawa, Shunsuke Minakuchi. Relationship between jaw-opening force and neck circumference in healthy older individuals. Geriatr Gerontol Int. 2019.04; 19(4); 330-334
14. G Ohwada, S Minakuchi, Y Sato, H Kondo, T Nomura, A Tsuboi, G Hong, Y Itoh, Y Kawai, S Kimoto, A Gunji, A Suzuki, T Suzuki, K Kimoto, N Hoshi, M Saita, Y Yoneyama, Y Sato, M Morokuma, J Okazaki, T Maeda, K Nakai, T Ichikawa, K Nagao, K Fujimoto, H Murata, T Kurogi, K Yoshida, M Nishimura, Y Nishi, M Murakami, T Hosoi, T Hamada. Subjective Evaluation of Denture Adhesives: A Multicenter Randomized Controlled Trial. JDR Clinical & Translational Research. 2019.04; 2380084419837607
15. Aung SSMP, Takagaki T, Lyann SK, Ikeda M, Inokoshi M, Sadr A, Nikaido T, Tagami J. Effects of alumina-blasting pressure on the bonding to super/ultra-translucent zirconia. Dent Mater. 2019.05; 35(5); 730-739
16. Kubota K, Kyosaka Y, Ueda K, Minakuchi S. Increase in pulse pressure on administration of a dental local anesthetic solution, prilocaine hydrochloride with felypressin in male diabetic patients with coronary heart disease. Clinical oral investigations. 2019.05; 239-246
17. Hiroyuki Suzuki, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Noriko Amagai, Shunsuke Minakuchi. Changes in the nutritional statuses of edentulous elderly patients after new denture fabrication with and without providing simple dietary advice. J Prosthodont Res. 2019.07; 63(3); 288-292
18. Yamaga Eijiro, Sato Yusuke, Soeda Hitomi, Minakuchi Shunsuke. Structural equation modeling of the impact of mandibular ridge form and denture quality on oral health-related quality of life in complete denture wearers. Journal of Prosthodontic Research. 2019.07; 63(3); 293-298
19. Yamaga Eijiro, Sato Yusuke, Soeda Hitomi, Minakuchi Shunsuke. Relationship between oral health-related quality of life and usage period of complete dentures. The International Journal of Prosthodontics. 2019.07; 32(4); 327-332
20. Khaing Myat Thu, Haruki Shimizu, Manabu Kanazawa, Shunsuke Minakuchi. Measuring the retention of removable mandibular prostheses by a standardized model: A technical report. J Indian Prosthodont Soc. 2019.07; 19(3); 272-275
21. Thu KM, Kanazawa M, Thuy VL, Asami M, Sato D, Minakuchi S. . Durability and Optimal Retentive Force of Single-implant Overdentures using Locator Attachment: A Preliminary Clinical Study. 口腔病学会雑誌. 2019.07; 86(2); 12-22

22. Yuriko Kurosawa, Koji Hara, Haruka Tohara, Chizuru Namiki, Ayako Nakane, Kazuharu Nakagawa, Kohei Yamaguchi, Kanako Yoshimi, Junichi Furuya, Shunsuke Minakuchi. Calf Circumference Is a Useful Index for Assessing Dysphagia among Community Dwelling Elderly Recipients of Long-Term Care. *Tohoku Journal of Experimental Medicine*. 2019.07; 248(3); 201-208
23. Nishi Y, Nomura T, Murakami M, Kawai Y, Nishimura M, Kondo H, Ito Y, Tsuboi A, Hong G, Kimoto S, Gunji A, Suzuki A, Ohwada G, Minakuchi S, Sato Y, Suzuki T, Kimoto K, Hoshi N, Saita M, Yoneyama Y, Sato Y, Morokuma M, Okazaki J, Maeda T, Nakai K, Ichikawa T, Nagao K, Fujimoto K, Murata H, Kurogi T, Yoshida K, Hosoi T, Hamada T. Effect of denture adhesives on oral moisture: A multicenter randomized controlled trial. *J Prosthodont Res*. 2019.09;
24. Kyosaka Y, Owatari T, Inokoshi M, Kubota K, Inoue M, Minakuchi S. Cardiovascular Comparison of 2 Types of Local Anesthesia With Vasoconstrictor in Older Adults: A Crossover Study. *Anesth Prog*. 2019.09; 66(3); 133-140
25. Iwaki M, Kanazawa M, Sato D, Miyayasu A, Minakuchi S. Masticatory function of immediately loaded two-implant mandibular overdentures: A 5-year prospective study. *The International journal of oral & maxillofacial implants*. 2019.09; 34(6); 1434-1440
26. Thuy Lam Vo, Manabu Kanazawa, Khaing Myat Thu, Mari Asami, Daisuke Sato, Shunsuke Minakuchi. Masticatory function and bite force of mandibular single-implant overdentures and complete dentures: a randomized crossover control study. *J Prosthodont Res*. 2019.10; 63(4); 428-433
27. Hada T, Suzuki T, Minakuchi S, Takahashi H. Reduction in maxillary complete denture deformation using framework material made by computer-aided design and manufacturing systems. *J Mech Behav Biomed Mater*. 2019.11; 103; 103514
28. Kimura Atsushi, Yamaguchi Kohei, Tohara Haruka, Sato Yusuke, Sawada Naoko, Nakagawa Yasuhide, Matsuda Yukako, Inoue Motoharu, Tamaki Kazuhiro. Addition Of Sauce Enhances Finger-Snack Intake Among Japanese Elderly People With Dementia. *Clinical Interventions in Aging*. 2019.11; 14; 2031-2040
29. Yamaguchi K, Tohara H, Hara K, Chantaramanee A, Nakagawa K, Yoshimi K, Nakane A, Minakuchi S. Tongue thickness is associated with masticatory performance of perioral muscles: Ultrasonographic study of perioral muscle characteristics in healthy young subjects. *Journal of Oral Rehabilitation*. 2019.11; 47(3); 325-331
30. Hiroyuki Suzuki, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Noriko Amagai, Shunsuke Minakuchi. Influence of simplified dietary advice combined with new complete denture fabrication on masticatory function of complete denture wearers. *J Oral Rehabil*. 2019.12; 46(12); 1100-1106

[Books etc]

1. Oral Health and Nutrition for Healthy Longevity An Evidence-based Perspective. 2019.08
2. Dysphagia Rehabilitation for Dental Hygienists. 2019.08
3. Manabu Kanazawa, Yuriko Komagamine, Mari Asami. The latest clinical evidence and practice of the implant overdenture. 2019.08

[Misc]

1. Manabu Kanazawa, Maiko Iwaki, Mari Asami. The latest clinical evidence and practice of the implant overdenture. 2019.04; 133(4); 694-707
2. Manabu Kanazawa, Yuriko Komagamine, Mari Asami. The latest clinical evidence and practice of the implant overdenture. 2019.08; 134(2); 294-308
3. Manabu Kanazawa, Anna Miyayasu, Masatoshi Negoro . The latest clinical evidence and practice of the implant overdenture (4th) Do not lower patient's quality of life " Immediate load IOD " *Dental Outlook* . 2019.10; 134(4); 720-733
4. Manabu Kanazawa, Maiko Iwaki , Yoko Uehara. The latest clinical evidence and practice of the implant overdenture-The Delivery and maintenance of implant overdenture(IOD) *Dental Outlook*. 2019.12; 134(6); 1124-1136

[Conference Activities & Talks]

1. KANAZAWA M. The new Stream of Implant Overdentures. International Expert Symposium in Bangkok featuring TMDU International Faculty Development Course 2019.01.23 Bangkok
2. Inokoshi M. Root caries of elderly patients: prevention and restoration. The Japan Denture Care Society 2019.02.02 Tokyo
3. Chantaramanee A, Hara K, Tohara H, Kazuharu Nakagawa, Yamaguchi K, Namiki C, Kurosawa Y, Nakane A, Minakuchi S. The Effect of Gender and Age differences on Echo Intensity of Tongue. Dysphagia Research Society 2019.03.07 San Diego
4. Hara K, Tohara H, Namiki C, Yamaguchi K, Chantaramanee A, Kurosawa Y, Nakagawa K, Nakane A, Minakuchi S. Jaw-opening exercise effect on geniohyoid muscle morphology and function in nursing home residents: A randomized controlled study. Dysphagia Research Society 2019.03.08 San Diego
5. Kurosawa Y, Hara K, Tohara H, Chantaramanee A, Yoshimi K, Nakane A, Minakuchi S. Relationship between cervical perimeter and cross sectional area of geniohyoid muscle of healthy elderly. Dysphagia Research Society 2019.03.08 San Diego
6. Hiroyuki Suzuki. What the dental practitioners could do for edentulous elderly. TMDU Seminar 2019.03.13 Ann Arbor
7. Inokoshi M, Shimizubata M, Hatano K, Wada T, Uo M, Takahashi R, Minakuchi S. Application of S-PRG filler containing materials for geriatric dentistry. The 4th Bioactive Materials S-PRG Research Meeting 2019.03.22 Kyoto
8. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matubara, Yuko Kagifuku, Haruka Tohara, Shunsuke Minakuchi. Investigation of oral health status and function in Mild Cognitive Impairment (MCI) patients -An interim report of cross sectional study-. The 1st TAGD-JSG Gerodontology Summit 2019.03.23 Taipei
9. Inokoshi M. Properties and bond strategy of highly translucent zirconia. The 1st Resin-bonded zirconia fixed dental prosthesis research meeting 2019.04.06 Osaka
10. Onuma H, Inokoshi M, Hirayama D, Inoue M, Minakuchi S. Stress analysis of soft reliners using SPH method-viscoelasticity analysis by creep tests. The 73rd General Session of the Japanese Society for Dental Materials and Devices 2018 2019.04.21 Tokyo
11. Hatano K, Inokoshi M, Wada T, Uo M, Takahashi R, Minakuchi S. Ion release capacity of a novel S-PRG filler containing denture adhesive. The 73rd General Session of the Japanese Society for Dental Materials and Devices 2018 2019.04.21 Tokyo
12. Hada T, Kanazawa M, Iwaki M, Arakida T, Soeda Y, Otake R, Katheng A, Ando K, Minakuchi S. Mechanical property evaluation of CAD/CAM custom disk produced with cold cure resin. 2019.05.10 Sapporo
13. Inokoshi M, Nozaki K, Minakuchi S. Degradation of dental zirconia stored in artificial saliva. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.11 Sapporo
14. Shimizubata M, Inokoshi M, Hatano K, Nozaki K, Minakuchi S. Degree of conversion of an ion-releasing S-PRG filler containing denture base resin. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.12 Sapporo
15. Inokoshi M. How to bond to zirconia ceramics. The 148th Meeting of the Japanese Society of Conservative Dentistry 2019.05.12 Sapporo
16. The effect of dental treatment on Metabolic syndrome -Randomized controlled trial-. 2019.05.12
17. Shimada R, Kanazawa M, Miyayasu A, Asami M, Negoro M, Uehara Y, Katheng A, Sato D, Kasugai S, Minakuchi S. Marginal bone loss, survival rate and complication of immediately loaded mandibular 2-IOD - a 5-year follow up-. The 128th Annual Meeting of the Japan Prosthodontic Society 2019.05.12 Sapporo
18. Hiroyuki Suzuki. The possibility of oral rehabilitation for preventing malnutrition in edentate elderly patients. 29th Annual congress of European College of Gerodontology 2019.05.18 Amersfoort

19. Seiko Kaneko, Shunsuke Minakuchi, Kazumasa Kubota, Eriko Tsugawa, Anri Hirai, Shiho Yaguchi. Analysis of diabetic patients at Special Care 1 based on HbA1c and blood sugar level. Japanese Society Gerodontology 2019.06.07 Sendai Miyagi
20. Hasegawa, S., Yoshimi, K., Yamaguchi, K., Hara, K., Nakagawa, K., Nakane, A., Tohara, H., Minakuchi, S. Jaw retraction exercise improves upper esophageal sphincter opening and anterior excursion of hyoid bone in an elderly patient with mild dysphagia : A Case Report. The 30th Annual Meeting of Japanese Society of Gerodontology 2019.06.07 Sendai, Japan
21. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Yuko Kagihuku, Haruka Tohara, Shunsuke Minakuchi. Investigation of oral function in patients with Mild Cognitive Impairment (MCI) by medical and dental cooperation. The 30th Annual Meeting of the Japanese Society of Gerodontology 2019.06.08 Sendai
22. Eriko Tsugawa, Kazumasa Kubota, Seiko Kaneko, Anri Hirai, Shiho Yaguchi, Shunsuke Minakuchi. Two cases of emergency for elders with bradycardia and hypotension. The Japanese Society of Gerodontology 2019.06.08 Sendai, Miyagi
23. Kenichiro Ozaki, Isamu Matsukawa, Hironori Hosoe, et al.. Questionnaire Survey Regarding Dentistry for Rehabilitation Staffs in Community Hospital: A Multicenter Study in Japan. 13th ISPRM World Congress – ISPRM 2019 2019.06.10
24. Inokoshi M, Zhang F, Nozaki K, Shimizu H, Vleugels J, Van Meerbeek B, Minakuchi S. Translucency, flexural strength and aging behavior of highly translucent zirconia. 97th General Session & Exhibition of the IADR 2019.06.21 Vancouver
25. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Ion release and acid buffering capacity of S-PRG containing cement. 97th General Session & Exhibition of the IADR 2019.06.21 Vancouver
26. Yohei Hama, Shunsuke Minakuchi, Keiichi Sasaki, Takeyasu Maeda, Akira Hamura, Tatsuya Ichinohe, Takashi Okiji, Tetsuro Watabe. The Dental Education Consortium to promote healthy longevity -Fifth report- Future prospects at the expiration of the five years project . 38th Japanese Dental Education Association Meeting 2019.07.19 Hakata
27. Maiko Iwaki , Manabu Kanazawa, Anna Miyayasu, Thuy Vo Lam, Khaing Myat Thu, Mari Asami, Ryo Shimada, Masatoshi Negoro, Awutsadaporn Katheng, Sai Tun Naing, Yoko Uehara, Yuriko Komagamine, Daisuke Sato, Shohei Kasugai, Shunsuke Minakuchi.. Complications of Immediate Loading of Two-implant Mandibular Overdentures: 5-year prospective study. ICP/EPA 2019 2019.09.05 Amsterdam, The Netherlands
28. Katheng A, Kanazawa M, Iwaki M, Arakida T, Hada T, Soeda Y, Otake R, Minakuchi S. Effect of Stereolithography post-curing in different conditions on the fitting accuracy of photopolymer 3D resins. ICP and EPA joint meeting 2019.09.05 Amsterdam, The Netherlands
29. Nakagawa K, Yamaguchi K, Yoshimi K, Nakane A, Hara K, Tohara H.. KINEMATIC ANALYSIS OF SWALLOWING FUNCTION BEFORE AND AFTER ANTERIOR CERVICAL DISTCECTOMY AND FUSION FOR CERVICAL SPONDYLOTIC AMYOTROPHY. 9th ESSD annual meeting 2019.09.20 Vienna
30. Kanako Yoshimi, Haruka Tohara, Kazuharu Nakagawa, Koji Hara, Kohei Yamaguchi, Chizuru Namiki, Ayako Nakane. RELATIONSHIP BETWEEN TONGUE PRESSURE AND BACK MUSCLE STRENGTH IN HEALTHY ELDERLY INDIVIDUALS. 9th ESSD annual meeting 2019.09.21 Vienna
31. Yamaguchi K Hara K Nakagawa K Chantaramanee A Namiki C Yoshimi K Nakane A Furuya J Tohara H. AGING AND TOOTH LOSS RELATED CHANGES OF MASSETER MUSCLE CHARACTERISTICS - ULTRASONOGRAPHIC STUDY ON YOUNG AND OLD SUBJECTS -. 9th ESSD annual meeting 2019.09.21 Vienna
32. Chizuru Namiki , Koji Hara , Kazuharu Nakagawa , Kohei Yamaguchi , Takuma Okumura , Ariya Chantaramanee , Ayako Nakane , Kanako Yoshimi , Haruka Tohara. RELATIONSHIP BETWEEN JAW-OPENING FORCE AND FORWARD HEAD POSTURE IN HEALTHY ELDERLY PEOPLE. 9th ESSD annual meeting 2019.09.21 Vienna

33. Yumika SOEDA, Manabu KANAZAWA, Maiko IWAKI, Toshio ARAKIDA, Tamaki HADA, Ryosuke OTAKE, Awutsadapornk KATHENG, Kazuo ANDO, Shunsuke MINAKUCHI. Final impression and jaw registration with CAD/CAM try-in dentures. The 5th Annual Meeting of the International Academy for Digital Dental Medicine 2019.10.04 奈良県
34. Hada T, Kanazawa M, Iwaki M, Arakida T, Soeda Y, Otake R, Katheng A, Ando K, Minakuchi S. Effects of printing direction on the strain of 3D printed rectangular specimens. The 5th Annual Meeting of the International Academy for Digital Dental Medicine 2019.10.04 奈良県
35. Hada T, Kanazawa M, Iwaki M, Arakida T, Soeda Y, Otake R, Katheng A, Ando K, Minakuchi S. Effects of printing direction on the strain of 3D printed rectangular specimens. The 10th Annual Meeting of the Japan Academy of Digital Dentistry 2019.10.05 Nara
36. Onuma H, Inokoshi M, Hirayama D, Inoue M, Minakuchi S. Stress analysis of soft reliners using SPH method- A comparison between acrylic type soft reliners and silicone type soft reliners. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki
37. Yamamoto M, Inokoshi M, Shimizubata M, Takagaki T, Yoshihara K, Minakuchi S. Degree of conversion of 4-META/MMA-TBB resin containing antibacterial agents. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki
38. Shimizubata M, Inokoshi M, Hatano K, Wada T, Takahashi R, Uo M, Minakuchi S. Fluoride recharge and release capacity of a S-PRG filler containing glass ionomer cement. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki
39. Thaw Di CT, Inokoshi M, Nozaki K, Minakuchi S. Influence of sintering conditions on translucency of highly translucent dental zirconia. The 74th General Session of the Japanese Society for Dental Materials and Devices 2018 2019.10.05 Nagasaki
40. Yumika SOEDA, Manabu KANAZAWA, Maiko IWAKI, Toshio ARAKIDA, Tamaki HADA, Ryosuke OTAKE, Awutsadapornk KATHENG, Kazuo ANDO, Shunsuke MINAKUCHI. Final impression and jaw registration with CAD/CAM try-in dentures. The 10th Annual Meeting of the Japan Academy of Digital Dentistry 2019.10.05 Nara
41. Mari Asami, Miyayasu Anna, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. Masticatory function of mandibular single-implant overdentures: A 2-year follow-up report. 2019.10.06
42. Maki Shirobe, Takeshi Kikutani, Tetsuro Sato, Tomoki Tanaka, Katsushi Tamaki, Haruka Tohara, Kazuko Nakajo, Misa Nishimoto, Hirohiko Hirano, Shouji Hironaka, Tatsuo Yamamoto, Yutaka Watanabe, Takuo Ishii, Shunsuke Minakuchi, Katsuya Iijima. Title Dealing with deterioration of oral frailty in dental clinics —a randomized comparative control study—. IAGG Asia / Oceania Congress of Gerontology and Geriatrics 2019.10.25 Taipei
43. Khanlar LN, Takagaki T, Inokoshi M, Ikeda M, Takahashi A, Yoshihara K, Nagaoka N, Nikaido T, Tagami J. Effect of glass-beads blasting on bonding performance of super-translucent zirconia. ConsAsia 2019 2019.11.09 Seoul
44. Awutsadaporn Katheng, Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Tamaki Hada, Yumika Soeda, Ryosuke Otake, Kazuo Ando, Shunsuke Minakuchi. Evaluation of Stereolithography Post-Curing on Dimensional Accuracy and Polymerization. IADR-APR 2019 2019.11.28 Brisbane, Australia
45. Seki N, Mizutani K, Hosaka K, Komada W, Kanazawa M, Komagamine Y, Moross J, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Essential Expertise for Clinical Dentistry (EECD), International Dental Clinical Education Course for Graduate School of Medical and Dental Sciences. The 84th annual meeting of the Stomatological Society 2019.12.07 Tokyo
46. Nakai H, Inokoshi M, Nozaki K, Minakuchi S. Crystallographic analysis of additive manufactured zirconia. The 23rd scientific meeting of Japan Prosthodontic Society, Tokyo branch 2019.12.08 Tokyo

[Patents]

1. ARTIFICIAL TOOTH, Patent Number : ZL201580007062.8
2. ARTIFICIAL TOOTH, Patent Number : ZL201580007062.8

[Awards & Honors]

1. GERIATRIC ORAL RESEARCH AWARD, 2019 RECIPIENTS OF THE IADR DISTINGUISHED SCIENTIST AWARDS (Shunsuke Minakuchi), International Association for Dental Research, 2019.06

[Others]

1. Inokoshi M. Grant-in-Aid for Scientific Research (C), 2019.04
Development of zirconia implant using additive manufacturing
2019-2021
2. Yamaga Eijiro Grant-in-Aid for for Young Scientists, 2019.04
Structural equation modeling to investigate the relationship between oral function and healthy aging.
2019-2021

[Social Contribution]

1. Inokoshi M. responsible person of the international program with the Chulalongkorn University, 2017.07.01
- Now
2. The enjoyment of eating with mastication -mastication, denture, and nutrition intake-, Japanese Society for Mastication Science and Health Promotion, The first follow up seminar in 2019, Tokyo Medical and Dental University, 2019.03.21
3. Inokoshi M. TMDU International Dental Program organizer for Clinical part, 2019.05 - 2019.09
4. The effect of prosthetic treatment for eating -Dietary advice as denture care-, Japan Denture Care Society, The first workshop of Denture care Meister, Tokyo Medical and Dental University, 2019.06.15

Laboratory Medicine

Professor Shuji TOHDA
Assistant Professor Mai ITOH
Graduate Students Mika OHTAKA, Yuki KODA, Erika SHIRATORI, Tatsuya SAITO,
Salwa MOHAMMAD, Yuri SONODA

(1) Outline

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

(2) Research

Our research subjects are as follows:

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

(3) Education

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

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

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

(6) Clinical Performances

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

(7) Publications

[Original Articles]

1. Kawaguchi-Ihara Noriko, Zhao Yan, Nakamura Suzune, Suzuki Keiko, Zhang Yi, Tohda Shuji, Murohashi Ikuo. Chloroquine Inhibits Self-Renewal of Blast Progenitors Synergistically With Phytochemicals or Non-steroidal Anti-inflammatory Drugs in Hematological Malignant Cell Lines ANTICANCER RESEARCH. 2019.01; 39(1); 87-98
2. Yuna Horiuchi, Ryunosuke Ohkawa, Shao-Jui Lai, Shitsuko Shimano, Michio Hagihara, Shuji Tohda, Takahiro Kameda, Minoru Tozuka. Usefulness of apolipoprotein B-depleted serum in cholesterol efflux capacity assays using immobilized liposome-bound gel beads. Biosci. Rep.. 2019.03;
3. Hamada S, Hasegawa Y, Oono A, Suzuki A, Takahashi N, Nishimura T, Koyama T, Hagihara M, Tohda S, Furukawa T, Hirao K, Sasano T. Author Correction: Differential Assessment of Factor Xa Activity and Global Blood Coagulability Utilizing Novel Dielectric Coagulometry. Scientific reports. 2019.03; 9(1); 4957
4. Mai Itoh, Yuki Okuhashi, Yusuke Takahashi, Yuri Sonoda, Salwa Mohammad, Tatsuya Saito, Erika Shiratori, Shuji Tohda. Hypoxia Up-regulates HIF Expression While Suppressing Cell Growth and NOTCH Activity in Leukaemia Cells. Anticancer Research. 2019.08; 39(8); 4165-4170
5. Yoko Nukui, Alafate Ayibieke, Makoto Taniguchi, Yoshibumi Aiso, Yuka Shibuya, Kazunari Sonobe, Jun Nakajima, Saki Kanehira, Yoshiro Hadano, Shuji Tohda, Ryuji Koike, Ryoichi Saito. Whole-genome analysis of EC129, an NDM-5-, CTX-M-14-, OXA-10- and MCR-1-co-producing Escherichia coli ST167 strain isolated from Japan. J Glob Antimicrob Resist. 2019.09; 18; 148-150
6. Ryoichi Saito, Yukino Usui, Alafate Ayibieke, Jun Nakajima, Isaac Prah, Kazunari Sonobe, Yoshibumi Aiso, Shiori Ito, Yasuhiro Itsui, Yoshiro Hadano, Yoko Nukui, Ryuji Koike, Shuji Tohda. Hypervirulent clade 2, ribotype 019/sequence type 67 Clostridioides difficile strain from Japan. Gut Pathog. 2019.11; 11; 54
7. Nukui Y, Chino T, Tani C, Sonobe K, Aiso Y, Tohda S, Koike R, Saito R. Molecular epidemiologic and clinical analysis of Helicobacter cinaedi bacteremia in Japan. Helicobacter. 2019.11; e12675

[Conference Activities & Talks]

1. Horiuchi Y., Ohkawa R., Lai SJ., Shimano S., Hagihara M., Tohda S., and Tozuka M. Availability of apoB-depleted serum in clinical assay for cholesterol efflux capacity using immobilized liposome-bound gel beads. 3rd IFCC-EFLM European Congress of Clinical Chemistry and Laboratory Medicine 2019.05.19 Barcelona
2. Tatsuya Saito, Mai Itoh, Shuji Tohda. Metformin inhibits the growth of myeloid leukemia cells partly due to suppression of TYRO3 expression.. The 24th Congress of the European Hematology Association 2019.06.14 Amsterdam, Holland
3. Tatsuya Saito, Mai Itoh, Shuji Tohda. Metformin inhibits the growth of myeloid leukemia cells partly due to suppression of tyro3 expression. 24th Congress of European Hematology Association 2019.06.14 Amsterdam
4. Fujii Y., Ohkawa R., Lai SJ., Horiuchi Y., Shimano S., Ohno K., Ichimura N., Hagihara M., Tozuka M., Tohda S. Analysis of Serum Amyloid A Containing HDL Formation in HepG2. 2019 KAMT congress & International conference 2019.08.31 Pyeongchang
5. Yamazaki A., Ohkawa R., Horiuchi Y., Lai SJ., Shimano S., Itoi A., Ichimura N., Hagihara M., Tozuka M., Tohda S. Analysis of Apolipoprotein C-II and C-III Transfers between High-density Lipoprotein and Very Low-density Lipoprotein. 2019 KAMT congress & International conference 2019.08.31 Pyeongchang

6. Chihiro Tani, Kazunari Sonobe, Ayuka Kobayashi, Jun Nakajima, Rieko Takahashi, Saki Kanehira, Sonoka Yuasa, Tomoko Motohashi, Michio Hagihara, Takashi Yaguchi, Shuji Tohda. The impact of the morphological difference of fungal colonies among several potato dextrose agars on the identification. The 30th World Congress of World Association of Societies of Pathology and Laboratory Medicine 2019.09.20
7. Ayako Nogami, Watanabe Daisuke, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Toshikage Nagao, Shuji Tohda and Osamu Miura. FLT3-ITD Enhances Proliferation and Survival of AML Cells through Activation of RSK1 to Upregulate the mTORC1/eIF4F Pathway Cooperatively with PIM or PI3K and to Inhibit Bad and Bim. 60th ASH Annual Meeting and Exposition 2019.12.01 FL, Orange County Convention Center

Intensive Care Medicine

Professor and Chairman
Hidenobu Shigemitsu (2016.9.1 -)

Professor
Hideo Takahashi(2017.4.1 -)

Associate Professor
Toyomu Ugawa (2018.11.1 -)

Junior Associate Professor
Michio Nagashima (2017.4.1 -)

Assistant Professor
Takahiro Masuda (Intensive Care Unit) (2014.4.1 -)
Kenji Wakabayashi (2015.4.1 -)
Fumi Maruyama (Intensive Care Unit) (2017.2.1 -)

Specially Appointed Assistant Professor
Nobuhiro Shiota (2017.4.1 -)
Shin Inukai (Intensive Care Unit) (2017.4.1 -)
Kensuke Hirasawa (Intensive Care Unit) (2018.4.1 -)

Fellow:
Yuka Mishima (Intensive Care Unit) (2017.4.1 -)
Sachiyo Sato (Intensive Care Unit) (2017.4.1 -)

Postgraduate students:
Mariko Senda (2014.4.1 -)
Shotaro Matsumoto (2016.4.1 -)
Nobuhiro Shiota (2017.4.1 -)
Yoichi Iki (2018.4.1 -)

Research student:
Michiko Abe (2018.4.1 -)

(1) Outline

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

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

mechanical ventilation, pharmacological support, cardiopulmonary support system, blood purification, and nutrition support.

(2) Research

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

Clinical research:

- 1) Effective Medical Creation (EMC) project, in liaison with Yamaha Co. and world-renowned designer Hiroko Koshino.
- 2) Clinical implementation of US-style bundle in the ICU (Shigemitsu, funded by Grant-in-Aid for Scientific Research C)

Basic research:

- 1) Role of microvesicles in patients on ECMO (Shiota, funded by Grant-in-Aid for Young Scientists B)
- 2) Role of microvesicles in bronchopulmonary dysplasia (Wakabayashi, funded by Grant-in-Aid for Young Scientists B)
- 3) Role of urinary microvesicles in acute liver failure (Wakabayashi, funded by National Center of Child Health and Development)
- 4) Impact of residual neuromuscular blockade in the ICU (Nagashima, funded by Grant-in-Aid for Young Scientists B)
- 5) Effect of nutrition status in the ICU (Masuda, funded by Grant-in-Aid for Young Scientists B)

(3) Education

Undergraduate education

Lectures: Fourth-year medical students

- 1) Mechanical ventilation (Wakabayashi)

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

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

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

Residents: Residents in training rotate 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) Lectures & Courses

US-based training system has been in place at the Department of Intensive Care Medicine under the Prof Shigemitsu who was a program director of ACGME-accredited fellowship program at the University of Nevada. We regularly hold educational conferences on every Tuesday called 'academic day'.

(5) Clinical Services & Other Works

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

Every morning, intensivists, nurses, pharmacist, nutritionist, rehabilitation staffs, infection control staffs, medical engineers, and attending physicians get together, go round, and talk about the best treatment of the patients. From March 2017, we also started a novel Rapid Response System (we named as RAS: Risk Assessment System), in collaboration with the Department of Acute Critical Care and Disaster Medicine.

(6) Clinical Performances

Our early rehabilitation program based on the multidisciplinary round was awarded a 'best team prize' in 2017, and presented at an invited seminar at the national conference of Japanese Society of Respiratory Care Medicine.

(7) Publications

[Books etc]

1. Kenji Wakabayashi. ICU practice handbook. Youdo-sha, 2019.03
2. Mizuho Asada, Kenji Wakabayashi. ICU practice handbook. Youdo-sha, 2019.03

[Misc]

1. Kenji Wakabayashi, Hidenobu Shigemitsu. Multidisciplinary Approach to Clinical Ethics and End-of-Life Care in ICU Emergency Medicine. 2019.02; 43(2);

Liaison Psychiatry and Palliative Medicine

Assistant Professor Miho Miyajima
 Visiting Lecture Eisuke Matsushima, Katsuya Ota,
 Kanako Ichikura, Tetsuya Matsuda,
 Takashi Hosaka, Kouichi Fujiwara,
 Toshitaka Yamakawa,
 Clinical Psychologist Nao Nakayama, Tomoko Sugano, Hitomi Satou,
 Graduate Student Hiroshi Koubou, Toshimi Takano, Rie Tani,
 Noriko Yoshida, Nami Kondou, Hiroki Sakurai,
 Mayo Fujiwara,
 Kanako Amano, Sayaka Ozaka,
 Saori Koshimoto, Shiho Matsuoka,
 Kazuhiro Kosugi, Takafumi Watanabe,
 Mayuko Iijima, Yu Okura, Jun Kakou,
 Kensuke Komatsu, Hiroyuki Tanaka,
 Takahiro kawata, Yukari Bandou,
 Research Student Okihiko Aihara, Ryuho Ibaraki.
 Technical Assistant Satoko Ogi, Wakana Takeshita,
 Takuya Seki, Takeshi Ono, Shintaro Takiguchi,
 Motoaki Iimori, Masato Serino,
 Takeshi Ohno, Sinterou takiguchi,
 Office Assistant Yoriko Mizukane, Hitomi Matsuda,

(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. Kako J, Kajiwar K, Miyashita M. Response to “The hand-held fan and the Calming Hand for people with chronic breathlessness: a feasibility trial” . J Pain Symptom Manage. 2019; 58(2); e1-e2
2. Kako J, Kajiwar K, Miyashita M. Response to Niki et al. (doi: 10.1089/jpm.2018.0233): A Novel Palliative Care Approach Using Virtual Reality for Improving Various Symptoms of Terminal Cancer Patients: A Preliminary Prospective, Multicenter Study. J Palliat Med. 2019; 22(5); 479
3. Kajiwar K, Kako J, Miyashita M. A Response to: “Prevalence, Severity and Correlates of Symptoms of Anxiety and Depression at the Very End of Life” J Pain Symptom Manage. 2019; 58(3); e3
4. Kako J, Kajiwar K, Miyashita M. Response to Li et al. (doi:10.1089/jpm.2019.0622): Symptom Assessment in Patients with Advanced Cancer: Are the Most Severe Symptoms the Most Bothersome? J Palliat Med. 2019; 22(11); 1300
5. Kajiwar K, Kako J, Tatematsu N. Letter by Kajiwar et al Regarding Article, “Caregiver-Delivered Stroke Rehabilitation in Rural China: The RECOVER Randomized Controlled Trial”. Stroke. 2019; 50; e319
6. Kajiwar K, Kako J, Noto H, Oosono Y, Kobayashi M. Response to “Factors associated with long-term impact on informal caregivers during Alzheimer’s disease dementia progression: 36-month results from GERAS” International Psychogeriatrics. 2019;
7. Kajiwar K, Kako J, Noto H, Oosono Y, Kobayashi M. Reply to “Barriers and facilitators of adherence to a perioperative physical activity intervention for older adults with cancer and their family caregivers” Journal of Geriatric Oncology. 2019;
8. Kako J, Oosono Y, Kajiwar K, Kobayashi M, Noto H. Hope, optimism, and the importance of caregivers in end - of - life care Cancer. 2019;
9. Kajiwar K, Kako J, Miyashita M. Response to: “Caring for the person with cancer and the role of digital technology in supporting carers” Supportive Care in Cancer. 2019;
10. Kajiwar K, Kako J, Noto H, Kobayashi M, Oosono Y. Letter to the editor: “Improving information to caregivers of cancer patients: the Herlev Hospital Empowerment of Relatives through More and Earlier information Supply (HERMES) randomized controlled trial” Supportive Care in Cancer. 2019;
11. Kako J, Kajiwar K, Noto H, Oosono Y, Kobayashi M. Response to “Prophylactic Fentanyl Sublingual Spray for Episodic Exertional Dyspnea in Cancer Patients: A Pilot Double-Blind Randomized Controlled Trial.” J Pain Symptom Manage. 2019; 58(4); e16-e17
12. Kako J, Kajiwar K, Kobayashi M, Oosono Y, Noto H. Response to: “Acupuncture for chemotherapy-induced peripheral neuropathy: a randomised controlled pilot study.” BMJ Supportive & Palliative Care. 2019;
13. Kajiwar K, Kako J, Noto H. “Mood, lifestyle and cardiovascular risk factors among older caregivers of patients with Alzheimer’s disease dementia: a case-control study” : A letter in response Aging Clin Exp Res. 2019;
14. Kajiwar K, Kako J, Noto H. Letter in response to: “Determinants of self- and carer-rated quality of life and caregiver burden in Alzheimer disease” International Journal of Geriatric Psychiatry. 2019;
15. Kako J, Kajiwar K, Kobayashi M, Oosono Y. Comment on: “Preventing chemotherapy-induced alopecia: a prospective clinical trial on the efficacy and safety of a scalp-cooling system in early breast cancer patients treated with anthracyclines” British Journal of Cancer. 2019;

16. Kako J, Ishiki H, Kajiwarara K. Biofeedback or loperamide for faecal incontinence in women *The Lancet Gastroenterology & Hepatology*. 2019; 4(12); 903-904
17. Kajiwarara K, Kako J, Noto H, Kobayashi M, Oosono Y. Response to the article "Informal caregivers in stroke: Life impact, support, and psychological well-being-A Swedish Stroke Register (Riksstroke) study". *International Journal of Stroke*. 2019;
18. Kajiwarara K, Kako J, Noto H, Kobayashi M, Oosono Y. Reply to: "Informal caregiver quality of life in a palliative oncology population" *Supportive Care in Cancer*. 2019; 27(12); 4387-4388
19. Kajiwarara K, Kako J, Noto H, Kobayashi M, Oosono Y. Reply to: "Providing care to a family member affected by head and neck cancer: a phenomenological study" *Supportive Care in Cancer*. 2019;
20. Kako J, Kajiwarara K, Kobayashi M, Oosono Y. Questioning the Acute effect of orange chromatic environment on perceived health status, pain, and vital signs during chemotherapy treatment *Supportive Care in Cancer*. 2019;
21. Kako J, Kajiwarara K, Kobayashi M, Oosono Y. Response to "Patient-reported symptom severity among 22,650 cancer outpatients in the last 6 months of life." *J Pain Symptom Manage*. 2019;
22. Kajiwarara K, Kako J, Noto H, Kobayashi M, Oosono Y. Reply to: "Breast cancer survivors' perspectives on a home-based physical activity intervention utilizing wearable technology" *Supportive Care in Cancer*. 2019;
23. Kako J, Kobayashi M, Oosono Y, Kajiwarara K, Miyashita M. Immediate Effect of Fan Therapy in Terminal Cancer with Dyspnea at Rest: A Meta-Analysis *Am J Hosp Palliat Care*. 2019; 1-6
24. Kajiwarara K, Kako J, Yamanaka M, Miyashita M. Determining caregiver burden using new technologies for informal caregivers of people with dementia: a systematic review *Geriatrics & Gerontology International*. 2019; 1069-1071
25. Kanako Amano, Kanako Ichikura, Kazuho Hisamura, Yuko Motomatsu, Eisuke Matsushima. Factors Associated with Social Support Needs of Spouses of Patients with Cancer: Online Survey *International Journal of Clinical Medicine*. 2019; 10; 270-292
26. Takafumi Watanabe, Miho Miyajima, Katsuya Ohta, Noriko Yoshida, Rie Omoya, Mayo Fujiwara, Yoko Suzuki, Issei Murata, Shigeru Ozaki, Mitsuru Nakamura, Eisuke Matsushima. Predicting postictal suppression in electroconvulsive therapy using analysis of heart rate variability. *J Affect Disord*. 2019.03; 246; 355-360
27. Suzuki Y, Miyajima M, Ohta K, Yoshida N, Watanabe T, Fujiwara M, Okumura M, Nakamura M, Sasano T, Kawara T, Matsuura M, Matsushima E. Changes in cardiac autonomic nervous system activity during a course of electroconvulsive therapy. *Neuropsychopharmacology reports*. 2019.03; 39(1); 2-9

[Conference Activities & Talks]

1. Kobayashi M, Kako J, Oosono Y. The Effect of Providing Information on Deceased Palliative Care Patients to Visiting Nurses. 22nd EAFONS 2019 2019.01.17
2. Kako J, Kobayashi M, Oosono Y, Kajiwarara K, Miyashita M. Fan Therapy for the Relief of Dyspnea in Malignant and Non-Malignant Diseases. *Oncology Nursing Society 44th Annual Congress* 2019.04.12
3. Miyashita M, Yamaguchi M, Tenda Y, Kako J, Kajiwarara K, Kadoya T. Effects of Cognitive Function as a Mediator on Quality of Life in Post-operative Elderly Patients with Breast Cancer. *Oncology Nursing Society 45th Annual Congress* 2019.04.12
4. Mori K, Miyashita M, Kako J, Kajiwarara K. Difficulties and Coping Strategies in Nursing and Medical Care for Cancer Patients with Dementia: A Qualitative Study. *Oncology Nursing Society 45th Annual Congress* 2019.04.12
5. Miho Miyajima, Koichi Fujiwara, Toshitaka Yamakawa, Motoaki Iimori, Takeshi Ohno, Takuya Seki, Motoki Inaji, Masaki Iwasaki, Eiji Nakagawa, Hideaki Shiraishi, Masami Fujii, Toshikazu Nagathuna, Shinji Yamamoto, Hidenori Sugano, Yasushi Iimura, Naoto Kunii, Haruhiko Kishima, Satoru Oshino, Hui Ming Khoo, Masako Watanabe, Manabu Kano, Taketoshi Maehara. Views of Medical Staff Members on the Use of a Wearable Seizure Prediction System in Hospitals. 2019 Annual Meeting of the American Epilepsy Society 2019.12.08

Pharmacokinetics and Pharmacodynamics

Associate Professor Masashi Nagata

Postgraduate student Kohta Tsuge, Xue Bingyang, Tomofumi Kobayashi

(1) Research

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

(2) Education

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

(3) Publications

[Original Articles]

1. Masatoshi Takagi, Chitose Ogawa, Yuki Aoki-Nogami, Tomoko Iehara, Eri Ishibashi, Minoru Imai, Tetsuro Kihara, Kiyoshi Nobori, Kazuhisa Hasebe, Shuki Mizutani, Toshimi Kimura, Masashi Nagata, Masato Yasuhara, Kenichi Yoshimura, Pariko Yorozu, Hajime Hosoi, Ryuji Koike. Phase I clinical study of oral olaparib in pediatric patients with refractory solid tumors: study protocol. BMC Pediatr. 2019.01; 19(1); 31
2. Suzuki S, Naito S, Numasawa Y, Asada M, Shoji N, Zeniya M, Takahashi D, Sato H, Iimori S, Nomura N, Sohara E, Okado T, Ishiwata Y, Nagata M, Rai T, Yokota T, Uchida S. Encephalopathy Induced by High Plasma and Cerebrospinal Fluid Ceftriaxone Concentrations in a Hemodialysis Patient. Internal medicine (Tokyo, Japan). 2019.02;

[Conference Activities & Talks]

1. Yasuhara M., Asada M., Nagata M., Mizuno T., Uchida T., Takahashi H., Makita K., Arai H., Echizen H.. Population pharmacokinetics of cefazoline before, during and after cardiopulmonary bypass in Japanese patients undergoing cardiothoracic surgery. 2019 AAPS PharmSci 360 2019.11

Medical Education Research and Development

Professor Yujiro TANAKA
 Junior Associate Professor Makoto TAKAHASHI
 Junior Associate Professor Eriko OKADA
 Junior Associate Professor Yasuhiro ITSUI
 Assistant Professor Nobutoshi NAWA
 Attending Staff Fukiko KITAHATA
 Attending Staff Ayako KASHIMADA
 Graduate Student Hisashi SHIMOZONO

(1) Outline

Department of General Medicine was established in 2000, we have aimed to coordinate and support a wide range of 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 patient support system including social casework, 3) Establishing the Center for Cell Therapy, 4) Reforming the undergraduate medical education, 5) Establishing the working group for ward management 6) Managing the medical safety committee, 7) Providing second opinion support system. Recently we have been focusing on providing systems for undergraduate and postgraduate education, such as reforming the undergraduate educational curriculum (e.g. educational cooperation with Harvard Medical School) and clinical training system. The medical training center was established for the clinical residency program. In 2006, the department of General Medicine was transformed into the Department of Medical Education Research and Development. We are working in close cooperation with Center for Extraprofessional Education which we took in part of its establishment to materialize the interprofessional education introduced due to a revision of a new curriculum in 2011.

(2) Research

* Research on continuing education in clinical EBM

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

* Research on medical education We are developing comprehensive research projects regarding under- and post-graduate medical education, e.g. Clinical reasoning, clinical competence, medical interview, PBL system, and informed consent, are our research themes.

(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 the 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.

Besides, 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 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 Japan Residency Matching Program, 2019 showed one of the highest satisfaction rates 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

We are aiming to improve initial clinical training through the recruitment of medical interns, training management, holding various workshops, such as Evening Seminars, and operation of the "Tasukigake" training system with each partner hospital. We also hold clinical training sessions for supervising physicians to learn better teaching methods, and staff training classes about medical safety, infection control and medical information throughout the year. We 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.

(5) Publications

[Original Articles]

1. Nawa N, Hirata K, Kawatani K, Nambara T, Omori S, Banno K, Kokubu C, Takeda J, Nishimura K, Ohtaka M, Nakanishi M, Okuzaki D, Taniguchi H, Arahori H, Wada K, Kitabatake Y, Ozono K. Elimination of protein aggregates prevents premature senescence in human trisomy 21 fibroblasts. *PloS one*. 2019; 14(7): e0219592
2. Nawa N, Fujiwara T. Association between social capital and second dose of measles vaccination in Japan: Results from the A-CHILD study. *Vaccine*. 2019.01; 37(6):877-881
3. Azuma S, Asahina Y, Kakinuma S, Azuma K, Miyoshi M, Inoue E, Tsunoda T, Sato A, Kaneko S, Nagata H, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Tomita M, Nakagawa M, Watanabe M. Diabetic Retinopathy as a Risk Factor Associated with the Development of Hepatocellular Carcinoma in Nonalcoholic Fatty Liver Disease. *Dig Dis*. 2019;37(3):247-254. Epub 2019.01.
4. Kashimada A, Hasegawa S, Nomura T, Shiraku H, Moriyama K, Suzuki T, Nakajima K, Mizuno T, Imai K, Sugawara Y, Morio T, Kumada S, Takagi M. Genetic analysis of undiagnosed ataxia-telangiectasia-like disorders. *Brain Dev*. 2019.02; 41(2): 150 -157
5. Miyoshi M, Kakinuma S, Kamiya A, Tsunoda T, Tsuchiya J, Sato A, Kaneko S, Nitta S, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Nakauchi H, Asahina Y, Watanabe M. LIM homeobox 2 promotes interaction between human iPS-derived hepatic progenitors and iPS-derived hepatic stellate-like cells. *Sci Rep*. 2019.02;9(1):2072.
6. Sato R, Fujiwara T, Kino S, Nawa N, Kawachi I. Pet Ownership and Children's Emotional Expression: Propensity Score-Matched Analysis of Longitudinal Data from Japan. *Inter*

- national journal of environmental research and public health. 2019.03; 16(5); pii: E758
7. Nitta S, Asahina Y, Kato T, Tsuchiya J, Inoue-Shinomiya E, Sato A, Tsunoda T, Miyoshi M, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Hikita H, Takehara T, Watanabe M. Impact of novel NS5A resistance-associated substitutions of hepatitis C virus detected in treatment-experienced patients. *Sci Rep*. 2019.04;9(1):5722.
 8. Tsunoda T, Kakinuma S, Miyoshi M, Kamiya A, Kaneko S, Sato A, Tsuchiya J, Nitta S, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Sogo T, Loss of fibrocystin promotes interleukin-8-dependent proliferation and CTGF production of biliary epithelium. *J Hepatol*. 2019.07;71(1):143-152.
 9. Nawa N, Black MM, Araya R, Richiardi L, Surkan PJ. Pre- and post-natal maternal anxiety and early childhood weight gain. *Journal of affective disorders*. 2019.07; 257; 136-142
 10. Surkan PJ, Hong X, Zhang B, Nawa N, Ji H, Tang WY, Ji Y, Kimmel MC, Wang G, Pearson C, Wang X. Can social support during pregnancy affect maternal DNA methylation? Findings from a cohort of African-Americans. *Pediatric research*. 2019.07; [Epub ahead of print]
 11. Mizuno T, Kashimada A, Nomura T, Moriyama K, Yokoyama H, Hasegawa S, Takagi M, Mizutani S. Infantile-onset spinocerebellar ataxia type 5 associated with a novel SPTBN2 mutation: A case report. *Brain Dev*. 2019.08;41(7)
 12. Shimozone, H., Takahashi, M., Tomita, M., Takada, K., & Tanaka, Y. (2019). "The 2-Dimensional Approach": a novel tool to help learners organize their knowledge and improve their clinical reasoning skills. *MedEdPublish*, 8.
 13. Hasegawa S, Kumada S, Tanuma N, Tsuji-Hosokawa A, Kashimada A, Mizuno T, Moriyama K, Sugawara Y, Shirai I, Miyata Y, Nishida H, Mashimo H, Hasegawa T, Hosokawa T, Hisakawa H, Uematsu M, Fujine A, Miyata R, Sakuma H, Kashimada K, Imai K, Morio T, Hayashi M, Mizutani S, Takagi M. Long-Term Evaluation of Low-Dose Betamethasone for Ataxia Telangiectasia. *Pediatr Neurol*. 2019.11; 100:60-66
 14. Saito R, Usui Y, Ayibieke A, Nakajima J, Prah I, Sonobe K, Aiso Y, Ito S, Itsui Y, Hadano Y, Nukui Y, Koike R, Tohda S. Hypervirulent clade 2, ribotype 019/sequence type 67 *Clostridioides difficile* strain from Japan. *Gut Pathog*. 2019.11;11:54.
 15. Nakagawa M, Sugihara K, Isobe K, Akasu M, Tsujimoto K, Itsui Y, Nakajima Y. A case of tracheal obstruction caused by reflux and aspiration of semi-solid nutrients via the nasogastric tube. *Int J Surg Case Rep*. 2019;65:217-220. Epub 2019.11.
 16. Kawai-Kitahata F, Asahina Y, Kaneko S, Tsuchiya J, Sato A, Miyoshi M, Tsunoda T, Inoue-Shinomiya E, Murakawa M, Nitta S, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Tanabe M, Sugawara E, Takemoto A, Ojima H, Sakamoto M, Muraoka M, Takano S, Maekawa S, Enomoto N, Watanabe M. Comprehensive genetic analysis of cholangiolocellular carcinoma with a coexistent hepatocellular carcinoma-like area and metachronous hepatocellular carcinoma. *Hepatol Res*. 2019.12;49(12):1466-1474.
 17. Sato A, Kakinuma S, Miyoshi M, Kamiya A, Tsunoda T, Kaneko S, Tsuchiya J, Shimizu T, Takeichi E, Nitta S, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Koshikawa N, Seiki M, Nakauchi H, Asahina Y, Watanabe M. Vasoactive Intestinal Peptide Derived From Liver Mesenchymal Cells Mediates Tight Junction Assembly in Mouse Intrahepatic Bile Ducts. *Hepatol Commun*. 2019.12;4(2):235-254.

[Conference Activities & Talks]

1. Eriko Okada, Makoto takahashi, Yasuhiro Itsui, Yuki Sumi, Kumiko Yamaguchi, Yujiro Tanaka. The learning of symptomatology in the first-year medical students is effective for

- better understanding preclinical medicine. The Association for Medical Education in Europe (AMEE) Conference 2019 2019.08 Vienna, Austria
2. Yasuhiro Itsui, Chikako Okawara, Eriko Okada, Makoto Takahashi, Yujiro Tanaka. Analysis of teaching doctor statue required by junior residents. The Association for Medical Education in Europe (AMEE) Conference 2019 2019.08 Vienna, Austria.
 3. Nobutoshi Nawa, Kumiko Yamaguchi, Chiharu Kawakami, Mina Nakagawa, Takeo Fujiwara, Keiichi Akita. Differences in effects of interprofessional education workshops by students' discipline and gender among medical and dental students. The Association for Medical Education in Europe (AMEE) Conference 2019 2019.08 Vienna, Austria
 4. Shimozono H, Takahashi M, Tanaka Y. The "5x5 Approach" for clinical reasoning has larger effect on male than female residents. The Association for Medical Education in Europe (AMEE) Conference 2019 2019.08 Vienna, Austria

Dentistry for Persons with Disabilities

Associate Professor
Osamu SHINOZUKA

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

Assistant Professor
Yasuka KUSUMOTO

Specially Appointed Assistant Professor
Taiji HOSHIAI

Graduate Student
Aiko HOSHIAI
Yusuke IWABUCHI

Hospital Staff
Takae AIDA
Anna KUMAKURAI
Ayana NATORI

Clinical Junior Associate Professor (Part-time)
Shohei TAMURA
Tomo SUZUKI
Yosuke KINOSHITA

(1) Research

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

(2) Lectures & Courses

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

The main objective of this course is to provide the opportunity for students to understand the outline of the reconstruction of functional and esthetic disorders of oral and/or maxillofacial areas by means of the high-advanced dental cares for patients with special needs.

(3) Clinical Performances

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

For example,

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

(4) Publications

[Original Articles]

1. Hidenobu Senpuku , Tomoyo Nakamura, Yusuke Iwabuchi, Satoru Hirayama, Ryoma Nakao, Makoto Ohnishi. Effects of Complex DNA and MVs with GTF Extracted from *Streptococcus mutans* on the Oral Biofilm Molecules. 2019.08; 24(17); 3131

General Dentistry

Professor Hiroshi Nitta
 Associate Professor Shigeru ODA
 Junior Associate Professor Masayuki HIDEISHIMA
 Junior Associate Professor Ken-ichi TONAMI
 Assistant Professor Sachi UMEMORI
 Assistant Professor Kanako NORITAKE
 Project Assistant Professor Maiko IWAKI
 Project Assistant Professor Shuuhei NAKAMURA
 Project Assistant Professor Yuko MITSUMA
 Project Assistant Professor Naoko HARADA
 Hospital Staff Naoki ISHIHARA
 Hospital Staff Yuna KANAMORI
 Hospital Staff Daisuke KIDO
 Hospital Staff Yasuyuki KIMURA
 Hospital Staff Yukako KUSUNOKI
 Hospital Staff Naoki SASAKI
 Hospital Staff Shogo TAKEUCHI
 Hospital Staff Shota HAYASHI
 Hospital Staff Kiichi MARUYAMA

(1) Outline

Recent dentistry is sectionalized into various specialized fields of research and education. On the other hand, as a general practitioner, a dentist must possess not only integrated knowledge and skills of all the fields but also should be competent to apply such generalized knowledge and skills to individual patients. The department of General Dentistry performs researches and education for practicing such general and holistic dentistry. General dentistry related to clinical and affective education for dental students and residents. Therefore, the research theme includes dental education as well as oral diagnosis and general dentistry, cooperating with the department of Educational System in Dentistry, Behavioral Dentistry and Educational Media Development. Researches for sleep apnea syndrome have been also conducted in association with Dental Clinic for Sleep Disorders. The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry which missions in the Dental Hospital are initial diagnosis for new outpatients and general dental practice. Clinics of General Dentistry 1 and 2, where dental students and residents are trained, also relate to the department of General Dentistry.

(2) Research

Recent research themes are listed below.

1. Study for structure of health problems and treatment planning for dental patients.
2. Study for verification and improvement of oral diagnosis.
3. Study for dental education for dental students and residents.

(3) Education

The educational objective of General Dentistry is that the students/residents acquire transversal academic framework of dental knowledge and skills and competency to provide patients with personalized treatment.

(4) Lectures & Courses

1. Introduction to the Behavioral Science. (For the 2nd-year dental students)
2. Holistic Oral Diagnosis. (For the 5th-year dental students)
3. Comprehensive Clinical Training Phase I Phase II. (For the 5th and 6th-year dental students)
4. Clinical training (For the dental residents)

(5) Clinical Services & Other Works

The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry. In the clinic, dental examination and health assessment for new outpatients are conducted to decide initial treatment plan and a clinic in charge for the patients. The patients who need comprehensive dental care and who cannot cooperate students' practice also attend this clinic to receive general dental practice.

(6) Clinical Performances

In the Dental Hospital, the clinic of Oral Diagnosis and General Dentistry is the first clinic for new outpatients. That is, the clinic is responsible for constructing good relationship between patients and the hospital. Therefore, the doctors pay attention actively to psychosocial aspects of patients during examination. In diagnosing and deciding clinic for patients, initial-treatment plans are introduced to patients. In this process, doctors think treatment plans together with patients thoroughly to obtain sound informed consent. Many patients who visits the dental hospital demands high medical level of the university hospital while not a few patients needs primary care. Oral Diagnosis and General Dentistry provides such patients with general dental practice to meet various kinds of patients' needs, makes effort to improve patients' satisfaction.

(7) Publications

[Original Articles]

1. Hiroshi Matsuura, Sai Yu, Koichi Sawasaki, Junichiro Wada, Masayuki Hideshima. Development and practical evaluation of a Japanese utterance education support system using phonetic segments and fundamental frequencies Journal of Japan e-Learning Association. 2019; (19); 15-26
2. Komagamine Y, Kanazawa M, Sato Y, Iwaki M, Jo A, Minakuchi S. Masticatory performance of different impression methods for complete denture fabrication: a randomized controlled trial. Journal of dentistry. 2019.01;
3. Ohtsu A, Takeuchi Y, Katagiri S, Suda W, Maekawa S, Shiba T, Komazaki R, Udagawa S, Sasaki N, Hattori M, Izumi Y. Influence of *Porphyromonas gingivalis* in gut microbiota of streptozotocin-induced diabetic mice. Oral diseases. 2019.01; 25(3); 868-880
4. Kouji Wada, Noriko Takei, Noriko Kanazawa, Tomoe Miyoshi, Kanako Noritake. Working Conditions of Dental Hygienists Employed in Japanese Hospitals INTERNATIONAL JOURNAL OF CLINICAL PREVENTIVE DENTISTRY. 2019.03; 15(1); 48-55
5. Hiroyuki Suzuki, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Noriko Amagai, Shunsuke Minakuchi. Changes in the nutritional statuses of edentulous elderly patients after new denture fabrication with and without providing simple dietary advice. J Prosthodont Res. 2019.07; 63(3); 288-292
6. Watanabe K, Ohsugi Y, Maekawa S, Sasaki N, Shiba T, Katagiri S, Arakawa S. Ozone Ultrafine Bubble Water improves wound healing via modification of inflammation Journal of the Stomatological Society. 2019.07; 86(2); 25-34

7. Iwaki M, Kanazawa M, Sato D, Miyayasu A, Minakuchi S. Masticatory function of immediately loaded two-implant mandibular overdentures: A 5-year prospective study. *The International journal of oral & maxillofacial implants*. 2019.09; 34(6); 1434-1440
8. Maekawa S, Onizuka S, Katagiri S, Hatasa M, Ohsugi Y, Sasaki N, Watanabe K, Ohtsu A, Komazaki R, Ogura K, Miyoshi-Akiyama T, Iwata T, Nitta H, Izumi Y. RNA sequencing for ligature induced periodontitis in mice revealed important role of S100A8 and S100A9 for periodontal destruction *Scientific Reports*. 2019.10; 9(1); 14663
9. Hiroyuki Suzuki, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Noriko Amagai, Shunsuke Minakuchi. Influence of simplified dietary advice combined with new complete denture fabrication on masticatory function of complete denture wearers. *J Oral Rehabil*. 2019.12; 46(12); 1100-1106
10. Wada J, Hideshima M, Uchikura K, Shichiri Y, Inukai S, Matsuura H, Wakabayashi N. Influence of the Covering Area of Major Connectors of Mandibular Dentures on the Accuracy of Speech Production: A Pilot Study *Folia Phoniatrica et Logopaedica*. 2019.12; 18; 1-10
11. Yuna Kanamori, Rena Takahashi, Toru Nikaido, Elias P Bamidis, Michael F Burrow, Junji Tagami. The effect of curing mode of a high-power LED unit on bond strengths of dual-cure resin cements to dentin and CAD/CAM resin blocks. *Dent Mater J*. 2019.12; 38(6); 947-954

[Misc]

1. Manabu Kanazawa, Maiko Iwaki, Mari Asami. The latest clinical evidence and practice of the implant overdenture. 2019.04; 133(4); 694-707
2. Masayuki HIDEISHIMA. Oral Appliance Therapy for Obstructive Sleep Apnea with Edentulous Dentition *Journal of Oral and Sleep Medicine*. 2019.10; 6(1); 47
3. Manabu Kanazawa, Maiko Iwaki, Yoko Uehara. The latest clinical evidence and practice of the implant overdenture-The Delivery and maintenance of implant overdenture(IOD) *Dental Outlook*. 2019.12; 134(6); 1124-1136

[Conference Activities & Talks]

1. Sachi Umemori et al.. Association between second-hand smoking and dental caries in children, results from the A-CHILD study. The 29th Annual scientific meeting of the Japan Epidemiological Association 2019.01.31 Tokyo
2. The effect of dental treatment on Metabolic syndrome -Randomized controlled trial-. 2019.05.12
3. Yuna Kanamori, Rena Takahashi, Toru Nikaido, Junji Tagami, Reinhard Hickel, Karl-Heinz Kunzelmann. Effect of Resin Coating Techniques on CAD/CAM Hybrid Ceramic Inlays. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
4. Kohei Takeda, Koji Mizutani, Takanori Matsuura, Daisuke Kido, Risako Mikami, Masahiro Noda, Prima Buranasin, Yoshiyuki Sasaki, Yuichi Izumi, Takanori Iwata. Periodontal regenerative effect of enamel matrix derivative in diabetes. IADR/AADR/CADR General Session & Exhibition 2019.06.20
5. Kanako Noritake, Jun Tsuruta, Mina Nakagawa, Kumiko Yamaguchi, Tomoe Miyoshi, Kouji Araki.. The effect of a program that medical students learn from dental students in dental student clinic.. The 51st annual meeting of Japan Society of Medical Education 2019.07.26 Kyoto
6. Sachi Umemori, Kenichi Tonami, Hiroshi Nitta, Araki Kouji. The Analysis of Unprofessional behavior in the class in Faculty of Dentistry, TMDU. The 51st Annual Meeting of the Japan Society for Medical Education 2019.07.27 Kyoto
7. Maiko Iwaki, Manabu Kanazawa, Anna Miyayasu, Thuy Vo Lam, Khaing Myat Thu, Mari Asami, Ryo Shimada, Masatoshi Negoro, Awutsadaporn Katheng, Sai Tun Naing, Yoko Uehara, Yuriko Komagamine, Daisuke Sato, Shohei Kasugai, Shunsuke Minakuchi.. Complications of Immediate Loading of Two-implant Mandibular Overdentures: 5-year prospective study. ICP/EPA 2019 2019.09.05 Amsterdam, The Netherlands

8. Katheng A, Kanazawa M, Iwaki M, Arakida T, Hada T, Soeda Y, Otake R, Minakuchi S. Effect of Stereolithography post-curing in different conditions on the fitting accuracy of photopolymer 3D resins. ICP and EPA joint meeting 2019.09.05 Amsterdam, The Netherlands
9. Akitaka Hattori ,Jun Turuta,Yasuyuki Kimura , Masayuki Hideshima, Kouji Araki. Study on the correlation between artificial tooth cutting and VR simulator. Japan Association for Simulation-based Education in Healthcare Professionals 2019.09.21 Tokyo
10. Yumika SOEDA, Manabu KANAZAWA, Maiko IWAKI, Toshio ARAKIDA, Tamaki HADA, Ryosuke OTAKE, Awutsadaporn KATHENG, Kazuo ANDO, Shunsuke MINAKUCHI. Final impression and jaw registration with CAD/CAM try-in dentures. The 10th Annual Meeting of the Japan Academy of Digital Dentistry 2019.10.05 Nara
11. Mari Asami, Miyayasu Anna, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. Masticatory function of mandibular single-implant overdentures: A 2-year follow-up report. 2019.10.06
12. Risako Mikami, Koji Mizutani, Takanori Matsuura, Daisuke Kido, Yoshiyuki Sasaki, Takanori Iwata 他. The impact of diabetes on periodontal parameters in Japanese hemodialysis patients: A cross-sectional study. 105th Annual Meeting of the American Academy of Periodontology 2019.11.03
13. Daisuke Kido, Koji Mizutani, Yuichi Izumi, Hiroshi Nitta. INSULIN RESISTANCE IMPROVEMENT WITH PERIODONTAL TREATMENT IN TYPE - 2 DIABETIC PATIENTS WITH LOCALIZED, SEVERE CHRONIC PERIODONTITIS. American Academy of Periodontology 105th ANNUAL MEETING 2019.11.03 Chicago, IL
14. 三間 裕子, 中村 周平, 飯田 知里, 犬飼 周佑, 玉岡 明洋, 秀島 雅之. 舌前方保持装置の臨床的有用性に関する検討. 第 18 回日本睡眠歯科学会総会 • 学術集会 2019.11.24 新潟
15. 秀島雅之. 教育セミナー：OA 治療における臨床でのヒント. 欠損歯列症例の OA 治療. . 第 18 回日本睡眠歯科学会総会 • 学術集会 2019.11.24 新潟
16. Akitaka Hattori ,Jun Turuta,Yasuyuki Kimura , Masayuki Hideshima, Kouji Araki. Study on the correlation between artificial tooth cutting and VR simulator. The Stomatological Society,Japan 2019.12.06 Tokyo
17. Yuna Kanamori, Kanako Noritake, Sachi Umemori, Maiko Iwaki, Daisuke Kido, Shogo Takeuchi, Akitaka Hattori, Ken-ichi Tonami, Arata Ebihara, Masayuki Hideshima, Kouji Araki, Hiroshi Nitta. Introduction of objective clinical skills examination for TMDU's trainee residents. 2019.12.07

[Awards & Honors]

1. Second Prize Poster Presentation, SEAADE 2019, 2019.08

[Others]

1. Maiko Iwaki. Grant-in-Aid for Scientific Research(C) (JSPS) , 2019.04
Prospective study of CAD/CAM complete denture for the Edentulous Patients. 2018-2020.

Psychosomatic Dentistry

Professor	Akira Toyofuku
Assistant Professor	Miho Takenoshita
Project Assistant Professor	Takeshi Watanabe
Hospital Staff	Takayuki Suga, Lou Mikuzuki
Graduate Student	Yukiko Shinohara, Kaoru Kawasaki, Shiori Sugawara, Tu Thi Huyen Trang, Takayuki Suga, Kazuya Watanabe, Yuma Aota, Mitsuhiro Asami, Chaoli Hong,
Lecturer (part-time)	Haruhiko Motomura, Ayano Katagiri, Jiro Kurata

(1) Outline

Psychosomatic dentistry is the only one department in Japan, which research and develop new diagnosis and treatment methods for MUOS such as BMS, AO, PBS etc.

(2) Research

- 1) Study on pathophysiological mechanisms of oral psychosomatic disorders
- 2) Psychosomatic study on oro-facial medically and psychiatrically unexplained symptoms
- 3) Brain imaging of oral psychosomatic disorders
- 4) Psychopharmacological study on oral psychosomatic disorders

(3) Education

It is not uncommon to see the patients diagnosed with “Oral Psychosomatic Disorders”, so there is a growing need for proper treatment of the disorders from both sides of doctors and patients. It is, therefore, extremely important for dental students to instruct in psychosomatic dentistry. However, few Dental Universities in Japan are following this. At the same time, there’s a great deal of misunderstanding about psychosomatic dentistry, in spite of we have many years of consistent education. For example, “Your work is only hearing to complaints from patients”, “Patients with not otherwise specified mental illness is eventually referred to your clinic”, or “The mission of your clinic is to calm down your patients with unidentified dental and oral complaints”.

So, regarding undergraduate medical education, we focus on not only lessons from lectures and books but also practical experience through clinical training. We have comprehensive medical teaching for fifth and sixth-year students. Students can listen to patient’s complaints directly and deepen their understanding. Actually

they can see patients with dental psychosomatic disorders, and they know that these disorders are treatable. Moreover, they can learn negative effects of wrong ideas as a psychogenic disorder, and they can understand serious distress in patients and family members.

This practice is arduous effort, but in the future, it is hoped that efforts will be made to facilitate uniformed services for patients with dental psychosomatic disorders, enhance coping skills for refractory cases, and reduce trouble with patients by the graduates of our department who mastered psychosomatic dentistry.

It is important to have identity as a dentist on practice of psychosomatic dentistry. Therefore we have advanced strengthening of human resource development. In particular, we focus on cultivation of dentists who can be readily applied their knowledge of psychosomatic medicine to clinical practice. And we are working towards establishment of ‘psychosomatic dentistry’ introduced psychotherapy.

Also regarding education for graduate student, we focus on clinical practice for development of dentists who have great skill in psychosomatic dentistry.

(4) Clinical Services & Other Works

We take charge of “Psychosomatic Dentistry clinic” in dental hospital of Tokyo Medical and Dental University. This special clinic is for patients with oral psychosomatic disorders, such as glossodynia (burning mouth syndrome), atypical facial pain, atypical odontalgia, oral dysesthesia, occlusal discomfort(dysesthesia).

Main psychosomatic treatment is psychopharmacological one with SSRIs(Selective Serotonin Reuptake Inhibitors), SNRI(Serotonin-Noradrenaline Reuptake Inhibitor), SDAs(Serotonin-Dopamin antagonists) etc. And supportive psychotherapies are applied.

Intractable cases are increasing year by year, we take care of every patient and have good clinical courses about 70% of them.

We believe there are exactly “oral psychosomatic disorders” , and dentists should be in charge of treatment. Psychosis, as a matter of course, should be taken care by psychiatrists, so we discriminate them from oral psychosomatic disorders, and properly refer to psychiatry.

On the other hand, on “functional somatic symptoms secondary to psychiatry disorders” , which are refer to us from psychiatrists, we do our best in cooperation with psychiatrists.

We have about 600 new outpatients per year, and almost of them were referred from other specialists not only in dentistry but also internal medicine, otorhinolaryngology, dermatology, psychosomatic medicine, and psychiatry. They come from the Metropolitan area, of course, Osaka, Kyushu, Hokkaido and so on. We take fine-grained care and follow up, total number of patients is up to 10,000 per year.

We have a mission to meet the demand of these patients and their families, so better treatment outcome and increasing efficiency are required, and cooperation with other medical specialists is needed.

(5) Clinical Performances

Psychosomatic dentistry clinic is very unique, specialized for patients with MUOS. We have treated a large number of patients with various oral psychosomatic problems. With our unrivalled clinical experiences for MUOS, we offer our best clinical setting for the treatments of every MUOS.

(6) Publications

[Original Articles]

1. Tu Trang T. H., Miura Anna, Shinohara Yukiko, Mikuzuki Lou, Kawasaki Kaoru, Sugawara Shiori, Suga Takayuki, Watanabe Takeshi, Aota Yuma, Umezaki Yojiro, Takenoshita Miho, Toyofuku Akira. Pharmacotherapeutic outcomes in atypical odontalgia: determinants of pain relief JOURNAL OF PAIN RESEARCH. 2019; 12; 831-839
2. Takenoshita Miho, Trang Tu T. H., Sugawara Shiori, Kawasaki Kaoru, Suga Takayuki, Watanabe Kazuya, Hong Chaoli, Sakuraba Yuka, Mikuzuki Lou, Watanabe Takeshi, Toyofuku Akira. A case study on halitophobia with oral dysesthesia treated with low-dose aripiprazole PSYCHOTHERAPY AND PSYCHOSOMATICS. 2019; 88; 125-126

3. Watanabe T, Nagamine T, Mikuzuki L, Aota Y, Suga T, Trang T.H Tu, Kawasaki K, Shinohara Y, Takenoshita M, Toyofuku A. . Changes in Corrected QT Interval may be associated with Clinical Responses in Burning Mouth Syndrome *Int Med J.* 2019.02; 26(1); 13-14
4. Yojiro Umezaki, Trang T H Tu, Akira Toriihara, Yusuke Sato, Toru Naito, Akira Toyofuku. Change of Cerebral Blood Flow After a Successful Pharmacological Treatment of Phantom Bite Syndrome: A Case Report. *Clin Neuropharmacol.* 2019.02;
5. Akihito Uezato, Akira Toyofuku, Yojiro Umezaki, Toru Nishikawa. Oral dysesthesia associated with autistic traits: a retrospective chart review. *Eur. J. Oral Sci.* 2019.05;
6. Yukiko Shinohara, Yojiro Umezaki, Ichiro Minami, Motoko Watanabe, Anna Miura, Lou Mikutsuki, Kaoru Kawasaki, Shiori Sugawara, Tu Thi Hyen Trang, Takayuki Suga, Takeshi Watanabe, Tatsuya Yoshikawa, Miho Takenoshita, Haruhiko Motomura, Akira Toyofuku.. Comorbid depressive disorders and left-side dominant occlusal discomfort in patients with phantom bite syndrome (PBS). *J Oral Rehabil.* 2019.08;
7. Takayuki Suga, Miho Takenoshita, Akira Toyofuku. Medical Comorbidities of Patients with Burning Mouth Syndrome. *Oral Dis.* 2019.08;
8. Durga Paudel, Masafumi Utsunomiya, Koki Yoshida, Sarita Giri, Osamu Uehara, Hirofumi Matsuoka, Itsuo Chiba, Akira Toyofuku, Yoshihiro Abiko. Pharmacotherapy in relieving the symptoms of burning mouth syndrome: A 1-year follow-up study. *Oral Dis.* 2019.11;
9. Shiori Sugawara, Masamichi Shinoda, Yoshinori Hayashi, Hiroto Saito, Sayaka Asano, Asako Kubo, Ikuko Shibuta, Akihiko Furukawa, Akira Toyofuku, Koichi Iwata. Increase in IGF-1 Expression in the Injured Infraorbital Nerve and Possible Implications for Orofacial Neuropathic Pain. *Int J Mol Sci.* 2019.12; 20(24);
10. Motoko Watanabe, Miho Takenoshita, Trang T H Tu, Akira Toyofuku. Real-world Discontinuation of Antidepressant Treatment in Patients with Burning Mouth Syndrome: A Chart Review. *Pain Med.* 2019.12;
11. Takayuki Suga, Miho Takenoshita, Takeshi Watanabe, Trang Th Tu, Lou Mikuzuki, Chaoli Hong, Kazuhito Miura, Tatsuya Yoshikawa, Takahiko Nagamine, Akira Toyofuku. Therapeutic Dose of Amitriptyline for Older Patients with Burning Mouth Syndrome. *Neuropsychiatr Dis Treat.* 2019.12; 15; 3599-3607

[Misc]

1. Trang T H Tu, Miho Takenoshita, Hirofumi Matsuoka, Takeshi Watanabe, Takayuki Suga, Yuma Aota, Yoshihiro Abiko, Akira Toyofuku. Current management strategies for the pain of elderly patients with burning mouth syndrome: a critical review. *Biopsychosoc Med.* 2019.01; 13; 1
2. T Trang, H Tu, Y Abiko, A Toyofuku. Mental health disorders. *Br Dent J.* 2019.12; 227(12); 1010

[Conference Activities & Talks]

1. Kazuya Watanabe, Trang T.H Tu, Lou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Takayuki Suga, Chaoli Hong, Asami Mitsuhiro, Takeshi Watanabe, Miho Takenoshita, Akira Toyofuku. The difference in the clinical characteristics of unilateral Oral Dysesthesia patients with or without trigeminal Neurovascular Compression. ICPM 25th World Congress 2019.09.11 Conference Centre Nuovo Ingresso di Careggi (NIC), Florence, Italy
2. Trang T.H Tu, Lou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Takayuki Suga, Chaoli Hong, Asami Mitsuhiro, Takeshi Watanabe, Miho Takenoshita, Akira Toyofuku. The impact of personality dimension in patients with medically unexplained oral symptoms. ICPM 25th World Congress 2019.09.12 Conference Centre Nuovo Ingresso di Careggi (NIC), Florence, Italy
3. MihoTakenoshita, Tu T H Trang, Shiori Sugawara, Kaoru kawasaki, Takayuki Suga, Kazuya Watanabe, Chaoli Hong, Yuka Sakuraba, Lou Mikuzuki,Takeshi Watanabe,Akira Toyofuku. A case study on halitophobia with oral dysesthesia treated with low- dose aripiprazole. ICPM 25th World Congress 2019.09.12 Conference Centre Nuovo Ingresso di Careggi (NIC), Florence, Italy

4. Takayuki Suga, Lou Mikuzuki, Takeshi Watanabe, TRANG T.H TU, Miho Takenoshita, Akira Toyofuku. Oral squamous cell carcinoma mimicking burning mouth syndrome in elderly patients: a case series. ICPM 25th World Congress 2019.09.13 Conference Centre Nuovo Ingresso di Careggi (NIC), Florence, Italy
5. Takeshi Watanabe, Shunsuke Takano, Kohsuke Abe, Shiori Sugawara, Kaoru Kawasaki, Kazuhito Miura, Takayuki Suga, Lou Mikuzuki, Chaoli Hong, Tu Thi Huyen Trang, Kazuya Watanabe, Miho Takenoshita, Akira Toyofuku. Effect of low dose aripiprazole on amitriptyline-intolerant burning mouth syndrome. ICPM 25th World Congress 2019.09.13 Conference Centre Nuovo Ingresso di Careggi (NIC), Florence, Italy
6. Yoshihiro Abiko, Masafumi Utsunomiya, Durga Paudel Hirofumi Matsuoka, Akira Toyofuku. . Therapeutic approaches for burning mouth syndrome. 2019 Conference meeting of the Korean Society of Psychosomatic Dentistry 2019.10.20 Preme Foundation Nexon Children's Rehabilitation Hospital, Seoul, Korea
7. Trang T.H Tu, Lou Mikuzuki, Kazuya Watanabe, Takayuki Suga, Chaoli Hong, Asami Mitsuhiro, Takeshi Watanabe, Miho Takenoshita and Akira Toyofuku . The impact of personality in patients with Burning Mouth Syndrome: Hit or Miss?. 2019 Conference meeting of the Korean Society of Psychosomatic Dentistry 2019/10/20 2019.10.20 Preme Foundation Nexon Children's Rehabilitation Hospital, Seoul, Korea
8. Takayuki Suga, Takeshi Watanabe, Lou Mikuzuki, Miho Takenoshita and Akira Toyofuku. Medical Comorbidities of Patients with Burning Mouth Syndrome. 2019 Conference meeting of the Korean Society of Psychosomatic Dentistry 2019/10/20 2019.10.20 Preme Foundation Nexon Children's Rehabilitation Hospital, Seoul, Korea
9. Takayuki Suga, Takeshi Watanabe, Lou Mikuzuki, Trang T.H Tu, Chaoli Hong, Miho Takenoshita and Akira Toyofuku. Social Indication of Jaw Deformity Surgery in Patients with Psychiatric Comorbidities. 2019 Conference meeting of the Korean Society of Psychosomatic Dentistry 2019/10/20 2019.10.20

Behavioral Dentistry

Professor Hiroshi Nitta
Research Associate Sachi Umemori

(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. Maekawa S, Onizuka S, Katagiri S, Hatasa M, Ohsugi Y, Sasaki N, Watanabe K, Ohtsu A, Komazaki R, Ogura K, Miyoshi-Akiyama T, Iwata T, Nitta H, Izumi Y. RNA sequencing for ligature induced periodontitis in mice revealed important role of S100A8 and S100A9 for periodontal destruction Scientific Reports. 2019.10; 9(1); 14663

[Conference Activities & Talks]

1. Sachi Umemori et al.. Association between second-hand smoking and dental caries in children, results from the A-CHILD study. The 29th Annual scientific meeting of the Japan Epidemiological Association 2019.01.31 Tokyo
2. Sachi Umemori, Kenichi Tonami, Hiroshi Nitta, Araki Kouji. The Analysis of Unprofessional behavior in the class in Faculty of Dentistry, TMDU. The 51st Annual Meeting of the Japan Society for Medical Education 2019.07.27 Kyoto
3. Daisuke Kido, Koji Mizutani, Yuichi Izumi, Hiroshi Nitta. INSULIN RESISTANCE IMPROVEMENT WITH PERIODONTAL TREATMENT IN TYPE - 2 DIABETIC PATIENTS WITH LOCALIZED, SEVERE CHRONIC PERIODONTITIS. American Academy of Periodontology 105th ANNUAL MEETING 2019.11.03 Chicago, IL

4. Yuna Kanamori, Kanako Noritake, Sachi Umemori, Maiko Iwaki, Daisuke Kido, Shogo Takeuchi, Akitaka Hattori, Ken-ichi Tonami, Arata Ebihara, Masayuki Hideshima, Kouji Araki, Hiroshi Nitta. Introduction of objective clinical skills examination for TMDU's trainee residents. 2019.12.07

Professional Development in Health Sciences

Professor Kazuki Takada

(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 provides 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

(3) Education

Undergraduate schools

Courses

- School of medicine (1st year): Medical Introductory Courses
- Schools of medicine/dentistry (2nd/3rd years): Global Communication for Health Professionals
- School of medicine (4th year): Preparation for Clinical Clerkship
- School of medicine (5th/6th years): Clinical Clerkship
- Health Sciences Leadership Program: Moral and Political Philosophy
- Health Sciences Leadership Program: Applied Critical Thinking for Health Sciences
- Health Sciences Leadership Program: Problem-solving in the Health Sciences

Graduate school

Course

- 【Master level】 Public Health Biology

(4) Clinical Services & Other Works

Medical Hospital

Kazuki TAKADA (Rheumatology)

(5) Publications

[Original Articles]

1. Shimozono H, M Takahashi, M Tomita, K Takada, Y Tanaka. The 2-Dimensional Approach: a novel tool to help learners organize their knowledge and improve their clinical reasoning skills MedEdPublish. 2019.06;
2. Takada K, Y Katada, S Ito, T Hayashi, J Kishi, K Itoh, H Yamashita, M Hirakata, K Kawahata, A Kawakami, N Watanabe, T Atsumi, Y Takasaki, N Miyasaka. Impact of adding tacrolimus to initial treatment of interstitial pneumonitis in polymyositis/dermatomyositis: a single-arm clinical trial Rheumatology (Oxford). 2019.09;

Family Medicine

Yosuke Takemura
Toru Yamada
Masashi Beppu
Suguru Mabuchi
Yoshiro Hadano
Kazuhisa Sakai
Mari Fukuhara
Yuiko Nagamine
Shoko Yoshida
Hiroshi Koike
Masako Sugihara
Yuya Ando
Hiroki Nin

(1) Outline

Greetings from Professor Yousuke C. Takemura

“Ambition” and “Passion”
Keys for Family Medicine/General Medicine
Share your “Ambition” with us.
You may think it impossible to become true.
Believe me, we are here for you.
We can take it with all our strength and our heart
Exert your passionate ebullience
We are ready to support you.

Professor Yousuke C. Takemura
Department of Family Medicine
Graduate School of Medical and Dental Sciences
Tokyo Medical and Dental University

Backgrounds and Aims

TMDU General Medicine/Family Medicine Network (TMUDGM/FM-N) is a network of hospitals and clinics which engage in practice, education, and research related to general medicine/family medicine or primary health care. More than ten healthcare institutions join the TMUDGM/FM-N in Tokyo Ward and a few prefectures surrounding Tokyo, Japan. The TMUDGM/FM-N is also known as a network for physicians and other professionals who engage in these activities. Members of the TMUDGM/FM-N build a weak tie with each other or facility, and collaborate closely in each activity.

The TMUDGM/FM-N engages in following activities for people in community all over the world to stay in healthy and happy lives:

1. To conduct research more efficiently and provide effective practices in general medicine/family medicine and primary health care.
2. To foster general medicine, family physicians, general practitioners, and healthcare professionals, who can

practice in the field of general medicine/family medicine and primary health care

3. To nurture more advanced personnel who can educate general medicine/family physicians, healthcare professionals, educators, or researchers in the field of general medicine/family medicine and primary health care.

Our Activity

Education

The TMUDGM/FM-N provide educations about general medicine/family medicine, and primary healthcare, for each generation of healthcare professionals, such as medical students, junior residents, and senior residents. As well, we provide inter-professional educations for the various medical professionals. Although some of our educations are provided in TMDU, lots of parts are undertaken in clinics and hospitals in community.

The TMUDGM/FM-N weighs importance on career-long education for general medicine/family physicians and other collaborating healthcare professionals. As well, we have activities of continuous medical education on themes related to general medicine/family medicine.

Graduate School

The TMUDGM/FM-N provides education and research for TMDU Graduate School of Medical and Dental Sciences. The TMUDGM/FM-N accepts international students from all over the world.

In our graduate school, we want students to learn how to resolve problems in the real community via research. Our research should not be mere finding or exploring the facts, but contribute towards people in communities. Research is only one of the tools for resolving problems in communities, improving clinical practices, and contributing to patients and people in community. Therefore, we should keep in our mind to implement the research findings into the real world.

To enable students to fulfill our aims above mentioned, we provide didactic lectures about general medicine/family medicine, biostatistics, clinical epidemiology, qualitative research, how to build questionnaire and so on. However, attending these lectures for students is not enough to resolve problems in communities and they should: approach the target community or field; get familiar with the people living there; feel known or unknown needs from the people living there; and suggest some resolution for their needs or problems. These processes require students not only technical and academic skills, but also communication or social skills. As well, these processes train students to learn by their own mistakes. Therefore, we provide students safe environments to think their own interests for themselves.

Research

The TMUDGM/FM-N conducts research several themes in general medicine/family medicine, communication, community medicine, and medical education. We especially focus on the behavioral aspects of patients and medical professionals, as well as collaborations between specialties or healthcare professionals. We use both quantitative and qualitative approaches.

The examples of ongoing research are as follows:

1. Research on the relationship between the characteristic of physicians and patients' medical seeking behavior or their health status
2. Research on non-verbal communication using artificial intelligence (AI)
3. reliability and validity of apparatus used in primary care setting (ultrasound, etc.)
4. Cost-effectiveness of the home care
5. Collaboration between primary care physicians and occupational physicians
6. To establish the method to build better team in medical setting
7. Relationship between the basis of the family medicine and health outcomes
8. Inter-professional education for students in medical school
9. Home visiting care for elderly in community
10. Other researches of family medicine/general medicine

Practice

The TMUDGM/FM-N provides care for the people living in their own community, in their own clinics or hospitals besides at outpatient department and wards in TMDU university hospital. Our practice is based on the principles and methods for the general medicine/family medicine, or primary healthcare. Additionally, we weigh importance on the collaboration between specialties, between healthcare professionals, between medical facilities, and between healthcare system and community. Moreover, we try to learn about the newest evidences for all the disease we can be involved.

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

1. Toru Yamada, Yasuaki Motomura, Eiji Hiraoka, Aki Miyagaki, Juichi Sato. Nasogastric Tubes Can Cause Intramural Hematoma of the Esophagus. *Am J Case Rep.* 2019.02; 20; 224-227
2. 鈴木 里彩, 沼沢 祥行, 竹村 洋典. 【内科サブスペシャリティから総合的に考える代謝内分泌疾患】総合内科における代謝内分泌疾患診断のポイント (総合内科)(解説/特集) 日本内科学会雑誌. 2019.04; 108(4); 722-728
3. Tomohiko Ukai, Shuhei Ichikawa, Miho Sekimoto, Satoru Shikata, Yousuke Takemura. Effectiveness of monthly and bimonthly follow-up of patients with well-controlled type 2 diabetes: a propensity score matched cohort study. *BMC Endocr Disord.* 2019.05; 19(1); 43
4. 竹村洋典. 総合診療医が心身症患者を診るときに必要な医療面接 日本のエビデンスに基づいて (解説) 心身医学. 2019.05; 59(4); 302-306
5. 松岡 尚則 (研医会), 田中 耕一郎, 牧野 利明, 別府 正志. 日本の薬・医療の始まりを考えさせられる出土物について 日本東洋医学雑誌. 2019.06; 70;
6. 別府 正志. 【難治性婦人科疾患の中医治療】難治性婦人科疾患に対する私の漢方・中医学治療 中医臨床. 2019.06; 40(2); 166-170
7. Tanizaki R, Ichikawa S, Takemura Y.. Clinical impact of perinephric fat stranding detected on computed tomography in patients with acute pyelonephritis: a retrospective observational study. *Eur J Clin Microbiol Infect Dis.* . 2019.08;
8. Nukui Y, Ayibieke A, Taniguchi M, Aiso Y, Shibuya Y, Sonobe K, Nakajima J, Kanehira S, Hadano Y, Tohda S, Koike R, Saito R.. Whole-genome analysis of EC129, an NDM-5-, CTX-M-14-, OXA-10- and MCR-1-co-producing *Escherichia coli* ST167 strain isolated from Japan. *J Glob Antimicrob Resist.* 2019.09; 18; 148-150
9. 笛木司, 谷村陽平, 田中耕一郎, 千葉浩輝, 松岡尚則, 並木隆雄, 藤田康介, 須永隆夫, 別府正志, 牧野利明. 『宋板傷寒論』の未修治附子配合処方煎煮時間と煎液に含まれるアコニチン型ジエステルアルカロイド量 — 処方中の乾姜と甘草が与える影響 — 日本東洋医学雑誌. 2019.10; 70(4); 313-323
10. Yuichiro Matsuo, Toru Yamada, Eiji Hiraoka. Unique presentation of cricoid cartilage fracture causing intermittent dyspnea without preceding trauma Nagoya Journal of Medical Science. 2019.11; 81(4); 687-691
11. Ryoichi Saito, Yukino Usui, Alafate Ayibieke, Jun Nakajima, Isaac Prah, Kazunari Sonobe, Yoshibumi Aiso, Shiori Ito, Yasuhiro Itsui, Yoshiro Hadano, Yoko Nukui, Ryuji Koike & Shuji Tohda . Hypervirulent clade 2, ribotype 019/sequence type 67 *Clostridioides difficile* strain from Japan Gut Pathog. . 2019.11; 11(54);
12. Jun Ehara, Eiji Hiraoka, Hsiang-Chin Hsu, Toru Yamada, Yosuke Homma, Shigeki Fujitani. The effectiveness of a national early warning score as a triage tool for activating a rapid response system in an outpatient setting: A retrospective cohort study. *Medicine (Baltimore).* 2019.12; 98(52); e18475

[Misc]

1. 羽田野義郎. ICD のホンネ 現場でプロジェクトをどう進めていくか J-IDEO. 2019; 622-623
2. Haya MAN, Ichikawa S, Wakabayashi H, Takemura Y. Family Caregivers' Perspectives for the Effect of Social Support on their Care Burden and Quality of Life: A Mixed-Method Study in Rural and Sub-Urban Central Japan. *The Tohoku journal of experimental medicine.* 2019.03; 247(3); 197-207

[Conference Activities & Talks]

1. 別府正志. 西洋医学と中医学における婦人科生理の考え方. イスクラ高円寺塾婦人科特別セミナー 2019.01.28 イスクラ高円寺塾東京都中野区
2. 別府正志. 月経周期中医調節法と日本における不妊症に対する応用. 第 89 届国医節第 11 届台北国際中医薬学術論壇 2019.03.10 台大医院国際会議中心 (台湾台北市)

3. 羽田野義郎. 外来での抗菌薬適正使用. 豊島区医師会シンポジウム 2019.03.20 豊島区医師会館
4. Suguru Mabuchi, Shuji Ouchi, Risa Suzuki, Norihiko Izumimoto, Yoshiyuki Numasawa, Yousuke Takemura. Severe Osteoporosis and Sarcopenia Caused by Vitamin D Deficiency due to Chronic Pancreatitis Treated with Pancreatic Enzyme: A Case Report. WONCA-APR (国際家庭医療学会アジア大洋州学会) 2019.05.17
5. Michiko Goto, Hideki Wakabayashi, Masaru Kitamura, Miho Sekimoto, Yousuke Takemura. Development of Video Review Assessment Sheet for Primary Care Resident in Mie University. WONCA-APR (国際家庭医療学会アジア大洋州学会) 2019.05.17
6. 羽田野義郎. Melioidosis. Tropical Medicine and Health 2019 Review Course 2019.08.30 順天堂大学
7. Toru Yamada. NDC-POCUS course. 2019.09.12
8. Toru Yamada. Basics of Lung ultrasound and DVT ultrasound. 2019.09.26
9. 竹村洋典. Community Health Care in Japan. 2019.12.09 Seoul National University (韓国 ソウル)

Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio
Assistant Professor: KAWAGISHI Masahiko
Assistant Professor: SAITO Kenta
Assistant Professor: SATO Keisuke
Graduate Student, MD-PhD Course : NAKAI Nori
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. Nori Nakai, Keisuke Sato, Tomomi Tani, Kenta Saito, Fumiya Sato, and Sumio Terada. Genetically encoded orientation probes for F-actin for fluorescence polarization microscopy. 2019;

[Misc]

1. Nakai Nori, Sato Keisuke, Tani Tomomi, Saito Kenta, Sato Fumiya, Terada Sumio. Genetically encoded orientation probes for F-actin for fluorescence polarization microscopy(和訳中) Microscopy. 2019.10; 68(5); 359-368

[Conference Activities & Talks]

1. Ayana Sugizaki, Keisuke Sato, Kazuyoshi Chiba, Shalin B. Mehta, Tomomi Tani, Sumio Terada. Development of a novel actin probe for fluorescence polarization microscopyda. The 124th Annual Meeting of The Japanese Association of Anatomists 2019.03.29 Niigata, Japan
2. N.Nakai,K.Sato,T.Tani,K.Saito,F.Sato,S.Terada. GFP-based F-actin Orientation Probes for Fluorescence Polarization Microscopy and Speckle F-actin Orientation Imaginag in Living Cells. 2019 The American Society for Cell Biology 2019.12.07 Washington,DC

Systems Neurophysiology

Professor Izumi Sugihara
Associate Professor Yuriko Sugiuchi
Lecturer Yoshiko Izawa
Assistant Professor Mayu Takahashi
Project Researcher Yuanjun Luo
Students (dorc) 8

(1) Outline

Department of Systems Neurophysiology, formerly Department of Physiology #1 of the medical school, is one of the basic medicine departments and take charge of research and education in the field of neurophysiology and related neurosciences.

(2) Research

Our main interest lies in clarifying the structures that underlies function of the central nervous system and then understanding their function. We are focused on the part of the central nervous system that is involved in control of eye movements. The eye movement control system is located in the cerebrum, brainstem and cerebellum, has been studied in great detail and is important clinically. The cerebellum itself is another site of focus. Dysfunction of the cerebellum causes ataxia, a movement disorder associated with impaired control of movement. We use electrophysiological, morphological and cell-biological approaches.

1) Cerebellar function

Distinct regions in the cerebellum make specific connections with different areas of the brain and are involved in the control of various movements including eye movements. For example, the neuronal circuitry that connects the lateral cerebrum, pontine nuclei, cerebellar cortex (hemisphere), cerebellar nucleus (dentate nucl.), thalamus and cerebrum is important for initiation, execution and control of movements. To understand cerebellar function, it is important to understand the organization of the cerebellum into distinct anatomical regions, to characterize the specific neuronal circuitry of these regions, and to identify how the cerebellum is organized into regions and functions by way of the input and output systems. Our systematic approach to this question includes (developmental) anatomy, molecular biology, and electrophysiology. We have expertise in neuronal labeling with marker molecules and tracers, single-axonal reconstruction, three-dimensional mapping of neuronal projection patterns.

(3) Education

We participate in Introductory Neurophysiology, Neuroscience and Physiology Lab courses for medical students (2nd year) as well as in courses for graduate students. We mainly teach the neurophysiology sections in these courses. Our goal is for students to understand normal function of nerve cells and the nervous system and, on this ground, to understand pathological states of the nervous system in disease. For this purpose, we give clinically-oriented lectures and laboratory courses linked with morphology and pharmacology.

(4) Lectures & Courses

Our lectures cover transport and electric potential of the cell membrane, excitation and synaptic transmission (Introductory Neurophysiology), sensory systems, motor systems, autonomic nervous systems, and higher brain function (Neuroscience), i.e. neurophysiology in general from the molecular, cellular through the organismic levels. To promote students' self-learning attitude, we sometimes employ an "active-learning" style. In the laboratory course, we promote student-teacher discussion in small groups. We have had two "elective research course" students.

(5) Publications

[Original Articles]

1. Shinoda Yoshikazu, Takahashi Mayu, Sugiuchi Yuriko. Brainstem neural circuits for fixation and generation of saccadic eye movements MATHEMATICAL MODELLING IN MOTOR NEUROSCIENCE: STATE OF THE ART AND TRANSLATION TO THE CLINIC. GAZE ORIENTING MECHANISMS AND DISEASE. 2019; 249; 95-104
2. Takahashi Mayu. Morphological and electrophysiological characteristics of the commissural system in the superior colliculi for control of eye movements MATHEMATICAL MODELLING IN MOTOR NEUROSCIENCE: STATE OF THE ART AND TRANSLATION TO THE CLINIC. GAZE ORIENTING MECHANISMS AND DISEASE. 2019; 249; 105-115
3. Nguyen-Minh Viet T., Khoa Tran-Anh, Luo Yuanjun, Sugihara Izumi. Electrophysiological Excitability and Parallel Fiber Synaptic Properties of Zebrin-Positive and -Negative Purkinje Cells in Lobule VIII of the Mouse Cerebellar Slice FRONTIERS IN CELLULAR NEUROSCIENCE. 2019.01; 12; 513
4. Biswas MS, Luo Y, Sarpong GA, Sugihara I. Divergent projections of single pontocerebellar axons to multiple cerebellar lobules in the mouse. The Journal of comparative neurology. 2019.02; 527(12); 1966-1985
5. Na J, Sugihara I, Shinoda Y. The entire trajectories of single pontocerebellar axons and their lobular and longitudinal terminal distribution patterns in multiple aldolase C positive compartments of the rat cerebellar cortex. The Journal of comparative neurology. 2019.03; 527(15); 2488-2511

[Conference Activities & Talks]

1. Mayu Takahashi. Brainstem neural circuits of saccadic eye movements and their frame of reference. The Kyoto Symposium on the Eye and Head Movement Control Systems, Pre-NCM 2019.04.21
2. Mayu Takahashi. New perspectives on the role of the superior colliculus in visually-guided motor behavior. 29th NCM (Neural Control of Movement) Annual Meeting 2019.04.25
3. Mayu Takahashi. Brainstem neural circuits of horizontal and vertical saccadic eye movements and their relation to quick phases of vestibular nystagmus. XLVIth Congress of the International Neurootological & Equilibrimetric Society 2019.05.31
4. Nguyen-Minh Viet Tuan, Tran Anh Khoa, Luo Yuanjun, Sugihara Izumi. Zebrin 陽性および陰性プルキンエ細胞の電気生理学的比較 (Electrophysiological comparison between zebrin-positive and -negative Purkinje cells). The Journal of Physiological Sciences 2019.06.01
5. Shimuta Misa, Sugihara Izumi, Ishikawa Taro. 新皮質の体性感覚シグナルの小脳統合 (Cerebellar integration of neocortical somatosensory signals). The Journal of Physiological Sciences 2019.06.01
6. Yoshiko Izawa, Hisao Suzuki. Suppressive control of reflexive eye movements by the frontal eye field in the monkey. The Gordon Research Conference 2019 on Eye Movements 2019.07.07 Bates College, Lewiston, ME, U.S.A.
7. Mayu Takahashi. Frame of reference of saccadic eye movements. The 42nd Annual meeting of the Japan Neuroscience Society 2019.07.27

8. Viet T Nguyen-Minh, Khoa Tran-Anh, Yuanjun Luo, Izumi Sugihara. Comparison of electrophysiological characteristics of Zebrin-positive and -negative Purkinje cells. The 75th Fujihara Seminar ‘cerebellum as a CNS hub’ 2019.12.03 Tokyo Medical and Dental University, Tokyo
9. Biswas MS, Luo Y, Sugihara I. Morphology of single pontocerebellar axons in relation to zebrin stripes and lobules in the mouse cerebellum. The 75th Fujihara Seminar ‘cerebellum as a CNS hub’ 2019.12.03 Tokyo Medical and Dental University, Tokyo

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. Tanaka DH, Li S, Mukae S, Tanabe T. Genetic Access to Gustatory Disgust-Associated Neurons in the Interstitial Nucleus of the Posterior Limb of the Anterior Commissure in Male Mice. *Neuroscience*. 2019.06; 413; 45-63
2. Wang, X., Saegusa, H., Huntula, S. and Tanabe, T. . Blockade of microglial Cav1.2 Ca²⁺ channel exacerbates the symptoms in a Parkinson' s disease model. *Scientific Reports* . 2019.06; 9(9138);
3. Huntula, S., Wang, X., Saegusa, H. and Tanabe, T.. Involvement of N-type Ca²⁺ channel in microglial activation and its implications to aging-induced exaggerated cytokine response. *Cell Calcium*. 2019.07; 82; 102059
4. Tanaka, D.H. and Tanabe, T. . CHANging consciousness epistemically (CHANCE): An empirical method to convert the subjective content of consciousness into scientific data. *J. Mind Behav.* . 2019.12; 40(3,4); 177-190

[Conference Activities & Talks]

1. Contribution of GPD2/mGPDH to an alternative respiratory chain of the mitochondrial energy metabolism and the stemness in CD133-positive HuH-7 cells. 2019.12.03

Molecular Neuroscience

Professor Kohichi Tanaka
Assistant Professor Saeko Ishida
Assistant Professor Yuichi Hiraoka

Graduate Student (doctor course)
Takehisa Handa
Bi Haining

Graduate Student (master course)
Haruna Aikawa
Yuuta Sawada
Zhao Di
Ryo Matsuura
Minami Kato

Technical Staff
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. Human genetic studies have suggested that de novo mutations in GLAST (EAAT1) is linked to schizophrenia. Consistent with this, GLAST null mice show phenotypes relevant to positive, negative and executive/cognitive symptoms of schizophrenia, including novelty-induced locomotor hyperactivity, abnormal social behavior characterized by reduced initiation of social interactions, poor nesting and impaired pairwise visual discrimination learning. Repeated phencyclidine (PCP) administration induces several schizophrenia-like psychobehavioral abnormalities and decreased extracellular glutamate levels, which are associated with increased expression of GLAST in the prefrontal cortex of mice. In this study, we investigated the functional roles of GLAST in the schizophrenia-like psychobehavioral abnormalities induced by repeated PCP administration using GLAST heterozygous (GLAST+/-) mice. PCP-administered GLAST wild-type (+/+) mice showed enhancement of immobility in a forced swimming test, impairments of visual recognition memory in a novel object recognition test, decrease in high potassium (K⁺)-induced extracellular glutamate release, and overexpression of GLAST

and S100 proteins in the PFC, compared to saline-administered GLAST+/+ mice. Such behavioral and neurochemical abnormalities were not observed in PCP-administered GLAST+/- mice. These results clearly suggest that overexpression of GLAST and glial activation play important roles in the development of emotional and cognitive abnormalities in PCP-administered GLAST+/+mice. It is therefore necessary to strictly regulate the expression of GLAST to maintain normal brain function. Studies targeting GLAST may lead to the development of medications for emotional (negative symptoms) and cognitive impairments in schizophrenia.

2. Elucidation of the effect of abnormalities in the GATOR1 complex on focal epilepsy

Epilepsy is characterized by recurrent seizures resulting from excessive neuronal discharge and presents a wide variety of clinical symptoms. Although epilepsy is a frequent neurological disorder that occurs in about 1% of the population, there is often no fundamental cure for it, forcing it to rely on symptomatic treatment with prolonged use of antiepileptic drugs. In addition, seizures in about 30% of patients fail to respond to the drugs. Therefore, the development of new treatment and prevention methods is urgent.

"Focal epilepsy", in which the site of abnormal neuronal firing is limited to a part of the cerebral hemisphere, accounts for half of adult epilepsy. Gap activity toward Rags 1 (GATOR1) complex abnormality is involved in about 10% of the onset of focal epilepsy. The GATOR1 complex is a complex composed of DEP domain-containing protein 5 (DEPDC5) and Nitrogen permease regulator 2 / 3-like protein (NPRL2, NPRL3). It suppresses the mechanical target of rapamycin complex1 (mTORC1) pathway that controls cell growth and proliferation (Fig.2). However, the function of the GATOR1 complex in the nervous system has not been clarified. We aim to elucidate the function of the GATOR1 complex and the role on epileptogenesis using mouse models.

Because conventional knockout (KO) of DEPDC5, NPRL2, and NPRL3 in mice results in embryonic lethal, it was impossible to analyze their functions in adults. In this year, we focused on the cerebral cortex where most seizure focus exist, and generated the conditional knockout (cKO) mice of each gene. Phenotypic analysis revealed that each cKO mouse exhibited spontaneous epileptic seizures and cerebral cortical dysplasia similarly to patients, indicating that they are useful as epilepsy model mice (Fig.3). Further analysis of these mice will promote our research on elucidation of the onset mechanism.

(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. Yang-Yang Feng, Miao Tang, Mitsuhiro Suzuki, Chinthika Gunasekara, Yuki Anbe, Yuichi Hiraoka, Jun Liu, Helmut Grasberger, Mamoru Ohkita, Yasuo Matsumura, Ji-Yang Wang and Takeshi Tsubata. Essential Role of NADPH Oxidase-Dependent Production of Reactive Oxygen Species in Maintenance of Sustained B Cell Receptor Signaling and B Cell Proliferation *J Immunol.* 2019.03;
2. Uchida Mizuki, Hida Hirotake, Mori Kentaro, Yoshimi Akira, Kitagaki Shinji, Yamada Kiyofumi, Hiraoka Yuichi, Aida Tomomi, Tanaka Kohichi, Ozaki Norio, Noda Yukihiro. Functional roles of the glial glutamate transporter (GLAST) in emotional and cognitive abnormalities of mice after repeated phencyclidine administration *EUROPEAN NEUROPSYCHOPHARMACOLOGY.* 2019.08; 29(8); 914-924

Neuropathology

Professor: Hitoshi Okazawa

Practical Professor: Kazuhiko Tagawa

Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone, Toshiki Uchihara(∼ 2019.3)

Assistant Professor: Kyota Fujita

Project Assistant Professor: Hidenori Homma,

Emiko Yamanishi(∼ 2019.3)

Assistant Administrative Staff: Shigemi Sato, Xuemei Zhang(∼ 2019.6)

Secretary: Marie Tanaka

Graduate Student : Kanoh Kondo, Hikari Tanaka,

Maiko Inotsume(∼ 2019.3), Yuki Yoshioka, Jin Meihua, Jin Xiaocen, Huang Yong

(1) Outline

The goals of our research are to elucidate molecular mechanisms of neurodegenerative disorders as well as of mental retardation, and to develop novel therapeutics for those intractable diseases. In neurodegeneration, we are now focusing on polyglutamine diseases including hereditary spinocerebellar degenerations and Huntington's disease. Knowledge from transcriptome and proteome analyses of the pathologies will lead to new types of molecular therapeutics. In reference to mental retardation, we are developing animal models and analyzing molecular pathologies of our original molecule PQBP1 whose mutations cause mental retardation with microcephaly. This line of research is also for developing new therapeutics of the common but intractable diseases.

(2) Research

Research Contents

Following studies have been intensively carried out in our laboratory.

- 1) Investigation of molecular pathologies of neurodegenerative diseases.
- 2) Studies on impairment of DNA-repair in polyglutamine diseases.
- 3) Development of new seed drugs for neurodegeneration.
- 4) Development of new seed drug for mental retardation.
- 5) Investigation of molecular functions of Oct-3/4

Below is the brief report of this year's progress.

1. YAP-dependent necrosis occurs in early stages of Alzheimer's disease and regulates mouse model pathology

The ability to diagnose AD at an early stage is eagerly anticipated, especially after clinical trials of anti-Aβ antibodies and γ-/β-secretase inhibitors in post-onset patients proved disappointing. A deeper understanding of MCI could play a pivotal role in the development of new therapeutic strategies for AD. Despite the importance of MCI, the pathological and molecular evaluation remains insufficient especially from the aspect of chronological change of neuronal function and cell death. Accordingly, no efficient single biomarker directly reflecting disease activity in MCI has yet been reported.

Cutting-edge techniques, including comprehensive analyses, have identified molecules in addition to Aβ and tau that could be targeted for therapeutic intervention at the early stage of AD. For instance, comparison

of neuroimaging and transcriptome data revealed that a genetic profile of lipid metabolism centered by APOE affects propagation patterns of both Abeta and tau in the brain. In another study, a meta-analysis of functional genomic data from AD showed that YAP, a co-transcriptional factor that regulates cell death and survival by binding to the different transcription factors p73 and TEA domain family member 1 (TEAD), is positioned at the center of the molecular network of AD. Elevated activity of TEAD mediated by YAP has been implicated in cell proliferation, differentiation, and survival, whereas elevated p73 activity and reduced TEAD activity promote apoptosis and necrosis, respectively.

Previously, we performed a comprehensive phosphoproteome analysis of four strains of AD model mice and human postmortem AD brains, and discovered three proteins whose phosphorylation state is altered at a very early stage before extracellular amyloid aggregates. One such protein is MARCKS, which anchors the actin cytoskeleton to the plasma membrane and plays a critical role in stabilizing the post-synaptic structure of dendritic spines. Phosphorylation of MARCKS at Ser46 decreases its affinity for actin and destabilizes dendritic spines. High mobility group box-1 (HMGB1) contributes to the MARCKS phosphorylation via Toll-like receptor 4 (TLR4) since blockade of HMGB1–TLR4 binding with monoclonal anti-HMGB1 antibodies suppresses the phosphorylation of MARCKS at Ser46, stabilizes dendritic spines, and rescues cognitive impairment in AD model mice. Given that HMGB1 is released from necrotic cells, it remains unclear how MARCKS phosphorylation, which occurs at the early stage of AD pathology, is connected to neuronal cell death, which is believed to occur at a relatively late stage.

In the current study, we found that HMGB1 levels were remarkably elevated in CSF of mild cognitive impairment (MCI), but not so elevated in AD patients. Consistent with this, active neuronal necrosis revealed by our original marker, myristoylated alanine-rich C-kinase substrate phosphorylated at serine 46 (pSer46-MARCKS), increased to the greatest extent during preclinical stages of AD mouse models and human MCI patients. Post-mortem brains of MCI rather than symptomatic AD patients reveal a remarkable increase of necrosis. In vivo imaging reveals instability of endoplasmic reticulum (ER) in mouse AD models and genome-edited human AD iPS cell-derived neurons, which were reminiscent of transcriptional repression-induced atypical cell death (TRIAD). In addition, we showed that the observed necrosis was caused by a deficiency of YAP, resulting in suppression of the transcriptional activity of TEAD, the final effector molecule of the Hippo pathway. The level of nuclear Yes-associated protein (YAP) is remarkably decreased in such neurons under AD pathology due to the sequestration into cytoplasmic amyloid beta (Abeta) aggregates, supporting the feature of YAP-dependent necrosis. Suppression of early-stage neuronal death by AAV-YAPdeltaC reduces the later-stage extracellular Abeta burden and cognitive impairment. These findings unravel the occurrence of cell death at the early stage in AD, suggesting that preclinical/prodromal YAP-dependent neuronal necrosis represents a target for AD therapeutics.

(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. Inoue S, Hayashi K, Fujita K, Tagawa K, Okazawa H, Kubo K, Nakajima K. Drebrin-like (Dbnl) controls neuronal migration via regulating N-cadherin expression in the developing cerebral cortex. *Journal of Neuroscience*. 2019.01; 39(4); 678-691

2. Bannai T, Mano T, Chen X, Ohtomo G, Ohtomo R, Tsuchida T, Koshi-Mano K, Hashimoto T, Okazawa H, Iwatsubo T, Tsuji S, Toda T, Iwata A. Chronic cerebral hypoperfusion shifts the equilibrium of amyloid beta oligomers to aggregation-prone species with higher molecular weight. *Scientific Reports*. 2019.02; 9(1); 2827
3. Rahmn SK, Okazawa H, Chen YW. Frameshift PQBP-1 mutants K192Sfs*7 and R153Sfs*41 implicated in X-linked intellectual disability form stable dimers *Journal of Structural Biology*. 2019.06; 206(3); 305-313

[Misc]

1. Xigui Chen, Kanoh Kondo, Hitoshi Okazawa. Methods to image macroautophagy in the brain in vivo. *Methods in Molecular Biology*. 2019.01; 1880; 529-534

[Conference Activities & Talks]

1. Hitoshi Okazawa. New Treatment Strategies in Huntington's Disease and Other Chorea. The 6th Asian and Oceanian Parkinson's Disease and Movement Disorders Congress 2019 2019.04.13 InterContinental-Hangzhou(China Hangzhou)
2. Kyota Fujita, Xigui Chen, Hidenori Homma, Kazuhiko Tagawa, Hitoshi Okazawa. Targeting Tyro3 ameliorates a model of PGRN-mutant FTLD-TDP via tau-mediated synaptic pathology. 60th annual meeting of the Japanese society of neurology 2019.05.22 Osaka International Convention Center(Osaka)
3. Hitoshi Okazawa. Gene therapy against SCA1 based on the molecular pathomechanism. 60th Annual Meeting Of The Japanese Society of Neurology 2019.05.25 Osaka International Convention Center(Osaka)
4. Hitoshi Okazawa. Gene therapy for spinocerebellar ataxia. The 25th Annual Meeting of Japan Society of Gene and Cell Therapy(JSGCT2019) 2019.07.21 The University of Tokyo(Tokyo)
5. Hitoshi Okazawa. Research and development of neurodegenerative diseases based on the all Japan Brain Bank Network. NEURO2019 2019.07.25 Toki Messe(Niigata)
6. Hikari Tanaka, Kanoh Kondo, Xigui Chen, Hidenori Homma, Kazuhiko Tagawa, Aurelian Kerever, Shigeki Aoki, Takashi Saito, Takaomi Saido, Shin-ichi Muramatsu, Kyota Fujita, Hitoshi Okazawa. The intellectual disability gene PQBP1 rescues Alzheimer's disease pathology. NEURO2019 2019.07.27 Toki Messe(Niigata)
7. Kyota Fujita, Hidenori Homma, Kanoh Kondo, Kazuhiko Tagawa, Hitoshi Okazawa. Ser46-phosphorylated MARCKS is a common mechanism of pre-aggregation neurite degeneration in across multiple dementia. NEURO2019 2019.07.27 Toki Messe(Niigata)
8. Hitoshi Okazawa. Targeting HMGB1-mediated expansion of neurodegeneration at the ultra-early phase pathology of Alzheimer's disease. AsCNP2019 2019.10.12 Fukuoka Sunpalace Hotel and Hall (Fukuoka)
9. Hitoshi Okazawa. HMGB1 and Neurodegeneration. 9th International DAMPs and Alarmins Symposium 2019.11.06 Okayama University Shikata Campus(Okayama)
10. Hitoshi Okazawa. Alzheimer's disease and Autophagy. The 38th Annual Meeting of Japan Society for Dementia Research 2019.11.07 Keio Plaza Hotel (Tokyo)
11. Hitoshi Okazawa. New therapeutics development against ultra-early phase AD pathology. The 38th Annual Meeting of Japan Society for Dementia Research 2019.11.07 Keio Plaza Hotel (Tokyo)
12. Hitoshi Okazawa. Ultra-early phase pathology of neurodegeneration. China-Japan High-end Forum on Medical and Health Cooperation 2019.12.21 Jinan University (China Guangzhou)

Ophthalmology and Visual Science

Professor;Kyoko Ohno-Matsui

Specially-appointed professor;Makoto Aihara

Associate Professor;Takeshi Yoshida

Junior Associate Professor;Hiroshi Takase, Koju Kamoi, Shintaro Horie

Assistant Professor; Tae Yokoi, Natsuko Nagaoka, Hiroyuki Takahashi, Yuko Iwasaki, Kengo Uramoto

Graduate student; Hisako Karube, keijia Cao, Yuxin Fang, Ran Du, Xie Shi Qi

(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. Minami Uchida, Koju Kamoi, Naoko Ando, Chenxi Wei, Hisako Karube, Kyoko Ohno-Matsui. Safety of Infliximab for the Eye Under Human T-Cell Leukemia Virus Type 1 Infectious Conditions in vitro. *Front Microbiol.* 2019; 10; 2148
2. Koju Kamoi, Kyoko Ohno-Matsui. Intraocular Infiltration. *American Journal of Tropical Medicine and Hygiene.* in press. 2019;
3. Koju Kamoi, Akihiko Okayama, Shuji Izumo, Isao Hamaguchi, Kaoru Uchimaru, Arinobu Tojo, Kyoko Ohno-Matsui. Adult T-Cell Leukemia/Lymphoma-Related Ocular Manifestations: Analysis of the First Large-Scale Nationwide Survey. *Front Microbiol.* 2019.01; 9; 3240
4. Pei-Chang Wu, Meng-Ni Chuang, Jessie Choi, Huan Chen, Grace Wu, Ohno-Matsui K, Jost B Jonas, Chui Ming Gemmy Cheung. Update in myopia and treatment strategy of atropine use in myopia control. *Eye (Lond).* 2019.01; 33(1); 3-13
5. Raja Narayanan, Ohno-Matsui K. Choroidal vasculature without angiography. *Indian J Ophthalmol.* 2019.01; 67(1); 141
6. Takashi Watanabe, Kaori Kasahara, Soh Futagami, Yuxin Fang, Ran Du, Muka Moriyama, Kengo Uramoto, Tae Yokoi, Yuka Onishi, Takeshi Yoshida, Koju Kamoi, Jost B Jonas, Ohno-Matsui K. Cilioretinal Arteries and Cilioretinal Veins in Eyes with Pathologic Myopia. *Sci Rep.* 2019.02; 9(1); 2451
7. Daniel Ian Flitcroft, Mingguang He, Jost B Jonas, Monica Jong, Kovin Naidoo, Ohno-Matsui K, Jugnoo Rahi, Serge Resnikoff, Susan Vitale, Lawrence Yannuzzi. IMI - Defining and Classifying Myopia: A Proposed Set of Standards for Clinical and Epidemiologic Studies. *Invest. Ophthalmol. Vis. Sci.* 2019.02; 60(3); M20-M30

8. Serge Resnikoff, Jost B Jonas, David Friedman, Mingguage He, Monica Jong, Jason J Nichols, Ohno-Matsui K, Earl L Smith, Christine F Wildsoet, Hugh R Taylor, James S Wolffsohn, Tien Y Wong. Myopia - A 21st Century Public Health Issue. *Invest. Ophthalmol. Vis. Sci.*. 2019.02; 60(3); Mi-Mii
9. Hiroyuki Takahashi, Hiroshi Takase, Yukiko Terada, Manabu Mochizuki, Kyoko Ohno-Matsui. Acquired myopia in Vogt-Koyanagi-Harada disease. *Int Ophthalmol.* 2019.03; 39(3); 521-531
10. Masaru Takeuchi, Takayuki Kanda, Toshikatsu Kaburaki, Rie Tanaka, Kenichi Namba, Koju Kamoi, Kazuichi Maruyama, Etsuko Shibuya, Nobuhisa Mizuki. Real-world evidence of treatment for relapse of noninfectious uveitis in tertiary centers in Japan: A multicenter study. *Medicine (Baltimore)*. 2019.03; 98(9); e14668
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14. Ohno-Matsui K, Fang Y, Shinohara K, Takahashi H, Uramoto K, Yokoi T. Imaging of Pathologic Myopia. *Asia-Pacific journal of ophthalmology (Philadelphia, Pa.)*. 2019.03;
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17. Tanaka Noriko, Shinohara Kosei, Yokoi Tae, Uramoto Kengo, Takahashi Hiroyuki, Onishi Yuka, Horie Shintaro, Yoshida Takeshi, Ohno-Matsui Kyoko. Posterior staphylomas and scleral curvature in highly myopic children and adolescents investigated by ultra-widefield optical coherence tomography PLOS ONE. 2019.06; 14(6); e0218107
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James Fujimoto. Consensus Nomenclature for Reporting Neovascular Age-Related Macular Degeneration Data: Consensus on Neovascular Age-Related Macular Degeneration Nomenclature Study Group. Ophthalmology. 2019.11;

37. Nagaoka N, Yoshida T, Cao K, Iwasaki Y, Nakahama KI, Morita I, Ohno-Matsui K. Visual arrestin modulates gene expression in the retinal pigment epithelium: Implications for homeostasis in the retina. Biochemistry and biophysics reports. 2019.12; 20; 100680
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[Books etc]

1. Ohno-Matsui K. Updates on Myopia. 2019.10 (ISBN : 978-9811384905)

[Misc]

1. Ohno-Matsui K, Jost B Jonas. Posterior staphyloma in pathologic myopia. Prog Retin Eye Res. 2019.05; 70; 99-109
2. Manabu Mochizuki, Koju Kamoi. F1000Prime Recommendation of [Gül A et al., Ann Rheum Dis 2012, 71(4):563-6] . F1000 Prime.

[Conference Activities & Talks]

1. Ohno-Matsui K. Vitreous imaging in pathologic myopia. 3rd International swept-source OCT and angiography conference 2019.02.10 Florida, USA
2. Ohno-Matsui K. Early signs of posterior staphyloma. 3rd International swept-source OCT and angiography conference 2019.02.10 Florida, USA
3. Takahashi H, Ohno-Matsui K. Ultra wide-field swept-source OCT imaging of posterior vitreous in eyes with high myopia. 42nd Annual meeting macula society 2019.02.13 Florida, USA
4. Yokoi T, Sakaguchi T, Terano Y, Ohno-Matsui K. Anti-VEGF therapy for myopic CNV. APAO 2019 2019.03.08 Bangkok, Thailand
5. Ohno-Matsui K. Mysteries on myopic CNV and dome-shaped macula. XXIII Congreso 2019.03.09 Madrid, Spain
6. Ohno-Matsui K. Ultra wide-field imaging of posterior staphyloma. XXIII Congreso 2019.03.09 Madrid, Spain
7. Ohno-Matsui K. Ultra wide-field OCT for myopic retinoschisis and myopic vitreous changes. XXIII Congreso 2019.03.09 Madrid, Spain
8. Yokoi T, Sakaguchi T, Terano Y, Ohno-Matsui K. Real-world data of intravitreal aflibercept for myopic choroidal neovascularisation: 6-month outcomes of Japan post-marketing surveillance. 2019.03.09 Bangkok, Thailand
9. Yoshida T, Suga M, Nomura T, Aihara M, Ohno-Matsui K. Two years follow-up of ExPress® implantation surgery for glaucoma in high myopic eyes. 8th World Glaucoma Congress 2019.03.29 Melbourne, Australia
10. Tatsuro Sakura, Hiroshi Takase. A Case of White Retinal Lesion. Ochanomizu advanced medical seminar 2019.04.09 Tokyo
11. Effect of adalimumab on noninfectious uveitis. 2019.04.19
12. A nationwide survey of PCR using intraocular fluids for infectious uveitis. 2019.04.19
13. GWC of rubella virus in vitreous opacity of unknown etiology. 2019.04.19

14. Hiroshi Takase, Mitsunao Ide, Kyoko Ohno-Matsui. Positivity of rubella virus in steroid-resistant intermediate uveitis of unknown etiology. The Association for Research in Vision and Ophthalmology Annual Meeting 2019.04.28 Vancouver, Canada
15. Vutipongsatorn K, Yoshida T, Li X, Cao K, Ohno-Matsui K. Constructing murine model of posterior staphyloma through targeted disruption of bruch's membrane. ARVO2019 2019.05.01 Vancouver, Canada
16. Nomura T, Yoshida T, Aihara M, Ohno-Matsui K. Identification of schlemm's canal by anterior segment optical coherence tomography in patients with high myopia. ARVO2019 2019.05.01 Vancouver, Canada
17. Jonas JB, Ohno-Matsui K, Holbach L, Panda-Jonas S. Histology of myopic scleral staphylomas. ARVO2019 2019.05.01
18. Tanaka N, Shinohara K, Yokoi T, Uramoto K, Takahashi H, Onishi Y, Horie S, Ohno-Matsui K. Detection of early changes of posterior staphylomas in children and young adults by Ultra wide-field OCT. ARVO2019 2019.05.01 Vancouver, Canada
19. Ohno-Matsui K. OCT-based classification of myopic maculopathy. MaculArt2019 2019.06.25 Paris, France
20. Mitsunao Ide, Hiroshi Takase, Kyoko Ohno-Matsui. Usefulness of vitreous biopsy for steroid-resistant intermediate uveitis. Global Ocular Inflammation Workshops 2019 2019.06.28 Sapporo
21. Hiroshi Takase, Justine Smith, Nisha Acharya, Narsing Rao. Manabu Mochizuki. International Questionnaire Survey on the Management of Ocular Sarcoidosis. 7th International Workshop on Ocular Sarcoidosis 2019.06.29 Sapporo
22. Ohno-Matsui K. Ultrawide-field OCT for myopic retinoschisis and myopic vitreous changes. APRIS(Asia-Pacific Retinal Imaging Society Congress)2019 2019.07.06 Seoul, Korea
23. Ohno-Matsui K. Ultra-widefield swept-source OCT imaging of pathologic myopia. 19th EURETINA Congress 2019.09.07 Paris, France
24. Yokoi T, Shinohara K, Fang Y, Ogata S, Yoshida T, Imanaka T, Yoshida H, Shibagaki K, Inoue H, Toshimori M, Togashi Y, Ohno-Matsui K. A Retrospective Study on the Development of Posterior Staphyloma in High Myopia Patients. 17th IMC(International myopia Conference) 2019.09.12 Tokyo, Japan
25. Nomura T, Yoshida T, Tobe M, Ito T, Suga M, Ohno-Matsui K. Identification of Schlemm's Canal by Anterior Segment Optical Coherence Tomography in patients with Pathologic Myopia. 17th IMC(International myopia Conference) 2019.09.12 Tokyo, Japan
26. Fang Y, Yokoi T, Shimada N, Du R, Shinohara K, Takahashi H, Uramoto K, Ohno-Matsui K. Pars Plana Vitrectomy-Associated Macular Atrophy in Pathologic Myopia. 17th IMC(International myopia Conference) 2019.09.12 Tokyo, Japan
27. Toyota S, Yoshida T, Nomura T, Yana M, Ohno-Matsui K. Relationship Between Microperimetry and Goldmann Visual Field Variability In Pathological Myopia. 17th IMC(International myopia Conference) 2019.09.12 Tokyo, Japan
28. Xie S, Fang Y, Du R, Yokoi T, Takahashi H, Uramoto K, Yoshida T, Ohno-Matsui K. Abruptly Emerging Vessels in Myopic Patchy Chorioretinal Atrophy. 17th IMC(International myopia Conference) 2019.09.12 Tokyo, Japan
29. Vutipongsatorn K, Yokoi T, Ohno-Matsui K. Current and Emerging Pharmaceutical Interventions for Myopia. 17th IMC(International myopia Conference) 2019.09.14 Tokyo, Japan
30. Watanabe T, Yokoi T, Moriyama M, Tanaka N, Shinohara K, Takahashi H, Yoshida T, Ohno-Matsui K. Comparison of Clinical Features in Highly Myopic Eyes with and without Posterior Staphyloma evaluated with Ultrawide-Field Swept-Source OCT. 17th IMC(International myopia Conference) 2019.09.15 Tokyo, Japan
31. Vutipongsatorn K, Yoshida T, Li X, Cao K, Ohno-Matsui K. Constructing murine model of posterior staphyloma through targeted disruption of bruch's membrane. 19th EURETINA Congress 2019.09.18 Paris, France

32. Azuma T, Yokoi T, Ohno-Matsui K. Case report: Is it really myopic CNV? . APAO Grand Rounds Around the World 2019.10.03 Hong Kong, China
33. Sugisawa K, Nagaoka N, Yokoi T, Horie S, Ohno-Matsui K. Mystery case with diffuse choroidal lesions. APAO Grand Rounds Around the World 2019.10.03 Hong Kong, China
34. Ohno-Matsui K. Ultra-widefield Swept Source OCT for Dynamic Observations of Posterior Vitreous. AAO2019 2019.10.12 San Francisco, USA
35. Hiroyuki T, Tanaka N, Shinohara K, Yokoi T, Yoshida T, Ohno-Matsui K. Ultra-widefield OCT imaging for posterior vitreous in eyes with myopic macular retinoschisis. AAO2019 2019.10.12 San Francisco, USA
36. Ohno-Matsui K, Cheung G, Lai T, Hirakata A. What You Need To Know about Pathologic Myopia?. AAO2019 2019.10.13 San Francisco, USA
37. Stanga PE, Fawzi A, Moussa MS, Ohno-Matsui K, Papayannis A, Sadda SR, Staurengi G. Spectral Domain and Swept Source Cross-Sectional, En Face, Angiographic, 3-D Rendering and Intraoperative OCT: Diagnosis and Management of Vitreoretinal and Retinochoroidal Disorders. AAO2019 2019.10.13 San Francisco, USA
38. Grzybowski A, Repka MX, Koffler BH, Ohno-Matsui K. New Approaches to the Prevention and Treatment of Myopia Update 2019. AAO2019 2019.10.14 San Francisco, USA
39. Yana M, Yokoi T, Ohno-Matsui K. To be determined. English pathologic myopia meeting 2019.10.24 Kyoto (TKP Garden city Kyoto)
40. Onishi Y, Yokoi T, Ohno-Matsui K. Three-year outcomes of intravitreal aflibercept for choroidal neovascularization in patients with pathologic myopia. English pathologic myopia meeting 2019.10.24 Kyoto (TKP Garden city Kyoto)
41. Azuma T, Yokoi T, Ohno-Matsui K. Polarization-sensitive optical coherence tomography (PS-OCT) reveals scleral structure in patients with pathologic myopia. English pathologic myopia meeting 2019.10.24 Kyoto (TKP Garden city Kyoto)
42. Onishi Y, Yokoi T, Ohno-Matsui K. Real-world data of intravitreal aflibercept for mCNV: 12-month outcomes of J-PMS. The 73rd Annual Congress of Japan Clinical Ophthalmology 2019.10.25 Kyoto
43. Azuma T, Yokoi T, Ohno-matsui K. Case Report: Is it really myopic CNV?. Capital Retina Club 4th Meeting 2019.11.08 Tokyo
44. Hiroshi Takase. A nationwide survey of acute retinal necrosis in Japan. The 15th International Ocular Inflammation Society (IOIS) Congress 2019.11.13 Kaohsiung, Taiwan
45. Takanashi T, Yokoi T, Ohno-matsui K. Communication between retinal, choroidal, and postbulbar circulation in a case with choroidal coloboma and parhologic myopia. International pathologic myopia forum 2019.11.21 Shanghai, China
46. Azuma T, Yokoi T, Ohno-matsui K. Polarization- sensitive optical coherence tomography(PS-OCT)reveals scleral structure in patients with pathologic myopia. International pathologic myopia forum 2019.11.21
47. Onishi Y, Yokoi T, Ohno-matsui K. Three-year outcomes of intravitreal afribercept for choroidal neovascularization in patients with pathologic myopia. International pathologic myopia forum 2019.11.21 Shanghai, China
48. Ohno-Matsui K. SS-OCT Findings of Pathological Myopia. 13th APVRS Congress 2019.11.23 Shanghai, China
49. Ohno-Matsui K. Diagnostic and Treatment Conundrums in Retinal Diseases: Mystery case presentation. 13th APVRS Congress 2019.11.23 Shanghai, China
50. Ohno-Matsui K. Great cases with inflammation and beyond: Is this really myopic CNV?. 13th APVRS Congress 2019.11.24 Shanghai, China
51. Yokoi T, Sato S, Terano Y, Ohno-Matsui K. Real-world data of intravitreal aflibercept for myopic choroidal neovascularization: 12-month outcomes of Japan post-marketing surveillance. 13th APVRS Congress 2019.11.24 Shanghai, China

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53. Ohno-Matsui K. Ultra wide-field OCT imaging of pathologic myopia. 2019 The korean retina socity 2019.12.06 Seoul, Korea
54. Ohno-Matsui K. Vitreous imaging with UWF-OCT. GBO-ASMHK2019 2019.12.15 HongKong, China
55. Ohno-Matsui K. Imaging of Pathologic Myopia. GBO-ASMHK2019 2019.12.15
56. Ohno-Matsui K. Myopic CNV. Busan–Gyeongnam POWER Forum 2019.12.20 Busan, Korea

Otorhinolaryngology

Professor: Takeshi Tsutsumi

Associate Professor: Yoshiyuki Kawashima

Junior Associate Professor: Yasuhiro Suzuki

Assistant Professor: Taku Itou, Tarou Fujikawa, Keiji Honda

Hospital Staff: Takamori Takeda, Hiroki Watanabe, Natsuko Kurata, Midori Inoue, Saki Tsukamoto, Ai Watanabe

Graduate Student: Ayane Makabe, Takamori Takeda, Ayako Maruyama, Ayame Yamazaki, Yusuke Kiyokawa, Motomu I

(1) Research

- 1) Deafness gene analysis
- 2) Neurophysiological study of hearing
- 3) Histoanatomical study of ear, nose, throat, head, and neck
- 4) Eye movement analysis in patients with dizziness
- 5) Clinical study of treatment and prognosis in patients with allergic rhinitis, acute and chronic sinusitis, and benign tumors
- 6) Treatment of tinnitus
- 7) Treatment using endoscope
- 8) Development of a new mapping procedure for cochlear implant
- 9) Bio-Marker of external ear canal carcinoma

(2) Lectures & Courses

Pre-graduate clinical education

Clinical systematic lecture covers anatomy, a general idea of diseases, their pathological conditions and treatments in the field of otorhinolaryngology. Clinical clerkship I (general diagnostic training) provides instruction in the diagnosis and testing techniques of the otorhinolaryngological field; clinical clerkship II (clinical training) provides detailed explanations of disease mechanisms, training in the performance of examinations, and clinical responsibilities involving both inpatient and outpatient care. Clinical clerkship III provides advanced training beyond the scope of clinical clerkship II. In particular, students develop an advanced understanding of otorhinolaryngological diseases by conducting outpatient procedures (including taking histories, visual inspection, and palpation), and gaining practical experience in assessment and diagnosis of patients' conditions. Furthermore, in the clinical clerkship III, students also attend a "micro-conference" on teaching. Finally, students are assigned to patients throughout their treatment, consistently dealing with the same individuals before, during, and after surgery; this allows the students to become familiar with the course of clinical care.

(3) Clinical Performances

Otorhinolaryngology clinic provides full examinations and treatment for diseases in ear, nose, throat, head, and neck, including dizziness, sudden deafness, facial palsy, infectious disease and benign as well as malignant disease in the otorhinolaryngeal area. We have performed the first implementation of bone anchored hearing aid implant in Japan and since then we have experienced many patients for this surgery. We also have performed surgery for patients with malignant disease as well as skull base lesions in collaboration with the Department of

the Head and Neck Surgery. Our outpatient clinic includes general ear, nose and throat clinic as well as allergy, sinusitis, dizziness, otitis media, tumor, deafness, and tinnitus clinic.

(4) Publications

[Original Articles]

1. Ito T, Kawashima Y, Fujikawa T, Honda K, Makabe A, Kitamura K, Tsutsumi T. Rapid screening of copy number variations in *STR* C by droplet digital PCR in patients with mild-to-moderate hearing loss. *Human genome variation*. 2019; 6; 41
2. A case of eosinophilic granulomatosis with polyangiitis associated with posterior auricular arteritis 2019.02; 29(1); 45-51
3. Masaru Yokokura, Yoshiyuki Kawashima, Taro Fujikawa, Takeshi Tsutsumi. Duplicated internal auditory canal associated with varicella zoster virus meningitis and facial palsy: a case report 2019.03; 38; 158-160
4. Takeda Takamori, Ikeda Takuo, Tsutsumi Takeshi. The evaluation of gravitational recognition in patients with spinocerebellar degeneration using Listing's plane *ACTA OTO-LARYNGOLOGICA*. 2019.04; 139(7); 581-587
5. Prevalence and clinical features of diverticulum-like cavity on the anterior wall of the internal auditory canal in patients with otosclerosis. 2019.05; 29(2); 168-173
6. Takeda T, Ikeda T, Tsutsumi T. The evaluation of gravitational recognition in patients with spinocerebellar degeneration using Listing's plane. *Acta Oto-Laryngologica*. 2019.07; 139(7); 581-587
7. Nomura Fuminori, Ariizumi Yosuke, Kiyokawa Yusuke, Tasaki Akihisa, Tateishi Yumiko, Koide Nobuaki, Kawabe Hiroaki, Sugawara Takashi, Tanaka Kentaro, Asakage Takahiro. 顎関節に生じた色素性絨毛結節性滑膜炎 (Pigmented villonodular synovitis occurring in the temporomandibular joint) *Auris· Nasus· Larynx*. 2019.08; 46(4); 609-617
8. Yamazaki Ayame, Ikeda Takuo, Tsutsumi Takeshi. Main sequence of torsional saccadic eye movement - analysis by three-dimensional video-oculography *ACTA OTO-LARYNGOLOGICA*. 2019.11; 139(11); 987-989
9. Transcanal stapedotomy with 4K ultra-high definition endoscope for congenital malformations of middle ear. 2019.12; 29(4); 297-301
10. 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

[Conference Activities & Talks]

1. Takamori Takeda, Taro Fujikawa, Yuriko Sakamaki, Masato Fujioka, Yoshiyuki Kawashima, Taku Ito, Ayane Makabe, Takeshi Tsutsumi, Michisuke Yuzaki. *GluD1 Deficiency Causes Progressive High-frequency Hearing Loss and Insufficient Efferent Synapse Formation on Outer Hair Cells*. ARO 42nd Annual Midwinter Meeting 2019.02
2. Taku Ito, Taro Fujikawa, Ayane Makabe, Keiji Honda, Yoshiyuki Kawashima, Takeshi Tsutsumi, Andrew Griffith. Correlation of micro-CT and histopathology in *Slc26a4*-null mice unveils the cochlear pathogenesis of incomplete partition type II. ARO 42th Annual MidWinter Meeting 2019.02.09
3. Takamori Takeda, Taro Fujikawa, Yuriko Sakamaki, Masato Fujioka, Yoshiyuki Kawashima, Taku Ito, Ayane Makabe, Takeshi Tsutsumi, Michisuke Yuzaki. *GluD1 deficiency causes progressive high-frequency hearing loss and insufficient efferent synapse formation on outer hair cells*. ARO 42th Annual MidWinter Meeting 2019.02.09
4. Taku Ito, Taro Fujikawa 他. Correlation of Micro CT and Histopathology in *SLC26A*-Null Mice Unveils the Cochlear Pathogenesis of Incomplete Partition Type II. 42nd annual meeting of ARO 2019.02.10
5. Takamori Takeda, Taro Fujikawa 他. *GluD1 Deficiency Causes Progressive High-Frequency Hearing Loss and Insufficient Efferent Synapse Formation on Outer Hair Cells*. 42nd annual meeting of ARO 2019.02.12

6. Kawashima Y, Maruyama A, Fujikawa T, Ito T, Takeda T, Tsutsumi T. Potential confounding factors may bias the association between configurations of the vertebrobasilar artery system and the incidence of idiopathic sudden sensorineural hearing loss and canal paresis.. Otolological Society 152nd Annual Meeting in Combined Otolaryngology Spring Meetings 2019 2019.05
7. Ayako Maruyama, Yoshiyuki Kawahima, Taro Fujikawa, Taku Ito, Takamori Takeda, Takeshi Tsutsumi.. Potential confounding factors may bias the association between configurations of the vertebrobasilar artery system and the incidence of idiopathic sudden sensorineural hearing loss and canal paresis.. COSM2019 (Combined Otolaryngology Spring Meetings)-AOS(The American Otological Society) 2019.05.01
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9. Taku Ito, Yoshiyuki Kawashima, Taro Fujikawa, Keiji Honda, Takamori Takeda, Ayane Makabe, Takeshi Tsutsumi. . Morphometric analysis of otoconia in a mouse model of Pendred Syndrome by X-ray computed microtomography.. Vestibular Oriented Research Meeting 2019.05.19
10. Takamori Takeda, Takuo Ikeda, Takeshi Tsutsumi.. The evaluation of gravitational recognition in patients with spinocerebellar degeneration.. Vestibular Oriented Research Meeting 2019.05.19
11. Takeda T, Ikeda T, Tsutsumi T. Evaluation of gravitational recognition in patients with spinocerebellar degeneration.. 2019 Vestibular Oriented Research Meeting 2019.05.21

Neurology and Neurological Science

Professor	YOKOTA Takanori
Associate Professor	ISHIBASHI Satoru
Junior Associate Professor	NISHIDA Yoichiro
Junior Associate Professor	OHKUBO Takuya
Assistant Professor	ISHIGURO Taro
Assistant Professor	HATTORI Takaaki
Assistant Professor	YAGI Yohsuke
Project Professor	SANJO Nobuo
Project Professor	UCHIHARA Toshiki
Project Associate Professor	NAGATA Tetsuya
Project Junior Associate Professor	HARA Rintaro
Project Assistant Professor	YOSHIOKA Kotaro
Project Assistant Professor	HIGASHI Miwa
Graduate Student	OHYAGI Masaki
Graduate Student	HASEGAWA Jyuri
Graduate Student	SHINTAKU Hiroshi
Graduate Student	FURUKAWA Fumiko
Graduate Student	MIYASHITA Akiko
Graduate Student	FUJITA Kyohe
Graduate Student	ONO Daisuke
Graduate Student	HIRATA Kose
Graduate Student	KUNIEDA Taiki
Graduate Student	SANO Tatsuhiko
Graduate Student	ISHINOSE Keiko
Graduate Student	MARUOKA Hiroyuki
Graduate Student	NISHI Rieko
Graduate Student	SUZUKI Motohiro
Graduate Student	YAMADA Akane
Graduate Student	KINA Satoko
Graduate Student	SATO Takefumi
Graduate Student	IIDA Shintaro
Graduate Student	TAKAHASHI Yuko
Graduate Student	OOHARA Masahiro
Graduate Student	MIURA Motoki
Graduate Student	AOKI Hanako
Graduate Student	YAMADA Hiroki
Graduate Student	OOTSU Shinichi
Graduate Student	MATSUDA Sakino
Graduate Student	YANAGIDAIRA Mitsugu
Graduate Student	OHYA Tai
Graduate Student	SHINYA Akiko
Research Student	TOIDE Nozomi
Graduate Student	SU SU Lei Mon
Graduate Student	JIA Chunyan
Graduate Student	CHIN Seimu
Graduate Student	THUNYARUT Bannawongsil
Graduate Student	YASUDA Eiji
Graduate Student	MORIFUJI Hiroshi
Graduate Student	KATO Tomotaka

(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]

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2. Amano E, Ozaki K, Ishibashi S, Sanjo N, Yokota T. Remarkable improvement in progressive multifocal leukoencephalopathy following acute pyelonephritis with bacteremia. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia*. 2019.01; 62; 226-228
3. Takahashi K, Yanai S, Takisawa S, Kono N, Arai H, Nishida Y, Yokota T, Endo S, Ishigami A. Vitamin C and vitamin E double-deficiency increased neuroinflammation and impaired conditioned fear memory. *Archives of biochemistry and biophysics*. 2019.01; 663; 120-128
4. Maeda Y, Iwata Hara R, Nishina K, Yoshida-Tanaka K, Sakamoto T, Yokota T, Wada T. Artificial cationic peptides that increase nuclease resistance of siRNA without disturbing RNAi activity. *Nucleosides, nucleotides & nucleic acids*. 2019.01; 38(5); 338-348

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6. Yokote H., Amano R., Toru S., Hattori T., Nishida Y., Sanjo N., Yokota T.. Brain Atrophy is Associated with Higher Serum Amyloid A Levels in Patients with Relapsing and Remitting Multiple Sclerosis and Clinically Isolated Syndrome *MULTIPLE SCLEROSIS JOURNAL*. 2019.03; 25(3); 442
7. Furukawa F, Ishikawa K, Yokota T, Sanjo N. Cross-Sectional Area Analysis of the Head of the Caudate Nucleus in Huntington's Disease. *European neurology*. 2019.04; 81(1-2); 13-18
8. Ebashi M, Toru S, Nakamura A, Kamei S, Yokota T, Hirokawa K, Uchihara T. Detection of AD-specific four repeat tau with deamidated asparagine residue 279-specific fraction purified from 4R tau polyclonal antibody. *Acta neuropathologica*. 2019.04; 138(1); 163-166
9. Hashimoto S, Inaji M, Nariai T, Kobayashi D, Sanjo N, Yokota T, Ishii K, Taketoshi M. Usefulness of [¹¹C] Methionine PET in the Differentiation of Tumefactive Multiple Sclerosis from High Grade Astrocytoma. *Neurologia medico-chirurgica*. 2019.04; 59(5); 176-183
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12. Guo L, Bertola DR, Takanohashi A, Saito A, Segawa Y, Yokota T, Ishibashi S, Nishida Y, Yamamoto GL, Franco JFDS, Honjo RS, Kim CA, Musso CM, Timmons M, Pizzino A, Taft RJ, Lajoie B, Knight MA, Fischbeck KH, Singleton AB, Ferreira CR, Wang Z, Yan L, Garbern JY, Simsek-Kiper PO, Ohashi H, Robey PG, Boyde A, Matsumoto N, Miyake N, Spranger J, Schiffmann R, Vanderver A, Nishimura G, Passos-Bueno MRDS, Simons C, Ishikawa K, Ikegawa S. Bi-allelic CSF1R Mutations Cause Skeletal Dysplasia of Dysosteosclerosis-Pyle Disease Spectrum and Degenerative Encephalopathy with Brain Malformation. *American journal of human genetics*. 2019.05; 104(5); 925-935
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15. Otsu S, Ishibashi S, Ozaki K, Yokota T. Elevated lipid peaks during the recovery phase of Baló's concentric sclerosis: A case report. *eNeurologicalSci*. 2019.06; 15; 100191
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25. Yanagidaira M, Hattori T, Emoto H, Kiyosawa M, Yokota T. Optic perineuritis with anti-myelin oligodendrocyte glycoprotein antibody. *Multiple sclerosis and related disorders*. 2019.10; 38; 101444
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30. Yanagidaira M, Nishida Y, Yokota T. Temporal correlation between serum CH₅₀ level and symptom severity of myasthenia gravis during eculizumab therapy. *Clinical neurology and neurosurgery*. 2019.12; 189; 105630

[Conference Activities & Talks]

1. 八木洋輔, 横田隆徳. Small RNA profiling of cerebrospinal fluid exosomes. 第6回 JMAC シンポジウム 2019.01.24 東京
2. Hashimoto Satoka, Inaji Motoki, Nariai Tadashi, Kobayashi Daisuke, Sanjo Nobuo, Yokota Takanori, Ishii Kenji, Maehara Taketoshi. 高グレード星細胞腫と tumefactive multiple sclerosis を鑑別するための [11C] Methionine PET の有用性 (Usefulness of [11C] Methionine PET in the Differentiation of Tumefactive Multiple Sclerosis from High Grade Astrocytoma). *Neurologia medico-chirurgica* 2019.05.01
3. Takahashi YK, Nishida Y, Nose Y, Ishibashi S, Sanjo N, Kanai T, Uzawa A, Oda F, Ozawa Y, Kuwabara S, Yokota T. Calcineurin inhibitors can be safely reduced in most patients with well-controlled myasthenia gravis. *American Academy of Neurology (AAN) 71st Annual Meeting* 2019.05.06 Philadelphia

4. Yagi Y, Iida S, Kanouchi T, Kusunoki S, Sobue G, Kaji R, Kuwabara S, Yokota T, Glovenin-I CIDP Study Group. Maintenance treatment with IVIg for CIDP can prevent disease progression. 60th Annual Meeting of the Japanese Society of Neurology 2019.05.22 Osaka
5. Ishibashi S, Li F, Iwasawa E, Suzuki M, Ichinose K, Yokota T. Upregulation of lipoprotein receptors on brain in the early phase of ischemic stroke in mice. 第60回日本神経学会学術大会 2019.05.22 大阪
6. New DNA/RNA heteroduplex oligonucleotide technology for regulating functions of lymphocytes in vivo. 第60回日本神経学会学術大会 2019.05.22 大阪
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8. Yokote H, Amano R, Toru S, Hattori T, Nishida Y, Sanjo N, Yokota T. Brain atrophy is associated with higher serum amyloid A levels in patients with multiple sclerosis. 第60回日本神経学会学術大会 2019.05.23 大阪
9. Yoshioka K, Lei Mon S, Jia C, Yamada H, Asami Y, Tanaka K, Wenying P, Kuwahara H, Nishina K, Nagata T, Yokota T. A novel antisense oligonucleotide therapy by overhanging heteroduplex oligonucleotide targeting CNS. 第60回日本神経学会学術大会 2019.05.23 大阪
10. Igarashi S, Otani T, Soga K, Irioka T, Kuhara T, Ozai K, Yokota T. Peri-insular sign: An MRI finding on acute fulminant hyperammonemia caused by a urea cycle disorder. 第60回日本神経学会学術大会 2019.05.23 大阪
11. Akaza Miho, Kawabata Shigenori, Watanabe Taishi, Hasegawa Yuki, Iida Shintaro, Sasaki Toru, Adachi Yoshiaki, Sekihara Kensuke, Kanouchi Tadashi, Sumi Yuki, Okawa Atsushi, Yokota Takanori. Diagnosis of C8 radiculopathy by magnetospinogram. 第60回日本神経学会学術大会 2019.05.23
12. Irioka Takashi, Motomura Masakatsu, Uchihara Toshiki, Shintaku Hiroshi, Ishikawa Kinuya, Igarashi Susumu, Majima Takamasa, Takahashi Yuko K, Iwase Ryo, Otani Tai, Kitanosono Hiroko, Shiraishi Hirokazu, Tsuura Yukio, Yokota Takanori. Clinicopathological study of a patient with calcium channels antibody-associated cerebellar ataxia. 第60回日本神経学会学術大会 2019.05.24
13. Ishiguro Taro, Yokota Takanori, Ishikawa Kinuya, Nagai Yoshitaka, Petrucelli Leonard. Spt4 knockdown suppressed SCA31-linked expanded UGAA repeat-induced toxicity in Drosophila. 第60回日本神経学会学術大会 2019.05.24
14. Hirata Kosei, Hattori Takaaki, Chen Qingmeng, Ohara Masahiro, Kina Satoko, Yokota Takanori. Striatal dopamine depletion correlates with variability of stride length in Parkinson's disease. 第60回日本神経学会学術大会 2019.05.24
15. Kim Yangsu, Iwase Ryo, Otani Tai, Igarashi Susumu, Soga Kazumasa, Irioka Takashi, Yokota Takanori. Varicella-zoster virus encephalitis followed by herpes zoster in hemodialysis patients. 第60回日本神経学会学術大会 2019.05.24
16. Otani Tai, Iwase Ryo, Takahashi Yuko K, Soga Kazumasa, Kim Yangsu, Igarashi Susumu, Kaneko Kimihiko, Takahashi Toshiyuki, Irioka Takashi, Yokota Takanori. A Variety of Myelin Oligodendrocyte Glycoprotein Antibody Positive Central Nervous System Disorders. 第60回日本神経学会学術大会 2019.05.25
17. Iwase Ryo, Irioka Takashi, Takahashi Yuko K, Igarashi Susumu, Otani Tai, Soga Kazumasa, Yokota Takanori. Clinical and neuroradiological study of 3 patients with intravascular lymphoma (IVL). 第60回日本神経学会学術大会 2019.05.25
18. Sanjo Nobuo, Shishido-hara Yukiko, Nose Yurie, Yokota Takanori. Progressive multifocal leukoencephalopathy in the era of disease-modifying therapies A controlled inflammation and a regulatory immune system are associated with better prognosis of PML. 第60回日本神経学会学術大会 2019.05.25
19. 高橋 直, 宮本 翔平, 三條 伸夫, 横田 隆徳. Width of the third ventricle is high-sensitive marker for chronic progressive neuro-Behcet's disease. 第60回日本神経学会学術大会 2019.05.25
20. Yokota Takanori. Oligonucleotide drug for treatment of ALS. 第60回日本神経学会学術大会 2019.05.25
21. A diagnostic decision tree for degenerative cerebellar ataxia based on pontine magnetic resonance imaging. 2019.05.25

22. Amano A, Sanjo N, Nakakido M, Tsumoto K, Matsubara E, Nishida Y, Hattori T, Nagata T, Tomiyama T, Yokota T. Quantitative measurement of amyloid-beta oligomer in mouse brain using dot blot assay. ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2019 2019.07.16 LOS ANGELES
23. 天野晶子, 三條伸夫, 仲木戸誠, 津本浩平, 松原悦朗, 古川迪子, 西田陽一郎, 齊藤貴志, 西道隆臣, 横田隆徳. ドットプロット法を用いたマウス脳中アミロイド β オリゴマーの定量法評価. 第7回日本アミロイドーシス学会学術集会 2019.08.30 東京
24. Takaaki Hattori. Neural correlates of compensatory process and impaired working memory in Parkinson's disease during disease progression. 23rd International Congress of Parkinson's Disease and Movement Disorders 2019.09.25 Nice
25. Taiki Matsubayashi, Miho Akaza, Nobuo Sanjo, Tsuyoshi Hamaguchi, Yuichi Hayashi, Takayoshi Shimohata, Masahito Yamada, Takanori Yokota. Focal sharp waves are specific in the early stage of MM2 cortical form of sCJD . Asian Pacific Prion Symposium 2019 2019.10.03 埼玉
26. Yokota T. BBB-penetrating DNA/RNA heteroduplex oligonucleotide efficiently regulating CNS gene.. Tokyo Medical and Dental University-Taipei Medical University Joint Symposium on Medical Innovation 2019.10.05 Taipei
27. Daisuke Ono, Ken Asada, Daishi Yui, Fumika Sakaue, Kotaro Yoshioka, Tetsuya Nagata, Takanori Yokota. Unwinding-related Rapid Nuclear Inflow of DNA/RNA Heteroduplex Oligonucleotide; Unveiling Distinctive Intracellular Trafficking. The 15th Annual Meeting of the Oligonucleotide Therapeutics Society 2019.10.14 Munich
28. Amano A, Sanjo N, Nakakido M, Tsumoto K, Matsubara E, Furukawa F, Nishida Y, Saito T, Saido T, Yokota T,. Quantitative evaluation of A β oligomer in mouse brain using dot blot method. 第38回日本認知症学会学術集会 2019.11.07 新宿
29. Takanori Yokota. Systemically Administered DNA/RNA Heteroduplex Oligonucleotides That Can Efficiently Regulate CNS Genes*. TIDES Europe 2019: Oligonucleotide & Peptide Therapeutics 2019.11.13 Amsterdam
30. Kotaro Yoshioka. Heteroduplex-Oligonucleotides for Highly Efficient Silencing of microRNA through a Novel intracellular Mechanism. 2019 Oligonucleotides Meeting 2019.11.16 Munich

Psychiatry and Behavioral Sciences

Professor, Chair

Hidehiko Takahashi

Professor

Takayuki OKADA

Associate Professor

Genichiro SUGIHARA

Junior Associate Professor

Takashi TAKEUCHI

Senior Assistant Professor

Daisuke JITOKU

Assistant Professor

Hitoshi MUTO, Takehiro TAMURA, Shunsuke TAKAGI, Hiroki SHIWAKU

Junior Assistant Professor

Ryota SHIOE, Nanase KOBAYASHI

Senior Resident

Kyoji MARUO

Clinical Psychologist

Yasuhiro OKA(-Dec.2018), Kazunori MURAKAMI, Yukari WAKAYAMA, Toshikazu SHINOTAKE, Hisashi YAMADA, Ryoko NAKAJIMA, Hikaru TANIGUCHI

Psychiatric Social Worker

Yoshifumi KANEKO, Noriko NUMAGUCHI, Sayaka KOJIMA, Norikazu MONTA(-Mar.2018), Sumiko NOGUCHI

Graduate Students

Shinichi UMINO(-Mar.2018), Kazuo TAKIGUCHI(-Mar.2018), Momoko KOBAYASHI(-Mar.2018), Megumi GOTO, Ko FURUTA, Shigehiro OGATA, Hidetoshi KINOSHITA, Ryotaro SAITO, Koji TAKEDA, Takehiro TAMURA(Diagnostic Radiology and Nuclear Medicine), Yosuke SEKIGUCHI, Yoshiko NOMURA, Asami ISHIZUYA

(1) Outline

Our laboratory is committed to comprehensive research on endogenous psychosis, neurosis, and epilepsy through biological, psychological and social approaches. We are also involved in social psychiatry, child and adolescent psychiatry. Brain imaging studies are our most interested and well skilled lesion. Neuro-feedback approaches to treat psychiatric diseases, AI and computational psychiatry is our new frontiers.

(2) Research

1) Studies in biological psychiatry

(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.

(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.

(iv) 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.

2) 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) Forensic Psychiatry Research

Our research includes projects in the development of forensic psychiatric evaluation methodology, risk assessment and management in forensic settings, exploring associations and mechanisms of criminal behavior.

(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

We 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 lesion of Sleep and Epilepsy, we have board certified specialist. 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. Takagi Shunsuke, Terasawa Yuuya, Takeuchi Takashi. Asystole a Few Seconds After the Electrical Stimulation of Electroconvulsive Therapy PSYCHOSOMATICS. 2019; 60(1); 66-69
2. Takagi Shunsuke, Terasawa Yuuya, Takeuchi Takashi. Asystole a Few Seconds After the Electrical Stimulation of Electroconvulsive Therapy PSYCHOSOMATICS. 2019; 60(1); 66-69
3. Nishina K, Takagishi H, Takahashi H, Sakagami M, Inoue-Murayama M. Association of Polymorphism of Arginine-Vasopressin Receptor 1A (< i> AVPR1a< /i>) Gene With Trust and Reciprocity. Frontiers in human neuroscience. 2019; 13; 230
4. Takeda K, Sugawara N, Yamada Y, Nagata T, Kashiwagi H, Kono T, Hirabayashi N, Okada T. Employment-Related Factors of Forensic Psychiatric Outpatients with Psychotic Disorders. Neuropsychiatric disease and treatment. 2019; 15; 3341-3350
5. Puhl Matthew D., Desai Rajeev I., Takagi Shunsuke, Presti Kendall T., Doyle Michelle R., Donahue Rachel J., Landino Samantha M., Bergman Jack, Carlezon William A. Jr., Coyle Joseph T.. N-Methyl-d-aspartate receptor co-agonist availability affects behavioral and neurochemical responses to cocaine: insights into comorbid schizophrenia and substance abuse ADDICTION BIOLOGY. 2019.01; 24(1); 40-50
6. Framework for Dialogue among Experts of Law and Psychiatry through Forensic Expert Testimony, Cross Examination, Deliberation and Case Study. 2019.03; 14(1); 42-45
7. Ubukata S, Oishi N, Sugihara G, Aso T, Fukuyama H, Murai T, Ueda K. Transcallosal Fiber Disruption and its Relationship with Corresponding Gray Matter Alteration in Patients with Diffuse Axonal Injury. Journal of neurotrauma. 2019.04; 36(7); 1106-1114
8. Nakagami Y, Sugihara G, Kuga H, Takahashi H, Murai T. Revision of road traffic law in Japan and mental health stigma. Psychiatry and clinical neurosciences. 2019.05; 73(5); 284-285
9. Nakagami Yukako, Sugihara Genichi, Kuga Hironori, Takahashi Hidehiko, Murai Toshiya. Revision of road traffic law in Japan and mental health stigma(和訳中) Psychiatry and Clinical Neurosciences. 2019.06; 73(5-6); 284-285
10. Tamura T, Shiwaku H, Jitoku D, Kurumaji A. Effect of Tandospirone, a Partial Agonist of the 5-HT1A Receptor, in a Patient With Chronic Poststroke Emotional Incontinence With Anxiousness. The primary care companion for CNS disorders. 2019.09; 21(5);
11. Fujino J, Tei S, Itahashi T, Aoki YY, Ohta H, Kubota M, Hashimoto RI, Nakamura M, Kato N, Takahashi H. Impact of past experiences on decision-making in autism spectrum disorder. European archives of psychiatry and clinical neuroscience. 2019.09;

12. Takayuki OKADA. Layer's issue from psychiatrists' perspective. Keiho Zasshi (Journal of Criminal Law). 2019.10; 58(2); 296-309
13. 吉村 健佑, 橋本 佐, 佐藤 泰憲, 佐藤 愛子, 竹内 崇, 渡邊 博幸, 寺尾 岳, 中里 道子, 伊豫 雅臣. Survey of anticonvulsant drugs and lithium prescription in women of childbearing age in Japan using public national insurance claims database of Japan(和訳中) 日本臨床精神神経薬理学会・日本神経精神薬理学会合同年会プログラム・抄録集. 2019.10; 29 回・49 回; 126
14. Koji Takeda, Norio Sugawara, Taro Matsuda, Akihiro Shimada, Takako Nagata, Hiroko Kashiwagi, Naot-sugu Hirabayashi, Takayuki Okada. Mortality and suicide rates in patients discharged from forensic psychiatric wards in Japan Comprehensive Psychiatry. 2019.11; 95; 152131
15. Tei S, Fujino J, Itahashi T, Aoki Y, Ohta H, Kubota M, Hashimoto RI, Nakamura M, Kato N, Takahashi H. Egocentric biases and atypical generosity in autistic individuals. Autism research : official journal of the International Society for Autism Research. 2019.11; 12(11); 1598-1608
16. Hatta K, Kishi Y, Wada K, Takeuchi T, Hashimoto N, Suda K, Taira T, Tsuchida K, Ohmori T, Akizuki N, Nishio Y, Nakanishi Y, Usui C, Kurata A, Horikawa N, Eguchi H, Ito S, Muto H, Nakamura H, Uchimura N. Real-World Effectiveness of Ramelteon and Suvorexant for Delirium Prevention in 948 Patients With Delirium Risk Factors. The Journal of clinical psychiatry. 2019.12; 81(1);
17. Shiwaku H, Nakano Y, Kato M, Takahashi H. Detection of autoantibodies against GABA< sub> A< /sub> R α 1 in patients with schizophrenia. Schizophrenia research. 2019.12;
18. Fujino J, Tei S, Itahashi T, Aoki YY, Ohta H, Kubota M, Hashimoto RI, Takahashi H, Kato N, Nakamura M. Role of the right temporoparietal junction in intergroup bias in trust decisions. Human brain mapping. 2019.12;
19. Kurumaji A, Narushima K, Takeda M, Jitoku D, Kyono H, Hobo M, Mitsusada H, Nishida M, Atsuta H, Tamai S, Takagi D, Fujita M, Kawamata K, Okuzumi S, Hino K, Tsutsui K, Nishikawa T.. A Comparison of Pharmacotherapy of Inpatients with Major Depressive Disorders between Single Episode and Recurrent One. Clinical Neuropsychopharmacology and Therapeutics.. (5); 5-10

[Misc]

1. An overview of the diagnosis, treatment and clinical studies of the bipolar II disorder with a comparison to the bipolar I disorder Psychiatria et Neurologia Japonica. 2019.08; 121(8); 612-618
2. Akeo Kurumaji. Glutamate hypothesis in schizophrenia Japanese Journal of Psychiatric Treatment. 2019.09; 34(9); 989-994

[Conference Activities & Talks]

1. H. TAKAHASHI. Neuroimaging of Gambling Disorder: Toward precision addiction psychiatry. 6th International Conference on Behavioral Addictions 2019.06.19 横浜
2. H. TAKAHASHI. Neuroimaging of Gambling Disorder. Neuro2019 2019.06.26 新潟
3. S. TAKAGI. Serine Racemase expression and its function in striatum and in striatal GABAergic interneuron.. Australasian Neuroscience society annual scientific meeting 2019.11.04 Adelaide
4. H. Shiwaku. Detection of autoantibodies against GABAAR α 1 in patients with schizophrenia. Australasian Neuroscience society annual scientific meeting 2019.11.04 Adelaide
5. H. TAKAHASHI. Altered decision-making as an endophenotype to bridge the gap between phenomenology and neurobiology.. International Symposium of Personalized value: Interdisciplinary approach 2019.11.16 京都

Neurosurgery

Professor: Taketoshi Maehara

Associate Professor: Tadashi Nariai

Assistant Professors: Yoji Tanaka and Motoki Inaji

Hospital stuffs:

Takashi Sugawara, Kaoru Tamura, Jun Karakama and Satoka Hashimoto

Graduate Students: Yasuhiro Ueda, Satoka Hashimoto, Kenji Yamada, Masataka, Yoshimura, Akitaka Muta, Jiro Aoyama, Tomoyuki Nakano, Motoshige Yamashina, Asumi Orihara and Satoru Takahashi

(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. Yoshimura Yuri, Hara Keiko, Akaza Miho, Ohta Kaseya, Sumi Yuki, Inaji Motoki, Yanagisawa Eriko, Maehara Taketoshi. Effects of antiepileptic monotherapy on hematological and biochemical parameters(和訳中) *Epilepsy & Seizure*. 2019; 11(1); 1-13
2. Hara S, Hori M, Ueda R, Hayashi S, Inaji M, Tanaka Y, Maehara T, Ishii K, Aoki S, Nariai T. Unraveling Specific Brain Microstructural Damage in Moyamoya Disease Using Diffusion Magnetic Resonance Imaging and Positron Emission Tomography. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2019.01;
3. Arita Hideyuki, Ohno Makoto, Nakamura Taishi, Tamura Kaoru, Miyake Yohei, Saito Kuniaki, Tanaka Shota, Higuchi Fumi, Kanemura Yonehiro, Ichimura Koichi. Prognostic impact of TERT promoter mutation suggests its utility as a surrogate marker for 1p/19q codeletion in IDH mutated gliomas *BRAIN PATHOLOGY*. 2019.02; 29; 193
4. Hashimoto S, Inaji M, Nariai T, Kobayashi D, Sanjo N, Yokota T, Ishii K, Taketoshi M. Usefulness of [¹¹C] Methionine PET in the Differentiation of Tumefactive Multiple Sclerosis from High Grade Astrocytoma. *Neurologia medico-chirurgica*. 2019.04; 59(5); 176-183
5. Hara S, Hori M, Ueda R, Hagiwara A, Hayashi S, Inaji M, Tanaka Y, Maehara T, Ishii K, Aoki S, Nariai T. Intravoxel incoherent motion perfusion in patients with Moyamoya disease: comparison with 15O-gas positron emission tomography. *Acta radiologica open*. 2019.05; 8(5); 2058460119846587
6. Hashimoto Satoka, Inaji Motoki, Nariai Tadashi, Kobayashi Daisuke, Sanjo Nobuo, Yokota Takanori, Ishii Kenji, Maehara Taketoshi. Usefulness of [¹¹C] Methionine PET in the Differentiation of Tumefactive Multiple Sclerosis from High Grade Astrocytoma *Neurologia medico-chirurgica*. 2019.05; 59(5); 176-183
7. Shirahata Mitsuaki, Adachi Junichi, Kobayashi Keiichi, Yamasaki Fumiyuki, Tamura Kaoru, Suzuki Tomonari, Mishima Kazuhiko, Nagane Motoo, Ichimura Koichi, Nishikawa Ryo. Stratified monotherapy approach according to MGMT methylation status in elderly patients with glioblastoma. *JOURNAL OF CLINICAL ONCOLOGY*. 2019.05; 37(15);
8. Obana M, Furuya J, Matsubara C, Haruka T, Inaji M, Miki K, Numasawa Y, Minakuchi S, Maehara T. Effect of a collaborative transdisciplinary team approach on oral health status in acute stroke patients. *Journal of oral rehabilitation*. 2019.07;
9. Tanaka Y., Miyasaka N., Hara S., Inaji M., Maehara T., Nariai T.. Changes in cerebral blood flow during pregnancy detected by arterial spin labeling MRI in healthy subjects and in the patients with moyamoya disease *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*. 2019.07; 39; 230
10. Inaji M., Hayashi S., Nariai T., Sakata M., Ishii K., Maehara T.. Adenosine A1 Receptor Imaging with [¹¹C-11] MPDX PET in mesial temporal lobe epilepsy patients *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*. 2019.07; 39; 547
11. Hayashi S., Inaji M., Nariai T., Wagatsuma K., Sakata M., Ishii K., Maehara T.. Gap filling and rebinning algorithms for 3D PET data *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*. 2019.07; 39; 594

12. Takami H., Fukushima S., Aoki K., Satomi K., Narumi K., Hama N., Matsushita Y., Fukuoka K., Yamasaki K., Nakamura T., Mukasa A., Saito N., Suzuki T., Yanagisawa T., Nakamura H., Sugiyama K., Tamura K., Maehara T., Nakada M., Nonaka M., Asai A., Yokogami K., Takeshima H., Luchi T., Kanemura Y., Kobayashi K., Nagane M., Kurozumi K., Yoshimoto K., Matsuda M., Matsumura A., Hirose Y., Tokuyama T., Kumabe T., Ueki K., Narita Y., Shibui S., Totoki Y., Shibata T., Nakazato Y., Nishikawa R., Matsutani M., Ichimura K.. Intratumoural immune cell landscape in germinoma reveals multipotent lineages and exhibits prognostic significance NEUROPATHOLOGY AND APPLIED NEUROBIOLOGY. 2019.07;
13. Nomura Shunsuke, Akagawa Hiroyuki, Yamaguchi Koji, Ishikawa Tatsuya, Kawashima Akitsugu, Kasuya Hidetoshi, Mukawa Maki, Nariai Tadashi, Maehara Taketoshi, Okada Yoshikazu, Kawamata Takakazu. Rare and Low-Frequency Variants in RNF213 Confer Susceptibility to Moyamoya Syndrome Associated with Hyperthyroidism WORLD NEUROSURGERY. 2019.07; 127; E460-E466
14. Taketoshi Maehara, Kazuko Kamiya, Takamitsu Fujimaki, Akira Matsumura, Kazuhiro Hongo, Satoshi Kuroda, Mitsunori Matsumae, Hideo Takeshima, Nobuo Sugo, Naoyuki Nakao, Nobuhito Saito, Fusao Ikawa, Noriko Tamura, Kaori Sakurada, Shoko Shimokawa, Hajime Arai, Kaoru Tamura, Kazutaka Sumita, Shoko Hara, Yoko Kato, . A Questionnaire to Assess the Challenges Faced by Women Who Quit Working as Full-Time Neurosurgeons. World Neurosurg. 2019.08;
15. Kofuji S, Hirayama A, Eberhardt AO, Kawaguchi R, Sugiura Y, Sampetean O, Ikeda Y, Warren M, Sakamoto N, Kitahara S, Yoshino H, Yamashita D, Sumita K, Wolfe K, Lange L, Ikeda S, Shimada H, Minami N, Malhotra A, Morioka S, Ban Y, Asano M, Flanary VL, Ramkissoon A, Chow LML, Kiyokawa J, Mashimo T, Lucey G, Mareninov S, Ozawa T, Onishi N, Okumura K, Terakawa J, Daikoku T, Wise-Draper T, Majd N, Kofuji K, Sasaki M, Mori M, Kanemura Y, Smith EP, Anastasiou D, Wakimoto H, Holland EC, Yong WH, Horbinski C, Nakano I, DeBerardinis RJ, Bachoo RM, Mischel PS, Yasui W, Suematsu M, Saya H, Soga T, Grummt I, Bierhoff H, Sasaki AT. IMP dehydrogenase-2 drives aberrant nucleolar activity and promotes tumorigenesis in glioblastoma. Nature cell biology. 2019.08; 21(8); 1003-1014
16. Hashimoto Satoka, Maeda Jun, Takuwa Hiroyuki, Takado Yuhei, Shimojo Masafumi, Inaji Motoki, Kumata Katsushi, Zhang Ming-Rong, Suhara Tetsuya, Maehara Taketoshi, Higuchi Makoto. Abnormal tryptophan metabolism and astrocyte functional failure in the pathology of epilepsy Journal of the Japan Epilepsy Society. 2019.09; 37(2); 551
17. Hasegawa Mitsuhiro, Hatayama Toru, Kondo Akinori, Nagahiro Shinji, Fujimaki Takamitsu, Amagasaki Kenichi, Arita Kazunori, Date Isao, Fujii Yukihiko, Goto Takeo, Hanaya Ryosuke, Higuchi Yoshinori, Hongo Kazuhiro, Inoue Toru, Kasuya Hidetoshi, Kayama Takamasa, Kawashima Masatou, Kohmura Eiji, Maehara Taketoshi, Matsushima Toshio, Mizobuchi Yoshihumi, Morita Akio, Nishizawa Shigeru, Noro Shusaku, Saito Shinjiro, Shimano Hirofumi, Shirane Reizo, Takeshima Hideo, Tanaka Yuichiro, Tanabe Hidenori, Toda Hiroki, Yamakami Iwao, Nishiyama Yuya, Ohba Shigeo, Hirose Yuichi, Suzuki Takeya. Prosthesis Used in Microvascular Decompressions: A Multicenter Survey in Japan Focusing on Adverse Events WORLD NEUROSURGERY. 2019.10; 130; E251-E258
18. S. Hara, Y. Tanaka, S. Hayashi, M. Inaji, T. Maehara, M. Hori, S. Aoki, K. Ishii and T. Nariai. Bayesian estimation of CBF measured by DSC-MRI in patients with Moyamoya disease: comparison with 15O-gas PET and singular value decomposition American Journal of Neuroradiology. 2019.11;
19. Hara S, Seida M, Kumagai K, Yamamoto T. Beneficial Effect of Carotid Artery Stenting on Cerebral Hemodynamic Impairment and Cognitive Function. Neurologia medico-chirurgica. 2019.11;
20. Yamada Kenji, Tanaka Yoji, Sumita Kazutaka, Nemoto Shigeru, Maehara Taketoshi. Computational Fluid Dynamics Analysis of the Offending Artery at Sites of Neurovascular Compression in Trigeminal Neuralgia Using Preoperative MRI Data NEUROLOGIA MEDICO-CHIRURGICA. 2019.11; 59(11); 415-422
21. Inaji M., Hayashi S., Nariai T., Sakata M., Ishii K., Maehara T.. [11C] MPDX Pet Imaging Of Adenosine A1 Receptors In Mesial Temporal Lobe Epilepsy Patients EPILEPSIA. 2019.11; 60; 97-98
22. Hashimoto S., Maeda J., Takuwa H., Takado Y., Shimojo M., Takahashi M., Urushihata T., Sampei K., Minamihisamatsu T., Inaji M., Kumata K., Ming-Rong Z., Suhara T., Maehara T., Higuchi M.. Astrocyte Dysfunction Induced By Abnormal Tryptophan Metabolism In The Pathology Of Epilepsy EPILEPSIA. 2019.11; 60; 178-179

23. Takahashi Satoru, Shimizu Kazuhide, Inaji Motoki, Hashimoto Satoka, Yamamoto Shinji, Maehara Take-toshi. Effectiveness of perampanel as a first add-on antiepileptic drug for the treatment of partial epilepsy EPILEPSY & BEHAVIOR. 2019.11; 100(Pt A); 106492
24. Arita Hideyuki, Matsushita Yuko, Ohno Makoto, Miyake Yohei, Saito Kuniaki, Tanaka Shota, Naka-mura Taishi, Tamura Kaoru, Higuchi Fumi, Sandika Eriel, Sabit Hemragul, Hattori Yasuhiko, Yamaguchi Shigeru, Okita Yoshiko, Sakamoto Daisuke, Fukai Junya, Uda Takehiro, Hata Nohuhiro, Shofuda Tomoko, Sasayama Takashi, Mori Kanji, Kurozumi Kazuhiko, Kanamori Masayuki, Sasaki Hikaru, Kishima Haruhiko, Kanemura Yonehiro, Nakada Mitsutoshi, Sonoda Yukihiro, Nagane Motoo, Ueki Keisuke, Nishikawa Ryo, Narita Yoshitaka, Ichimura Koichi. PROGNOSTIC ROLE OF TERT PROMOTER MUTATIONS IM-PROVES THE STRATIFICATION OF IDH-MUTATED LOWER GRADE GLIOMA NEURO-ONCOLOGY. 2019.11; 21; 151
25. Hara S, Tanaka Y, Ueda Y, Abe D, Hayashi S, Inaji M, Maehara T, Ishii K, Nariai T. Detection of hemodynamic impairment on 15O gas PET using visual assessment of arterial spin-labeling MR imaging in patients with moyamoya disease. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2019.12;
26. Takami Hirokazu, Fukuoka Kohei, Fukushima Shintaro, Nakamura Taishi, Mukasa Akitake, Saito Nobuhito, Yanagisawa Takaaki, Nakamura Hideo, Sugiyama Kazuhiko, Kanamori Masayuki, Tominaga Teiji, Mae-hara Taketoshi, Nakada Mitsutoshi, Kanemura Yonehiro, Asai Akio, Takeshima Hideo, Hirose Yuichi, Iuchi Toshihiko, Nagane Motoo, Yoshimoto Koji, Matsumura Akira, Kurozumi Kazuhiko, Nakase Hi-royuki, Sakai Keiichi, Tokuyama Tsutomu, Shibui Soichiro, Nakazato Yoichi, Narita Yoshitaka, Nishikawa Ryo, Matsutani Masao, Ichimura Koichi. Integrated clinical, histopathological, and molecular data anal-ysis of 190 central nervous system germ cell tumors from the iGCT Consortium NEURO-ONCOLOGY. 2019.12; 21(12); 1565-1577
27. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. Am J Otolaryngol. 35(3); 402-404

[Books etc]

1. Shoko Hara. Unraveling Specific Brain Microstructural Damage in Moyamoya Disease Using Diffusion Magnetic Resonance Imaging and Positron Emission Tomography. Biomedical Advances ISSN 2573-0355, 2019.08

[Conference Activities & Talks]

1. Takashi Sugawara. Anatomy of the Cavernous sinus - Focus on Oculomotor Nerve and Cave -. ACNS On-Line Symposium, Anatomy of the Skull Base & Ventricles 2019.02.03 Live web lecture
2. Shoko Hara. Microstructural Damage in Normal-Appearing Brain Parenchyma and Neurocognitive Dys-function in Adult Moyamoya Disease. The 48th Annual Meeting of the Japanese Society of Neuroradiology 2019.02.15
3. Hara S, Hori M, Aoki S, Nariai T. Microstructural correlates of personality in patients with Moyamoya disease measured by neurite orientation dispersion and density imaging. ECR2019 2019.02.27 Vienna, Austria
4. Takashi Sugawara, Taketoshi Maehara. Surgical Technique for the Cavernous sinus lesion -Oculomotor Cave Exposure and Oculomotor Mobilization-. GRAND OPENING ARKANSAS NEUROSCIENCE IN-STITUTE RESEARCH AND EDUCATION CENTER & Grand Opening Symposium & Live Microneu-rosurgery course 2019.05.16 Little Rock, Arkansas, USA
5. Hara S, Kudo T, Hayashi S, Inaji M, Maehara T, Ishii K, Nariai T. Insights into the improvement of neurocognitive dysfunction after indirect bypass surgery in adult Moyamoya disease; 15O-gas positron emission tomography study. Brain & Brain PET 2019 2019.07.06
6. Takashi Sugawara. Surgical Technique for the Cavernous sinus lesion -Oculomotor Cave Exposure and Oculomotor Mobilization-. 2019 WFNS foundation ACNS seminar Tianjin 2019.08.10 Tianjin, China
7. Takashi Sugawara. Tentorium Resection and Oculomotor Nerve Mobilization for Safe and Reliable Aneurysm Clipping. 2019 WFNS foundation ACNS seminar Tianjin 2019.08.10 Tianjin, China

[Awards & Honors]

1. Kato Award, The Japanese Society of Neuroradiology, 2019.02

Endovascular Surgery

Professor Shigeru Nemoto
Associate Professor Kazutaka Sumita
Assistant Professor Kazunori Miki
Clinical Fellow Shoko Fujii
Clinical Fellow Yuki Aizawa
Secretary 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. Ishibashi T, Toyama S, Miki K, Karakama J, Yoshino Y, Ishibashi S, Tomita M, Nemoto S.. Effects of propofol versus sevoflurane on cerebral circulation time in patients undergoing coiling for cerebral artery aneurysm: a prospective randomized crossover study. *Journal of Clinical monitoring and computing*. 2019.01;
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[Conference Activities & Talks]

1. Shoko Fujii, Kazutaka Sumita, Kazunori Miki, Yuki Aizawa, Jun Karakama, Taketoshi Maehara, Shigeru Nemoto. Characteristics of the cases resulted in restenosis and retreatment after carotid artery stenting. 2019.10.09
2. Shoko Fujii, Kazutaka Sumita, Yuki Aizawa, Jun Karakama, Shigeru Nemoto. Long and mid-term outcomes of stenting for symptomatic carotid artery total occlusion . 2019.11.21

NCNP Brain Physiology and Pathology

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Yu-ichi GOTO
Collaborative Professor	Hiroshi KUNUGI
Collaborative Professor	Takashi HANAKAWA
Collaborative Professor	Noritaka ICHINOHE
Collaborative Associate Professor	Yoshitsugu AOKI

(1) Research

1) **Investigation of the molecular machinery underlying brain development.**

(Mikio Hoshino; Department of Biochemistry and Cellular Biology, National Institute of Neuroscience, NCNP)

We are investigating molecular machinery underlying nervous system development, especially focusing on neuron-subtype specification, nervous system regionalization and neuronal migration. We are also interested in human diseases/disorders caused by disorganized development of the nervous system. We published papers on the development of the cerebellum and midbrain (Shiraishi et al, Arimura et al).

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 including mitochondrial disease, Rett syndrome, and diseases with cortical and white matter dysplasia. In 2019, we detected a new mutation in mitochondrial DNA or mitochondria-associated nuclear genes (Nomura E, et al. J Neurol Sci, 2019; Inoue M, et al. Ann Neurol 2019), and causal genes of Rett syndrome by next-generation sequencing and MLPA analysis (Iwama K, et al. J Med Genet, 2019; Takeshita et al. Hum Genome Var, 2019) .

3) **Clinical research on mood disorders and schizophrenia**

(Hiroshi Kunugi, Department of Mental Disorder Research, National Institute of Neuroscience, NCNP)

The pathogenesis and physiology of mood disorders and schizophrenia remain elusive, and their biomarkers have not yet been established. Our department, which is in collaboration with the National Center of Neurology and Psychiatry Hospital, is trying to develop objective diagnostic markers for these diseases, employing omics approach, brain imaging, and physiological studies. We also aim to develop new treatment on the basis of key molecules and nutrition. In this year, we reported reduced brain-derived neurotrophic factor (BDNF) pro-peptide level in the cerebrospinal fluid of patients with depressive disorder (J Psychiatr Res, 2019) and reduced plasma n-3 polyunsaturated fatty acid level in patients with bipolar disorder (Transl Psychiatry, 2019). We established “common space” of mice to monitor spontaneous brain activity (BBRC, 2019).

4) Noninvasive study on pathophysiology of human higher brain function.

(Takashi Hanakawa, Department of Advanced Neuroimaging, Integrative Brain Imaging Center, NCNP)

We aim at revealing neural mechanisms underlying higher brain functions including sensory, motor, thought, emotion, and decision-making functions in humans, by integrating innovative brain imaging techniques. Translational approach based on this methodological development is to find imaging biomarkers related to the pathophysiology of neuro-psychiatric disorders and to develop new diagnostic tools using the biomarkers and machine learning. We also develop new rehabilitation methods using non-invasive brain stimulation and brain-machine interface.

In 2019, we found the neural correlates of motivation during operant learning in rats (Hori et al. Neuroimage 2019) and the pathophysiological mechanisms of musicians' dystonia (Uehara et al. Hum Brain Mapp 2019). We also discovered the site of cerebellar atrophy correlated with the degree of prism adaptation failure in spinocerebellar ataxia (Bando et al. Front Neurol 2019).

5) Elucidation of the pathogenesis of autism and development of treatment methods using an autism model primate (marmoset)

(Noritaka Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, NCNP)

Autism is a disorder in which the main symptom is difficulty in adjusting relationships with others. Primates, including humans, live in groups and coordinate their relationships with others, and non-human primate autism models are considered to be excellent models for reproducing the symptoms and studying the underlying pathophysiology. We have developed an animal model of autism in the New World monkey marmoset, and are analyzing the animal using multimodal research methods to elucidate the pathophysiology of autism and to develop therapeutic methods.

Our repertoire of methods includes molecular biology, micro-, meso- and macro-scale neuroanatomy, physiology, imaging, and animal behavior. In this year, we identified a decrease in FZD3, a gene important for anterior commissure coupling, in the cerebral cortex of the neonatal animal model. In addition, we observed a decrease in the size of the anterior commissure by MRI imaging. This suggests that the gene FZD3 is involved in the background of reduced commissural connectivity in human autism (Mimura et al., 2019). It is also known that microglial overactivity occurs in human autism. We observed a similar change in microglial morphology in this animal model (Sanagi et al., 2019). In addition, gene expression analysis of the brain revealed upregulation of microglia-related genes. These genetic changes are similar to those observed in the human postmortem brain, suggesting that this animal model may serve as a model for studying the relationship between microglial abnormalities in autism and its autistic symptoms.

6) Molecular pathogenesis and gene therapies for neuromuscular diseases

(Yoshitsugu Aoki, Department of Molecular Therapy, National, National Institute of Neuroscience, NCNP)

Our department integrates molecular, pharmacologic, proteomic, and genomic methodologies to clarify the molecular mechanisms of disease pathogenesis and develop novel genetic or stem cell-based therapies for the diseases (Mol Ther. 2019;27:2005-2017., Mol Ther. 2019;27:76-86.) . Primarily, our research focuses on novel genetic therapies targeting messenger RNA and DNA (Mol Ther Nucleic Acids. 2019;14:520-535.) . We also investigate RNA interference-based and genome editing therapies for several neuromuscular disorders. We have successfully shown the proof of exon skipping concept in our unique animal models, such as canine X-linked muscular dystrophy in Japan and mdx52 mice with an exon 52 deletion of the Dmd gene. We are currently developing an exon 53-skipping drug (NS-065/NCNP-01) in collaboration with a Japanese pharmaceutical company. Additionally, our department has drawn on research worldwide to create a picture of the current state of urine-derived stem cells and induced pluripotent stem cell (iPSC) research in this area (Sci Rep. 2019;9:3807.). Furthermore, to elucidate the complex molecular mechanisms of muscular dystrophy, we focus on the functional analysis of intracellular calcium regulation and mechanosensing in muscle cells, entailing several promising discoveries and offering hope to patients afflicted with the potentially life-limiting condition of DMD.

(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]

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3. Arimura N, Dewa KI, Okada M, Yanagawa Y, Taya SI, Hoshino M. Comprehensive and cell-type-based characterization of the dorsal midbrain during development. *Genes Cells.* 24, 41-59, 2019
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9. Ota M, Nemoto K, Ishida I, Sato S, Asada T, Arai T, Kunugi H. Structural brain network correlated with the resilience to traumatic events in the healthy participants: An MRI study on healthy people in a stricken area of the Great East Japan Earthquake. *Psychol Trauma*. 2019 Oct 17.
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- BDNF pro-peptide levels in major depressive disorder and schizophrenia. *J Psychiatr Res.* 2019 Jun;113:190-198.
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 32. Hori Y, Ihara N, Sugai C, Ogura J, Honda M, Kato K, Isomura Y, Hanakawa T: Ventral striatum links motivational and motor networks during operant-conditioned movement in rats. *Neuroimage* 184:943-953, 2019.

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[Review Articles • Books]

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- Dystrophin Expression in Duchenne Muscular Dystrophy: Current Status of Therapeutic Approaches. *J Pers Med*. 2019 Jan 7;9(1):1.
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 6. Nordin JZ, Aoki Y. Autoimmune response and its long-term consequences after exon-skipping therapy in a Duchenne muscular dystrophy mouse model. *J Pathol*. 2019 Nov;249(3):271-273.
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Immune Regulation

Professor Hajime Karasuyama, M.D., Ph.D.
Associate Professor Yoshinori Yamanishi, M.D., Ph.D.
Assistant Professor Yohei Kawano, Ph.D.
Assistant Professor Soichiro Yoshikawa, Ph.D.
Specially Appointed Assistant Professor Kensuke Miyake, M.D., Ph.D.

(1) Research

- 1) Role of basophils in immune disorders such as allergy
- 2) Role of basophils in protective immunity against infections
- 3) in vivo imaging of basophil-mediated immune responses

(2) Education

Main objective of the immunology course for undergraduate students is to provide them the basic ideas how the immune system works and is regulated in various physiological and pathological settings including infections, cancer, autoimmune and allergic disorders, and organ transplantation. In the immunology course for graduate students, they study molecular mechanisms underlying the development of immune diseases including allergy and parasitic infection, by employing advanced technology in molecular biology, biochemistry, cellular biology and developmental engineering.

(3) Publications

[Original Articles]

1. Adachi T, Yoshikawa S, Tezuka H, Tsuji NM, Ohteki T, Karasuyama H, Kumazawa T. Propolis induces Ca²⁺ signaling in immune cells. *Bioscience of Microbiota, Food and Health*. 2019; 38(4); 141-149
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3. Nagao T, Yamanishi Y, Miyake K, Teranishi M, Takahashi S, Yoshikawa S, Kawano Y, Karasuyama H. Aggregation makes a protein allergenic at the challenge phase of basophil-mediated allergy in mice. *Int. Immunol.* 2019.02; 31(1); 41-49
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[Conference Activities & Talks]

1. Miyake K, Shiozawa N, Nagao T, Yoshikawa S, Yamanishi Y, Karasuyama H. Basophils exert antigen presentation through trogocytosis of peptide-MHC class II complexes from DCs. 8th NIF Winter School on Advanced Immunology 2019.01.20 Singapore
2. Miyake K, Yoshikawa S, Yamanishi Y, Karasuyama H. Basophils promote the differentiation of monocytes into M2-like macrophages which dampen IL-1 α -mediated aggravation of allergic inflammation. 17th IUIS 2019 (International Congress of Immunology) 2019.10.21 Beijing, China
3. Yoshikawa S, Oh-hora M, Hashimoto R, Miyake K, Adachi T, Kawano Y, Yamanishi Y, Kamiya A, Karasuyama H. Pivotal role of STIM2, but not STIM1, in IL-4 production by IL-3-stimulated basophils. 17th IUIS 2019 (International Congress of Immunology) 2019.10.23 Beijing, China
4. Miyake K, Yoshikawa S, Yamanishi Y, Karasuyama H. Monocyte-derived M2-like macrophages induced by activated basophils dampen IL-1 α -mediated aggravation of allergic inflammation. The 48th Annual Meeting of The Japanese Society for Immunology 2019.12.13 Hamamatsu, Japan
5. Mogi K, Takahashi K, Miyake K, Yoshikawa S, Karasuyama H, Yamanishi Y. Basophil-derived IL-4 promotes disease progression in a hapten-elicited murine model of atopic dermatitis. The 48th Annual Meeting of The Japanese Society for Immunology 2019.12.13 Hamamatsu, Japan
6. Ito J, Miyake K, Shichino S, Yamanishi Y, Karasuyama H. Identification of immature-type basophils that are distinguishable from mature ones in terms of surface phenotype and activation property. The 48th Annual Meeting of The Japanese Society for Immunology 2019.12.13 Hamamatsu, Japan

Immunotherapeutics

Professor: Mari Kannagi

Associate Professor: Takao Masuda

Assistant Professor: Atsuhiko Hasegawa (Lecturer)

Assistant Professor: Yoshiko Nagano

Visiting Researcher: Sayaka Ito

Research Assistant: Kuniko Katagiri

Graduate Student: Undrakh Ganbaatar, Yu-Lun HUANG, Tomokma Fujikawa, Atsushi Otsuka, Jianchun Zhang, Te

(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. Br J Haematol, 2015) (Kannagi, M., et al. Cancer Sci, 2019).

② Involvement of innate immune response in HTLV-1 pathogenesis.

There are several enigmas in HTLV-1 pathogenesis. The level of HTLV-1 expression in infected cells is very low in vivo but rapidly induced in vitro. Despite the low viral expression, NF κ B is constitutively activated, which plays an important role in leukemogenesis of adult T-cell leukemia/lymphoma (ATL). In addition, the combination therapy of AZT/IFN- α used for ATL outside Japan, while its transient anti-ATL mechanism has been unclear because HTLV-1-infected cells are resistant to this therapy in vitro. We found that host innate immune responses against HTLV-1 are involved in these long-puzzling phenomena. (Kinpara, et al. J Virol. 2009, Retrovirol, 2013, Leukemia, 2015). Furthermore, our findings elucidated that IL-10-dominant microenvironment is critical for HTLV-1 leukemogenesis partly explaining how HTLV-1 induces totally different lymphoproliferative or inflammatory diseases without differences in viral strains (Sawada, et al. PLOS Pathog, 2017). These findings indicate that both innate and acquired immune response against HTLV-1 are deeply involved in HTLV-1 pathogenesis (Kannagi, et al. Retrovirology. 2019).

③ Novel molecular basis to regulate HIV-1 replication.

Reverse transcription of viral genomic RNAs into DNA forms followed by integration of the viral DNA into host cell chromosome is an essential step for retroviral replication including human immunodeficiency virus type 1 (HIV-1). We have proposed that essential roles of integrase (IN) during reverse transcription step which could be the next target for novel anti-HIV drug development (Masuda. Front Microbiol, 2011). Recently we found that critical contribution of HIV-1 IN in facilitating reverse transcription is exerted through the IN precursor fusion form with reverse transcriptase (RT) (Takahata et al., J. Virol. 2017). Furthermore, we established in vitro cell-free HIV-1 reverse transcription assay to delineate the contribution of other cis- and trans-acting candidate factors in regulating HIV-1 reverse transcription. We revealed unprecedented roles of the 5' -end nucleotide of HIV-1 genomic RNA for reverse transcription (Masuda et al, Sci. Rep. 2015, Huang et al, BBRC. 2019). These studies have provided novel molecular basis and concept to regulate HIV-1 replication.

(3) Education

① For under graduate students of the medical school, we participate in education of basic immunology I, and II, the project semester, and the preclinical clerkship.

② Graduate students are trained for basic skills in the field of immunology and virology to handle biohazard materials. We provide the opportunity to research for mechanisms of the retro-virus-mediated diseases and development of immunological therapeutics. All the staffs and students participate in maintenance of the laboratory and periodical seminars to discuss about their own studies and keep up with the latest knowledge and information in the area.

(4) Lectures & Courses

We always think of the clinical significance of the results of basic research. We try to find an effective therapy by approaching from basic research to understand the disease mechanisms and solve the problem. The disease mechanisms that we study include leukemogenesis, inflammation, immunosuppression, and autoimmunity in persistent virus infection. Through these studies, we contribute to clinical therapies as well as medical sciences.

(5) Clinical Services & Other Works

We held the 5th Annual Meeting of Japanese Society of HTLV-1 Associated Diseases in Tokyo on Aug 31 through Sept 2, 2018.

(6) Clinical Performances

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.

(7) Publications

[Original Articles]

1. Kannagi Mari, Hasegawa Atsuhiko, Nagano Yoshiko, Iino Tadafumi, Okamura Jun, Suehiro Youko. Tax 標的化ワクチンによる成人 T 細胞白血病の長期寛解維持 疾患予防治療としての期待 (Maintenance of long remission in adult T-cell leukemia by Tax-targeted vaccine: A hope for disease-preventive therapy) *Cancer Science*. 2019.03; 110(3); 849-857
2. Yu-Lun Huang, Gota Kawai, Atsuhiko Hasegawa, Mari Kannagi, Takao Masuda. Impact of 5'-end nucleotide modifications of HIV-1 genomic RNA on reverse transcription. *Biochem. Biophys. Res. Commun.* 2019.07;
3. Huang, Y. L., Kawai, G., Hasegawa, A., Kannagi, M., Masuda, T.. Impact of 5'-end nucleotide modifications of HIV-1 genomic RNA on reverse transcription *Biochemical and biophysical research communications*. 2019.07; 516(4); 1145-1151
4. Kannagi M, Hasegawa A, Nagano Y, Kimpara S, Suehiro Y. Impact of host immunity on HTLV-1 pathogenesis: potential of Tax-targeted immunotherapy against ATL. *Retrovirology*. 2019.08; 16(1); 23

[Misc]

1. Mari Kannagi, Atsuhiko Hasegawa, Yoshiko Nagano, Tadafumi Iino, Jun Okamura, Youko Suehiro. Maintenance of long remission in adult T- cell leukemia by Tax- targeted vaccine: A hope for disease-preventive therapy *Cancer Science*. 2019.01; 110; 849-857
2. Kannagi M, Hasegawa A, Nagano Y, Iino T, Okamura J, Suehiro Y. Maintenance of long remission in adult T-cell leukemia by Tax-targeted vaccine: A hope for disease-preventive therapy. *Cancer Science*. 2019.03; 110(3); 849-857
3. Kannagi M, Hasegawa A, Nagano Y, Kimpara S, Suehiro Y. Impact of host immunity on HTLV-1 pathogenesis: potential of Tax-targeted immunotherapy against ATL. *Retrovirology*. 2019.08; 16(1); 23
4. Kannagi M., Hasegawa A., Nagano Y., Kimpara S., Suehiro Y.. Impact of host immunity on HTLV-1 pathogenesis: Potential of Tax-targeted immunotherapy against ATL. *Retrovirology*. 2019.08; 16(1); 23

[Conference Activities & Talks]

1. Hasegawa A, Iino T, Shiratsuchi M, Utsunomiya H, Ohno H, Kitaura K, Matsutani T, Suxuki R, Nagano Y, Matsuoka M, Kannagi M, Suehiro Y. Clonal analysis of residual ATL cells and anti-HTLV-1 Tax CTL following a dendritic cell-based anti-ATL immunotherapy targeting Tax. 2019.04.24 Peru
2. JIANCHUN ZHANG、永野 佳子、長谷川 温彦、片桐 邦子、倉橋 初実、増田 貴夫、神奈木 真理. IRF4 制御による HTLV-1 感染細胞の増殖低下は SOCS3 発現の増大を伴う. 第 6 回日本 HTLV-1 学会学術集会 2019.08.24
3. Camille Michiko Obayashi, Yoko Shinohara, Takao Masuda, Gota Kawai. Influence of the 5'-terminal sequences on the structure and function of the HIV-1 genomic RNA. 2019.09.18
4. Yoshiko Nagano, Jianchun Zhang, Atsuhiko Hasegawa, Takao Masuda, Mari Kannagi. Growth inhibition of HTLV-1-infected cells by regulation of IRF4 is accompanied by increased SOCS3 expression. 第 78 回日本癌学会学術集会 2019.09.26
5. Mari Kannagi, Yoshiko Nagano, Takeru Yoneda, Jian-Chun Zhang, Takao Masuda, Atsuhiko Hasegawa. Lenalidomide inhibits proliferation of HTLV-1-infected cells through suppression of IRF4 and IL-10. 2019.09.28
6. 米田 建、永野 佳子、長谷川 温彦、近藤 伸世、石澤 未来、松岡 将太郎、増田 貴夫、神奈木 真理. 免疫調節薬レナリドミドは HTLV-1 感染細胞のサイトカイン産生に影響し増殖を抑制する. 第 67 回日本ウイルス学会学術集会 2019.10.30
7. 大林カミーユ美智子, 篠原陽子, 増田貴夫, 河合剛太. HIV-1 ゲノム RNA の 5' 末端の違いが構造と機能に与える影響. 第 42 回 分子生物学会 2019.12.03 福岡

Biodefense Research

Professor Toshiaki Ohteki
 Junior Associate Professor Taku Sato
 Adjunct Lecturer Nobuyuki Onai
 Assistant Professor Masashi Kanayama
 Project Assistant Professor Mihoko Kajita
 Graduate Student Minako Inazawa
 Graduate Student Kana Minamide
 Graduate Student Miwako Sase
 Graduate Student Shun Ishikawa
 Graduate Student Hirona Yamamoto
 Graduate Student Yuta Izumi
 Research Technician Shoko Kuroda
 Research Technician Kisho Shiseki
 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 myeloid cells (dendritic cells and macrophages), tissue stem cells, and their functional interplay in the immunological and non-immunological organs. 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 myeloid cells

1) Identification of novel sources of mononuclear phagocytes

Mononuclear phagocytes contain monocytes, macrophages and dendritic cells (DCs). In a recent decade, it has been continuing epoch-making discoveries in the field of mononuclear phagocytes and their functions are now beyond classical Immunology and extend to broad life phenomenon, e.g. tissue development/regeneration, wound-healing, and establishment of tumor environments and various inflammatory diseases.

DCs consist of conventional DCs (cDCs) and plasmacytoid DCs (pDCs), both of which play critical regulatory roles in the immune system. cDCs exhibit prominent antigen-presenting ability, whereas pDCs are characterized by their capacity to produce large amounts of type I interferons (IFNs). We have discovered the DC progenitors in the mouse bone marrow, and named common DC progenitors (CDPs) (Immunity 2013; Nat Immunol 2007). Interestingly, CDPs are divided into 2 subpopulations. One is M-CSF receptor (R)+ CDPs mainly producing cDCs, and the other M-CSFR-CDPs producing a large number of pDCs. In addition to CDPs, common monocyte/macrophage progenitors, cMoP, identified in the mouse bone marrow and spleen by other group in 2013.

Based on these achievements in mouse, we have been trying to identify human progenitors of mononuclear phagocytes, and most recently succeeded to identify human cMoP (Immunity 2017; Int Immunol 2018). Human cMoP gives rise to only monocytes but not other hematopoietic cells including DCs. Given that monocytes

and monocyte-derived macrophages cause a variety of inflammatory disorders, including metabolic syndromes and tumor development, our studies shed light on possible therapeutic applications for infectious diseases, cancers and autoimmune diseases. Collaborations with pharmaceutical company and Department of Hematology of TMDU toward the development of therapeutic agents targeting cMoP and monocyte lineage and with Department of Pediatrics of TMDU for the pathology clarification of congenital pulmonary alveolar proteinosis (PAP) are currently in progress.

2) Mechanism of brain function impairment by spatiotemporal transformation of microglial enhancer

The decline in tissue regeneration and homeostasis associated with life-stage progression is closely related to the functional alteration of macrophages. Microglia, a macrophage in the brain, is actively contributing to the brain development and maintenance during young age (regenerative microglia). However, with age, microglial inflammatory trait becomes prominent with impaired phagocytosis and brain-derived neurotrophic factor (BDNF) production etc (inflammatory microglia). As a result, functional neurons and synapses are decreased and destroyed. However, the overall picture and entire process of the microglial functional alteration and causative epigenomic transformation have not been clarified.

In this study, using a novel technology that can detect the active enhancer region and its activity with high sensitivity, we will identify the super enhancers (hereafter, SEs) responsible for the microglial transformation during life-stage progression, and elucidate the entire process of transformation dynamics. As SEs are activated in a cell-type specific manner, one can expect that it will lead to the development of novel technology to specifically control the age-related functional alteration of microglia. To date, we have identified 36,320 new microglial enhancers including 937 regions that become different with age (unpublished).

3) Mechanism of emergency myelopoiesis

Unlike steady-state hematopoiesis, hematopoiesis triggered at infection, irradiation and anti-cancer therapy is biased toward myeloid cell differentiation and production, that is “emergency myelopoiesis”. However, due to the fluctuation of cell-surface marker(s) on hematopoietic stem progenitor cells (HSPCs), it has long been difficult to understand bona-fide emergency myelopoiesis. Recently, our laboratory succeeded in identifying a novel marker with less fluctuation during emergency myelopoiesis. Using this unique marker, we will elucidate the mechanism of emergency myelopoiesis.

2. Research on tissue stem cells

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

We found that type I IFNs induce proliferation and exhaustion in hematopoietic stem cells (HSCs), and that interferon regulatory factor-2 (IRF2), a transcriptional suppressor of type I IFN signaling, preserves the self-renewal and multi-lineage differentiation capacity of HSCs (Nat Med 2009). Based on this finding, we show that type I IFN preconditioning, without irradiation or DNA alkylating agents, significantly enhanced the HSC engraftment efficiency in wild type (WT) recipient mice (Blood 2013). Based on these achievements, we have further found that physiological levels of type I IFN signaling also affect other tissue stem cells (submitted).

2) Establishment of biobank for human tongue cancer

Oral cancer has an increasing trend of 270,000 new cases per year worldwide. Two-thirds of them are tongue cancers, and in advanced cases, they become refractory to treatment and have a poor prognosis, and causal genes have not been identified. Under these backgrounds, we succeeded in establishing a human tongue cancer organoid culture system. In the future, we aim to develop fundamental technologies that lead to personalized treatment.

(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. Adachi Takahiro, Yoshikawa Soichiro, Tezuka Hiroyuki, Tsuji Noriko M., Ohteki Toshiaki, Karasuyama Hajime, Kumazawa Toshihiko. Propolis induces Ca²⁺ signaling in immune cells BIOSCIENCE OF

MICROBIOTA FOOD AND HEALTH. 2019; 38(4); 141-149

2. Zi Wang, Soichiro Adachi, Lingling Kong, Daisuke Watanabe, Yusuke Nakanishi, Toshiaki Ohteki, Namiko Hoshi, Yuzo Kodama. Role of eosinophils in a murine model of inflammatory bowel disease. *Biochem. Biophys. Res. Commun.*. 2019.03; 511(1); 99-104
3. Kanayama Masashi, Izumi Yuta, Ohteki Toshiaki. Hematopoiesis and Immune Environment Analysis with an alternative marker for Sca-1 revealed bona fide hematopoietic responses during infection(和訳中) 日本免疫学会総会・学術集会記録. 2019.11; 48(Proceedings); 1-H

[Misc]

1. Hiroyuki Tezuka, Toshiaki Ohteki. Regulation of IgA Production by Intestinal Dendritic Cells and Related Cells. *Front Immunol.* 2019.08; 10; 1891

[Conference Activities & Talks]

1. Ohteki Toshiaki. Clonal hematopoiesis and radiation-associated diseases. Radiation Effects Research Foundation International Workshop 2019.01.10 Hiroshima
2. Ohteki Toshiaki. Chronic inflammatory milieu causes differentiation and exhaustion of tissue stem cells. . France - Japan Symposium Implications of Senescence in Age Related Disorders:Towards Healthy Aging 2019.09.05 France

Pathological Cell Biology

Professor : Shigeomi SHIMIZU

Associate Professor : Norio SHIMIZU

Junior Associate Professor : Satoko ARAKAWA

Project Associate Professor : Masatsune TSUJIOKA, Satoshi TORII

Assistant Professor : Shinya HONDA, Hirofumi YAMAGUCHI

Project Assistant Professor : Michiko MUROHASHI, Hajime SAKURAI, Minkyon SHIN, Saori NOGUCHI, Hatuki ENDO

Graduate Student : Toyokazu SEKI, Tomoyo YOSHIDA, Kazuma OHSHIMA,

Joshua KUBOTA, Chinami OGAWA, Mizuki KATOH

Research Assistant : Ikuyo YOSHINO, Naomi KOJIMA, Hikari SHIMADA

Secretary : Hitomi Fukabori, Setsu TAMAI

(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. Masatsune Tsujioka, Taro Q P Uyeda, Yoshiaki Iwade, Hitesh Patel, Keitaro Shibata, Tenji Yumoto, Shigenobu Yonemura. Actin-binding domains mediate the distinct distribution of two Dictyostelium Talins through different affinities to specific subsets of actin filaments during directed cell migration. PLoS ONE. 2019; 14(4); e0214736
2. Okuno Y, Murata T, Sato Y, Muramatsu H, Ito Y, Watanabe T, Okuno T, Murakami N, Yoshida K, Sawada A, Inoue M, Kawa K, Seto M, Ohshima K, Shiraishi Y, Chiba K, Tanaka H, Miyano S, Narita Y, Yoshida M, Goshima F, Kawada JI, Nishida T, Kiyoi H, Kato S, Nakamura S, Morishima S, Yoshikawa T, Fujiwara S, Shimizu N, Isobe Y, Noguchi M, Kikuta A, Iwatsuki K, Takahashi Y, Kojima S, Ogawa S, Kimura H. Defective Epstein-Barr virus in chronic active infection and haematological malignancy. Nature microbiology. 2019.01; 4(3); 404-413
3. Sugimoto Y, Murohashi M, Arakawa S, Honda S, Shimizu S. Prediction of intracellular targets of a small compound by analyzing peptides presented on MHC class I. Biochemical and biophysical research communications. 2019.01; 508(2); 480-486
4. Noguchi S, Honda S, Saitoh T, Matsumura H, Nishimura EK, Akira S, Shimizu S. Beclin 1 regulates recycling endosome and is required for skin development in mice. Communications Biology. 2019.01; 2(37);
5. Noguchi Saori, Honda Shinya, Saitoh Tatsuya, Matsumura Hiroyuki, Nishimura Emi, Akira Shizuo, Shimizu Shigeomi. Beclin 1 regulates recycling endosome and is required for skin development in mice COMMUNICATIONS BIOLOGY. 2019.01; 2;
6. Muraoka Naoto, Nara Kaori, Tamura Fumiya, Kojima Hidenori, Yamakawa Hiroyuki, Sadahiro Taketaro, Miyamoto Kazutaka, Isomi Mari, Haginiwa Sho, Tani Hidenori, Kurotsu Shota, Osakabe Rina, Torii Satoru, Shimizu Shigeomi, Okano Hideyuki, Sugimoto Yukihiko, Fukuda Keiichi, Ieda Masaki. Role of cyclooxygenase-2-mediated prostaglandin E2-prostaglandin E receptor 4 signaling in cardiac reprogramming NATURE COMMUNICATIONS. 2019.02; 10;
7. Okuno Y, Murata T, Sato Y, Muramatsu H, Ito Y, Watanabe T, Okuno T, Murakami N, Yoshida K, Sawada A, Inoue M, Kawa K, Seto M, Ohshima K, Shiraishi Y, Chiba K, Tanaka H, Miyano S, Narita Y, Yoshida M, Goshima F, Kawada JI, Nishida T, Kiyoi H, Kato S, Nakamura S, Morishima S, Yoshikawa T, Fujiwara S, Shimizu N, Isobe Y, Noguchi M, Kikuta A, Iwatsuki K, Takahashi Y, Kojima S, Ogawa S, Kimura H. Publisher Correction: Defective Epstein-Barr virus in chronic active infection and haematological malignancy. Nature microbiology. 2019.03; 4(3); 544
8. Funakoshi Y, Ito K, Morino S, Kinoshita K, Morikawa Y, Kono T, Doan YH, Shimizu H, Hanaoka N, Konagaya M, Fujimoto T, Suzuki A, Chiba T, Akiba T, Tomaru Y, Watanabe K, Shimizu N, Horikoshi Y. Enterovirus D68 respiratory infection in a children's hospital in Japan in 2015. Pediatrics international : official journal of the Japan Pediatric Society. 2019.05;
9. Koushiro Fujimoto, Masahito Tanaka, A Y K Md Masud Rana, Md Golam Sarowar Jahan, Go Itoh, Masatsune Tsujioka, Taro Q P Uyeda, Shin-Ya Miyagishima, Shigehiko Yumura. Contributes to Cytokinesis Cooperatively with Other Dynamins. Cells. 2019.07; 8(8);
10. Funakoshi Yu, Ito Kenta, Morino Saeko, Kinoshita Kazue, Morikawa Yoshihiko, Kono Tatsuo, Doan Yen Hai, Shimizu Hiroyuki, Hanaoka Nozomu, Konagaya Masami, Fujimoto Tsuguto, Suzuki Ai, Chiba Takashi, Akiba Tetsuya, Tomaru Yasuhiro, Watanabe Ken, Shimizu Norio, Horikoshi Yuho. Enterovirus D68 respiratory infection in a children's hospital in Japan in 2015(和訳中) Pediatrics International. 2019.08; 61(8); 768-776
11. 清水 重臣, 山口 啓史, 桜井 一, 荒川 聡子. ゴルジ体の機能と構造 (Molecular mechanisms and physiological roles of alternative autophagy) 日本生化学会大会プログラム・講演要旨集. 2019.09; 92 回; [3S12m-05]
12. Nakano S, Tomaru Y, Kubota T, Takase H, Mochizuki M, Shimizu N, Sugita S, Strip PCR Project Group.. Evaluation of a multiplex Strip PCR test for infectious uveitis: a prospective multi-center study. American journal of ophthalmology. 2019.11;

13. Kato Y, Arakawa S, Terasawa K, Inokuchi JI, Iwata T, Shimizu S, Watabe T, Hara-Yokoyama M. The ceramide analogue N-(1-hydroxy-3-morpholino-1-phenylpropan-2-yl)decanamide induces large lipid droplet accumulation and highlights the effect of LAMP-2 deficiency on lipid droplet degradation. *Bioorganic & medicinal chemistry letters*. 2019.12; 126891
14. Ng SB, Ohshima K, Selvarajan V, Huang G, Choo SN, Miyoshi H, Shimizu N, Reghunathan R, Chua HC, Yeoh AE, Quah TC, Koh LP, Tan PL, Chng WJ. . 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*.. 56; 2408-2415
15. Wu T, Wang S, Wu J, Lin Z, Sui X, Xu X, Shimizu N, Chen B, Wang X.. Icaritin induces lytic cytotoxicity in extranodal NK/T-cell lymphoma. *J Exp Clin Cancer Res*. . 34; 17
16. Kozaki T, Komano J, Kanbayashi D, Takahama M, Misawa T, Satoh T, Takeuchi O, Kawai T, Shimizu S, Matsuura Y, Akira S, Saitoh T.. Mitochondrial damage elicits a TCDD-inducible poly(ADP-ribose) polymerase-mediated antiviral response. *PNAS*..

[Books etc]

1. Shimizu S. *Autophagic Cell Death and Cancer Chemotherapeutics*. . Springer,

[Misc]

1. Shigeomi Shimizu. Organelle zones in mitochondria. *J. Biochem*.. 2019.02; 165(2); 101-107
2. Arakawa S, Honda S, Torii S, Tsujioka M, Shimizu S.. Monitoring of Atg5-independent Mitophagy. *Methods in Molecular Biology*, "Mitophagy".

[Conference Activities & Talks]

1. Satoru Torii. Regulation of DNA damage-induced apoptosis by autophagy. 湯島若手塾 2019.03.18 東京都文京区湯島
2. Satoko Arakawa, Shinya Honda, Shigeomi Shimizu. Electron microscopic analysis of mitophagy during erythrocyte maturation. Joint Annual Meeting of 71st JSCB & 19th PSSJ 2019.06.25 Kobe

Lipid Biology

Professor Takehiko Sasaki
 Associate Professor Junko Sasaki
 Assistant Professor Junya Hasegawa
 Technical Assistant Toshiyoshi Yamamoto
 Technical Assistant Emi Tokuda
 JSPS Research Fellow Morioka Shin
 Graduate student (master) Takumi Ikeda
 Graduate research student Yixin Zhang
 Secretary Masayo Mita

(1) Outline

Lipids are biological molecules essential for the integrity of cell membranes, energy storage, and intra/extracellular signal transduction. What our group is mostly focused on now is the roles of phosphoinositide metabolism in health and disease. Phosphoinositides (PIPs) are bipolar lipids that contain a phosphatidylinositol (PI). PI has a glycerol backbone, an inositol head group linked to the glycerol through a phosphate group, and two long-chain fatty acids linked to the glycerol through ester bonds. Phosphorylation patterns of the hydroxyls of the inositol moiety give rise to seven other PIPs classes. In humans and mice, there are 18 interconversion reactions involving all eight PIPs classes, and these reactions are orchestrated by as many as 48 genes encoding 19 lipid kinases and 29 phosphatases. Three acyltransferases that modify the acyl moiety of phosphoinositides have also been identified.

Our goal is to achieve a comprehensive understanding of this whole metabolic system to propose new strategies for the treatment and diagnosis of incurable diseases. To this end, we have been systematically generating and characterizing knockout mouse mutants for each PIPs metabolizing enzyme. Another unique strength of the group is our original methods for lipid profiling based on LC-MS/MS technique, which will help explore novel therapeutic targets as well as biomarkers.

(2) Research

We are proposing the **"Department of Lipid Biology's Four Postulates"** to find out the relationship between lipids and diseases, and proceed with basic research to prove it scientifically.

1. Find specific lipid changes (deficiency/accumulation) in certain human pathological conditions.
2. Identify the lipid metabolizing (production/degradation) enzyme.
3. Cause the same disease state by deleting/expressing the metabolizing enzyme in mice.
4. Find the same lipid changes as in 1.

Based on this basic concept, we are trying to elucidate the true nature of the following various pathologies and to develop medical applications based on these new findings.

- Stratification method of lymphomas based on lipid acyl group composition
- Prediction method for the sensitivity of cancers (breast cancer, pancreatic cancer, lymphoma) to molecular target drugs by lipid profile.
- Identification of phospholipids involved in the pathogenesis of inflammatory diseases (pneumonia, colitis, and non-alcoholic steatohepatitis).
- Identification of phospholipids involved in basal ganglia neurodegeneration.

- Discovery of new phospholipids, their metabolic enzymes, and target proteins.
- Elucidation of target protein activation mechanism by phospholipid (MD simulation, Shotgun proteomics)

(3) Education

Topics of research for graduate student

1. Exploring bioactive lipids that cause disease conditions
2. Exploring bioactive lipids that reflect disease conditions
3. Elucidation of the true nature of cancer, inflammatory diseases, and neurodegenerative diseases by lipid profiling
4. Development of lipid analysis technology based on mass spectrometry
5. Pathological analysis of mice lacking lipid metabolizing enzymes (PI3K, PTEN, etc.)

(4) Lectures & Courses

Each student has an independent research theme.

Systematically teach experimental science knowledge and skills through research and practice, including cell culture, genome editing, and how to use knockout mice, multivariate analysis, chromatography, and mass spectrometer technology.

It is aiming for scientifically original discovery that is useful for medical progress.

The goal is to be able to plan, execute, and present original research in cooperation with other researchers.

(5) Publications

[Original Articles]

1. Fujioka Yoichiro, Satoh Aya O., Horiuchi Kosui, Fujioka Mari, Tsutsumi Kaori, Sasaki Junko, Nepal Prabha, Kashiwagi Sayaka, Paudel Sarad, Nishide Shinya, Nanbo Asuka, Sasaki Takehiko, Ohba Yusuke. A Peptide Derived from Phosphoinositide 3-kinase Inhibits Endocytosis and Influenza Virus Infection CELL STRUCTURE AND FUNCTION. 2019; 44(1); 61-74
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4. Takemasu Shinya, Ito Masaki, Morioka Shin, Nigorikawa Kiyomi, Kofuji Satoshi, Takasuga Shunsuke, Eguchi Satoshi, Nakanishi Hiroki, Matsuoka Isao, Sasaki Junko, Sasaki Takehiko, Hazeki Kaoru. Lysophosphatidylinositol-acyltransferase-1 is involved in cytosolic Ca^{2+} oscillations in macrophages. Genes to Cells. 2019.03; 24(5); 366-376
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7. Sasaki Junko, Eguchi Satoshi, Nakanishi Hiroki, Sasaki Takehiko. Regulation of cell functions by phosphoinositides Molecular mechanisms of phosphoinositide signaling(和訳中) The Journal of Physiological Sciences. 2019.06; 69(Suppl.1); S36

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9. McCormick Barry, Craig Helen E., Chu Julia Y., Carlin Leo M., Canel Marta, Wollweber Florian, Toivakka Matilda, Michael Melina, Astier Anne L., Norton Laura, Lilja Johanna, Felton Jennifer M., Sasaki Takehiko, Ivaska Johanna, Hers Ingeborg, Dransfield Ian, Rossi Adriano G., Vermeren Sonja. A Negative Feedback Loop Regulates Integrin Inactivation and Promotes Neutrophil Recruitment to Inflammatory Sites *JOURNAL OF IMMUNOLOGY*. 2019.09; 203(6); 1579-1588
10. Koizumi Atsushi, Narita Shintaro, Nakanishi Hiroki, Ishikawa Masaki, Eguchi Satoshi, Kimura Hiro-taka, Takasuga Shunsuke, Huang Mingguo, Inoue Takamitsu, Sasaki Junko, Yoshioka Toshiaki, Habuchi Tomonori, Sasaki Takehiko. Increased fatty acyl saturation of phosphatidylinositol phosphates in prostate cancer progression *SCIENTIFIC REPORTS*. 2019.09; 9(1); 13257
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[Conference Activities & Talks]

1. Junko Sasaki, Satoshi Eguchi, Hiroki Nakanishi, Takehiko Sasaki. Molecular mechanisms of phosphoinositide signaling. 9th Federation of the Asian and Oceanian Physiological Societies Congress 2019.03.27
2. Junko Sasaki. Molecular mechanisms of phosphoinositide signaling. 9th FAOPS Congress 2019.03.29 Kobe Convention Center
3. Takehiko Sasaki, Eiji Yamamoto, Toshiyoshi Yamamoto, Junko Sasaki. Lipoquality of phosphoinositides in biological systems. 60th International Conference on the Bioscience of Lipids 2019.06.17
4. 山本利義、阿部史人、田川博之、佐々木雄彦. リンパ腫細胞株ホスホイノシタイド脂肪酸組成の多変量解析を用いた抗がん剤感受性予測について. 第 18 回生命科学研究会 2019.06.28
5. 佐々木雄彦. 良い脂質、悪い脂質、普通の脂質. 文の京・最先端生命科学講座 第 24 回 2019.06.28
6. Junko Sasaki, Eiji Yamamoto, Toshiyoshi Yamamoto, Takehiko Sasaki. Molecular dissection of phosphoinositides. The 14th International Symposium of the Institute Network for Biomedical Sciences 2019 2019.10.03
7. Takehiko Sasaki, Eiji Yamamoto, Toshiyoshi Yamamoto, Junko Sasaki. Phosphoinositide Fingerprinting in Cancer. TOHOKU FORUM for CREATIVITY Thematic Program “Cancer – from Biology to Acceptance” International Symposium 2: New Technology for Diagnosis and Therapeutics of Cancer 2019.12.02

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Department of Pediatrics, Neonatal and Maternal Medicine

Professor: Shozaburo DOI (~ September, 2019)

Associate Professor: Kohsuke IMAI

Project Assistant Professor: Susumu HOSOKAWA, Tomohiro WATANABE

Department of Lifecourse Clinical Immunology

Professor: Masaaki MORI

Project Assistant Professor: Susumu Yamazaki

(1) Outline

Our department is providing advanced medical service for infants, children, adolescents and young adults. The specialties cover most pediatric diseases, including hematology-oncology, immunology, cardiology, neurology, endocrinology, nephrology, neonatology, allergy and rheumatology. On the other hand, our scientific and academic activities encompass a wide spectrum, from basic to clinical research. By focusing on innovative strategies for clarifying pathogenesis, diagnostic tests, and therapeutic interventions, we are looking at comprehensive resolution of the child's health problems, improving their future.

(2) Research

Our research covers many specialties of pediatric diseases, and the research spans from bench to bedside. Our current main projects are

1. Identification of responsible genes for primary immunodeficiency (PID).
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 ex vivo cell therapy after hematopoietic stem cell transplantation.
7. Effect of dexmedetomidine on progress of pulmonary hypertension
8. Effect of Automated External Defibrillator (AED) for sudden cardiac death in young people
9. Effectiveness evaluation of live attenuated vaccines for patients using immunosuppressants
10. Multicenter Registry study on Kawasaki Disease with coronary aneurysm
11. Identifying the pathological mechanisms of periventricular leukomalacia and pulmonary damage using model rats
12. Elucidating the molecular mechanisms of gonadal development
13. Molecular pathology of congenital adrenal diseases and disorder of sex development
14. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
15. Identifying pathological mechanisms of neurological diseases caused by defective DNA damage response
16. Investigation of molecule marker determine the prognosis of infant leukemia
17. Development of therapeutic strategy targeting homologous recombination repair
18. Genetic background of leukemia development
19. Genetic analysis and development of therapeutic approach for epilepsy syndrome
20. Developing data base of JIA (juvenile inflammatory arthritis), CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan)
21. Clarifying immunological profiles of the patients with autoimmune diseases
22. Developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker
23. Development of newborn screening for treatable childhood diseases including spinal muscular atrophy
24. Kinetic and functional analysis of novel T and B cell subsets in patients with autoimmune disease

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Science, Hiroshima University, 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, Kyoto University, Tokyo University and many other laboratories.

● Hematology/Oncology/Immunology Group (Basic Research)

Hematology/Oncology/Immunology group includes 9 staff members, 3 medical staff, 10 graduate students, collaborating researchers, and several technical assistants.

Identifying the pathophysiology of primary immunodeficiency (PID)

We are performing candidate gene hunting of PID using whole exon sequencing analysis by a next generation sequencer and identified several responsive or candidate genes, and we will also analyze further pathogenesis. Among them, in 2018, Kanegane et al studied X linked lymphoproliferative disorder, and CTLA4 deficiency from the view from EBV infection, and reported in a scientific journal. We also reported about application methods such as flow cytometric analysis method and digital PCR necessary for PID diagnosis and/or treatment standardization. As clinical research, the results of a nationwide survey of hematopoietic cell transplantation to PI3K δ abnormality was reported. Sugawara et al. reported the usefulness of cimetidine for Aicardi-Goutières syndrome with IFIH1 mutation.

As the ongoing study, research of PAPA syndrome, PID with lymphoma susceptibility, PID with pulmonary alveolar proteinosis a disease with immunoglobulin class switch abnormality. Takagi revealed variety of autoantibodies in IPEX syndrome Imai pursues the research on the execution of nationwide neonatal mass screening using TREC/KREC test for PID, and research using early diagnosis and patient registration database. Development of adoptive immunotherapy, virus-specific T cell therapy, to promote immunological reconstitution after hematopoietic transplantation was performed by Mori and Yanagimachi. The clinical trial of specific T cell therapy was launched this year.

Regenerative medicine

Morio organized a research group to evaluate the quality of the clinical uses of iPS cell. The comprehensive microbe monitoring system has been developing in collaboration with Dr. Shimizu at TMDU Medical research institute, and non-invasive genomic alteration detection system has been in development in collaboration with

Dr. Inazawa at TMDU Medical research institute and Dr. Ohara at Kazusa genome institute.

Oncology

TCF3-PBX1 chimeric gene is known to be a responsible gene for B progenitor leukemia development. In our research, it also revealed that TCF3-PBX1 chimeric gene is also involved in the development of B cell lymphoblastic lymphoma. We are focusing on identifying the mechanisms that suppress oncogenic transformation by DNA damage response. In addition, the development of therapeutics targeting DNA damage and repair pathway is conducted. Comprehensive genome research for leukemia has been conducted. This research will lead to the identification of novel therapeutic approaches for pediatric leukemia and neuroblastoma. The research was expanded to Phase I clinical trial of Olaparib for refractory solid tumor.

● Cardiology Group

We have two graduate school students. One is struggling to elucidate the mechanism of pulmonary arterial hypertension as a basic research, his current project is to examine the effect of dexmedetomidine for monocrotaline-induced pulmonary hypertension in rats. The other is engaged in a clinical research, he has two projects which are “Effect of Automated External Defibrillator (AED) for sudden cardiac death in young people” and “Effectiveness evaluation of live attenuated vaccines for patients using immunosuppressants”.

We join multicenter clinical studies too, which is “Multicenter Registry study of Kawasaki Disease with coronary aneurysm”.

● Neurology Group

< Basic research >

We are trying to establish the gene therapy using viral vectors for ataxia telangiectasia (AT), one of the major neurodegenerative diseases. Our another project is to establish diagnostic tools for early detection and early treatment of spinal muscular atrophy (SMA). We are also investigating the pathological mechanism of Moyamoya syndrome.

To Elucidate cytoprotective effect of astrocyte in oxygen-glucose deprivation condition, we have investigated the role of Nuclear Receptor 4A (NR4A) subfamily and another cytoprotective transcription factor associated with hypoxic-induced factor 1 alpha (HIF-1 α). Another study is to establish rat neonatal white matter injury model. (collaborative project with Hi-roshi Sakuma, Tokyo Metropolitan Institute of Medical Science).

< Clinical research >

“Genetic analysis and development of therapeutic approach for epilepsy syndrome” (collaboration with Showa University)

“Research for rare epilepsy syndrome” (collaboration with Institute of Epilepsy and Neurological Disorders)

“Systematic measurement and functional analysis of autoantibody in immunologic neurological diseases” (collaboration with Tokyo Metropolitan Institute of Medical Science)

“Evaluation of adrenocortical function in the patients with West syndrome treated with ACTH therapy”

“Development of newborn screening for treatable childhood diseases including spinal muscular atrophy”

● Endocrinology Group

Molecular mechanisms of gonadal development

To understand the pathophysiology of DSD, our current research focuses on the elucidation of the molecular mechanisms of sex determination and gonadal development, especially in the understanding of the transcriptional network of sex determination and gonadal development. Another of our major target is to identify the precise functions of transcription factors, such as Nr5a1 (Sf1), Foxl2, and Sox9, in gonadal development.

Molecular analysis of pathological mechanisms in congenital adrenal hyperplasia (CAH)

Our institute contributed to the introduction of CAH neonatal mass-screening in Tokyo city. Recently, in addition to adrenal insufficiency and androgen excess, metabolic syndrome during adulthood is reported to be another major concern of the disease. The precise pathophysiology is not known. We are thus focusing on the elucidation of the molecular mechanisms of the metabolic syndrome in CAH patients through the use of a mouse model.

Identifying novel molecules of congenital endocrinological diseases

We aim to identify novel molecules responsible for the development of congenital endocrine disorders such as insulin resistance. Current ongoing projects will be integrated systematically, and will be applicable to develop innovative approach for the treatment of congenital endocrine disorder, including regenerative medicine.

● Rheumatology group

We are establishing an evidence based guideline of pediatric rheumatoid diseases including juvenile idiopathic arthritis: JIA. Developing a novel database system, CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan), clarifying immunological profiles of the patients with autoimmune dis-

eases, developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker, and Kinetic and functional analysis of novel T and B cell subsets in patients with autoimmune disease are other our current projects. In addition, in joint research with the department of rheumatology, we are analyzing the current status and effectiveness of treatment for childhood and adult onset of collagen disease.

● Neonatology group

We are examining changes of profile in umbilical cord-derived mesenchymal stem cells due to the intrauterine environment in humans through joint clinical research with related hospitals.

We are trying to elucidate the mechanism and effect of umbilical cord-derived mesenchymal stem cell therapy for diseases in preterm infant and the involvement of mesenchymal stem cells in the establishment of diseases.

● Allergy Group

One of our main project goals is to elucidate the immunological mechanisms of food allergy such as that against milk and eggs. In addition, we carry out immunological and epidemiological studies on therapeutic effects of oral immunotherapy against food allergy.

In collaboration with the Japanese Society of Pediatric Allergy and Clinical Immunology, we are conducting several clinical studies to refine pharmacologic therapy listed in the Japanese pediatric guideline for the treatment and management of asthma.

(3) Education

Block Lecture

The systematic lecture was performed for M4 students. One third of lectures “were performed using an active-learning” style. The number of frames of the active-learning from nine frames in the previous fiscal year to 12 frames. Two frames of team-based learning (TBL) were also provided. Although one frame of active-learning alone cannot cover the whole area of pediatrics, about 85% of students reach the passing point in the final test covering the whole area of pediatrics by student self-study. At this point, we believe that the usefulness of active learning has been demonstrated.

Project semester

This provides the opportunities of basic research for the 4th grade students for half a year. This year, one student was committed to the research of our department and presented at a scientific meeting.

Pre-clinical clerkship (PCC).

We proposed 6 programs providing the opportunities to learn the logical skills of clinical practice.

After the curriculum, The students undertake the examination of clinical practice, i.e., OSCE, CBT.

Clinical clerkship (CC)

Clinical clerkship (CC) is a compulsory course for one month. The practical training of medicine, and every month, approximately 10 students have the training in our department. The students involved in each group of sub-specialty (Hematology, Oncology, Immunology, Cardiology, Neurology, Nephrology, Rheumatology, Endocrinology, Neonatology). In addition to our university hospital, the students visit the satellite hospitals for the training of common diseases.

Once a week, the students round the pediatric ward of the hospital with the professor to learn the physical examination skills. This fiscal year, we made an effort to eliminate the disparity between inside and outside clinical practice among students by increasing the facilities performing extracurricular clinical training from five to six institutes (NICU at Kawaguchi Municipal Medical Center, Musashino Red Cross Hospital, Soka Municipal Hospital, Tokyo North Medical Center, Tsuchiura Kyodo General Hospital ot Tokyo Metropolitan Bokuto Hospital). Every Friday, we made a practical training program to conduct student conferences for further understanding of clinical practice.

Training of junior clinical fellows

We provide clinical training courses in cooperation with satellite hospitals (Tsuchiura Kyodo Hospital, Soka Municipal Hospital or Tokyo North 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

Primary care of pediatrics covers a wide spectrum of health care and clinical problems in children, and all pediatricians should be well trained in those subjects. Further, Tokyo Medical and Dental University is one of the top ranked national medical universities in Japan, and achieving cutting edge research is another social

responsibility. For students, we provide educational programs to learn primary pediatric care, management of the diseases in every organ during neonatal period childhood, and basic science. For residents, our educational program is mainly focused on producing physician scientists who possess the skills of pediatrics for primary care, of physician specialist and of basic researcher.

(5) Clinical Services & Other Works

● Hematology/Oncology/Immunology Group

Treating children with primary immunodeficiency, hematological malignancies, hematological disorders, and malignant solid tumors.

Collaboration with other professional facilities including St. Luke' s International Hospital and Juntendo University Hospital. Joint clinical conference and trainee exchange program are regularly held in the collaborating system.

Medical care

By collaborating with national co-operative clinical research group, such as the Tokyo Children' s Cancer Study Group (TCCSG) and Japanese Children' s Cancer Study Group (JCCG), we offer our patients opportunities to participate in the latest clinical trials, contributing to establishment of both standard and novel therapies for childhood cancers and other non-malignant diseases.

In 2019, we performed HCT for 15, and 10 cases were for PID patients. Our experience of HCT exceeds 230 cases including more than 100 cases with primary immunodeficiency diseases, so far.

Clinical trial

Three doctor-initiated clinical trials led by the pediatric department of Tokyo Medical and Dental University are ongoing.

” Phase I Clinical Study of Oral Olaparib in Pediatric Patients with Refractory Solid Tumors ” .

” Multi-virus (Cytomegalovirus, EB virus, Adenovirus, BK virus, and HHV-6) specific Cytotoxic T-Lymphocytes from HLA-haploidentical or more HLA-matched relative donor to persistent viral infection after hematopoietic cell transplantation (multi-center, prospective phase I/II study) ”

” Clinical Phase II Study of hematopoietic stem cell transplantation for ataxia telangiectasia and related diseases ” is carried out.

● Cardiology Group

We provide medical care in a wide range of pediatric cardiovascular diseases. Especially, our department is one of the major center hospitals providing medical care of pediatric pulmonary hypertension.

In 2019, the number of inpatients was 137, which consisted of 71 congenital heart disease, 22 pulmonary hypertension, 21 Kawasaki Disease, 11 arrhythmia, 7 cardiomyopathy and 5 others. Cardiac catheterizations were performed in 57 patients and cardiac surgery was performed in 20 patients (18 open-heart surgery), which consisted of 12 VSDs, 4 ASDs, 2AVSDs (1 complete, 1 incomplete), 1 ccTGA, 1 DORV. The number of outpatients was 1,918, echocardiogram was performed in 1,745, Treadmill exercise-induced electrocardiogram was performed in 95, and Holter 24hr electrocardiogram was performed in 74 patients.

● Neurology Group

We provide medical care in a wide range of pediatric neurologic diseases.

In particular, collaborating with the department of neurosurgery, we run an epilepsy center, providing advanced medical care for pediatric patients with intractable epilepsy.

The medical services in our department are long-term video EEG monitoring, high magnetic field MRI/PET, ACTH therapy, ketogenic diet, vagus nerve stimulation and surgical operation, such as focal brain resection and callosotomy. We also focus on diagnosis, genetic analysis and treatment for rare neurologic diseases.

● Endocrinology Group

We provide comprehensive diagnostic and treatment services for children with endocrinological abnormality and diabetes, such as disorders of growth, pubertal development, Ca/P metabolism (including skeletal dysplasia), gonadal development and adrenal cortex function. Especially, we are focusing on providing advanced medical service for congenital adrenal hyperplasia (CAH) and disorders of sex development (DSD). Our institute is one of the DSD central facilities approved by the Japanese Society for Pediatric Endocrinology (JSPE). For social contribution, we supervise the neonatal screening system for CAH in Tokyo metropolitan city and peer support group of type 1 diabetes, “Tokyo Wakamatsu-kai” .

● Nephrology Group

Nephrology Group provides diagnosis and treatment for patients with various kidney diseases. We perform kidney biopsy (30/year) and imaging examination.

We performed peritoneal dialysis for low-body-weight children and provided acute hemodialysis for children who developed acute kidney injury and for children with collagen diseases.

● Rheumatology group

Medical treatment and treatment of children with collagen disease and rheumatic diseases in general, but not limited to these cases, undiagnosed cases such as unknown fever and joint pain, and autoinflammatory syndrome represented by periodic fever. Is going. In addition, the current status of pediatric rheumatic diseases. The emphasis is on the issues and challenges of transitional care in adulthood for pediatric rheumatic diseases, depending on the situation and the actual situation.

The medical treatment started in July 2015, and the number of outpatients in 2019 exceeded 1600 mainly for referrals. The total number of hospitalized patients in one year is 157, all of which are increasing year by year.

● Neonatology group

Collaborating with other medical departments or special care groups in pediatrics, we are treating preterm infants (≥ 27 weeks gestation, birth weight ≥ 800 g), neonates with complications and babies born from mothers with complication.

● Allergy Group

The qualified allergists of the group attend both inpatient and outpatient care units for allergic diseases in the allergy medical center of our university and extramural, affiliated hospitals, where not only the standard medical services following clinical guidelines for allergic diseases are provided, but also highly advanced treatment such as oral immunotherapy for food allergy as well.

(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. Specifically, 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 the approval of industry-based clinical trials for drugs (such as anticancer drugs).

● Cardiology Group

Cardiology group performs diagnosis, evaluation of treatment and decision of treatment strategy for pediatric pulmonary hypertension patients. We actively treat severe idiopathic/hereditary pulmonary arterial hypertension (IPAH/HPAH) patients by upfront combination therapy (uCT) with two or three kinds of disease targeted drugs including continuous venous infusion of epoprostenol. We made considerable achievements of treatment in severe IPAH/HPAH patients with epoprostenol/treprostinil.

● Neurology Group

Neurology group provide highly specialized diagnostic approach and medical care for neurological disorders such as intractable epilepsy, cerebellar ataxia, involuntary movement, immune-mediated neurological disease, perinatal brain damage, infection of nervous system, acute encephalopathy/encephalitis, neurodegenerative disease and neuromuscular disorder.

● 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 hemodial-

ysis treatment and peritoneal dialysis for low-body-weight patients (under 10kg) in cooperation with department of blood purification.

● Rheumatology group

Clinically, our target is not only pediatric collagen and rheumatic disease, but also inflammatory diseases which require biopharmaceutical medicine, such as periodic fever unknown origin, and repeated arthritis affecting multiple joints. We are also actively involved in the expansion and standardization of treatment indications through participation in clinical trials and formulation of guidelines. Further, for developing a therapeutic approach, we are planning to register international clinical trials of a novel biopharmaceutical medicine, such as belimumab for pediatric SLE.

● Neonatology Group

Our NICU provides intensive care for preterm infants and critically ill newborns. As a designated perinatal medical center in Tokyo, we accept maternal and neonatal transfer from various areas in Tokyo and contribute to perinatal medicine in Tokyo.

● Allergy Group

We focus on clinical care of severe and complicated allergic diseases such as food allergy-induced anaphylaxis, food-dependent exercise-induced anaphylaxis, food protein-induced enterocolitis syndrome and oral allergy syndrome induced by cross-reactivity between 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. We introduce new biological medicines to the long-term management for severe persistent asthma patients.

(7) Publications

[Original Articles]

1. Kei Takasawa, Atsumi Tsuji-Hosokawa, Shigeru Takishima, Yasunori Wada, Keisuke Nagasaki, Sumito Dateki, Chikahiko Numakura, Atsushi Hijikata, Tsuyoshi Shirai, Kenichi Kashimada, Tomohiro Morio. Clinical characteristics of adolescent cases with Type A insulin resistance syndrome caused by heterozygous mutations in the β -subunit of the insulin receptor (INSR) gene. *J Diabetes*. 2019.01; 11(1); 46-54
2. Keiichi Iwanami, Tsubasa Okano, Osamu Ohara, Tomohiro Morio. Recurrent Acute Abdomen as the Main Manifestation of Hereditary Angioedema. *Intern Med*. 2019.01; 58(2); 213-216
3. Mari Kubota-Tanaka, Tomoo Osumi, Shouko Miura, Hiroshi Tsujimoto, Toshihiko Imamura, Akira Nishimura, Kentaro Oki, Kozue Nakamura, Satoshi Miyamoto, Kento Inoue, Maiko Inoue, Takahiro Kamiya, Masakatsu Yanagimachi, Tsubasa Okano, Noriko Mitsuki, Takeshi Isoda, Kohsuke Imai, Hirokazu Kanegane, Tomohiro Morio, Shinji Kounami, Mikiya Endo, Motohiro Kato, Masatoshi Takagi. B-lymphoblastic lymphoma with the TCF3-PBX1 fusion gene. *Haematologica*. 2019.01; 104(1); 35-37
4. Egawa M, Imai K, Taketani Y, Morio T, Miyasaka N.. Two Prenatal Cases of Hyper-IgE Syndrome. *J. Clin. Immunol.*. 2019.01;
5. Masatoshi Takagi, Chitose Ogawa, Yuki Aoki-Nogami, Tomoko Iehara, Eri Ishibashi, Minoru Imai, Tetsuro Kihara, Kiyoshi Nobori, Kazuhisa Hasebe, Shuki Mizutani, Toshimi Kimura, Masashi Nagata, Masato Yasuhara, Kenichi Yoshimura, Pariko Yoroze, Hajime Hosoi, Ryuji Koike. Phase I clinical study of oral olaparib in pediatric patients with refractory solid tumors: study protocol. *BMC Pediatr*. 2019.01; 19(1); 31
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[Misc]

1. Takeshi Isoda, Tomohiro Morio, Masatoshi Takagi. Noncoding RNA transcription at enhancers and genome folding in cancer. *Cancer Sci*. 2019.08; 110(8); 2328-2336

[Conference Activities & Talks]

1. Hematopoietic cell transplantation with reduced intensity conditioning regimen using fludarabine/busulfan and fludarabine/melphalan for primary immunodeficiency diseases . 2019.02.02
2. Tanita K, Cardinez C, Miraghanzadeh B, Hoshino A, Okada S, Asano T, Tsumura M, Ohnishi H, Kato Z, Morio T, Vinuesa CG, Kanegane H, Cook MC. Gain-of-function IKBKB mutation causes human combined immune deficiency. 第2回日本免疫不全・自己炎症学会総会・学術集会 2019.02.02 東京
3. An adult case of cytotoxic T-lymphocyte antigen 4 (CTLA-4) insufficiency treated successfully with abatacept. 2019.02.03
4. An experience of allogeneic stem cell transplantation for NFKB1 deficiency. 2019.02.03
5. Combined immunodeficiency of ICF syndrome. 2019.02.03
6. Three families with X-linked agammaglobulinemia caused by transcriptional. 2019.02.03
7. Shozaburo Doi. Comprehensive evaluation is essential for diagnosis and treatment of PH with CHD. The 4th Mt. Fuji Network Forum 2019.02.22 Shizuoka
8. Chantaramanee A, Hara K, Tohara H, Kazuharu Nakagawa, Yamaguchi K, Namiki C, Kurosawa Y, Nakane A, Minakuchi S. The Effect of Gender and Age differences on Echo Intensity of Tongue. Dysphagia Research Society 2019.03.07 San Diego
9. Influence of genetic mutation of CGD on the outcome of HSCT (a collaboration of JDCHCT and PIDJ). 2019.03.08
10. Impact of GVHD on the clinical outcome of allogeneic HSCT for non-malignant diseases. 2019.03.08
11. Multivirus specific T cell therapy for refractory viral infection after HSCT. 2019.03.08

12. Nishimura Akira, Aoki Yuki, Ishiwata Yasuyoshi, Inoue Maiko, Ichimura Takuya, Ueyama Junichi, Matsumoto Kazuaki, Inoue Kento, Hiroki Haruka, Ono Shintaro, Okano Tsubasa, Tanaka Mari, Miyamoto Satoshi, Ashiarai Miho, Miyawaki Reiji, Yamagishi Chika, Tezuka Mari, Okawa Teppei, Hoshino Akihiro, Endo Akifumi, Yasuhara Masato, Kamiya Takahiro, Mitsuiki Noriko, Ono Toshiaki, Yanagimachi Masakatsu, Isoda Takeshi, Tomizawa Daisuke, Nagasawa Masayuki, Kajiwara Michiko, Takagi Masatoshi, Mizutani Shuki, Kanegane Hirokazu, Imai Kohsuke, Morio Tomohiro. Hematopoietic cell transplantation with reduced intensity conditioning regimen using fludarabine/busulfan and fludarabine/melphalan for primary immunodeficiency diseases . The 45th Annual Meeting of the European Society for Blood and Marrow Transplantation 2019.03.25 Frankfurt
13. Shozaburo Doi. Valuable Algorithm for the Management of Patients with CHD-PAH. The 15th Korea-Japan-China Pediatric Heart Forum 2019.04.06 Korea
14. Shozaburo Doi. Japanese Guideline of pediatric PH. 2019 1st EASOPH and 4th TPHA Pulmonary Hypertension Forum 2019.04.13 Taiwan
15. Kenichi Kashimada. Diagnosis and clinical management of DSD in past and present. Pediatric Academic Societies Meeting 2019.04.28 Baltimore, USA
16. Morio T. Primary immunodeficiency disorders caused by a mutation in IKAROS family gene. RIKEN IMS-JSI International Symposium on Immunology 2019 2019.06.25 Tokyo
17. Morio T. Disorders caused by a defect in IKAROS family protein. 2019 Samsung Medikal Center Primary Immunodeficiency Symposium 2019.07.06 Seoul
18. Shozaburo Doi. Therapeutic Approach to PAH associated with CHD - Pulmonary Vascular Science in CHD-PAH -. 11th Long March National Vascular Medicine Conference 2019.08.03 Nanchang, China
19. Okano T, Imai K, Naruto T, Okada S, Okamoto K, Yamashita M, Yeh T. W, Takagi M, Kanegane H, Morio T. Diagnostic Approach by Whole Exome Sequencing for 141 Patients of Inborn Errors of Immunity. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.19 Brussels
20. Cardinez C, Miraghazadeh B, Tanita K, da Silva E, Hoshino A, Okada S, Chand R, Asano T, Tsumura M, Yoshida K, Ohnishi H, Kato Z, Yamazaki M, Okuno Y, Miyano S, Kojima S, Ogawa S, Andrews TD, Field MA, Burgio G, Morio T, Vinuesa CG, Kanegane H, Cook M. Gain-of-Function IKBKB Mutation Causes Human Combined Immune Deficiency. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.19 Brussels
21. Sakata S, Okada S, Matsubayashi T, Tamaura M, Tsumura M, Okano T, Imai K, Bustamante J, Morio T, Casanova JL, Kobayashi M. The First Intronic Mutations Which Caused Autosomal Recessive Complete STAT1 Deficiency. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.19 Brussels
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23. Morio T, Baheti G, Tortorici MA, Hofmann J, Rojavin MA. Pharmacokinetic Properties of IgPro10 in Japanese Patients with Primary Immunodeficiency. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.20 Brussels
24. Hoshino A, Okano T, Matsumoto K, Nishimura A, Shintaku H, Tokoro S, Okamoto H, Wada T, Mitsuiki N, Kajiwara M, Takagi M, Imai K, Kanegane H, Morio T. Plasmacytoma-Like Post-Transplant Lymphoproliferative Disorder with Multiple Autoantibodies in a XIAP Deficient Patient. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.20 Brussels
25. Nishimura A, Naruto T, Hoshino A, Amano K, Iwamoto S, Hirayama M, Grigg A, Bosco J J, Migita M, Takagi M, Ohara O, Morio T, van Zelm MC, Kanegane H. Genomics Analysis of Leukemia Predisposition in X-Linked Agammaglobulinemia. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.20 Brussels
26. Miyamoto T, Imai K. Japanese experience with UCBT in SCID. IEWP 2019.10.11 London

27. Genetic test for the suspected patients of inborn errors of immunity. 2019.11.07
28. Efficacy of Azacitidine for MDS due to germline GATA2 haploinsufficiency. 2019.11.14
29. Clonal evolution of leukemia with MLL-AF9 from myeloid to T-lineage. 2019.11.14
30. Treatment of platelet transfusion refractoriness in patients with Wiskott-Aldrich syndrome. 2019.11.14
31. Gene expression profiling defines clinical subgroups of pediatric BCP-ALL lacking major pathogenic. 2019.11.14
32. PARP inhibition sensitize BCR-ABL1 positive cell. 2019.11.14
33. Genome-wide association study of childhood acute lymphoblastic leukemia risk in Japanese: A report from the Tokyo Children's Cancer Study Group. 2019.11.14
34. A case with relapsed acute lymphoblastic leukemia treated with blinatumomab under the active GVHD after unrelated bone marrow transplantation. 2019.11.15
35. NUDT15 variants confer high incidence of secondary malignancies of ALL in children. 2019.11.15
36. Primary immunodeficiency (in bone error of immunity) from the view from pediatric hematological. 2019.11.15
37. BMP4 suppresses the tumor growth of neuroblastoma via MYCN downregulation. 2019.11.15
38. Intrinsically Vancomycin resistant enterococcal (*Enterococcus gallinarum*) meningitis occurred early after hematopoietic stem cell transplantation for activated PI3K delta syndrome type2. 2019.11.16
39. Successful case of donor lymphocyte infusion for refractory T cell acute lymphoblastic leukemia which lead to one year of remission. 2019.11.16
40. Pay attention to selective Immunoglobulin G2 deficiency - a case of Invasive pneumococcal infection after allogeneic hematopoietic stem cell transplantation. 2019.11.16
41. Usefulness of respiratory infection early diagnosis with multiplex PCR method for immunocompromised patients. 2019.11.16
42. A study for implementation of genomic medicine for pediatric cancer predispositions. 2019.11.16
43. Kenichi Kashimada. Endocrine Late Effects of childhood cancer. ISPAE PET School 2019 2019.11.26 Kolkata, India
44. Satoshi Miyamoto, Takuya Naruto, Tomohiro Morio, Kevin Y Urayama, Atsushi Manabe, Masatoshi Takagi. Association of Germline Variants of TCF3 and PAX5 with Pediatric Acute Lymphoblastic Leukemia Development. 61st American Society of Hematology (ASH) Annual Meeting and Exposition 2019.12.07 Orlando
45. Yoichi Tanaka, Kevin Y Urayama, Makiko Mori, Daisuke Hasegawa, Yasushi Noguchi, Masakatsu Yanagimachi, Dai Keino, Setsuo Ota, Koshi Akahane, Mayumi Hangai, Takahisa Kawaguchi, Masatoshi Takagi, Katsuyoshi Koh, Fumihiko Matsuda, Atsushi Manabe. NUDT15 Genetic Variation Is the Strongest Predictive Marker of Tolerance to 6-Mercaptopurine in Japanese Childhood ALL Patients: A Genome-Wide Association Study. 61st American Society of Hematology (ASH) Annual Meeting and Exposition 2019.12.07 Orlando
46. Hisashi Ishida, Takeo Sarashina, Katsutsugu Umeda, Tetsuo Mitsui, Naoto Fujita, Daisuke Tomizawa, Kevin Y Urayama, Yasushi Ishida, Takashi Taga, Masatoshi Takagi, Souichi Adachi, Atsushi Manabe, Toshihiko Imamura, Katsuyoshi Koh, Akira Shimada, Risa Matsumura. Clinical Features of Children with Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis in Japan: Retrospective Nationwide Survey. 61st American Society of Hematology (ASH) Annual Meeting and Exposition 2019.12.08 Orlando

47. Masanori Yoshida, Kazuhiko Nakabayashi, Aiko Sato-Otsubo, Shinichi Tsujimoto, Kaoru Yoshida, Ryota Shirai, Tomoo Osumi, Yuki Yuza, Masatoshi Takagi, Hiroyuki Takahashi, Katsuyoshi Koh, Akitoshi Kinoshita, Moeko Hino, Toshihiko Imamura, Yozo Nakazawa, Okuya Mayuko, Harumi Kakuda, Masashi Sanada, Kimikazu Matsumoto, Daisuke Tomizawa, Nobutaka Kiyokawa, Akira Ohara, Atsushi Manabe, Kenichiro Hata, Jun J. Yang, Motohiro Kato. NUDT15 Variants Confer High Incidence of Secondary Malignancies of ALL in Children. 61st American Society of Hematology (ASH) Annual Meeting and Exposition 2019.12.08 Orlando
48. Haruka Hiroki, Masatoshi Takagi, Yuko Ishi, Jinhua Piao, Tomohiro Morio. PARP Inhibition Sensitize BCR-ABL1 Positive Cel. 61st American Society of Hematology (ASH) Annual Meeting and Exposition 2019.12.08 Orlando
49. Anne Pieta De Groot, Yoriko Saito, Eiryo Kawakami, Mari Hashimoto, Yuki Aoki, Rintaro Ono, Ikuko Ogahara, Saera Fujiki, Akiko Kaneko, Takashi Watanabe, Masatoshi Takagi, Daisuke Tomizawa, Katsuyoshi Koh, Mariko Eguchi, Eiichi Ishii, Osamu Ohara, Leonard Shultz, Shuki Mizutani, Fumihiko Ishikawa. Targeting Critical Kinases and Anti-Apoptotic Molecules Overcomes Steroid Resistance in Infant MLL-Rearranged Leukemia. 61st American Society of Hematology (ASH) Annual Meeting and Exposition 2019.12.09 Orlando

Rheumatology

Professor	Ryuji KOIKE (2) Masaaki MORI (1) Tetsuo KUBOTA (2) Kazuki TAKADA (3)
Professor emeritus	Nobuyuki MIYASAKA
Associate Professor	Takahiko SUGIHARA
Junior Associate Professor	Hideyuki IWAI
Assistant Professor	Fumitaka MIZOGUCHI, Tadashi HOSOYA, Naoki KIMURA, Hisanori HASEGAWA, Natsuka UMEZAWA, Hirokazu SASAKI, Mari KAMIYA
Visiting Lecturer	Kimito KAWAHATA, Kenji NAGASAKA, Akito TAKAMURA, Makoto SOEJIMA, Hiroyuki HAGIYAMA, Yusuke MATSUO, Fumihito SUZUKI, Reiko TSUBATA, Kaori WATANABE, Jyunko NISHIO, Mari KIHARA, Toshihiro MATSUI, Tokishige MIYABE
Affiliated Hospital	Fumiaki KONDO, Takeshi KUSUDA, Wakako KAWSAKI, Marina TSUCHIDA, Takuji ITAKURA, Masami TOKURA, Seiya OBA, Yuriko YAGYU, Motohiko SATO, Yuichi KIRI
Resident	Tomoko NIWANO, Takahiro NAKAHARA, Daisuke KAWADA, Riku YOSHITUKA
Graduate Student	Akiou YAMAMOTO, Yasuhiro TAGAWA, Takumi MATSUMOTO, Fumiaki KONDO, Youji KOMIYA, Seiji NODA, Nao TANAKA, Tasuku SASAKI
Researcher	Hiroyuki BABA
Office Administrator	Kaori KONNO, Tomoko TAKAHASHI (1)
Technical Staff	Kazuko YAMAZAKI, Naoko FUJITA

(1) Department of Lifetime Clinical Immunology, (2) Medical Innovation Promotion Center,
(3) Institute of global affairs

(1) Research

Following studies have been extensively carried out in our laboratory with various biochemical, immunological, molecular biological and statistical techniques:

1) Investigation of mechanism and development of new therapeutics for the treatment of rheumatoid arthritis and dermato/polymyositis.

2) Establishment of evidence-based treatment of rheumatic diseases by implementing several cohort studies. We collaborate with department of lifetime clinical immunology and pediatrics.

(2) Education

We have provided medical students and graduates with the opportunity to obtain the ability to identify important clinical problems and to solve them by clinical reasoning through their active participation into the diagnosis and management of various rheumatic diseases.

(3) Clinical Services & Other Works

We have provided care to many patients with diverse rheumatic diseases. We have aimed to practice evidence-based medicine and to provide care that is in accordance with the global standard. We have contributed to the development of potential new drugs and treatments through participation into industry- as well as investigator-initiated clinical trials for chemical and biological agents. We have also contributed to the refinement of the care of rheumatic disease patients through the conduct of various pharmacovigilance studies.

We cooperate with department of lifetime clinical immunology and pediatrics.

(4) Publications

[Original Articles]

1. [Pediatrics and Developmental Biology : TAKAGI Masatoshi] Masatoshi Takagi, Chitose Ogawa, Yuki Aoki-Nogami, Tomoko Iehara, Eri Ishibashi, Minoru Imai, Tetsuro Kihara, Kiyoshi Nobori, Kazuhisa Hasebe, Shuki Mizutani, Toshimi Kimura, Masashi Nagata, Masato Yasuhara, Kenichi Yoshimura, Pariko Yorozu, Hajime Hosoi, Ryuji Koike. Phase I clinical study of oral olaparib in pediatric patients with refractory solid tumors: study protocol. BMC Pediatr. 2019.01; 19(1); 31
2. [Department of Lifetime Clinical Immunology : TAKAHIKO Sugihara] Miyazawa R, Tanei R, Tsuchida M, Sugihara T. MPO-ANCA-positive cutaneous polyarteritis nodosa with livedo racemosa arising from immune-deposit-positive necrotizing vasculitis. Giornale italiano di dermatologia e venereologia : organo ufficiale, Societa italiana di dermatologia e sifilografia. 2019.01;
3. [- : HIRANO Fumio] Natsumi Namba, Aya Kawasaki, Ken-Ei Sada, Fumio Hirano, Shigeto Kobayashi, Hidehiro Yamada, Hiroshi Furukawa, Kota Shimada, Atsushi Hashimoto, Toshihiro Matsui, Kenji Nagasaka, Takahiko Sugihara, Aika Suzuki, Kunihiro Yamagata, Takayuki Sumida, Shigeto Tohma, Sakae Homma, Shoichi Ozaki, Hiroshi Hashimoto, Hirofumi Makino, Yoshihiro Arimura, Masayoshi Harigai, Naoyuki Tsuchiya, . Association of *MUC5B* promoter polymorphism with interstitial lung disease in myeloperoxidase-antineutrophil cytoplasmic antibody-associated vasculitis. Annals of the Rheumatic Diseases. 2019.02;
4. [Department of Lifetime Clinical Immunology : TAKAHIKO Sugihara] Matsuda Y, Itabashi M, Tachibana Y, Sugihara T, Sakashita Y, Matsubara T, Murayama S, Yumura W, Shimizu A, Takei T, Arai T. Citrullinated histone H3 expression in anti-neutrophil cytoplasmic antibody-associated vasculitis in older Japanese autopsy patients. Geriatrics & gerontology international. 2019.03; 19(3); 259-264
5. [Pediatrics and Developmental Biology : MORIO Tomohiro] H Sasaki, A Takamura, K Kawahata, T Takashima, K Imai, T Morio, H Kohsaka. Peripheral blood lymphocyte subset repertoires are biased and reflect clinical features in patients with dermatomyositis. Scand J Rheumatol. 2019.05; 48(3); 225-229
6. [Rheumatology : MIZOGUCHI Fumitaka] Fan Zhang, Kevin Wei, Kamil Slowikowski, Chamith Y Fonseka, Deepak A Rao, Stephen Kelly, Susan M Goodman, Darren Tabechian, Laura B Hughes, Karen Salomon-Escoto, Gerald F M Watts, A Helena Jonsson, Javier Rangel-Moreno, Nida Meednu, Cristina Roza, William Apruzzese, Thomas M Eisenhaure, David J Lieb, David L Boyle, Mandelin AM 2nd; Accelerating Medicines Partnership Rheumatoid Arthritis and Systemic Lupus Erythematosus (AMP RA/SLE) Consortium, Brendan F Boyce, Edward DiCarlo, Ellen M Gravallese, Peter K Gregersen, Larry Moreland, Gary S Firestein, Nir Hacohen, Chad Nusbaum, James A Lederer, Harris Perlman, Costantino Pitzalis, Andrew Filer, V Michael Holers, Vivian P Bykerk, Laura T Donlin, Jennifer H Anolik, Michael B Brenner, Soumya Raychaudhuri. Defining inflammatory cell states in rheumatoid arthritis joint synovial tissues by integrating single-cell transcriptomics and mass cytometry. Nat. Immunol.. 2019.05;

7. [Pediatrics and Developmental Biology : MORIO Tomohiro] Takashi Okumura, Yumi Horie, Chen-Yi Lai, Huan-Ting Lin, Hirofumi Shoda, Bunki Natsumoto, Keishi Fujio, Eri Kumaki, Tsubasa Okano, Shintaro Ono, Kay Tanita, Tomohiro Morio, Hirokazu Kanegane, Hisanori Hasegawa, Fumitaka Mizoguchi, Kimito Kawahata, Hitoshi Kohsaka, Hiroshi Moritake, Hiroyuki Nunoi, Hironori Waki, Shin-Ichi Tamaru, Takayoshi Sasako, Toshimasa Yamauchi, Takashi Kadowaki, Hiroyuki Tanaka, Sachiko Kitanaka, Ken Nishimura, Manami Ohtaka, Mahito Nakanishi, Makoto Otsu. Robust and highly efficient hiPSC generation from patient non-mobilized peripheral blood-derived CD34+ cells using the auto-erasable Sendai virus vector. *Stem Cell Res Ther.* 2019.06; 10(1); 185
8. [Rheumatology : KIMURA Naoki] Kamiya M, Mizoguchi F, Takamura A, Kimura N, Kawahata K, Kohsaka H. A new in vitro model of polymyositis reveals CD8+ T cell invasion into muscle cells and its cytotoxic role. *Rheumatology (Oxford, England).* 2019.06;
9. [Department of Molecular Microbiology : SAITO Ryoichi] Yoko Nukui, Alafate Ayibieke, Makoto Taniguchi, Yoshibumi Aiso, Yuka Shibuya, Kazunari Sonobe, Jun Nakajima, Saki Kanehira, Yoshiro Hadano, Shuji Tohda, Ryuji Koike, Ryoichi Saito. Whole-genome analysis of EC129, an NDM-5-, CTX-M-14-, OXA-10- and MCR-1-co-producing *Escherichia coli* ST167 strain isolated from Japan. *J Glob Antimicrob Resist.* 2019.09; 18; 148-150
10. [- : KOIKE Ryuji] Kasai Shoko, Sakai Ryoko, Koike Ryuji, Kohsaka Hitoshi, Miyasaka Nobuyuki, Harigai Masayoshi. Higher risk of hospitalized infection, cardiovascular disease, and fracture in patients with rheumatoid arthritis determined using the Japanese health insurance database *Modern Rheumatology.* 2019.09; 29(5); 788-794
11. [Department of Molecular Microbiology : SAITO Ryoichi] Ryoichi Saito, Yukino Usui, Alafate Ayibieke, Jun Nakajima, Isaac Prah, Kazunari Sonobe, Yoshibumi Aiso, Shiori Ito, Yasuhiro Itsui, Yoshiro Hadano, Yoko Nukui, Ryuji Koike, Shuji Tohda. Hypervirulent clade 2, ribotype 019/sequence type 67 *Clostridioides difficile* strain from Japan. *Gut Pathog.* 2019.11; 11; 54
12. [Laboratory Medicine : TOHDA Shuji] Nukui Y, Chino T, Tani C, Sonobe K, Aiso Y, Tohda S, Koike R, Saito R. Molecular epidemiologic and clinical analysis of *Helicobacter cinaedi* bacteremia in Japan. *Helicobacter.* 2019.11; e12675
13. [Department of Lifetime Clinical Immunology : TAKAHIKO Sugihara] Yokoyama N, Kawasaki A, Matsushita T, Furukawa H, Kondo Y, Hirano F, Sada KE, Matsumoto I, Kusaoi M, Amano H, Nagaoka S, Setoguchi K, Nagai T, Shimada K, Sugii S, Hashimoto A, Matsui T, Okamoto A, Chiba N, Suematsu E, Ohno S, Katayama M, Migita K, Kono H, Hasegawa M, Kobayashi S, Yamada H, Nagasaka K, Sugihara T, Yamagata K, Ozaki S, Tamura N, Takasaki Y, Hashimoto H, Makino H, Arimura Y, Harigai M, Sato S, Sumida T, Tohma S, Takehara K, Tsuchiya N. Association of NCF1 polymorphism with systemic lupus erythematosus and systemic sclerosis but not with ANCA-associated vasculitis in a Japanese population. *Scientific reports.* 2019.11; 9(1); 16366

[Books etc]

1. [Rheumatology : MIZOGUCHI Fumitaka] Fumitaka Mizoguchi. *TODAY'S THERAPY 2019.* 2019.01 (ISBN : 978-4-260-03650-4)
2. [Rheumatology : MIZOGUCHI Fumitaka] Guideline for the management of systemic lupus erythematosus 2019. 2019.11 (ISBN : 978-4-525-23471-3)

[Misc]

1. [- : KOIKE Ryuji] Kameda Hideto, Fujii Takao, Nakajima Ayako, Koike Ryuji, Sagawa Akira, Kanbe Katsuaki, Tomita Tetsuya, Harigai Masayoshi, Suzuki Yasuo, Japan College of Rheumatology subcommittee on the guideline for the use of methotrexate in patients with rheumatoid arthritis. Japan College of Rheumatology guideline for the use of methotrexate in patients with rheumatoid arthritis *Modern Rheumatology.* 2019.01; 29(1); 31-40

[Conference Activities & Talks]

1. [Rheumatology : KIMURA Naoki] An adult case of cytotoxic T-lymphocyte antigen 4 (CTLA-4) insufficiency treated successfully with abatacept. 2019.02.03
2. [Rheumatology : KAMIYA Mari] Mari Kamiya, Fumitaka Mizoguchi, Kimito Kawahata, Hitoshi Kohsaka. Inhibition of necroptosis ameliorates in vitro and in vivo models of polymyositis. 63rd Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2019.04.16 Kyoto International Conference Center, Kyoto, Japan
3. [Rheumatology : MIZOGUCHI Fumitaka] Fumitaka Mizoguchi. Molecular and cellular deconstruction of tissue pathology in rheumatoid arthritis. 2019.04.17
4. [Rheumatology : KIMURA Naoki] Naoki Kimura, Hitoshi Kohsaka. Branched chain amino acids in the treatment of polymyositis and dermatomyositis : results from the BTOUGH study.. Annual European Congress of Rheumatology 2019 (EULAR 2019) 2019.06.14 Madrid, Spain
5. [Rheumatology : KAMIYA Mari] Mari Kamiya, Kimito Kawahata, Hitoshi Kohsaka, Fumitaka Mizoguchi. Inhibition of Necroptosis Suppresses Muscle Cell Death and Inflammatory Infiltrate, and Improves Muscle Strength in Experimental Polymyositis. 2019 ACR/ARP Annual meeting 2019.11.10 Atlanta, GA, USA

Dermatology

Professor: Hiroo YOKOZEKI
 Associate Professor: Takeshi NAMIKI
 Junior Associate Professor: Tsukasa UGAJIN, Makiko NISHIDA
 Project Junior Associate Professor: Kaoru TAKAYAMA
 Assistant Professor: Shown TOKORO, Takashi HASHIMOTO,
 Yusuke YOSHIOKA
 Senior Resident: Masahiro KATAGIRI, Mayo KONDO
 Resident: Tadatune IIDA, Sizuka OZASA, Atushi ODA, Taku NAMATAME,
 Syougo WADA
 Doctoral Student: Minako INAZAWA, Aiko FURUI, Michiko NAKAMURA, Kohei NOJIMA, Kohei KATO,
 Sally ESHIBA, Takahiro ISHIKAWA, Al-Busani Hind Abdullah Ahmed, Yukari MORI, Atushi SHIRANE, Daiki FUKAE
 Technical Assistant: Chiyako MIYAGISHI
 Staff Assistant: Masae SAKATA, Mayuko HAYASHI,

(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. Hashimoto T, Satoh T, Yokozeki H. Prurigo successfully treated with duloxetine hydrochloride. The Australasian journal of dermatology. 2019.01;
2. Handa Y, Ugajin T, Igawa K, Hamamoto H, Kobayashi K, Komatsuno T, Yamamoto T, Kawahara K, Yokozeki H. STAT6 decoy oligodeoxynucleotide (ODN)-containing ointment more potently inhibits mouse skin inflammation when formulated with ionic liquid technology than as a traditional Vaseline ointment. Allergology international : official journal of the Japanese Society of Allergology. 2019.01;
3. Omigawa Chika, Namiki Takeshi, Ueno Makiko, Ugajin Tsukasa, Miura Keiko, Yokozeki Hiroo. Case of Wells' syndrome: A rare association with the clinical course of chronic lymphocytic leukemia JOURNAL OF DERMATOLOGY. 2019.02; 46(2); E57-E59
4. Omigawa Chika, Namiki Takeshi, Ueno Makiko, Ugajin Tsukasa, Miura Keiko, Yokozeki Hiroo. Case of Wells' syndrome: A rare association with the clinical course of chronic lymphocytic leukemia(和訳中) The Journal of Dermatology. 2019.02; 46(2); e57-e59
5. Amano M, Namiki T, Munetsugu T, Nakamura M, Hashimoto T, Fujimoto T, Yokozeki H. Dyshidrosis associated with diabetes mellitus: Hypohidrosis associated with diabetic neuropathy and compensated hyperhidrosis. The Journal of dermatology. 2019.03;
6. Hashimoto T, Satoh T, Karasuyama H, Yokozeki H. Amphiregulin from basophils amplifies basophil-mediated chronic skin inflammation. The Journal of investigative dermatology. 2019.03;
7. Namiki T, Hsieh M, Iwamoto Y, Ugajin T, Tanaka K, Mori H, Miura K, Yokozeki H. Subcutaneous ossifying fibromyxoid tumor of the scalp: a potential importance of CT, MRI, and PET/CT on the diagnosis. International journal of dermatology. 2019.03;
8. Furusawa E, Ohno T, Nagai S, Noda T, Komiyama T, Kobayashi K, Hamamoto H, Miyashin M, Yokozeki H, Azuma M. Silencing of PD-L2/B7-DC by Topical Application of Small Interfering RNA Inhibits Elicitation of Contact Hypersensitivity. The Journal of investigative dermatology. 2019.04;
9. アルブサニ・ヘンドウ, 横関 博雄, 並木 剛. 多様な皮膚腫瘍における NIAK2 と p-Akt の発現 (Expression of NIAK2 and p-Akt in various skin tumors) 日本皮膚悪性腫瘍学会学術大会プログラム・抄録集. 2019.04; 35 回; 123
10. Namiki Takeshi, Hashimoto Takashi, Omigawa Chika, Fujimoto Tomoko, Ugajin Tsukasa, Miura Keiko, Satoh Takahiro, Nakano Hajime, Yokozeki Hiroo. び慢性網状色素沈着過剰および合指症に全身性無汗症を合併した 1 症例 (Case of generalized anhidrosis associated with diffuse reticular hyperpigmentation and syndactyly) The Journal of Dermatology. 2019.05; 46(5); e154-e155
11. Al-Busani Hind, Al-Sobaili Saber, Yokozeki Hiroo, Namiki Takeshi. 多様な皮膚腫瘍における NIAK2 と Phospho-Akt 発現についての免疫組織化学的分析 (Immunohistochemical Analysis of NIAK2 and Phospho-Akt Expression in Various Skin Tumors) 日本皮膚科学会雑誌. 2019.05; 129(5); 1148
12. Ogawa Shinji, Namiki Takeshi, Uchida Chie, Nojima Kohei, Miura Keiko, Tanaka Masaru, Yokozeki Hiroo. 色素性 Bowen 病とよく似た低メラニン色素性黒色腫と、その鑑別が困難なダーモスコピー像 (Hypomelanotic melanoma simulating pigmented Bowen's disease and its challenging dermoscopic features) The Journal of Dermatology. 2019.05; 46(5); e173-e175
13. Namiki Takeshi, Nojima Kohei, Chikazawa Sakiko, Iwamoto Yutaro, Otsuki Yuki, Albusani Hind, Miura Keiko, Kiyokawa Yusuke, Asakage Takahiro, Yokozeki Hiroo. 黒色腫に対するニボルマブの劇的な効果と免疫関連肝毒性 ニボルマブによる肝毒性の詳細な組織病理学および免疫組織化学的分析 (Dramatic effect of nivolumab against melanoma and immune-related liver toxicity: A detailed histopathological and

- immunohistochemical analysis of nivolumab-induced liver toxicity) *The Journal of Dermatology*. 2019.05; 46(5); e182-e183
14. Ugajin Tsukasa, Yokozeki Hiroo. 痒疹患者における抗免疫グロブリン E 療法の有効性 パイロットスタディー (Efficacy of anti-immunoglobulin E therapy in patients with prurigo: A pilot study) *Journal of Cutaneous Immunology and Allergy*. 2019.06; 2(3); 75-81
 15. Minghsiu Hsieh, Shown Tokoro, Tsukasa Ugajin, Takeshi Namiki, Keiko Miura, Hiroo Yokozeki. Ultrasonography as an auxiliary diagnostic tool for morphea profunda: A case report. *J. Dermatol.*. 2019.07; 46(7); 626-630
 16. Hashimoto T, Kursewicz CD, Fayne RA, Nanda S, Shah SM, Nattkemper L, Yokozeki H, Yosipovitch G. Pathophysiologic mechanisms of itch in bullous pemphigoid. *Journal of the American Academy of Dermatology*. 2019.07;
 17. Handa Yutaro, Ugajin Tsukasa, Igawa Ken, Hamamoto Hidetoshi, Kobayashi Katsunori, Komatsuno Takao, Yamamoto Toshinori, Kawahara Kazuo, Yokozeki Hiroo. STAT6 decoy oligodeoxynucleotide(ODN) 含有軟膏は従来のワセリン軟膏として製剤化するよりもイオン液体技術を用いて製剤化するほうがマウス皮膚炎症をより強力に抑制する (STATE decoy oligodeoxynucleotide(ODN)-containing ointment more potently inhibits mouse skin inflammation when formulated with ionic liquid technology than as a traditional Vaseline ointment) *Allergology International*. 2019.07; 68(3); 380-382
 18. Hsieh Minghsiu, Tokoro Shown, Ugajin Tsukasa, Namiki Takeshi, Miura Keiko, Yokozeki Hiroo. Ultrasonography as an auxiliary diagnostic tool for morphea profunda: A case report(和訳中) *The Journal of Dermatology*. 2019.07; 46(7); 626-630
 19. Ishikawa Takahiro, Hashimoto Takashi, Munetsugu Takichi, Yokozeki Hiroo, Satoh Takahiro. Increased β -endorphin and autotaxin in patients with prurigo(和訳中) *Journal of Cutaneous Immunology and Allergy*. 2019.08; 2(4); 94-101
 20. Amano Maki, Namiki Takeshi, Munetsugu Takichi, Nakamura Michiko, Hashimoto Takashi, Fujimoto Tomoko, Yokozeki Hiroo. 糖尿病を伴う発汗異常 糖尿病性ニューロパチーおよび代償性多汗症と関連する乏汗症 (Dyshidrosis associated with diabetes mellitus: Hypohidrosis associated with diabetic neuropathy and compensated hyperhidrosis) *The Journal of Dermatology*. 2019.08; 46(8); e292-e293
 21. Okiyama Naoko, Yamaguchi Yukie, Kodera Masanari, Hamaguchi Yasuhito, Yokozeki Hiroo, Ishiguro Naoko, Fujimoto Manabu. Distinct Histopathologic Patterns of Finger Eruptions in Dermatomyositis Based on Myositis-Specific Autoantibody Profiles *JAMA DERMATOLOGY*. 2019.09; 155(9); 1080-1082
 22. Hashimoto Takashi, Satoh Takahiro, Yokozeki Hiroo. Pruritus in ordinary scabies: IL-31 from macrophages induced by overexpression of thymic stromal lymphopoietin and periostin *ALLERGY*. 2019.09; 74(9); 1727-1737
 23. Hashimoto T, Kursewicz CD, Fayne RA, Nanda S, Shah SM, Nattkemper L, Yokozeki H, Yosipovitch G. Mechanisms of Itch in Stasis Dermatitis: Significant Role of IL-31 from Macrophages. *The Journal of investigative dermatology*. 2019.10;
 24. Al-Busani Hind, Yokozeki Hiroo, Al-Sobaihi Saber, Namiki Takeshi. NUA2 localization in the normal skin and its contribution to skin carcinogenesis with Yes-associated protein(和訳中) 日本研究皮膚科学会 年次学術大会・総会プログラム. 2019.10; 44 回; 212
 25. Shown Tokoro, Takeshi Namiki, Tsukasa Ugajin, Keiko Miura, Masaru Tanaka, Hiroo Yokozeki. Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber's disease): detailed assessment of skin lesions by dermoscopy and ultrasound. *Int. J. Dermatol.*. 2019.11; 58(11); e224-e226
 26. Chinuki Y, Yagami A, Adachi A, Matsunaga K, Ugajin T, Yokozeki H, Hayashi M, Katayama I, Kohno K, Shiwaku K, Morita E. In vitro basophil activation is reduced by short-term omalizumab treatment in hydrolyzed wheat protein allergy. *Allergology international : official journal of the Japanese Society of Allergology*. 2019.11;
 27. Murota H, Yamaga K, Ono E, Murayama N, Yokozeki H, Katayama I. Why does sweat lead to the development of itch in atopic dermatitis? *Experimental dermatology*. 2019.12; 28(12); 1416-1421

NCCHD Child Health and Development

1. Stuffs and Students

Collaborative Professor	Akutsu, Hidenori
Collaborative Professor	Onodera, Masashi
Collaborative Professor	Fukami, Maki
Collaborative Professor	Hata, Kenichiro
Collaborative Professor	Takada, Shuji
Collaborative Professor	Matsumoto, Kenji

2. Purpose of Education

The goal of this course is to learn the developmental process of human life from the viewpoints of latest molecular biology and genetics. Medical science for child health and development is the study to comprehensively grasp various health problems related to “human life cycle” to begin with the fertilization and to continue to the next generation through generation and development. Students of this course are required to understand a role and a function of medical care for child health and development, to acquire ability to handle such health problems and support relevant person with specialized theory and technique.

3. Research Subjects

1) Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells
Application studies for reproductive medicine and regenerative medicine

(Akutsu, Hidenori; Center for Regenerative Medicine, National Institute for Child Health and Development)

Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells.
Application studies for reproductive medicine and regenerative medicine.

2) Studying for cellular model in human severe disease by advancing flow cytometry

(Onodera, Masashi; Dept. of Human Genetics, National Institute for Child Health and Development)

We aim to identify causative genes for child intractable hereditary diseases and analyze their functions to develop new gene-based therapeutic options. We also establish iPS cells from peripheral blood or skin fibroblasts obtained from patients with intractable hereditary diseases such as primary immunodeficiencies and congenital metabolic disorders.

3) Elucidation of genetic abnormality in congenital severe metabolic diseases using advanced genetic analysis

(Fukami, Maki; Dept. of Molecular Endocrinology, National Institute for Child Health and Development)

Our objective is to clarify the molecular basis of congenital endocrine-related disorders and apply our findings to new innovations in clinical medicine. We investigate the molecular basis of single gene disorders, epigenetic/inprinting disorders, and multifactorial disorder.

4) Elucidating for molecular mechanism of perinatal abnormality using system biology

(Hata, Kenichiro; Dept. of Maternal-Fetal Biology, National Institute for Child Health and Development)

We aim to clarify mechanisms underlying abnormalities in fetal development and placentation, and/or perinatal diseases with developmental defects. To identify the underlying mechanisms of perinatal diseases, we take advantage of post-genomic technologies and investigate etiologies using an integrated genomic and epigenomic approach.

5) Identification of target molecules in severe diseases and establishment of disease model mice by studying molecular mechanisms of genomic imprinting, gametogenesis and sexual differentiation

(Takada, Shuji; Dept. of Systems Biomedicine, National Institute for Child Health and Development)

Our aim is to reveal the molecular mechanisms underlying embryonic development, cell differentiation and tissue formation and apply our findings to understand the causes of developmental diseases.

6) Elucidation for allergic disease mechanism and target molecules using molecular biology and ‘omics’ technology

(Matsumoto, Kenji; Dept. of Allergy and Clinical Immunology, National Institute for Child Health and Development)

Our mission is to clarify the precise pathogenic mechanisms of various immunological and allergic diseases, such as Kawasaki disease, various allergic diseases, allogeneic immune tolerance, congenital viral infections and severe infectious diseases. To achieve this, we employ various experimental approaches, including epidemiology, clinical and basic research. Our ultimate aim is to develop better means of preventing, diagnosing and treating allergic and immunological and infectious diseases based on our research findings and cumulative knowledge.

4. Publications

[OriginalArticles]

1. Inoue M, Kajiwarra K, Yamaguchi A, Kiyono T, Samura O, Akutsu H, Sago H, Okamoto A, Umezawa A. Autonomous trisomic rescue of Down syndrome cells. *Lab Invest*. 2019; 99 (6): 885-897.
2. Ogawa S, Yamada M, Nakamura A, Sugawara T, Nakamura A, Miyajima S, Harada Y, Ooka R, Okawa R, Miyauchi J, Tsumura H, Yoshimura Y, Miyado K, Akutsu H, Tanaka M, Umezawa A, Hamatani T. Zscan5b Deficiency Impairs DNA Damage Response and Causes Chromosomal Aberrations During Mitosis. *Stem Cell Reports*. 2019 Jun 11; 12(6): 1366-1379.
3. Yoshida T, Miyado M, Mikami M, Suzuki E, Kinjo K, Matsubara K, Ogata T, Akutsu H, Kagami M, Fukami M. Aneuploid rescue precedes X-chromosome inactivation and increases the incidence of its skewness by reducing the size of the embryonic progenitor cell pool. *Hum Reprod*. 2019 Sep 29;34(9):1762-1769.
4. Ito C, Akutsu H, Yao R, Yoshida K, Yamatoya K, Mutoh T, Makino T, Aoyama K, Ishikawa H, Kunitomo K, Tsukita S, Noda T, Kikkawa M, Toshimori K. Odf2 haploinsufficiency causes a new type of decapitated and decaudated spermatozoa, Odf2-DDS, in mice. *Sci Rep*. 2019 Oct 3;9(1):14249.
5. Tsuchida N, Kojima J, Fukuda A, Oda M, Kawasaki T, Ito H, Kuji N, Isaka K, Nishi H, Umezawa A, Akutsu H*. Placenta. Transcriptomic features of trophoblast lineage cells derived from human induced pluripotent stem cells treated with BMP 4. 2019 Oct 9; 89: 20-32.
6. Muraya K, Kawasaki T, Yamamoto T, Akutsu H. Enhancement of Cellular Adhesion and Proliferation in Human Mesenchymal Stromal Cells by the Direct Addition of Recombinant Collagen I Peptide to the Culture Medium. *Biores Open Access*. 2019 Nov 22;8(1):210-218.
7. Tanase-Nakao K, Mizuno K, Hayashi Y, Kojima Y, Hara M, Matsumoto K, Matsubara Y, Igarashi M, Miyado M, Fukami M. Dihydrotestosterone induces minor transcriptional alterations in genital skin fibroblasts of children with and without androgen insensitivity. *Endocr J* 2019;66:387-93.
8. Ohki K, Kiyokawa N, Saito Y, Hirabayashi S, Nakabayashi K, Ichikawa H, Momozawa Y, Okamura K, Yoshimi A, Ogata-Kawata H, Sakamoto H, Kato M, Fukushima K, Hasegawa D, Fukushima H, Imai M, Kajiwarra R, Koike T, Komori I, Matsui A, Mori M, Moriwaki K, Noguchi Y, Park MJ, Ueda T, Yamamoto S, Matsuda K, Yoshida T, Matsumoto K, Hata K, Kubo M, Matsubara Y, Takahashi H, Fukushima T, Hayashi Y, Koh K, Manabe A, Ohara A. Clinical and molecular characteristics of MEF2D fusion-positive B-cell precursor acute lymphoblastic leukemia in childhood, including a novel translocation resulting in MEF2D-HNRNP1 gene fusion. *Haematologica* 2019;104:128-37.
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[Conference Activities & Talks]

1. Hidenori Akutsu. Symposium; Stem Cell Research “Xeno-free generation of multi-functional gut organoids (Mini-Guts) from Human embryonic stem cells] The 9rd Asian Cellular Therapy Organization Meeting”2019, Oct 26, Chiangmai, Thailand
2. Hidneori Akutsu. Second International Summit on Human Genome Editing—Update: Governmental Actions and Advisory Opinions Regarding Human Genome Editing—“Regulatory Actions for Researches Using Genome Editing Technology on Human Embryos in Japan”2019, Nov 26 Hong Kong
3. Masafumi Onodera. How to establish the management system for CAR-T therapy in Japan. ISFA2019 and JSFA2019. Kyoto. 2019.10.18
4. Masafumi Onodera. What we have learnt from stem cell gene therapy for primary immunodeficiencies. In session 5 (gene therapy) of the 10th ACTO. Sapporo. 2019.11.7
5. Masafumi Onodera. Where GMP/GCTP starts from in ex vivo gene therapy? In evening seminar of the 10th ACTO. Sapporo. 2019.11.7
6. Masafumi Onodera. Gene therapy, Past, Present, and Future. Select Bio Cell and Gene therapy Asia 2019. Kobe. 2019.11.11
7. Masafumi Onodera. Points to consider of comparability in viral vectors. 4th DIA cell and gene therapy products symposium in Japan. 2019.12.17
8. Masafumi Onodera. A good practice for the Cartagena protocol in clinical sides. 4th DIA cell and gene therapy products symposium in Japan. Tokyo. 2019.12.17
9. Fukami M. New aspects in human sex development. In: Topic symposium, Pediatric Academic Societies Meeting, Baltimore, 2019.4.27

Human Pathology

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Secretary: Miho IWAMITSU

(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. Kobayashi Zen, Ishihara Shoichiro, Tomimitsu Hiroyuki, Ogawa Shinichi, Numasawa Yoshiyuki, Kobayashi Daisuke, Shintani Shuzo. Persisting subacute infarct pattern as early MRI feature of brain intravascular lymphoma(和訳中) *Neurology and Clinical Neuroscience*. 2019.01; 7(1); 34-36
2. Yamamoto Kurara, Uchida Keisuke, Furukawa Asuka, Tamura Tomoki, Ishige Yuki, Negi Mariko, Kobayashi Daisuke, Ito Takashi, Kakegawa Tomoya, Hebisawa Akira, Awano Nobuyasu, Takemura Tamiko, Amano Tomonari, Akashi Takumi, Eishi Yoshinobu. Catalase expression of *Propionibacterium acnes* may contribute to intracellular persistence of the bacterium in sinus macrophages of lymph nodes affected by sarcoidosis *IMMUNOLOGIC RESEARCH*. 2019.06; 67(2-3); 182-193
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Physiology and Cell Biology

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(1) Outline

One of the major goals of the Department of Physiology and Cell Biology is to elucidate the basic principles of the brain networks that are responsible for behavioral expression in rodents. Our neurophysiological research focuses mainly on the neural networks of the cerebral cortex, hippocampus, basal ganglia and thalamus that regulate particular behavioral tasks in rats; this research utilizes multichannel electrode-based multineuronal recording technology, optogenetics involving genetically modified animals and adeno-associated virus vectors, and theoretical analysis technologies.

(2) Research

Research Agenda – What do we want to know?

In the sensory, association and motor cortices in the cerebral cortex, the excitatory pyramidal cells and inhibitory interneurons form an intracortical circuit. These brain areas, which play important roles in appropriate behavioral expression, are connected with each other and form the interareal circuit that consists of complex intercortical and subcortical connections through the hippocampus, striatum, substantia nigra and thalamus. In the 20th century, the spike (unit) activity of single neurons in the brain that are related to behavior was actively studied using the single-unit recording technique. From a technical point of view, however, it was extremely difficult to investigate neuron subtypes and axonal connections by this method. Therefore, we developed a new experimental technique and used it to initiate a study of the basic principles whereby neural networks, particularly those in the cerebral cortex, encode behavioral information.

Research Techniques – How do we find answers?

1. Operant Learning Task

With the conventional technique of operant conditioning, it took weeks to months to train rats to obtain rewards by pushing a lever with their forelimb. Therefore, we developed a “spout-lever” by integrating a lever and a spout, and this enabled us to train rats to perform the forelimb movement task in a short period of time. This method allows for more rapid generation of rats to perform particular behavioral tasks in physiological experiments.

2. Multineuronal Recording

Multineuronal recording is a physiological technique in which spike activities of a large number of neurons are simultaneously recorded using silicon probes (multichannel electrodes). Signals recorded with electrode are distinguished by spike sorting, an analysis technique, to separate the spike (unit) activity produced by each neuron. Multineuronal recording also makes it possible to simultaneously record local field potentials and spike activities to permit the analysis of functional synchronous oscillation activities such as gamma and ripple waves.

3. Optogenetics

To understand the mechanism of information processing in neuronal networks, it is useful to demonstrate causality by optogenetically manipulating signals flowing in the networks. We are conducting experiments using gene-expressing virus vectors as well as transgenic rats that express channelrhodopsin-2, which uses blue light to depolarize membrane potentials. In addition, we are conducting research to establish a multi-line analysis technique that identifies axonal projections of recorded neurons by combining multineuronal recording technology with optogenetics.

4. Theoretical Analysis – Simulation Modeling

In collaboration with computational neuroscientists, we are conducting sophisticated and efficient theoretical analyses of multineuronal recording data. Our goal is to fuse experiment and theory by utilizing simulation and modeling techniques.

Research Methodologies – Pursuing Originality

Our research targets the brain networks in rats that are responsible for behavioral expression in order to understand essential brain mechanisms. Conventional neuroscience has often explored the functional localization in the brain by “averaging” brain activities. However, brain activities dynamically change every second, and there is no doubt that it is not just single areas that play a role in information processing, but rather the whole network, which consists of multiple areas. Therefore, we aim to perform truly original research by increasing the sophistication of our methods and extending our interests to multidisciplinary research without fear of failure, from the viewpoints of “from static to dynamic states” and “from points to lines.”

see

<https://researchmap.jp/yoshikazuisomura/>

(3) Education

The Department of Physiology and Cell Biology supports excellent next-generation researchers such as post-doctoral research fellows and graduate students through research activities that aim to elucidate the basic principles of brain networks. In principle, students define their research topics based on their future goals. One experimental setup is provided per one or two students/researchers. They receive curricula to learn a series of experimental techniques, join discussions that develop their logical thinking ability rather than simply increasing their knowledge, and receive opportunities to effectively conduct collaborative research in and out of the laboratory.

The Department is responsible for a lecture and laboratory practice on General Physiology for medical school students. It also provides research training for students during the project semester and MD-PhD courses that aim to foster basic researchers in the early stages of their education. The field of physiology is essential for comprehensively understanding body functions and providing the foundation for doctors to treat patients. We hope that you will voluntarily and actively participate in the activities of the department to immerse yourself in physiology.

(4) Publications

[Original Articles]

1. Hori Y, Ihara N, Sugai C, Ogura J, Honda M, Kato K, Isomura Y, *Hanakawa T. Ventral striatum links motivational and motor networks during operant-conditioned movement in rats. *NeuroImage*. 2019.01; 184; 943-953
2. *Soma S, Yoshida J, Kato S, Takahashi Y, Nonomura S, Sugimura YK, Ríos A, Kawabata M, Kobayashi K, Kato F, Sakai Y, Isomura Y. Ipsilateral-dominant control of limb movements in rodent posterior parietal cortex. *The Journal of neuroscience*. 2019.01; 39(3); 485-502
3. Sopak Supakul, Kenta Yao, Hiroki Ochi, Tomohito Shimada, Kyoko Hashimoto, Satoko Sunamura, Yo Mabuchi, Miwa Tanaka, Chihiro Akazawa, Takuro Nakamura, Atsushi Okawa, Shu Takeda, Shingo Sato. Pericytes as a Source of Osteogenic Cells in Bone Fracture Healing. *Int J Mol Sci*. 2019.03; 20(5);

4. Rios A, Soma S, Yoshida J, Nonomura S, Kawabata M, Sakai Y, *Isomura Y. Differential changes in the lateralized activity of identified projection neurons of motor cortex in hemiparkinsonian rats. *eNeuro*. 2019.06; 6(4); ENEURO.0110-19
5. Tsutsumi S, Hidaka N, Isomura Y, Matsuzaki M, Sakimura K, Kano M, Kitamura K. Modular organization of cerebellar climbing fiber inputs during goal-directed behavior. *eLife*. 2019.10; 8; e47021
6. Satoshi Nonomura, Kazuyuki Samejima. Neuronal Representation of Object Choice in the Striatum of the Monkey. *Front Neurosci*. 2019.11; 13; 1283

[Conference Activities & Talks]

1. Soma S, Yoshida J, Kato S, Nonomura S, Sugimura YK, Rios A, Kawabata M, Kobayashi K, Kato F, Sakai Y, Isomura Y. Rodent posterior parietal cortex controls ipsilateral as well contralateral movement. The 9th Federation of the Asian and Oceanian Physiological Societies Congress (FAOPS2019) 2019.03.30 Kobe Convention Center, Kobe, Hyogo
2. Kawabata M, Nonomura S, Yoshizawa T, Rios AA, Sakairi T, Sakai Y, Isomura Y. Distribution of sensory/motor-related information in the rat cerebral cortex. The 42nd Annual Meeting of the Japan Neuroscience Society (Neuro2019) 2019.07.26 Toki Messe, Niigata, Niigata
3. Nonomura S, Kato S, Sakai Y, Nambu A, Kobayashi K, Isomura Y, Kimura M. Differential activity of indirect pathway neurons in the dorsolateral and dorsomedial striatum for action selection. The 42nd Annual Meeting of the Japan Neuroscience Society (Neuro2019) 2019.07.26 Toki Messe, Niigata, Niigata
4. Rios AA, Satoshi N, Yoshizawa T, Kawabata M, Sakairi T, Sakai Y, Isomura Y. Modification of motor cortex forelimb lateralization preference in a hemiparkinsonian rat model. The 42nd Annual Meeting of the Japan Neuroscience Society (Neuro2019) 2019.07.27 Toki Messe, Niigata, Niigata
5. Yoshikazu Isomura. Exploring functional spike signals in cortical/subcortical circuits of rodents. The 42nd Annual Meeting of the Japan Neuroscience Society (Neuro2019) 2019.07.28 Toki Messe, Niigata, Niigata
6. Yoshikazu Isomura. An exception to contralateral dominance of cerebral cortex - from abstract to concrete - . Dynamic Brain Forum (DBF) 1, in The 7th International Congress on Cognitive Neurodynamics (ICCN2019) 2019.09.30 Università di Sassari, Alghero, Italy
7. Rios A, Soma S, Nonomura S, Yoshida J, Kawabata M, Sakai Y, Isomura Y. Differential changes in the forelimb selectivity of IT and PT projection neurons of motor cortex in hemiparkinsonian rats. The Annual Meeting of Society for Neuroscience (Neuroscience 2019) 2019.10.20 McCormick Place, Chicago, IL, USA

Stem Cell Regulation

Professor Tetsuya TAGA

Associate Professor Ikuo NOBUHISA

Assistant Professor Kouichi TABU

Technical Assistant/Administrative Assistant Kazuko INOUE

(1) Outline

Research in this department has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. Particular attention is given to cell-external cues (such as cytokines) and cell-intrinsic programs (including epigenetic modification), taking cross-interactions of transcriptional regulatory signals into consideration.

(2) Research

Research Subjects in this department are as follows:

- 1) Molecular basis for the maintenance of neural stem cells
- 2) Regulation of the neural stem cell fate
- 3) Characterization of hematopoietic stem cells in fetal hematopoietic organs
- 4) Characterization of cancer stem cells and their niche
- 5) Epigenetic regulation of neural development

(3) Education

Our education has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. The projects have been performed, for instance by elucidation of stem cell characteristics, analysis of transcriptional regulatory signaling pathways, and identification of niche signals.

(4) Lectures & Courses

Under our education program, students will learn the molecular basis of stem cell regulation in view of cell-extrinsic signals and cell intrinsic-programs during tissue development, maintenance, and regeneration from molecular to whole-body levels. Students will receive exposure to cutting edge concepts and research technologies, and study regulatory mechanisms in neural, hematopoietic, and cancer stem cells. With emphasis also on physiological and pathological conditions surrounding the stem cells, we aims to improve student's understanding of stem cells from multiple viewpoints.

(5) Publications**[Conference Activities & Talks]**

1. Taga T and Tabu K. Development of Treatment Strategies Targeting Cancer Stem Cells. The 3rd Meeting of International Society of Precision Cancer Medicine 2019.03.14 Seoul, Korea
2. Hagihara H, Shoji H, Kohno T, Hayata A, Tamada K, Hori K, Tatsukawa T, Shibutani M, Wakatsuki S, Hagino Y, Kasahara T, Numakawa T, Ohtabi H, Nobuhisa I, Hoshiba Y, Nakamura H, Katori S, Yamanishi K, Takamiya Y, Tanaka M, Yalcin I, Matsushita M, Hattori M, Hashimoto H, Takumi T, Hoshino M, Tabuchi K, Yamakawa K, Hatada I, Ikeda K, Kato T, Kunugi H, Toyoda A, Taga T, Hayashi-Takagi A, Goshima Y, Iwasato T, Okabe S, Meltzer HY, Miyakawa T. Systematic analysis of brain pH and lactate levels in animal models: relationships and implications for behavioral outcomes. The 21st Annual Meeting of the International Behavioural and Neural Genetics Society 2019.05.10 the University of Edinburgh, Edinburgh, Scotland, UK
3. Taga T and Tabu K. Exploration of molecular mechanisms regulating cancer stem cells and their niche. TMDU International Summer Program (ISP) 2019 2019.07.09 TMDU, Bunkyo-ku, Japan
4. Taga T. Pathogenesis in the mouse model of psychomotor disorder caused by histone demethylase Gasc1 gene mutation. The 40th Annual Meeting of the Japanese Society of Inflammation and Regeneration 2019.07.16 Kobe International Conference Center, Kobe, Japan
5. Tabu K and Taga T. Visualization and validation of monocyte-recruiting cells as a potential target of glioma stem cells. The 78th Annual Meeting of the Japanese Cancer Association 2019.09.28 Kyoto, Japan
6. Aimaitijiang A, Tabu K and Taga T. Glioma stem cells modulate erythropoiesis in mouse bone marrow. The 78th Annual Meeting of the Japanese Cancer Association 2019.09.28 Kyoto, Japan
7. Tabu K and Taga T. Visualization and validation of monocyte-recruiting cells as a potential target of glioma stem cells. The 78th Annual Meeting of the Japanese Cancer Association 2019.09.28 Kyoto, Japan
8. Aimaitijiang A, Tabu K and Taga. Glioma stem cells modulate erythropoiesis in mouse bone marrow. The 78th Annual Meeting of the Japanese Cancer Association 2019.09.28 Kyoto, Japan
9. Tsukahara Y, Nobuhisa I, Saito K, Kanai Y, Kanai M, and Taga T. The role of GIMAP family in the maintenance of hematopoietic capacity in hematopoietic cell cluster in midgestation mouse dorsal aorta. The 42th Annual Meeting of the Molecular Biology Society of Japan 2019.12.02 Fukuoka Convention Center, Fukuoka, Japan
10. Tabu K, Wenyu L and Taga T. A self-expanding strategy of glioma stem cells via promoting the development of M1-like tumor-associated macrophages. . The 42nd Annual Meeting of the Molecular Biology Society of Japan 2019.12.04 Fukuoka Convention Center, Fukuoka, Japan
11. Nobuhisa I, Saito K, Tsukahara R, Azuma K, Melig G, Itabashi A, Taga T. Involvement of TET1 in the maintenance of the hematopoietic capacity in hematopoietic cell clusters in the dorsal aorta in midgestation mouse embryo. The 48th Annual Meeting of The Japanese Society for Immunology 2019.12.11 Act City Hamamatsu, Hamamatsu, Japan

Stem Cell Biology

Professor : Emi Nishimura, M.D., Ph.D.
Associate Professor: Daisuke Nanba, Ph.D
Assistant Professor : Hiroyuki Matsumura, Ph.D.
Project Assistant Professor :Yasuaki Mohri, Ph.D.
Hironobu Morinaga, Ph.D.
Kyosuke Asakawa, Ph.D.
Liu Nan, M. D., Ph. D.
Joint Researcer : Yuko Muroyama, Ph. D.

(1) Outline

Stem cell systems play fundamental roles in sustaining tissue turnover and homeostasis. Our goal is to understand the mechanisms of tissue homeostasis driven by stem cell systems in mammals and to apply that knowledge to better understand the mechanisms underlying tissue/organ aging, cancer development and other diseases associated with aging. We further aim to apply this knowledge to drug discovery, regenerative medicine and the prevention and treatment of age-associated diseases.

(2) Research

1) Identification of stem cells in the skin

The skin is the largest organ in the body. Hair follicles are mini-organs located in the skin that 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 in each hair cycle. We previously identified the source of those melanocytes, “melanocyte stem cells” (McSCs), which are located in the hair follicle bulge and supply mature melanocytes required for hair and skin pigmentation (Nishimura EK et al. *Nature*, 2002). Subsequently, we identified similar McSCs in non-hair-bearing skin areas (Okamoto N et al. *PCMR*, 2014). Further, we recently succeeded in identifying epidermal stem cells with sufficient self-renewing potential by using genetic tracing of stem cell clones (Liu N et al. *Nature*, 2019).

2) Mechanisms of stem cell maintenance

The underlying mechanisms of stem cell maintenance are a fundamental issue in stem cell biology and medicine. We previously found that the niche microenvironment plays a dominant role in the fate determination of McSCs (Nishimura EK et al. *Nature*, 2002). That finding prompted us to further study the mechanisms involved and led us to demonstrate that hair follicle stem cells (HFSCs), which reside in the hair follicle bulge, serve as a functional niche for the maintenance of McSCs (Nishimura EK et al. *Cell Stem Cell*, 2010)(Tanimura S et al. *Cell Stem Cell*, 2011). The niche functions of HFSCs are mediated by extrinsic niche factors, including transforming growth factor β (TGF- β), that are secreted from HFSCs to maintain McSCs in a quiescent and immature state. Meanwhile, intrinsic defects in stem cells, such as those caused by *Mitf* or *Bcl2* deficiencies in mice, also induce the depletion of McSCs, which leads to the progressive expression of the hair graying phenotype. Therefore, we concluded that the incomplete maintenance of McSCs either by defective signaling from the stem cell niche or by intrinsic defects in stem cells, results in an insufficient supply of mature melanocytes for hair pigmentation in mice expressing the progressive hair graying phenotype.

3) A stemness checkpoint underlies the quality maintenance of tissues

Physiological hair graying and hair thinning are typical outward signs of aging in mammals, yet the mechanisms underlying those phenotypes had been largely unclear. We found that the incomplete maintenance of McSCs during the course of aging causes hair graying (Nishimura EK et al. *Science*, 2004). We then showed that genotoxic stress triggers/accelerates the aging process and abrogates the self-renewal of McSCs by triggering their differentiation without inducing cellular senescence. Further study of aged wild-type mice and progeroid mouse models, including ATM-deficient mice, revealed that a “stemness checkpoint”, which determines whether stem cells are qualified to self-renew or rather are forced to differentiate, maintains the quality of the stem cell pool and eliminates stressed/damaged stem cells from tissues (Inomata K et al. *Cell*, 2009). Similar checkpoint mechanisms have been found in HFSCs (Matsumura H et al. *Science*, 2016) and in epidermal stem cells (Liu N et al. *Nature*, 2019) by us and also in other somatic stem cells by other groups. We are currently studying the underlying molecular mechanism.

4) Dynamic elimination of aged stem cells causes hair follicle aging

To study the fate and dynamics of aged somatic stem cells, we performed in vivo fate tracing analysis of HFSCs and demonstrated that the dynamic elimination of HFSCs through their epidermal differentiation causes the stepwise miniaturization of hair follicles and eventual hair loss in mice. The DNA damage response in HFSCs causes proteolysis of Type XVII Collagen (COL17A1/BP180), a critical molecule for HFSC maintenance, to trigger HFSC aging that is characterized by the loss of stemness signatures and epidermal differentiation. Aged HFSCs are thus cyclically eliminated from the skin through their epidermal differentiation-mediated shedding from the skin surface, thereby causing hair follicle miniaturization (Figure 2). The aging process can be recapitulated by Col17a1-deficiency and prevented by the forced maintenance of COL17A1 in HFSCs, demonstrating that COL17A1 in HFSCs orchestrates the stem cell-centric aging program of the epithelial mini-organ (Matsumura H et al. *Science*, 2016). We are currently trying to identify the stem cell division program for organ aging.

5) Stem cell competition in the epidermis underlies skin homeostasis and aging

The skin protects living organisms from the outside world by acting as a barrier throughout the life-span, suggesting that the skin has more robust and flexible anti-aging mechanisms than mini-organs such as hair follicles. We have performed in vivo clonal analysis in mice by focusing on the expression of the hemidesmosomal protein COL17A1 by epidermal stem cells. Those studies revealed that the expression of COL17A1 fluctuates physiologically through genomic/oxidative stress-induced proteolysis, and that the resulting differential expression of COL17A1 in individual stem cells generates a driving force for cell competition (Figure 3). Clones that express high levels of COL17A1 divide symmetrically and outcompete/eliminate adjacent stressed clones that express low levels of COL17A1 and divide asymmetrically. Stem cells with higher potential or quality are thus selected for homeostasis, but their eventual loss of COL17A1 limits their competition, thereby causing aging. The resulting hemidesmosome fragility and stem cell delamination depletes adjacent melanocytes and fibroblasts to promote skin aging. Conversely, the forced maintenance of COL17A1 rescues skin organ aging, thereby indicating potential new approaches for anti-aging therapeutic intervention.

(3) Publications

[Original Articles]

1. Noguchi S, Honda S, Saitoh T, Matsumura H, Nishimura EK, Akira S, Shimizu S. Beclin 1 regulates recycling endosome and is required for skin development in mice. *Communications Biology*. 2019.01; 2(37);
2. Liu N, Matsumura H, Nishimura EK. et al.. Stem cell competition orchestrates skin homeostasis and ageing *Nature*. 2019.04; 568(7752); 344-350

3. Muraguchi Taichi, Nanba Daisuke, Nishimura Emi K., Tashiro Tomoko. IGF-1R deficiency in human keratinocytes disrupts epidermal homeostasis and stem cell maintenance JOURNAL OF DERMATOLOGICAL SCIENCE. 2019.05; 94(2); 298-305
4. Kinoshita K, Munesue T, Toki F, Higashiyama S, Barrandon Y, Nishimura EK, Yanagihara Y, Nanba D. Automated collective motion analysis validates human keratinocyte stem cell cultures. Scientific Reports. 2019.12; 9(1);

[Conference Activities & Talks]

1. Emi K. Nishimura. Epidermal stem cell competition coupled with stem cell divisions in mammalian epidermis. 2019 Keystone Symposia Conference-Cell Competition in Development and Disease- 2019.02.24 Tahoe City, USA
2. Emi K. Nishimura. Stem cell competition underlies skin homeostasis and aging. Japan-singapore international skin conference 2019 2019.04.10 Singapore
3. 西村 栄美. Stem cell competition orchestrates skin homeostasis and ageing. 第 17 回幹細胞シンポジウム 2019.05.24 兵庫県
4. Emi K. Nishimura. Stem cell competition orchestrates skin homeostasis and ageing. Nature conference 2019-aging, health & rejuvenation 2019.06.23 Netherlands
5. Emi K. Nishimura. Stem cell competition in skin homeostasis and aging. Gordon research conference-epithelial differentiation and keratinization 2019.07.07 USA
6. Emi K. Nishimura. Stem cell fate changes in skin organ aging. Fondation des treilles Stem Cells, Aging and stress response mechanisms 2019.10.07 France
7. Emi K. Nishimura. Stem cell competition underlies skin homeostasis and aging. 日本研究皮膚科学会第 44 回年次学術大会 2019.11.08 青森県

Respiratory Medicine

Professor: Yasunari Miyazaki

Respiratory and Nervous System Science, Graduate School of Professor Department of Medical and Dental Sciences:
Yuki Sumi

Professor Health Administration Center: Ryushi Tazawa

Associate Professor, RESPIRATORY Physiology and Sleep Medicine: Meiyo Tamaoka

Assistant Professor: Tomoya Tateishi, Tsukasa Okamoto, Masahiro Ishizuka, Tuyoshi Shirai,
Takayuki Honda

Project Assistant Professor: Takahiro Mitsumura, Rie Sakakibara, Yuki Iijima

Assistant Professor Health Administration Center: Keiko Komatsuzaki

Clinical Fellow: Takahiro Ando, Takuya Shinmura, Tatsuya Ito, Shun Endo, Kentaro Nakamura

Ph.D. student: Hiroaki Saito, Satoshi Hanzawa, Takashi Yamana, Naoki Nishiyama, Shinji Katayanagi, Masaru Ejima,
Takafumi Suzuki, Tatuo Kawahara, Yuri Tasaka, Hidetaka Majima, Rei Sagawa,

Seiko Takazawa, Hikaru Aoki, Shohei Yamashita

Specially-appointed Professor: Yasuhiro Setoguchi

(1) Outline

Respiratory Medicine deals with a variety of pulmonary diseases including tumors, infectious diseases, allergic diseases, non-allergic inflammatory diseases, and genetic disorders. The aim of our department is to understand the pathophysiology of a variety of lung diseases and to discover the development of the diseases.

(2) Research

1. Pathogenesis of hypersensitivity pneumonitis and identification of environmental causative antigens
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
6. Pathophysiology of sleep apnea
7. Treatment of drug-resistance bacteria

(3) Education

Main objective in the graduate course is to provide our 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. Iijima Y, Tateishi T, Tsuchiya K, Sumi Y, Akashi T, Miyazaki Y. A Case of Pneumoconiosis Caused by Inhalation of Metallic Titanium Grindings. *Internal Medicine*. 2019.02; 59(3); 425-428
2. Nishiyama N, Honda T, Sema M, Kawahara T, Jin Y, Natsume I, Chiaki T, Yamashita T, Tsukada Y, Taki R, Miyashita Y, Saito K, Tateishi T, Sakashita H, Miyazaki Y. The utility of ground-glass attenuation score for anticancer treatment-related acute exacerbation of interstitial lung disease among lung cancer patients with interstitial lung disease. *International Journal of Clinical Oncology*. 2019.02; 25(2); 282-291
3. Nagashima R, Kosai H, Masuo M, Izumiyama K, Noshikawaji T, Morimoto M, Kumaki S, Miyazaki Y, Motohashi H, Yamamoto M, Tanaka N. Nrf2 Suppresses Allergic Lung Inflammation by Attenuating the Type 2 Innate Lymphoid Cell Response. *Journal of Immunology*. 2019.03; 202(5); 1331-1339
4. Saito H, Tsuchiya K, Chiba S, Ogata T, Imase R, Yagi T, Mishima Y, Jinta T, Saito K, Taki R, Isogai S, Jin Y, Kawasaki T, Natsume I, Miyashita Y, Takagiwa J, Ishiwata N, Chiaki T, Kishi M, Tsukada Y, Yamasaki M, Inase N, Miyazaki Y. Treatment of asthma in smokers: A questionnaire survey in Japanese clinical practice. *Respiratory Investigation*. 2019.03; 57(2); 126-132
5. Wong JYY, Zhang H, Hsiung CA, Shiraishi K, Yu K, Matsuo K, Wong MP, Hong YC, Wang J, Seow WJ, Wang Z, Song M, Kim HN, Chang IS, Chatterjee N, Hu W, Wu C, Mitsudomi T, Zheng W, Kim JH, Seow A, Caporaso NE, Shin MH, Chung LP, An SJ, Wang P, Yang Y, Zheng H, Yatabe Y, Zhang XC, Kim YT, Cai Q, Yin Z, Kim YC, Bassig BA, Chang J, Ho JCM, Ji BT, Daigo Y, Ito H, Momozawa Y, Ashikawa K, Kamatani Y, Honda T, Hosgood HD, Sakamoto H, Kunitoh H, Tsuta K, Watanabe SI, Kubo M, Miyagi Y, Nakayama H, Matsumoto S, Tsuboi M, Goto K, Shi J, Song L, Hua X, Takahashi A, Goto A, Minamiya Y, Shimizu K, Tanaka K, Wei F, Matsuda F, Su J, Kim YH, Oh IJ, Song F, Su WC, Chen YM, Chang GC, Chen KY, Huang MS, Chien LH, Xiang YB, Park JY, Kweon SS, Chen CJ, Lee KM, Blechter B, Li H, Gao YT, Qian B, Lu D, Liu J, Jeon HS, Hsiao CF, Sung JS, Tsai YH, Jung YJ, Guo H, Hu Z, Wang WC, Chung CC, Burdett L, Yeager M, Hutchinson A, Berndt SI, Wu W, Pang H, Li Y, Choi JE, Park KH, Sung SW, Liu L, Kang CH, Zhu M, Chen CH, Yang TY, Xu J, Guan P, Tan W, Wang CL, Hsin M, Sit KY, Ho J, Chen Y, Choi YY, Hung JY, Kim JS, Yoon HI, Lin CC, Park IK, Xu P, Wang Y, He Q, Perng RP, Chen CY, Vermeulen R, Wu J, Lim WY, Chen KC, Li YJ, Li J, Chen H, Yu CJ, Jin L, Chen TY, Jiang SS, Liu J, Yamaji T, Hicks B, Wyatt K, Li SA, Dai J, Ma H, Jin G, Song B, Wang Z, Cheng S, Li X, Ren Y, Cui P, Iwasaki M, Shimazu T, Tsugane S, Zhu J, Chen Y, Yang K, Jiang G, Fei K, Wu G, Lin HC, Chen HL, Fang YH, Tsai FY, Hsieh WS, Yu J, Stevens VL, Laird-Offringa IA, Marconett CN, Rietveld L, Chao A, Yang PC, Shu XO, Wu T, Wu YL, Lin D, Chen K, Zhou B, Huang YC, Kohno T, Shen H, Chanock SJ, Rothman N, Lan Q. Tuberculosis infection and lung adenocarcinoma: Mendelian randomization and pathway analysis of genome-wide association study data from never-smoking Asian women. *Genomics*. 2019.03; 112(2); 1223-1232

6. Hanzawa S, Tateishi T, Takemura T, Okada Y, Yamada Y, Noda M, Miyazaki Y, Inase N. The analysis of surgical lung biopsy and explanted lung specimens sheds light on the pathological progression of chronic bird-related hypersensitivity pneumonitis. *Internal Medicine*. 2019.04; 58(8); 1145-1150
7. Saito H, Sakakibara Y, Sakata A, Kurashige R, Murakami D, Kageshima H, Saito A, Miyazaki Y. Antibacterial activity of lysozyme-chitosan oligosaccharide conjugates (LYZOX) against *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and Methicillin-resistant *Staphylococcus aureus*. *PloS One*. 2019.05; 14(5); e0217504
8. Nukui Y, Miyazaki Y, Masuo M, Okamoto T, Furusawa H, Tateishi T, Kishino M, Tateishi U, Ono J, Ohta S, Izuhara K, Inase N. Periostin as a predictor of prognosis in chronic bird-related hypersensitivity pneumonitis. *Allergology International*. 2019.06; 68(3); 321-328
9. Inoue Y, Ishizuka M, Furusawa H, Honda T, Kawahara T, Tateishi T, Miyazaki Y. Acute inflammatory and immunologic responses against antigen in chronic bird-related hypersensitivity pneumonitis. *Allergology International*. 2019.07; 68(3); 321-328
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[Misc]

1. Tao M, Liu Q, Miyazaki Y, Canning BJ. Nicotinic receptor dependent regulation of cough and other airway defensive reflexes. *Pulmonary pharmacology & therapeutics.* 2019.06; 58; 101810

[Conference Activities & Talks]

1. Honda T, Sakashita H, Masai K, Motoi N, Kobayashi M, Akashi T, Mimaki S, Tsuchihara K, Shiraishi K, Okubo K, Watanabe S, Tsuta K, Inase N, Miyazaki Y, Kohno T. Distribution of Tumor Mutation Burden in Lung Adenocarcinoma Patients with Usual Interstitial Pneumonia. The 59th Annual Meeting of the Japanese Respiratory Society 2019.04.12
2. Inoue Y, Yamaguchi E, Setoguchi Y, Ichiwata T, Ebina M, et al. Prognostic Impacts of Comorbidities in Pulmonary Alveolar Proteinosis: A Nationwide Surveillance in Japan. American Thoracic Society International Conference 2019.05.17
3. Tateishi T, Shibata S, Karasuyama H, Miyazaki Y. Basophil Depletion Leads to Promotion of the Lung Fibrosis in Bleomycin-Mouse Model. American Thoracic Society International Conference 2019.05.17
4. Hanzawa S, Tateishi T, Kawahara T, Ishizuka M, Miyazaki Y. Antigen Avoidance Test Is Beneficial for Predicting The Prognosis of Patients with Chronic Hypersensitivity Pneumonitis Treated with Corticosteroid Therapy. American Thoracic Society International Conference 2019.05.17
5. Furusawa H., J. Cardwell, Okamoto T., A.D. Walts, M.I. Schwarz, C.D. Cool, P.J. Wolters, J.S.Lee, I.V. Yang, D.A. Schwartz. Chronic Hypersensitivity Pneumonitis (CHP), an ILD with Distinct Molecular Signatures. American Thoracic Society International Conference. American Thoracic Society International Conference 2019.05.17
6. Ishizuka M, Inoue Y, Honda T, Miyazaki Y. A Single-Center Prospective Cohort Study of Diagnostic Procedure of Interstitial Pneumonia in Clinical Setting; The Importance of Distinguishing Chronic Hypersensitivity Pneumonitis from Idiopathic Pulmonary Fibrosis. American Thoracic Society International Conference 2019.05.17
7. Sakakibara R, Kobayashi M, Takahashi N, Inamura K, Ninomiya H, Wakejima R, Kitazono S, Yanagitani N, Horiike A, Ichinose J, Matsuura Y, Nakao M, Mun M, Nishio M, Okumura S, Motoi N, Ito T, Miyazaki Y, Inase N, Ishikawa Y. INSM1 Is a Good Marker for Diagnosis of Small Cell Lung Carcinoma Even When Neuroendocrine Marker Negative. IASLC 2019 World Conference on Lung Cancer 2019.09.07
8. Setoguchi Y, Kitagawa S, Katayanagi S, Okamoto T, Miyazaki Y. Serum galectin-3 could be useful biomarker to know progression of pulmonary fibrosis. Asian Pacific Society of Respirology International Conference. 2019.11.14

Gastroenterology and Hepatology

Distinguished Professor

Mamoru WATANABE

Professor

Yasuhiro ASAHINA (Department of Liver Disease Control)

Kazuo OHTSUKA (Endoscopy)

Ryuichi OKAMOTO (Center for Stem Cell and Regenerative Medicine)

Tetsuya NAKAMURA (Department of Advanced Therapeutics for GI Diseases)

Associate Professor

Seishin AZUMA (Department of Collaborative Medicine for Gastroenterology and Hepatology)

Sei KAKINUMA (Department of Liver Disease Control)

Kiichiro TSUCHIYA (Gastroenterology and Hepatology)

Mina NAKAGAWA (Curricular Management Division)

Takashi NAGAISHI (Department of Advanced Therapeutics for GI Diseases)

Masakazu NAGAHORI (Clinical Research Center)

Junior Associate Professor

Yasuhiro ITSUI (Professional Development Center)

Shigeru OSHIMA (Gastroenterology and Hepatology)

Eriko OKADA (Department of Medical Education Research and Development)

Assistant Professor

Toshimitsu FUJII, Eiko SAITO (Gastroenterology and Hepatology)

Yasuhiro NEMOTO (Department of Gastroenterology and Hepatology)

Michio ONIZAWA (Department of Advanced Therapeutics for GI Diseases)

Shiro YUI (Center for Stem Cell and Regenerative Medicine)

Miyako MURAKAWA (Clinical Laboratory)

Masayoshi FUKUDA (Endoscopy)

Kento TAKENAKA (Department of Collaborative Medicine for Gastroenterology and Hepatology)

Project Assistant Professor

Ryu NISHIMURA (Department of Gastroenterology and Hepatology)

Specially Appointed Assistant Professor

Taro WATABE, Nobukatsu HORITA, Yuka MATSUMOTO, Sayuri NITTA,

Shuji HIBIYA, Hiromichi SHIMIZU, Fukiko KITAHATA, Ami KAWAMOTO,

Masato MIYOSHI (Gastroenterology and Hepatology)

Kohei SUZUKI, Masanori KOBAYASHI, Maiko MOTOBAYASHI (Endoscopy)

Fukiko KITAHATA (General Medicine)

Yoshihito KANO (Department of Clinical Oncology)

Senior Resident

Takeshi WATANABE, Shiori ITO, Miyuki KANESHIRO, Hiromune KATSUDA (Gastroenterology and Hepatology)

Maiko MOTOBAYASHI, Sho WATANABE, Tomoaki SHIRASAKI (Endoscopy)

Resident

Yohei ITO, Shu KATO (Gastroenterology and Hepatology)

Graduate Student

Noriaki HOSOYA, Emi INOUE, Tomoyuki TSUNODA, JOSE Nisha, Yuta KOJIMA,

Minami HAMA, Yuria TAKEI, Sho ANZAI, Tomoaki SHIRASAKI, Shohei TANAKA,

Ayako WATANABE, Kana OTSUBO, Sho WATANABE, Nobuhiro KATSUKURA,

Hiroki MATSUDA, Takehito ASAKAWA, Reiko KUNO, Ai MASUMOTO,

Emi AONUMA, Mao KAWAI, Ryo MORIKAWA, Junichi TAKAHASHI,

Naoya TSUGAWA, Akiko TAMURA, Jun TSUCHIYA, Taro SHIMIZU,

Sakurako KOBAYASHI, Eiko TAKEICHI, Daiki YAMADA, Satoshi WATANABE

(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 disease-specific 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 assisted 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 enterography).
- 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. Seishin Azuma, Yasuhiro Asahina, Sei Kakinuma, Keiko Azuma, Masato Miyoshi, Emi Inoue, Tomoyuki Tsunoda, Ayako Sato, Shun Kaneko, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Makoto Tomita, Mina Nakagawa, Mamoru Watanabe. Diabetic Retinopathy as a Risk Factor Associated with the Development of Hepatocellular Carcinoma in Nonalcoholic Fatty Liver Disease. *Dig Dis.* 2019; 37(3); 247-254
2. Masanori Kobayashi, Shomei Ryozaawa, Hirotoishi Iwano, Ryuichiro Araki, Yuki Tanisaka, Akashi Fujita, Tsutomu Kobatake. The usefulness of wire-guided endoscopic snare papillectomy for tumors of the major duodenal papilla. *PLoS ONE.* 2019; 14(1); e0211019
3. Makoto Naganuma, Fumihito Hirai, Kiyonori Kobayashi, Kenji Watanabe, Ken Takeuchi, Nobuo Aoyama, Hiroshi Nozawa, Satoshi Motoya, Toshihide Ohmori, Akio Harada, Yushi Nagai, Takayuki Abe, Yoji Yamada, Katsutoshi Inagaki, Naoki Shimizu, Takanori Kanai, Mamoru Watanabe. Middle-term prognosis in patients with ulcerative colitis who achieved clinical and endoscopic remission by budesonide rectal foam. *PLoS ONE.* 2019; 14(8); e0220413
4. Yoshio Kitazume, Tomoyuki Fujioka, Kento Takenaka, Jun Oyama, Kazuo Ohtsuka, Toshimitsu Fujii, Ukihide Tateisi. Crohn Disease: A 5-Point MR Enterocolonography Classification Using Enteroscopic Findings. *AJR Am J Roentgenol.* 2019.01; 212(1); 67-76
5. Ryu Nishimura, Tomoaki Shirasaki, Kiichiro Tsuchiya, Yoshihide Miyake, Yusuke Watanabe, Shuji Hibiya, Sho Watanabe, Tetsuya Nakamura, Mamoru Watanabe. Establishment of a system to evaluate the therapeutic effect and the dynamics of an investigational drug on ulcerative colitis using human colonic organoids. *J Gastroenterol.* 2019.01; 54(7); 608-620
6. Masato Miyoshi, Sei Kakinuma, Akihide Kamiya, Tomoyuki Tsunoda, Jun Tsuchiya, Ayako Sato, Shun Kaneko, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. LIM homeobox 2 promotes interaction between human iPS-derived hepatic progenitors and iPS-derived hepatic stellate-like cells. *Sci Rep.* 2019.02; 9(1); 2072
7. Yasuharu Maeda, Shin-Ei Kudo, Yuichi Mori, Masashi Misawa, Noriyuki Ogata, Seiko Sasanuma, Kuni-hiko Wakamura, Masahiro Oda, Kensaku Mori, Kazuo Ohtsuka. Fully automated diagnostic system with artificial intelligence using endocytoscopy to identify the presence of histologic inflammation associated with ulcerative colitis (with video). *Gastrointest Endosc.* 2019.02; 89(2); 408-415
8. Satoshi Motoya, Kenji Watanabe, Haruhiko Ogata, Takanori Kanai, Toshiyuki Matsui, Yasuo Suzuki, Mitsuhiko Shikamura, Kenkichi Sugiura, Kazunori Oda, Tetsuharu Hori, Takahiro Araki, Mamoru Watanabe, Toshifumi Hibi. Vedolizumab in Japanese patients with ulcerative colitis: A Phase 3, randomized, double-blind, placebo-controlled study. *PLoS ONE.* 2019.02; 14(2); e0212989
9. Kaho Yamasaki, Kento Takenaka, Kazuo Ohtsuka. Laterally Spreading Tumor-like Early Cancer in Ileum. *Intern Med.* 2019.03; 58(6); 885-886

10. Hiroshi Fukamachi, Seon-Kyu Kim, Jiwon Koh, Hye Seung Lee, Yasushi Sasaki, Kentaro Yamashita, Taketo Nishikawaji, Shu Shimada, Yoshimitsu Akiyama, Sun-Ju Byeon, Dong-Hyuck Bae, Keisuke Okuno, Masatoshi Nakagawa, Toshiro Tanioka, Mikito Inokuchi, Hiroshi Kawachi, Kiichiro Tsuchiya, Kazuyuki Kojima, Takashi Tokino, Yoshinobu Eishi, Yong Sung Kim, Woo Ho Kim, Yasuhito Yuasa, Shinji Tanaka. A subset of diffuse-type gastric cancer is susceptible to mTOR inhibitors and checkpoint inhibitors. *J. Exp. Clin. Cancer Res.* 2019.03; 38(1); 127
11. Motohiro Esaki, Takayuki Matsumoto, Naoki Ohmiya, Ema Washio, Toshifumi Morishita, Kei Sakamoto, Hiroo Abe, Shojiro Yamamoto, Tetsu Kinjo, Kazutomo Togashi, Kenji Watanabe, Fumihito Hirai, Masanaka Nakamura, Sadaharu Nouda, Shinya Ashizuka, Teppei Omori, Shuji Kochi, Shunichi Yanai, Yuta Fuyuno, Atsushi Hirano, Junji Umeno, Takanari Kitazono, Fukunori Kinjo, Mamoru Watanabe, Toshiyuki Matsui, Yasuo Suzuki. Capsule endoscopy findings for the diagnosis of Crohn's disease: a nationwide case-control study. *J Gastroenterol.* 2019.03; 54(3); 249-260
12. Sayuri Nitta, Yasuhiro Asahina, Takanobu Kato, Jun Tsuchiya, Emi Inoue-Shinomiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Hayato Hikita, Tetsuo Takehara, Mamoru Watanabe. Impact of novel NS5A resistance-associated substitutions of hepatitis C virus detected in treatment-experienced patients. *Sci Rep.* 2019.04; 9(1); 5722
13. Nagaishi T, Yamada D, Suzuki K, Fukuyo R, Saito E, Fukuda M, Watabe T, Tsugawa N, Takeuchi K, Yamamoto K, Arai A, Ohtsuka K, Watanabe M. Indolent T cell lymphoproliferative disorder with villous atrophy in small intestine diagnosed by single-balloon enteroscopy. *Clinical journal of gastroenterology.* 2019.04;
14. Atsushi Yoshida, Noriko Kamata, Akihiro Yamada, Yoko Yokoyama, Teppei Omori, Toshimitsu Fujii, Ryohei Hayashi, Tetsu Kinjo, Akira Matsui, Norimasa Fukata, Sakuma Takahashi, Ryosuke Sakemi, Noriyuki Ogata, Shinya Ashizuka, Shigeki Bamba, Makoto Ooi, Shuji Kanmura, Katsuya Endo, Takuya Yoshino, Hiroki Tanaka, Toshio Morizane, Shinichiro Shinzaki, Taku Kobayashi. Pneumonia in Patients with Inflammatory Bowel Disease. *Inflamm Intest Dis.* 2019.04; 3(4); 167-172
15. Emi Inoue-Shinomiya, Miyako Murakawa, Yasuhiro Asahina, Mina Nakagawa, Jun Tsuchiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Sayuri Nitta, Fukiko Kawai-Kitahata, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Kazumoto Murata, Masashi Mizokami, Mamoru Watanabe. Association of serum interferon- λ 3 levels with hepatocarcinogenesis in chronic hepatitis C patients treated with direct-acting antiviral agents *Hepatology Res.* 2019.05; 49(5); 500-511
16. Akira Doi, Hayato Hikita, Yugo Kai, Yuki Tahata, Yoshinobu Saito, Tasuku Nakabori, Ryoko Yamada, Takahiro Kodama, Ryotaro Sakamori, Asako Murayama, Sayuri Nitta, Yasuhiro Asahina, Hiroshi Suemizu, Tomohide Tatsumi, Takanobu Kato, Tetsuo Takehara. Combinations of two drugs among NS3/4A inhibitors, NS5B inhibitors and non-selective antiviral agents are effective for hepatitis C virus with NS5A-P32 deletion in humanized-liver mice. *J Gastroenterol.* 2019.05; 54(5); 449-458
17. Jordi Guiu, Edouard Hannezo, Shiro Yui, Samuel Demharer, Svetlana Ulyanchenko, Martti Maimets, Anne Jørgensen, Signe Perlman, Lene Lundvall, Linn Salto Mamsen, Agnete Larsen, Rasmus H Olesen, Claus Yding Andersen, Lea Langhoff Thuesen, Kristine Juul Hare, Tune H Pers, Konstantin Khodosevich, Benjamin D Simons, Kim B Jensen. Tracing the origin of adult intestinal stem cells. *Nature.* 2019.06; 570(7759); 107-111
18. Tomoyuki Tsunoda, Sei Kakinuma, Masato Miyoshi, Akihide Kamiya, Shun Kaneko, Ayako Sato, Jun Tsuchiya, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Tsuyoshi Sogo, Haruki Komatsu, Ryutaro Mukouchi, Ayano Inui, Tomoo Fujisawa, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Loss of fibrocystin promotes interleukin-8-dependent proliferation and CTGF production of biliary epithelium. *J Hepatol.* 2019.07; 71(1); 143-152
19. Sho Watanabe, Kiichiro Tsuchiya, Ryu Nishimura, Tomoaki Shirasaki, Nobuhiro Katsukura, Shuji Hibiya, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Mutation by CRISPR System Enhances the Malignant Potential of Colon Cancer. *Mol Cancer Res.* 2019.07; 17(7); 1459-1467
20. Kento Takenaka, Toshimitsu Fujii, Kohei Suzuki, Hiromichi Shimizu, Maiko Motobayashi, Shuji Hibiya, Eiko Saito, Masakazu Nagahori, Mamoru Watanabe, Kazuo Ohtsuka. Small Bowel Healing Detected by Endoscopy in Patients With Crohn's Disease After Treatment With Antibodies Against Tumor Necrosis Factor.[Epub ahead of print] *Clin Gastroenterol Hepatol.* 2019.08;

21. Tadakazu Hisamatsu, Takayuki Matsumoto, Kenji Watanabe, Hiroshi Nakase, Satoshi Motoya, Naoki Yoshimura, Tetsuya Ishida, Shingo Kato, Tomoo Nakagawa, Motohiro Esaki, Masakazu Nagahori, Toshiyuki Matsui, Yuji Naito, Takanori Kanai, Yasuo Suzuki, Masanori Nojima, Mamoru Watanabe, Toshifumi Hibi, . Concerns and side effects of azathioprine during adalimumab induction and maintenance therapy for Japanese patients with Crohn's disease: a sub-analysis of a prospective randomized clinical trial (DIA-MOND study). *J Crohns Colitis*. 2019.09; 13(9); 1097-1104
22. Hajime Yamazaki, Katsuyoshi Matsuoka, Jovelle Fernandez, Toshifumi Hibi, Mamoru Watanabe, Tadakazu Hisamatsu, Shunichi Fukuhara. Ulcerative colitis outcomes research in Japan: protocol for an observational prospective cohort study of YOURS (YOU and Ulcerative colitis: Registry and Social network). *BMJ Open*. 2019.09; 9(9); e030134
23. Sayaka Tsuda, Azusa Sameshima, Michikazu Sekine, Haruna Kawaguchi, Daisuke Fujita, Shintaro Makino, Akio Morinobu, Yohko Murakawa, Kiyoshi Matsui, Takao Sugiyama, Mamoru Watanabe, Yasuo Suzuki, Masakazu Nagahori, Atsuko Murashima, Tatsuya Atsumi, Kenji Oku, Nobuaki Mitsuda, Syuji Takei, Takako Miyamae, Naoto Takahashi, Ken Nakajima, Shigeru Saito, . Pre-conception status, obstetric outcome and use of medications during pregnancy of systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) in Japan: Multi-center retrospective descriptive study. *Mod Rheumatol*. 2019.09; 1-10
24. Wan Wang, Kaoru Tsuchiya, Masayuki Kurosaki, Yutaka Yasui, Kento Inada, Sakura Kirino, Koji Yamashita, Shuhei Sekiguchi, Yuka Hayakawa, Leona Osawa, Mao Okada, Mayu Higuchi, Kenta Takaura, Chiaki Maeyashiki, Shun Kaneko, Nobuharu Tamaki, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Yasuhiro Asahina, Nobuyuki Enomoto, Namiki Izumi. Sorafenib-Regorafenib sequential therapy in Japanese patients with unresectable hepatocellular carcinoma-relative dose intensity and post-regorafenib therapies in real world practice. *Cancers (Basel)*. 2019.10; 11(10); E1517
25. Tomoo Nakagawa, Taku Kobayashi, Kiyohiro Nishikawa, Fumika Yamada, Satoshi Asai, Yukinori Sameshima, Yasuo Suzuki, Mamoru Watanabe, Toshifumi Hibi. Infliximab biosimilar CT-P13 is interchangeable with its originator for patients with inflammatory bowel disease in real world practice. *Intest Res*. 2019.10; 17(4); 504-515
26. Shintaro Akiyama, Katsuyoshi Matsuoka, Kyoko Fukuda, Shunsuke Hamada, Mikiko Shimizu, Kosaku Nanki, Shinta Mizuno, Hiroki Kiyohara, Mari Arai, Shinya Sugimoto, Yasushi Iwao, Haruhiko Ogata, Tadakazu Hisamatsu, Makoto Naganuma, Maiko Motobayashi, Kohei Suzuki, Kento Takenaka, Toshimitsu Fujii, Eiko Saito, Masakazu Nagahori, Kazuo Ohtsuka, Mayumi Mochizuki, Mamoru Watanabe, Masayuki Hashiguchi, Takanori Kanai. Long-term effect of NUDT15 R139C on hematologic indices in inflammatory bowel disease patients treated with thiopurine. *J Gastroenterol Hepatol*. 2019.10; 34(10); 1751-1757
27. Tadakazu Hisamatsu, Shingo Kato, Reiko Kunisaki, Minoru Matsuura, Masakazu Nagahori, Satoshi Motoya, Motohiro Esaki, Norimasa Fukata, Satoko Inoue, Takeshi Sugaya, Hirotake Sakuraba, Fumihito Hirai, Kenji Watanabe, Takanori Kanai, Makoto Naganuma, Hiroshi Nakase, Yasuo Suzuki, Mamoru Watanabe, Toshifumi Hibi, Masanori Nojima, Takayuki Matsumoto. Withdrawal of thiopurines in Crohn's disease treated with scheduled adalimumab maintenance: a prospective randomised clinical trial (DIA-MOND2). *J Gastroenterol*. 2019.10; 54(10); 860-870
28. Shun Kaneko, Masayuki Kurosaki, Nobuharu Tamaki, Jun Itakura, Tsuguru Hayashi, Sakura Kirino, Leona Osawa, Keiya Watakabe, Mao Okada, Wan Wang, Takao Shimizu, Mayu Higuchi, Kenta Takaura, Yutaka Yasui, Kaoru Tsuchiya, Hiroyuki Nakanishi, Yuka Takahashi, Mamoru Watanabe, Namiki Izumi. Tenofovir alafenamide for hepatitis B virus infection including switching therapy from tenofovir disoproxil fumarate. *J Gastroenterol Hepatol*. 2019.11; 34(11); 2004-2010
29. Kento Takenaka, Maiko Kimura, Kazuo Ohtsuka. Colonic strictures mimicking Crohn's disease.[Epub ahead of print] *Gut*. 2019.11;
30. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Emi Inoue-Shinomiya, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Minoru Tanabe, Emiko Sugawara, Akira Takemoto, Hidenori Ojima, Michiie Sakamoto, Masaru Muraoka, Shinichi Takano, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive genetic analysis of cholangiolocellular carcinoma with a coexistent hepatocellular carcinoma-like area and metachronous hepatocellular carcinoma. *Hepatol Res*. 2019.12; 49(12); 1466-1474

31. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient.[Epub ahead of print] *Hepatol Res.* 2019.12;
32. Ayako Sato, Sei Kakinuma, Masato Miyoshi, Akihida Kamiya, Tomoyuki Tsunoda, Shun Kaneko, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Naohiko Koshikawa, Motoharu Seiki, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Vasoactive intestinal peptide derived from liver mesenchymal cells mediates tight junction assembly in mouse intrahepatic bile ducts. *Hepatol Commun.* 2019.12; 4(2); 235-254

[Misc]

1. Sei Kakinuma, Akihida Kamiya. A rodent model for cell transplantation of hepatic progenitor cells. *Methods Mol Biol.* 2019; 1905; 211-219
2. Sei Kakinuma, Mamoru Watanabe. Analysis of the mechanism underlying liver diseases using human induced pluripotent stem cells. *Immunol Med.* 2019.06; 42(2); 71-78
3. Hiromichi Shimizu, Kohei Suzuki, Mamoru Watanabe, Ryuichi Okamoto. Stem cell-based therapy for inflammatory bowel disease. *Intest Res.* 2019.07; 17(3); 311-316
4. Sei Kakinuma. Research of hepatic fibrosis using human induced pluripotent stem cells. *Gastroenterology & Hepatology.* 2019.12; 6(6); 548-554

[Conference Activities & Talks]

1. Shigeru Oshima, Yoichi Nibe, Akiko Tamura, Hiroki Matsuda, Emi Aonuma, Kana Otsubo, Mamoru Watanabe. K33-linked polyubiquitin is recruited by SQSTM1/p62. *Keystone Symposia: Autophagy(B2)* 2019.02.19 New Mexico (USA)
2. Suzuki K, Shimizu H, Kawai M, Takahashi J, Anzai S, Kawamoto A, Nagata S, Hiraguri Y, Yui S, Tsuchiya K, Nakamura T, Ohtsuka K, Okamoto R, Watanabe M . UC-related and segment-specific properties of patient-derived colonic organoids. *ECCO2019* 2019.03.07 Copenhagen (Denmark)
3. Okamoto R, Watanabe M. 【Session 2: Clinical assessment and therapeutic modulation of intestinal regeneration in IBD】 Epithelial transplantation to facilitate mucosal healing. *ECCO2019* 2019.03.07 Copenhagen (Denmark)
4. Kawamoto A, Nagata S, Anzai S, Takahashi J, Kawai M, Hama M, Nogawa D, Yamamoto K, Kuno R, Suzuki K, Shimizu H, Hiraguri Y, Yui S, Oshima S, Tsuchiya K, Nakamura T, Ohtsuka K, Kitagawa M, Okamoto R, Watanabe M. Synergy of Notch signalling and TNF- α in the inflamed intestinal epithelia of IBD patients leads to up-regulation of UBD, a ubiquitin-like protein. *ECCO2019* 2019.03.08 Copenhagen (Denmark)
5. Shuji Hibiya, Kiichiro Tsuchiya, Ryu Nishimura, Tomoaki Shirasaki, Sho Watanabe, Nobuhiro Katsukura, Tetsuya Nakamura, Mamoru Watanabe. Establishment of an in vitro system to evaluate the therapeutic effect of the investigational drug on ulcerative colitis using human colonic organoids.. *ECCO2019* 2019.03.08 Copenhagen (Denmark)
6. Takashi Nagaishi, Yudai Kojima, Daiki Yamada, Taro Watabe, Naoya Tsugawa, Nisha Jose, Michio Onizawa, Mamoru Watanabe.. APL expression is downregulated in an animal model of chronic colitis.. *ECCO2019* 2019.03.08 Copenhagen (Denmark)
7. Tsuchiya K, Watanabe S, Shirasaki T, Nishimura R, Katsukura N, Hibiya S, Okamoto R, Nakamura T, Watanabe M. TP53 mutation in human colonic organoids acquires resistance to in vitro long-term inflammation.. *ECCO2019* 2019.03.09 Copenhagen (Denmark)
8. Kiichiro Tsuchiya. Organoid model for the carcinogenesis process of CAC. *IMKASID 2019* 2019.04.12 Seoul (Korea)

9. Shun Kaneko, Masayuki Kurosaki, Nobuharu Tamaki, Jun Itakura, Sakura Kirino, Leona Osawa, Keiya Watakabe, Mao Okada, Wan Wang, Takao Shimizu, Mayu Higuchi, Kenta Takaura, Yutaka Yasui, Kaoru Tsuchiya, Hiroyuki Nakanishi, Yuka Takahashi, Namiki Izumi. Efficacy and safety of switching therapy from tenofovir disoproxil fumarate to tenofovir alafenamide for hepatitis B virus infection. EASL, The International Liver Congress 2019 2019.04.12 Vienna (Austria)
10. Miyako Murakawa, Yasuhiro Asahina, Emi Inoue, Mina Nakagawa, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Fukiko Kawai-Kitahata, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. The association of serum IFN-lambda 3 levels with liver fibrosis and hepatocarcinogenesis in chronic hepatitis C patients treated with direct-acting antiviral agents. EASL, The International Liver Congress 2019 2019.04.13 Vienna (Austria)
11. Mina Nakagawa, Yasuhiro Asahina, Jun Tsuchiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Emi Inoue, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Makoto Tomita, Mamoru Watanabe. Impact of HCV clearance on HCC development and patient survival: Propensity score-matched analysis of an ongoing database of 2173 CHC patients. EASL, The International Liver Congress 2019 2019.04.13 Vienna (Austria)
12. Ryuichi Okamoto, Mao Kawai, Minami Hama, Sayaka Nagata, Ami Kawamoto, Kohei Suzuki, Hiromichi Shimizu, Sho Anzai, Junichi Takahashi, Reiko Kuno, Sayaka Takeoka, Yui Hiraguri, Shiro Yui, Mamoru Watanabe. **【The 6th JSGE International Topic Conference Lifestyle-related Diseases in Gastroenterology】** Gastrointestinal tract (role of gut microbiome and diet) :Food-borne factors in inflammatory bowel disease. The105th General Meeting of the Japanese Society of Gastroenterology 2019.05.10 Kanazawa (Japan)
13. Kawai M, Hama M, Nagata S, Kawamoto A, Suzuki K, Shimizu H, Anzai S, Takahashi J, Kuno R, Takeoka S, Hiraguri Y, Yui S, Okamoto R, Watanabe M. Functional analysis of isoflavones using patient-derived intestinal organoids. AOCC2019 2019.06.14 Taipei (Taiwan)
14. Eiko Saito, Kohei Suzuki, Shuuji Hibiya, Maiko Motobayashi, Kento Takenaka, Nobukatsu Horita, Hiromichi Shimizu, Michio Onizawa, Toshimitsu Fujii, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. The clinical efficacy of ustekinumab (UST) in patients with Crohn' s disease (CD). AOCC2019 2019.06.15 Taipei (Taiwan)
15. Kento Takenaka, Kazuo Ohtsuka, Toshimitsu Fujii, Kohei Suzuki, Hiromichi Shimizu, Maiko Motobayashi, Shuji Hibiya, Eiko Saito, Masakazu Nagahori, Mamoru Watanabe. Small bowel endoscopic healing of Crohn' s disease treated with anti-TNF antibodies. AOCC2019 2019.06.15 Taipei (Taiwan)
16. Shuji Hibiya, Kiichiro Tsuchiya, Ryu Nishimura, Tomoaki Shirasaki, Sho Watanabe, Nobuhiro Katsukura, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Long-term inflammation model using human colonic organoids. AOCC2019 2019.06.15 Taipei (Taiwan)
17. Daiki Yamada, Takashi Nagaishi, Yudai Kojima, Taro Watabe, Naoya Tsugawa, Nisha Jose, Akinori Hosoya, Masahiro Suzuki, Michio Onizawa, Mamoru Watanabe. APL downregulation in an animal model of chronic colitis. AOCC2019 2019.06.15 Taipei (Taiwan)
18. Shiro Yui, Mamoru Watanabe. Stem Cells in Gut, Who are They and How They Work, What Can We Count on Them. AOCC2019 2019.06.16 Taipei (Taiwan)
19. Takashi Nagaishi, Yudai Kojima, Taro Watabe, Naoya Tsugawa, Daiki Yamada, Nisha Jose, Akinori Hosoya, Masahiro Suzuki, Michio Onizawa, Mamoru Watanabe. Analysis of APL expression in an animal model of chronic colitis. FOCIS2019 2019.06.20 Boston (USA)
20. Okamoto R, Watanabe M. **【Focus Session: Cutting Edge Regenerative Medicine Using Stem Cells】** Intestinal Epithelial Stem Cell Organoids and IBD. ISSCR2019 2019.06.26 Los Angeles (USA)
21. Daiki Yamada, Takashi Nagaishi, Taro Watabe, Naoya Tsugawa, Yudai Kojima, Takahiro Adachi, Mamoru Watanabe. Analysis of Ileocecal Immune Response in an Animal Model of Colitis. ICMI2019 2019.07.17 Brisbane (Australia)
22. Kana Otsubo, Yoichi Nibe, Chiaki Maeyashiki, Akiko Tamura, Emi Aonuma, Hiroki Matsuda, Mamoru Watanabe, Shigeru Oshima. The role of ubiquitination in crosstalk of intestinal epithelial cell death and autophagic signaling was revealed by a novel polyubiquitin imaging system.. ICMI2019 2019.07.17 Brisbane (Australia)

23. Mina Nakagawa, Kanako Noritake, Kumiko Yamaguchi, Janelle Moross, Jun Tsuruta, Keiichi Akita. Introduction of Clinical Exchange Training for Medical and Dental Students. AMEE 2019 2019.08.26 Vienna (Austria)
24. Yasuhiro Asahina. Prevention and Risk for Liver Cancer after Anti-Viral Therapy in Patients with HBV/HCV. JSH International Liver Conference 2019.10.02 Osaka (Japan)
25. Shuji Hibiya, Kiichiro Tsuchiya, Ryu Nishimura, Sho Watanabe, Nobuhiro Katsukura, Tomoaki Shirasaki, Ryuichi Okamoto, Mamoru Watanabe. Establishment of chronic inflammation model using human small intestinal and colonic organoids. UEG Week 2019 2019.10.23 Barcelona (Spain)
26. Yasuhiro Asahina, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma. Comprehensive analysis of cancer gene mutations and viral integration in hepatocellular carcinoma arising from non-fibrotic liver. AASLD The Liver Meeting 2019 2019.11.10 Boston (USA)
27. Naoya Tsugawa, Takashi Nagaishi, Daiki Yamada, Toshimitsu Fujii, Yudai Kojima, Arisa Tokai, Taro Watabe, Shuang Wang, Michio Onizawa, Takahiro Adachi, Mamoru Watanabe. BCR signaling in the activated B cells may be regulated by the long isoform of Ceacam1. The 48th Annual Meeting of the Japanese Society for Immunology 2019.12.11 Hamamatsu (Japan)
28. Takahiro Adachi, Taro Watabe, Takashi Nagaishi, Mamoru Watanabe, Hajime Karasuyama, Soichiro Yoshikawa. IgA-deficiency causes spontaneous enteritis.. The 48th Annual Meeting of the Japanese Society for Immunology 2019.12.13 Hamamatsu (Japan)

Cardiovascular Surgery

Professor: Hirokuni ARAI

Associate Professor: Tomohiro MIZUNO

Junior Associate Professor: Keiji OI, Eiki NAGAOKA(from July)

Assistant Professor:

Masafumi YASHIMA, Eiki NAGAOKA(until June, sabbatical leave),

Hidehito KUROKI(until June), Tatsuki FUJIWARA, Kiyotoshi OISHI, Masashi TAKESHITA

Graduate Student:

Hidehito KUROKI, Dai TASAKI, Kenji SAKAI,

Ryoji KINOSHITA, Kiyotoshi OISHI, Kenji YOKOYAMA, Masashi TAKESHITA, Hironobu SAKURAI, Haruna SEKI,

Hospital Staff: 5

Department of Advanced Surgical Technology Research and Development

Associate Professor: Katsuhiro OUCHI

(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. Shun Nakagama, Taishi Yonetsu, Shinya Shiohira, Yuji Matsuda, Taro Sasaoka, Yu Hatano, Atsuhiko Yagishita, Tomoyuki Umemoto, Shingo Maeda, Takanobu Yamamoto, Tomohiro Yoneyama, Yoshio Kitazume, Yoshihide Takahashi, Yasuhiro Maejima, Mihoko Kawabata, Masahiko Goya, Takashi Ashikaga, Hirokuni Arai, Kenzo Hirao. Exertional syncope caused by myocardial ischemia due to arterial steal syndrome in left internal mammary artery graft. *Coron. Artery Dis.* 2019.03;
2. Kazuo Kimura, Takeshi Kimura, Masaharu Ishihara, Yoshihisa Nakagawa, Koichi Nakao, Katsumi Miyauchi, Tomohiro Sakamoto, Kenichi Tsujita, Nobuhisa Hagiwara, Shunichi Miyazaki, Junya Ako, Hirokuni Arai, Hideki Ishii, Hideki Origuchi, Wataru Shimizu, Hirofumi Takemura, Yoshio Tahara, Yoshihiro Morino, Kenji Iino, Tomonori Itoh, Yoshitaka Iwanaga, Keiji Uchida, Hirohisa Endo, Ken Kongoji, Kenji Sakamoto, Hiroki Shiomi, Takao Shimohama, Atsushi Suzuki, Jun Takahashi, Ichiro Takeuchi, Akihito Tanaka, Toshihiro Tamura, Takahiro Nakashima, Teruo Noguchi, Daisuke Fukamachi, Tomohiro Mizuno, Junichi Yamaguchi, Kenji Yodogawa, Masami Kosuge, Shun Kohsaka, Hideaki Yoshino, Satoshi Yasuda, Hiroaki Shimokawa, Atsushi Hirayama, Takashi Akasaka, Kazuo Haze, Hisao Ogawa, Hiroyuki Tsutsui, Tsutomu Yamazaki, . JCS 2018 Guideline on Diagnosis and Treatment of Acute Coronary Syndrome. *Circ. J.* 2019.04; 83(5); 1085-1196
3. Teruhiko Imamura, Koichiro Kinugawa, Minoru Ono, Osamu Kinoshita, Norihide Fukushima, Akira Shiose, Yoshiro Matsui, Kenji Yamazaki, Yoshikatsu Saiki, Akihiko Usui, Hiroshi Niinami, Goro Matsumiya, Hirokuni Arai, Yoshiki Sawa. Implication of Preoperative Existence of Atrial Fibrillation on Hemocompatibility-Related Adverse Events During Left Ventricular Assist Device Support. *Circ. J.* 2019.05; 83(6); 1286-1292
4. Takeshita M, Arai H, Mizuno T, Yashima M. Successful mitral valve repair involving division of bridging tissue in a patient with double orifice mitral valve. *J Thorac Cardiovasc Surg.* 2019.05; 157(5); e293-e295
5. Takeshi Miyairi, Yukihiro Orime, Goro Matsumiya, Hideyuki Shimizu, Yoshinori Watanabe, Hirokuni Arai, Yukiyasu Sezai. Coronary Artery Surgery in Japan in 2017. *Ann Thorac Cardiovasc Surg.* 2019.06; 25(3); 176-178
6. Yusuke Ebana, Yihan Sun, Xiaoxi Yang, Taiju Watanabe, Satoru Makita, Kouichi Ozaki, Toshihiro Tanaka, Hirokuni Arai, Tetsushi Furukawa. Pathway analysis with genome-wide association study (GWAS) data detected the association of atrial fibrillation with the mTOR signaling pathway. *Int J Cardiol Heart Vasc.* 2019.09; 24; 100383
7. Nagaoka E, Sato K, Hage A, Bagur R, Harle C, Asopa S, Kiai B. Rescue Balloon Aortic Valvuloplasty After Sutureless Aortic Valve Replacement for Severe Paravalvular Leak. *Innovations (Phila).* 2019.10; 14(5); 476-479
8. Oi Keiji, Arai Hirokuni, Mizuno Tomohiro, Ouchi Katushiro, Yashima Masafumi, Nagaoka Eiki, Fujiwara Tatsuki, Takeshita Masashi, Oishi Kiyotoshi, Okumura Yushi, Sai Youshun, Seki Haruna. Minimally invasive mitral valve procedures: MICS, MitraClip, NeoChord, and Transcatheter Mitral Valve Replacement A Novel Peel-away Type Device for Artificial Chordae Reconstruction with Tube Technique(和訳中) 人工臓器. 2019.10; 48(2); S-19
9. Takeshita M, Mizuno T, Yashima M, Oi K, Kuroki H, Fujiwara T, Oishi K, Kubo T, Arai H. Surgical Repair of an Arch and Descending Aortic Aneurysm in a Child. *The Annals of thoracic surgery.* 2019.11; 108(5); e315-317
10. Oishi K, Arai H, Oi K, Yashima M, Kuroki H, Fujiwara T, Takeshita M, Mizuno T. Safe and effective ultrasound-guided myectomy and mitral valve repair for HCM. *The Annals of thoracic surgery.* 2019.12; 108(6); e369-e371

[Books etc]

1. Yashima M, Arai H. . ONE-POINT ADVICE: The Significance of Performing Aortic Valvuloplasty in Young Patients. SpringerLink , 2019.03

[Conference Activities & Talks]

1. Arai H, Oishi K, Oi T, Mizuno T, Yashima M, Kuroki H, Fujiwara T, Takeshita T, Kubo T, Okumura Y, Nabeshima J. Ultrasound-Guided Septal Myectomy Using High-Resolution Intracardiac Probe and Mitral Leaflet Height Reduction for Systolic Anterior Motion in Hypertrophic Obstructive Cardiomyopathy. The Society of Thoracic Surgeons 55th Annual Meeting 2019.01.29 San Diego, USA
2. Mizuno T, Fujiwara T, Kuroki H, Oishi K, Takeshita M, Yashima M, Oi K, Arai H.. What Should Be Done for Improving the Outcomes of Salvage from Cardiogenic Shock on ECMO Support?. 39th Annual Meeting and Scientific Sessions 2019.04.05 Florida USA
3. H.Kuroki, H.Arai, K.Oi, M.Yashima, T.Fujiwara, K.Oishi, M.Takeshita, Y.Okumura, T.Kubo, J. Nabeshima, T.Mizuno. Mitral and Tricuspid Valve Repair Using Subvalvular Procedures in Non-Ischemic Cardiomyopathy. AATS Mitral Conclave 2019 2019.05.02 New York, USA
4. Takeshita M, Arai H, Mizuno T, Oi K, Yashima M, Kuroki H, Fujiwara T, Oishi K, Kubo T, Okumura Y, Nabeshima J. Impact of Subvalvular Procedures in Tricuspid Valve Repair. AATS Mitral Conclave 2019 2019.05.03 New York, USA
5. Arai H. Is there still a role for subvalvular techniques? (Breakout Session) . AATS Mitral Conclave 2019 (Breakout Session) 2019.05.03 New York, USA
6. Arai H. When and How I Use the Gastroepiploic Artery (Scientific Simultaneous Breakout Session) . AATS Annual Meeting 2019 2019.05.04 Toronto, Canada
7. Kiyotoshi Oishi, Katsuhiko Ouchi, Tomohiro Mizuno, Tatsuki Fujiwara, Hirokuni Arai. Real-time Three-dimensional Imaging of Coronary Artery Bypass Grafting using High-frequency Epicardial Ultrasound. ISMICS 2019 Annual Meeting 2019.05.30 New York, USA
8. Arai H. THE INSPIRIS RESILIA Aortic Valve. AVR Thailand 2019 2019.06.29 Bangkok, Thailand
9. Arai H. Tips and Pitfalls of AVR. AVR Thailand 2019 2019.06.29 Bangkok, Thailand
10. Arai H. Intraoperative Ultrasonic Quality Assessment and Surgical Guidance to improve CABG outcomes. The 15th Annual Meeting of the Chinese Association of Cardiovascular Surgeons 2019.09.28 Nanjing, China
11. Arai H. Innovative Exposure Technique in OPCAB using “TENTACLES” Heart Positioner. The 15th Annual Meeting of the Chinese Association of Cardiovascular Surgeons 2019.09.29 Nanjing, China
12. Arai H. Ischemic MR: Novel surgical repair. The 15th Annual Meeting of the Chinese Association of Cardiovascular Surgeons 2019.09.29 Nanjing, China
13. Arai H. Posterior leaflet prolapse: Resect or respect?. The 15th Annual Meeting of the Chinese Association of Cardiovascular Surgeons 2019.09.29 Nanjing, China
14. Arai H. Evolution of the Choice of Prosthetic Heart Valve. 52nd Anniversary of the E hospital Establishment 2019.10.18 Hanoi, Vietnam
15. Oi K, Arai H, Mizuno T, Ouchi K, Yashima M, Nagaoka E, Fujiwara T, Takeshita M, Oishi K, Okumura Y, Sai Y, Seki H.. A Novel Peel-away Type Device for Artificial Chordae Reconstruction with Tube Technique. The 8th Meeting of the International Federation for Artificial Organs 2019.11.13 Osaka
16. Seki H, Fujiwara T, Hijikata W, Ohuchi K, Murashige T, Maruyama T, Tahara T, Ogata A, Yokota S, Arai H. Evaluation of thrombus detection methods in a magnetically levitated blood pump in an animal experiment. IFAO2019 The 8th meeting of the international federation for artificial organs 2019.11.14
17. Seki H, Fujiwara T, Hijikata W, Ohuchi K, Murashige T, Maruyama T, Tahara T, Ogata A, Yokota S, Arai H. Development of a thrombus induction method at a target site using fibrinogen coating solution. IFAO2019 The 8th meeting of the international federation for artificial organs 2019.11.14
18. Fujiwara T, Ohuchi K, Hijikata W, Maruyama O, Seki H, Tahara T, Arai H. Transition of an acute LVAD experimental animal model at our experimental facility. The 8th Meeting of the International Federation for Artificial Organs 2019.11.14 Osaka, Japan

19. Oi K, Arai H, Mizuno T, Nagaoka E, Yashima M, Fujiwara T, Oishi K, Takeshita M, Okumura Y, Sai Y, Seki H. Patient Characteristics For Long-term Patency Of Saphenous Vein Graft In Coronary Artery Bypass Surgery. International Coronary Congress 2019 2019.12.06 New York USA
20. Arai H. GEA Grafting in the Redo CABG Patient (Simultaneous Session). International Coronary Congress 2019 2019.12.06 New York, USA
21. Arai H. (chair) Parallel Session: BITA Grafting: When, Why and How to Do It . International Coronary Congress 2019 2019.12.06 New York, USA
22. Arai H. Off-pump coronary CABG with the Tentacles Device(Simultaneous Session). International Coronary Congress 2019 2019.12.07 New York, USA
23. Arai H. The Combined use of TTFM and HFUS Imaging to Optimize Outcomes (Simultaneous Session). International Coronary Congress 2019 2019.12.07 New York, USA
24. Arai H. (chair) Parallel Session: Diffuse CAD, Endarterectomy and Full Metal Jacket. International Coronary Congress 2019 2019.12.07 New York, USA
25. Arai H. Development of Tentacles. International Coronary Congress 2019, Lunch Symposium, 2019.12.07 New York, USA
26. Arai H. High Frequency Ultrasound: What it adds to TTFM. International Coronary Congress 2019, Lunch Symposium 2019.12.07 New York, USA
27. Arai H. (panelist) Panel Discussion : The Future of CABG and How We Can Invent It Together. International Coronary Congress 2019 2019.12.08 New York, USA

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:

Soichiro IIMORI (Dept. of Blood Purification)

Takayasu MORI (Dept. of Blood Purification)

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Yu NANAMATSU (Project Assistant Professor)

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(first half) Yuriko MITSUHASHI, Ryo YASUHARA, Mariko YOSHIDA

(second half) Jun OHTA, Misa HATA, Sasaki MASATO

Technician:

Chieko IIJIMA, 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 pioneering institutes that introduced 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 2019, our 12 presentations including two oral presentations were adopted in the annual meeting of American Society of Nephrology (ASN KIDNEY WEEK). Moreover, our research manuscripts were published in *Kidney International* (IF: 8.3), *Bone* (IF: 4.4), and *Scientific Reports* (IF: 4.0). We published 26 reports in English and one of them were presented as "press release".

In addition to them, a lot of our members have got prizes in various medical meetings regardless of whether they are in or out of the country. Further, comprehensive diagnosis of inherited kidney diseases using next generation sequencer (NGS) and clinical studies on genome information are now on track and is contributing to various genetic diagnosis of many patients. Genetic diagnosis was carried out for about 200 cases a year. 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, which enabled us to publish 9 clinical research papers (5 in *Clin Exp Nephrol.*, 1 in *Nephrology* and others).

(3) Education

"Undergraduate education"

(Systematic lectures)

For third grade medical students, we are conducting lectures organized in a three-week 'block form' in collaboration with the Urology and Pathology sections. Under the name of "Body Fluid Regulation and Urology" Block, students can learn intensively about kidney and urologic diseases during this period. In this lecture, we incorporate PBL (Problem-based Learning) lectures and lectures held by actual patients, so that the students will be able to study independently and bi-directionally.

(Project semester)

We accept several students every year in the project semester, in which the students are expected to participate in the forefront research with the assistance of graduate students.

(Clinical clerkship)

For the last three months of fourth grade following the project semester, we provide the Pre-Clinical Clerkship (PCC) lectures for ten weeks (two weeks of large-class comprehensive lectures and eight weeks of small-class lectures), which are more practical and interactive than the previous lectures held in the classroom. After PCC, fifth grade 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 regular ward conference, and are expected to learn about the pathophysiology of various kidney diseases in depth.

"Postgraduate education"

After the two-year initial training after graduation, postgraduate doctors will be engaged in clinical training as nephrologists either in the University Hospital or affiliated hospitals as senior trainees. During this period, we teach them so that they can be aware about unsolved clinical problems. We are planning to bring them up as "academic doctors". Research activities in the graduate school are very active, and by carrying out the state-of-the-art research, we are training doctors to be able to excel in both basic and clinical works.

(4) Clinical Services & Other Works

We are one of the first groups that introduced the hemodialysis therapy in Japan, and thus, have a long experience of clinical practice of kidney diseases. We have close coordination with our 20 affiliated hospitals. 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 kidney disease patients, vascular access surgery, peritoneal dialysis-related surgery, and induction of dialysis are consistently carried out in our department. Our hemopurification center is one of the biggest institutions among 42 hospitals belonging to national universities. In 2019, the number of newly started dialysis patients and plasma exchange were in 1st place, the total number of blood purifications and the number of hemodialysis were in 2nd place. Furthermore, we developed diagnostic panel for comprehensive genetic diagnosis for hereditary kidney diseases like nephrogenic diabetes insipidus, pseudohypoaldosteronism type II, Liddle syndrome, and Polycystic kidney diseases. Currently, we receive requests of genetic tests from all over the country. Genetic screening using next-generation sequencing technology enables definite diagnosis for rare hereditary diseases.

(5) Publications

[Original Articles]

1. Kikuchi H, Sasaki E, Nomura N, Mori T, Minamishima YA, Yoshizaki Y, Takahashi N, Furusho T, Arai Y, Mandai S, Yamashita T, Ando F, Maejima Y, Isobe K, Okado T, Rai T, Uchida S, Sohara E. Failure to sense energy depletion may be a novel therapeutic target in chronic kidney disease *Kidney Int.* 2019.01; 95(1); 123-137
2. Suzuki S, Naito S, Numasawa Y, Asada M, Shoji N, Zeniya M, Takahashi D, Sato H, Iimori S, Nomura N, Sohara E, Okado T, Ishiwata Y, Nagata M, Rai T, Yokota T, Uchida S. Encephalopathy Induced by High Plasma and Cerebrospinal Fluid Ceftriaxone Concentrations in a Hemodialysis Patient. *Internal medicine (Tokyo, Japan)*. 2019.02;
3. Sekine A, Fujimaru T, Hoshino J, Suwabe T, Oguro M, Mizuno H, Kawada M, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Mandai S, Chiga M, Kikuchi H, Ando F, Mori T, Sohara E, Uchida S, Sawa N, Takaichi K, Ubara Y. Genotype-Clinical Correlations in Polycystic Kidney Disease with No Apparent Family History. *American journal of nephrology*. 2019.02; 49(3); 233-240
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8. Sakoh T, Sekine A, Mori T, Mizuno H, Kawada M, Hiramatsu R, Hasegawa E, Hayami N, Yamanouchi M, Suwabe T, Sawa N, Ubara Y, Fujimaru T, Sohara E, Shinichi U, Hoshino J, Takaichi K. A familial case of pseudohypoaldosteronism type II (PHA2) with a novel mutation (D564N) in the acidic motif in WNK4. *Molecular genetics & genomic medicine*. 2019.06; 7(6); e705
9. Kita Masahiro, Uchida Shinichi, Yamada Koji, Ano Yasuhisa. Anxiolytic effects of theaflavins via dopaminergic activation in the frontal cortex *Bioscience, Biotechnology, and Biochemistry*. 2019.06; 83(6); 1157-1162
10. Suzuki Soichiro, Naito Shotaro, Numasawa Yoshiyuki, Asada Mizuho, Shoji Norikazu, Zeniya Moko, Takahashi Daiei, Sato Hidehiko, Iimori Soichiro, Nomura Naohiro, Sohara Eisei, Okado Tomokazu, Ishiwata Yasuyoshi, Nagata Masashi, Rai Tatsumitsu, Yokota Takanori, Uchida Shinichi. Encephalopathy Induced by High Plasma and Cerebrospinal Fluid Ceftriaxone Concentrations in a Hemodialysis Patient *Internal Medicine*. 2019.06; 58(12); 1775-1779
11. Fujiki T, Ando F*, Murakami K, Isobe K, Mori T, Susa K, Nomura N, Sohara E, Rai T, Uchida S. Tolvaptan activates the Nrf2/HO-1 antioxidant pathway through PERK phosphorylation *Scientific Reports*. 2019.06; 9(1); 9245
12. Ohkubo Atsushi, Okado Tomokazu, Sakurasawa Takatoshi, Maeda Takuma, Itagaki Ayako, Yamamoto Hiroko, Miyamoto Satoko, Seshima Hiroshi, Kurashima Naoki, Mori Takayasu, Iimori Soichiro, Sohara Eisei, Rai Tatsumitsu, Uchida Shinichi, Naito Shotaro. Removal Characteristics of Immunoabsorption with the Tryptophan-Immobilized Column Using Conventional and Selective Plasma Separators in the Treatment of Myasthenia Gravis *Therapeutic Apheresis and Dialysis*. 2019.06; 23(3); 271-278

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14. Sohara Eisei, Kikuchi Hiroaki, Uchida Shinichi. New Frontiers in Regenerative Medicine of Renal Function Failure to sense energy depletion in chronic kidney disease The Journal of Physiological Sciences. 2019.06; 69(Suppl.1); S56
15. Suzuki S, Naito S, Uchida S. Author's Reply: Why did the Patient Not Show Any Neurological Symptoms on the Day of the Higher Serum Level of Ceftriaxone? Internal medicine (Tokyo, Japan). 2019.07;
16. Nomura N, Shoda W, Uchida S. Clinical importance of potassium intake and molecular mechanism of potassium regulation. Clinical and experimental nephrology. 2019.07;
17. Ishigami Junichi, Padula William V, Grams Morgan E., Chang Alexander R., Jaar Bernard, Gansevoort Ron T., Bridges John E. P., Kovesdy Csaba P., Uchida Shinichi, Coresh Josef, Matsushita Kunihiro. Cost-effectiveness of Pneumococcal Vaccination Among Patients with CKD in the United states AMERICAN JOURNAL OF KIDNEY DISEASES. 2019.07; 74(1); 23-35
18. Matsuura Y, Nomura N, Shoda W, Mori T, Isobe K, Susa K, Ando F, Sohara E, Rai T, Uchida S. Tacrolimus ameliorates the phenotypes of type 4 Bartter syndrome model mice through activation of sodium-potassium-2 chloride cotransporter and sodium-chloride cotransporter. Biochemical and biophysical research communications. 2019.09; 517(2); 364-368
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21. Nomura Naohiro, Shoda Wakana, Uchida Shinichi. Clinical importance of potassium intake and molecular mechanism of potassium regulation Clinical and Experimental Nephrology. 2019.10; 23(10); 1175-1180
22. Chinen T, Saeki E, Mori T, Sohara E, Uchida S, Akimoto T. A case of Gitelman syndrome: our experience with a patient treated in clinical practice on a local island. Journal of rural medicine : JRM. 2019.11; 14(2); 258-262

[Conference Activities & Talks]

1. Hiroaki Kikuchi, Eisei Sohara, Naohiro Nomura, Takayasu Mori, Yoji Andrew Minamishima, Naohiro Takahashi, Taisuke Furusho, Fumiaki Ando, Kiyoshi Isobe, Koichiro Susa, Tatemitsu Rai, and Shinichi Uchida. AMPK activation bypassing AMP sensing mechanism is a novel therapeutic strategy for chronic kidney disease. The 8th CKD Frontier Meeting 2019.02.23 Nagoya
2. EISEI SOHARA. Failure to sense energy depletion in chronic kidney disease. The 9th Federation of the Asian and Oceanian Physiological Societies Congress 2019.03.30 Kobe, Hyogo, Japan
3. EISEI SOHARA. Whole exome data in rare disease gene discovery. International Society of Nephrology, World Congress of Nephrology 2019 2019.04.15 Melbourne, Australia
4. Furusho T, Sohara E, Mandai S, Kikuchi H, Takahashi N, Fujimaru T, Hashimoto H, Arai Y, Ando F, Mori T, Susa K, Isobe K, Nomura N, Okado T, Rai T, Yamamoto K, Uchida S. Renal TNF α activates WNK phosphorylation cascade and contributes to salt-sensitive hypertension in CKD.. The 62nd Annual Meeting of the Japanese Society of Nephrology 2019.06 Nagoya
5. Eisei Sohara. WNK signaling in salt-sensitive hypertension and electrolyte disorder. JSN/ASN Joint Symposium, The 62nd Annual Meeting of the Japanese Society of Nephrology 2019.06.21
6. Fujiki T, Ando F, Isobe K, Susa K, Mori T, Nomura N, Sahara E, Rai T, Uchida S. Tolvaptan activates the Nrf2/HO-1 pathway through PERK phosphorylation. The 62nd Annual Meeting of the Japanese Society of Nephrology 2019.06.22 Nagoya

7. Yoshiaki Matsuura, Naohiro Nomura, Wakana Shoda, Kiyoshi Isobe, Takayasu Mori, Koichiro Susa, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Tacrolimus improved symptoms of type 4 Bartter syndrome model mice.. 2019.06.22
8. Sohara Eisei. Failure to sense energy depletion in chronic kidney disease.. The 6th Diabetes Research Innovation Symposium 2019 2019.07.14 Kyoto
9. Furusho T, Sohara E, Mandai S, Kikuchi H, Takahashi N, Fujimaru T, Hashimoto H, Arai Y, Ando F, Zeniya M, Mori T, Susa K, Isobe K, Nomura N, Okado T, Rai T, Uchida S. Renal TNF α activates WNK phosphorylation cascade and contributes to salt-sensitive hypertension in CKD . The 10th Meeting of the Japanese Conference of Molecular Nephrology. 2019.09 Kyoto
10. Takuya Fujimaru, Takayasu Mori, Michio Nagata, Shintaro Mandai, Motoko Chiga, Hiroaki Kikuchi, Fumiaki Ando, Yutaro Mori, Koichiro Susa, Kiyoshi Isobe, Soichiro Iimori, Naohiro Nomura, Shotaro Naito, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara.. Tubular basement membrane duplication and cell interposition are distinctive histological findings in the adult patients genetically diagnosed with NPHP-RCs. ASN Kidney Week 2019 2019.11
11. Yoshiaki Matsuura, Naohiro Nomura, Wakana Shoda, Kiyoshi Isobe, Takayasu Mori, Koichiro Susa, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Tacrolimus improved symptoms of type 4 Bartter syndrome model mice. ASN Kidney Week 2019 2019.11
12. Ando F, Yui N, Mandai S, Isobe K, Mori T, Susa K, Nomura N, Sohara E, Rai T, Uchida S. Derivatives of FMP-API-1/27 Robustly Activate AQP2 Water Channels Independently of Vasopressin. ASN Kidney Week 2019 2019.11
13. Furusho T, Mandai S, Kikuchi H, Takahashi N, Fujimaru T, Hashimoto H, Arai Y, Ando F, Mori T, Susa K, Isobe K, Nomura N, Okado T, Rai T, Yamamoto K, Uchida S, Sohara E. Renal TNF α activates WNK phosphorylation cascade and contributes to salt-sensitive hypertension in CKD. ASN Kidney Week 2019 2019.11 Washington D.C., USA
14. Mori T, Chiga M, Fujimaru T, Mandai S, Nanamatsu A, Sohara E, Rai T, Uchida S. More than half of patients clinically diagnosed as Gitelman syndrome in adulthood do not have causal mutations in known pathogenic genes. ASN Kidney Week 2019 2019.11
15. Fumiaki Ando, Naofumi Yui, Shintaro Mandai, Kiyoshi Isobe, Takayasu Mori, Koichiro Susa, Naohiro Nomura, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida.. Derivatives of FMP-API-1/27 Robustly Activate AQP2 Water Channels Independently of Vasopressin.. The 52nd Annual Meeting of American Society of Nephrology. 2019.11.07 Washington DC
16. Fujiki T, Ando F, Mandai S, Isobe K, Susa K, Mori T, Nomura N, Sohara E, Rai T, Uchida S.. Tolvaptan and Bardoxolone Methyl Synergistically Activate the Nrf2/HO-1 pathway.. ASN Kidney Week 2019 2019.11.08
17. Koichiro Susa, Akitoshi Tamura, Pierre Galichon, Navin R. Gupta, Takuya Matsumoto, Tomoya Miyoshi, Venkata Sabbiseti, Joseph V. Bonventre, Ryuji Morizane.. A Drug-Specific Nephrotoxicity Prediction System Using Kidney Organoids.. The 52nd Annual Meeting of American Society of Nephrology. 2019.11.08 Washington DC
18. Navin R. Gupta, Ken Hiratsuka, Tomoya Miyoshi, Koichiro Susa, Narihito Tatsumoto, Michifumi Yamashita, Ryuji Morizane.. Fibrotic Kidney Organoids and Human CKD Samples Demonstrate Loss of Homologous Recombination as a Critical Mediator of Maladaptive Repair. The 52nd Annual Meeting of American Society of Nephrology.. The 52nd Annual Meeting of American Society of Nephrology. 2019.11.08 Washington DC
19. Naohiro Takahashi, Hiroaki Kikuchi, Makoto Arita, Fumiaki Ando, Shintaro Mandai, Kiyoshi Isobe, Koichiro Susa, Takayasu Mori, Naohiro Nomura, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara.. 12/15-Lipoxygenase Knockout Mice Exhibit a Resistance to Kidney Damage in CKD.. The 52nd Annual Meeting of American Society of Nephrology. 2019.11.08 Washington DC
20. Tamami Fujiki, Fumiaki Ando, Shintaro Mandai, Kiyoshi Isobe, Takayasu Mori, Koichiro Susa, Naohiro Nomura, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida.. Tolvaptan and Bardoxolone Methyl Synergistically Activate the Nrf2/ HO-1 Pathway.. The 52nd Annual Meeting of American Society of Nephrology. 2019.11.08 Washington DC

21. Taisuke Furusho, Shintaro Mandai, Hiroaki Kikuchi, Naohiro Takahashi, Takuya Fujimaru, Hiroko Hashimoto, Yohei Arai, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Kiyoshi Isobe, Naohiro Nomura, Tomokazu Okado, Tatemitsu Rai, Kohei Yamamoto, Shinichi Uchida, Eisei Sohara.. Renal TNF α Activates WNK Phosphorylation Cascade and Contributes to Salt-Sensitive Hypertension in CKD.. The 52nd Annual Meeting of American Society of Nephrology. 2019.11.08 Washington DC
22. Takuya Fujimaru, Takayasu Mori, Michio Nagata, Shintaro Mandai, Motoko Chiga, Hiroaki Kikuchi, Fumiaki Ando, Yutaro Mori, Koichiro Susa, Kiyoshi Isobe, Soichiro Iimori, Naohiro Nomura, Shotaro Naito, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara.. Tubular Basement Membrane Duplication and Cell Interposition Are Distinctive Histological Findings in the Adult Patients Genetically Diagnosed with Nephronophthisis-Related Ciliopathies.. The 52nd Annual Meeting of American Society of Nephrology. 2019.11.08 Washington DC
23. Naohiro Takahashi. 12/15-Lipoxygenase Knockout Mice Exhibit a Resistance to Kidney Damage in CKD. Kidney Week 2019 2019.11.08
24. Sohara Eisei. Failure to sense energy depletion in chronic kidney disease.. The 42nd Annual Meeting of the Molecular Biology Society of Japan 2019.12.04 Kobe, Japan
25. Fujiki T, Ando F, Mandai S, Isobe K, Susa K, Mori T, Nomura N, Sohara E, Rai T, Uchida S. Tolvaptan activates the Nrf2/HO-1 pathway through PERK phosphorylation. The 23rd International Joint Conference on Cardiovascular and Metabolic diseases 2019.12.14

[Awards & Honors]

1. Hiroaki Kikuchi. CKD Frontier Award, The 8th Chronic Kidney Disease Frontier (Nagoya), 2019.02

Comprehensive Reproductive Medicine

Professor : Naoyuki MIYASAKA
Associate Professor : Naoyuki YOSHIKI
Project Professor : Masakazu TERAUCHI
Junior Associate Professor : Kimio WAKANA
Project Associate Professor : Tomonori ISHIKAWA
Assistant Professor : Noriko OSHIMA, Yuki IWAHARA, Masaki SEKIGUCHI, Shiro HIRAMITSU,
Takafumi TUKADA, Asuka HIROSE, Reiko NAKAMURA
Project Assistant Professor : kazuki SAITO, Takayuki TATSUMI
Hospital Staff : Junichiro MITSUI, Sayako KAWAHARA
Graduate Student : Takuto MATSUURA, Tamami ODAI, Kenta TAKAHASHI,
Mayumi KOBAYASHI, Shiho YAUCHI, Misako IWATA, Nobuyuki KIDERA, Ayako FUDONO, Yuan FANG, Kotoi TURANE, Jun

(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. Kenta Takahashi, Mayu Yunokawa, Shinsuke Sasada, Yae Takehara, Naoyuki Miyasaka, Tomoyasu Kato, Kenji Tamura. A novel prediction score for predicting the baseline risk of recurrence of stage I-II endometrial carcinoma. J Gynecol Oncol. 2019.01; 30(1); e8
2. Egawa M, Imai K, Taketani Y, Morio T, Miyasaka N.. Two Prenatal Cases of Hyper-IgE Syndrome. J. Clin. Immunol.. 2019.01;
3. Ishihara Osamu, Jwa Seung Chik, Kuwahara Akira, Ishikawa Tomonori, Kugu Koji, Sawa Rintaro, Banno Kouji, Irahara Minoru, Saito Hidekazu. Assisted reproductive technology in Japan: A summary report for 2016 by the Ethics Committee of the Japan Society of Obstetrics and Gynecology(和訳中) Reproductive Medicine and Biology. 2019.01; 18(1); 7-16
4. Kotoi Tsurane, Serabi Tanabe, Naoyuki Miyasaka, Minako Matsuda, Megumi Takahara, Tsutomu Ida, Akira Kohyama. Management of labor and delivery in myasthenia gravis: A new protocol. J. Obstet. Gynaecol. Res.. 2019.02;
5. Takahashi Kenta, Oshima Noriko, Nakamura Reiko, Iwahara Yuki, Wakana Kimio, Yoshida Masayuki, Miyasaka Naoyuki. Detection of hereditary gynecologic cancer by screening and risk assessment using questionnaires in gynecological outpatient clinic(和訳中) 日本産科婦人科学会雑誌. 2019.02; 71(臨増); S-196
6. Yamada Ichiro, Miyasaka Naoyuki, Kobayashi Daisuke, Wakana Kimio, Oshima Noriko, Wakabayashi Akira, Saida Yukihisa, Tateishi Ukihide, Eishi Yoshinobu. Endometrial Carcinoma: Texture Analysis of Apparent Diffusion Coefficient Maps and its Correlation with Histopathologic Findings and Prognosis(和訳中) 日本医学放射線学会学術集会抄録集. 2019.02; 78 回; S290
7. Saitou Kazuki, Ishikawa Tomonori, Tatsumi Kenichi, Nakasuji Takashi, Hiramitsu Shiro, Iwahara Yuki, Miyasaka Naoyuki. Successful delivery of a patient with P450 oxidoreductase deficiency(和訳中) 日本産科婦人科学会雑誌. 2019.02; 71(臨増); S-223
8. Fudono Ayako, Sato Noriko, Miyasaka Naoyuki. Trimester specific difference in exosomal microRNA expression(和訳中) 日本産科婦人科学会雑誌. 2019.02; 71(臨増); S-200
9. Jwa Seung Chik, Nakashima Akira, Kuwahara Akira, Saito Kazuki, Irahara Minoru, Sakumoto Tetsuro, Ishihara Osamu, Saito Hidekazu. Neonatal outcomes following different ovarian stimulation protocols in fresh single embryo transfer SCIENTIFIC REPORTS. 2019.02; 9(1); 3076

10. Hiramitsu Shiro, Ishikawa Tomonori, Umetani Michihisa, Miyasaka Naoyuki. 27-ヒドロキシコレステロールのエストロゲン受容体 β を介した肺がん細胞の増殖の調節 (Estrogen Receptor Beta-Mediated Modulation of Lung Cancer Cell Proliferation by 27-Hydroxycholesterol) 日本産科婦人科学会雑誌. 2019.02; 71(臨増); S-149
11. Hirose Asuka, Terauchi Masakazu, Odai Tamami, Yomogita Hiroshi, Tsurane Kotoi, Egawa Makiko, Miyasaka Naoyuki. 産後うつは出産後数日以内の抗酸化活性と関連している (Postpartum depression is associated with antioxidative activity within few days after delivery) 日本産科婦人科学会雑誌. 2019.02; 71(臨増); S-263
12. Pavethynath S, Imai C, Jin X, Hichiwa N, Takimoto H, Okamitsu M, Tarui I, Aoyama T, Yago S, Fudono A, Muramatsu M, Miyasaka N, Sato N. Metabolic and Immunological Shifts during Mid-to-Late Gestation Influence Maternal Blood Methylation of *CPT1A* and *SREBF1*. International journal of molecular sciences. 2019.03; 20(5);
13. Mayumi Kobayashi-Kato, Mayu Yunokawa, Seiko Bun, Naoyuki Miyasaka, Tomoyasu Kato, Kenji Tamura. Platinum-free interval affects efficacy of following treatment for platinum-refractory or -resistant ovarian cancer. Cancer Chemother. Pharmacol.. 2019.04;
14. Ryuji Kawaguchi, Koji Matsumoto, Shigeo Akira, Ken Ishitani, Kazuhiro Iwasaku, Yutaka Ueda, Ryugo Okagaki, Hiroya Okano, Toshimichi Oki, Kaori Koga, Michiko Kido, Takumi Kurabayashi, Yasushi Kuribayashi, Yuichi Sato, Kaori Shiina, Yasushi Takai, Satoshi Tanimura, Osamu Chaki, Masakazu Terauchi, Yukiharu Todo, Yasuyuki Noguchi, Sayaka Nose-Ogura, Tsukasa Baba, Akira Hirasawa, Takuma Fujii, Tsuneo Fujii, Tetsuo Maruyama, Etsuko Miyagi, Kaoru Yanagida, Osamu Yoshino, Mitsutoshi Iwashita, Tsugio Maeda, Takashi Minegishi, Hiroshi Kobayashi. Guidelines for office gynecology in Japan: Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG) 2017 edition J. Obstet. Gynaecol. Res.. 2019.04; 45(4); 766-786
15. Nakasuji Takashi, Kawai Kiyotaka, Ishikawa Tomonori, Teraoka Kaori, Takeuchi Shiho, Miyagawa Tomoko, Nara Kazuko, Kidera Nobuyuki, Harada Tatsuya, Miyasaka Naoyuki. Random-start ovarian stimulation with aromatase inhibitor for fertility preservation in women with Japanese breast cancer(和訳中) Reproductive Medicine and Biology. 2019.04; 18(2); 167-172
16. Nakasuji T, Kawai K, Ishikawa T, Teraoka K, Takeuchi S, Miyagawa T, Nara K, Kidera N, Harada T, Miyasaka N. Random-start ovarian stimulation with aromatase inhibitor for fertility preservation in women with Japanese breast cancer. Reproductive medicine and biology. 2019.04; 18(2); 167-172
17. Sekiguchi M, Mikami M, Nakagawa C, Ozaki M, Tanigaki S, Kobayashi T, Miyasaka N, Sago H. An ultrasonographic estimated fetal weight reference for Japanese twin pregnancies. Journal of Medical Ultrasonics. 2019.04; 46(2); 209-215
18. Diffusion kurtosis imaging of endometrial carcinoma: Correlation with histopathological findings Magn Reson Imaging. 2019.04; 57; 337-346
19. Oi R, Miyasaka N, Yamashita T, Adachi T. Associations of temporal changes in cervical length and lower uterine segment length with spontaneous preterm delivery risk: a prospective study of 727 Japanese women J Med Ultrason (2001). 2019.04; 46(2); 201-207
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[Misc]

1. Masakazu Terauchi. The effect of estradiol on muscle breakdown may be different between women in early and late postmenopause Menopause Live. 2019.07; (7/22);

[Conference Activities & Talks]

1. Arvand Asghari, Shiro Hiramitsu, Kevin Dao, Michihisa Umetani. 27-Hydroxycholesterol a Selective Estrogen Receptor Modulator: Profiling 27-Hydroxycholesterol Effects on Estrogen Receptor Activity in Mice. ENDO 2019 Meeting 2019.03.24 New Orleans, USA
2. Asuka Hirose, Masakazu Terauchi, Odai Tamami, Ayako Fudono, Makiko Egawa, Mihoko Akiyoshi, Kiyoko Kato, and Naoyuki Miyasaka.. Postpartum depression is associated with psychological symptom in the second trimester and antioxidative activity in the immediate postpartum period. 第71回日本産科婦人科学会学術講演会 2019.04.12 名古屋
3. Ayako Fudono, Noriko Sato, Naoyuki Miyasaka. Trimester specific difference in exosomal microRNA expression. 第71回日本産科婦人科学会学術講演会 2019.04.12 名古屋
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7. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Chilliness in Japanese middle-aged women is associated with low intake of n-3 fatty acids: a cross-sectional study. 12th European Congress on Menopause and Andropause 2019.05.15 Berlin
8. Tamami Odai, Masakazu Terauchi, Kiyoko Kato, Asuka Hirose, Naoyuki Miyasaka. Effects of grape seed proanthocyanidin extract on vascular endothelial function in patients with prehypertension: a randomized, double-blind, placebo-controlled study. 12th European Congress on Menopause and Andropause 2019.05.15 Berlin
9. Pavethynath Shilpa, 今井千裕, JIN Xin, 飛知和尚美, 瀧本秀美, 岡光基子, 樽井依織, 青山友子, 矢郷哲志, 不殿絢子, 宮坂尚幸, 佐藤憲子. 妊娠後半期の末梢血における脂質関連遺伝子の DNA メチル化. 第73回日本栄養・食糧学会大会 2019.05.18
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11. Masakazu Terauchi. Is the combined transdermal estradiol and micronized progesterone the better and safer MHT?. 7th Scientific Meeting of the Asia Pacific Menopause Federation 2019.05.29 Manila, Philippines
12. Shiro Hiramitsu, Tomonori Ishikawa, Takayuki Tatsumi, Kazuki Saito, Takashi Nakasuji, Yuki Iwahara, Kiyotaka Kawai, Naoyuki Miyasaka. Hysteroscopic Resection of Endometrial Polyps for Infertility. The 37th Japan Society of Fertilization and Implantation congress 2019.08.01

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14. Shiro Hiramitsu, Takayuki Tatsumi, Kazuki Saito, Takashi Nakasuji, Yuki Iwahara, Tomonori Ishikawa, Naoyuki Miyasaka. Hysteroscopic Resection of Endometrial Polyps for Infertility. The 59th Japan Society of Gynecologic and Obstetric Endoscopy and Minimally Invasive Therapy Congress 2019.09.12 Kyoto
15. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Chilliness in Japanese middle-aged women is associated with anxiety and low intake of n-3 fatty acids: a cross-sectional study. 19th International Society of Psychosomatic Obstetrics and Gynecology Congress 2019.10.12 Den Haag
16. Tamami Odai, Masakazu Terauchi, Risa Suzuki, Asuka Hirose, Kiyoko Kato, Naoyuki Miyasaka. Depressive symptoms in middle-aged and elderly women are inversely associated with dietary intake of vitamin B6. The 19th Congress of the International Society of Psychosomatic Obstetrics and Gynaecology 2019.10.12 Dutch
17. Sato N, Miyasaka N. Gestational Weight Gain and Birthweight-for-Gestational Age: TMDU Hospital Cohort Study. DOHAD 2019 Congress 2019.10.22 Melbourne, Australia
18. Imai C, Pavethynath S, Xin J, Hichiwa N, Takimoto H, Okamitsu M, Tarui I, Aoyama T, Yago S, Fudono A, Muramatsu M, Miyasaka N, Sato N. Intra- and Inter- individual Differences in CPT1A and SREBF1 Methylation of Maternal Leukocytes During Mid-to-Late Gestation. DOHAD 2019 Congress 2019.10.22 Melbourne, Australia
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21. Oshima N, Takahashi K, Nakamura R, Yoshino Y, Wakana K, Ikeda S, Miyasaka N. Precision Medicine for gynecologic tumors in our hospital. 第 57 回日本癌治療学会 2019.10.24
22. TAKAHASHI KENTA, Kumaki Yuichi, Yokobori Junko, Takamine Eriko, Oshima Noriko, Wakana Kimio, Ishikawa Toshiaki, Ban Daisuke, Kudo Atsushi, Kimura Koichiro, Nakagawa Tsuyosh, Tanabe Minoru, Miyasaka Naoyuki, Miyake Satoshi, Ikeda Sadakatsu. Prospects of Liquid biopsy in precision medicine; From the result of PROFILE study: a prospective observational study of precision medicine approach in solid tumors in Japan.. 2019.10.26

[Awards & Honors]

1. JSOG Congress Encouragement Award , The Japan Society of Obstetrics and Gynecology , 2019.04

Urology

Professor and Chairman: Yasuhisa Fujii

Associate Professor: Kazutaka Saito

Junior Associate Professor: Yoh Matsuoka,

Junichiro Ishioka (Department of Insured Medical Care Management), Minato Yokoyama

Assistant Professor: Soichiro Yoshida, Toshiki Kijima, Yosuke Yasuda, Sho Uehara

Project Assistant Professor: Shingo Moriyama (April -), Yuma Waseda (April - June), Shohei Fukuda (April -)

Hospital Staff: Yuma Waseda (- March), Hiroshi Fukushima (July -), Shohei Fukuda (- March), Masahiro Toide, Yuichi Fukuda (- June), Kasumi Kaneko (April -), Kenji Tanabe (April -)

Graduate Student: Saori Araki, Yosuke Yasuda (- March), Sho Uehara (- March), Yuma Waseda, Hiroshi Fukushima,

Shingo Moriyama, Shohei Fukuda (April -), Yusuke Uchida (April -), Masahiro Toide (April -)

Project Professor: Kazunori Kihara

(1) Outline

Urology is the branch of medicine that focuses on surgical and medical diseases of the male and female urinary-tract system and the male reproductive organs. 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” .

(2) Research

Clinical Research

1. A minimally invasive surgery, minimum-incision endoscopic urological surgery
2. Optimal MRI-ultrasonography fusion prostate needle biopsy
3. Curative and minimally invasive bladder preservation using transurethral resection of bladder tumor, low-dose chemoradiotherapy and partial cystectomy
4. Minimum-incision endoscopic clampless partial nephrectomy against kidney cancer
5. Focal brachytherapy against localized prostate cancer
6. Diffusion-weighted MRI to diagnosis, assessment of therapeutic effects and monitoring of relapse in urological cancer
7. Whole body MRI using DWIBS technique
8. Imaging diagnosis for prostate and kidney cancers using deep learning
9. Serum C-reactive protein as a prognostic biomarker of urological malignancies
10. Prognostic prediction model for non-muscle-invasive bladder cancer
11. Renal function after kidney cancer surgery
12. Prevention of postoperative inguinal hernia after robot assisted radical prostatectomy

Translational Research

1. Biomarker in bladder preservation therapy using chemoradiotherapy

2. Overcoming therapeutic resistance to immune-check point inhibitors for urological cancers
3. Mechanisms of abscopal effect of immune-check point inhibitors and radiation in urothelial cancer

(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 including robot-assisted surgery and laparoscopic sacrocolpopexy, we are making a continuous effort to improve daily practices. To realize the mission, we have been developing various procedures with high quality and affordable cost.

1. Minimum-incision endoscopic urological surgery which can be applied to most of patients with urological tumors
2. Tetra-modal bladder sparing treatment consisting of transurethral resection of bladder tumor, low-dose chemoradiotherapy and partial cystectomy with pelvic lymph node dissection
3. Clamless partial nephrectomy
4. Focal brachytherapy
5. Prediction model of non-muscle invasive bladder cancer
6. Diagnostic model for small renal masses
7. Clinical implication of diffusion-weighted MRI

(5) Publications

[Original Articles]

1. Hiroshi Watanabe, Hajime Tanaka, Yasuhisa Fujii, Makoto Kodama, Takumi Akashi, Tomoyuki Fujioka, Kazunori Kubota, Yukihisa Saida, Ukihide Tateishi. A case of immunoglobulin G4-related inflammatory pseudotumor mimicking renal cell carcinoma. *Abdom Radiol (NY)*. 2019.01;
2. Kawamura Naoko, Yokoyama Minato, Tanaka Hajime, Nakayama Takayuki, Yasuda Yosuke, Kijima Toshiki, Yoshida Soichiro, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Acute kidney injury and intermediate-term renal function after clamless partial nephrectomy(和訳中) *International Journal of Urology*. 2019.01; 26(1); 113-118
3. Hiroshi Fukushima, Yasuhisa Fujii, Fumitaka Koga. Metabolic and Molecular Basis of Sarcopenia: Implications in the Management of Urothelial Carcinoma. *Int J Mol Sci*. 2019.02; 20(3);
4. Kijima T, Tanaka H, Koga F, Masuda H, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Selective Tetramodal Bladder Preservation Therapy Incorporating Induction Chemoradiotherapy and Consolidative Partial Cystectomy with Pelvic Lymph Node Dissection for Muscle-Invasive Bladder Cancer: Oncological and Functional Outcomes of 107 Patients. *BJU international*. 2019.02;
5. Jitao Wu, Chalairat Suk-Ouichai, Wen Dong, Zhiling Zhang, Hajime Tanaka, Yanbo Wang, Elvis Caraballo, Erick M Remer, Jianbo Li, Sudhir Isharwal, Robert Abouassaly, Steven C Campbell. Vascularized Parenchymal Mass Preserved with Partial Nephrectomy: Functional Impact and Predictive Factors. *Eur Urol Oncol*. 2019.02; 2(1); 97-103
6. Waseda Yuma, Saito Kazutaka, Ishikawa Yudai, Kawano Keizo, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Morimoto Shinji, Kihara Kazunori, Fujii Yasuhisa. Predictive ability of renal cortex enhancement in dynamic computed tomography for residual renal function after nephroureterectomy: Comparison with 99m Tc-diethylenetriaminopentacetic acid renography and validation study. *International Journal of Urology*. 2019.02; 26(2); 266-272

7. Yajima S, Yoshida S, Takahara T, Arita Y, Tanaka H, Waseda Y, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Usefulness of the inchworm sign on DWI for predicting pT1 bladder cancer progression. *European radiology*. 2019.03;
8. Elvis R Caraballo, Diego Aguilar Palacios, Chalairat Suk-Ouichai, Jitao Wu, Wen Dong, Hajime Tanaka, Yanbo Wang, Brian R Lane, Steven C Campbell. Open partial nephrectomy when a non-flank approach is required: indications and outcomes. *World J Urol*. 2019.03; 37(3); 515-522
9. Kijima Toshiaki, Fukuda Shohei, Fukushima Hiroshi, Moriyama Shingo, Uehara Sho, Yasuda Yosuke, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Fujii Yasuhisa. Clinical outcomes of muscle-invasive bladder cancer patients with hydronephrosis treated with tetra-modality bladder sparing therapy incorporating consolidative partial cystectomy. *JOURNAL OF CLINICAL ONCOLOGY*. 2019.03; 37(7);
10. Hajime Tanaka, Yanbo Wang, Chalairat Suk-Ouichai, Diego Aguilar Palacios, Elvis R Caraballo, Yunlin Ye, Erick M Remer, Jianbo Li, Robert Abouassaly, Steven C Campbell. Can We Predict Functional Outcomes after Partial Nephrectomy? *J. Urol.*. 2019.04; 201(4); 693-701
11. Arita Yuki, Takahara Taro, Yoshida Soichiro, Kwee Thomas C, Yajima Shugo, Ishii Chikako, Ishii Ryota, Okuda Shigeo, Jinzaki Masahiro, Fujii Yasuhisa. Quantitative Assessment of Bone Metastasis in Prostate Cancer Using Synthetic Magnetic Resonance Imaging. *Invest Radiol*. 2019.05;
12. Toshiaki Kijima, Thomas Prince, Len Neckers, Fumitaka Koga, Yasuhisa Fujii. Heat shock factor 1 (HSF1)-targeted anticancer therapeutics: overview of current preclinical progress. *Expert Opin. Ther. Targets*. 2019.05; 23(5); 369-377
13. Yoshida S, Takahara T, Arita Y, Ishii C, Uchida Y, Nakagawa K, Toda K, Sakamoto T, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Yoshimura R, Fujii Y. Progressive Site-Directed Therapy for Castration-Resistant Prostate Cancer: Localization of the Progressive Site as a Prognostic Factor. *International journal of radiation oncology, biology, physics*. 2019.06;
14. Yoshida Soichiro, Sugimoto Maki, Fukuda Shohei, Taniguchi Naoji, Saito Kazutaka, Fujii Yasuhisa. Mixed reality computed tomography-based surgical planning for partial nephrectomy using a head-mounted holographic computer. *Int J Urol*. 2019.06; 26(6); 681-682
15. Yoshida Soichiro, Maeda Takeshi, Yokoyama Minato, Toide Masahiro, Saito Kazutaka, Fujii Yasuhisa. Application of eye tracking as a user interface for urological surgery. *Int J Urol*. 2019.06; 26(6); 680-681
16. Chalairat Suk-Ouichai, Hajime Tanaka, Yanbo Wang, Jitao Wu, Yunlin Ye, Sevag Demirjian, Jianbo Li, Steven C Campbell. Renal Cancer Surgery in Patients without Preexisting Chronic Kidney Disease-Is There a Survival Benefit for Partial Nephrectomy? *J. Urol.*. 2019.06; 201(6); 1088-1096
17. Yoshida Soichiro, Fujii Yasuhisa. Editorial Comment to Virtual reality of three-dimensional surgical field for surgical planning and intraoperative management. *Int J Urol*. 2019.07;
18. Kobayashi Masaki, Tanaka Hajime, Tateishi Ukihide, Numao Noboru, Yonese Junji, Ito Masaya, Koga Fumitaka, Fukushima Hiroshi, Uehara Sho, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Impact of fluorodeoxyglucose uptake on positron emission tomography/computed tomography on chemosensitivity and survival in patients with metastatic urothelial carcinoma. *Int J Urol*. 2019.08; 26(8); 820-826
19. Hajime Tanaka, Xiaobo Ding, Yunlin Ye, Yanbo Wang, Rebecca A Campbell, Molly E DeWitt-Foy, Chalairat Suk-Ouichai, Ryan D Ward, Erick M Remer, Jianbo Li, Steven C Campbell. Infiltrative Renal Masses: Clinical Significance and Fidelity of Documentation. *Eur Urol Oncol*. 2019.08;
20. Yanbo Wang, Hajime Tanaka, Yunlin Ye, Xiaobo Ding, Ryan D Ward, Rebecca A Campbell, Molly E DeWitt-Foy, Chalairat Suk-Ouichai, Erick M Remer, Steven C Campbell. The Complete Spectrum of Infiltrative Renal Masses: Clinical Characteristics and Prognostic Implications. *Urology*. 2019.08; 130; 86-92
21. Kobayashi Masaki, Tanaka Hajime, Tateishi Ukihide, Numao Noboru, Yonese Junji, Ito Masaya, Koga Fumitaka, Fukushima Hiroshi, Uehara Sho, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Impact of fluorodeoxyglucose uptake on positron emission tomography/computed tomography on chemosensitivity and survival in patients with metastatic urothelial carcinoma *International Journal of Urology*. 2019.08; 26(8); 820-826

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23. Hiroshi Fukushima, Yasuhisa Fujii. Editorial Comment to Does asymptomatic bacteriuria affect the response to intravesical bacillus Calmette-Guérin? *Int. J. Urol.*. 2019.10;
24. Masahiro Toide, Minato Yokoyama, Motohiro Fujiwara, Toshiki Kijima, Kazutaka Saito, Yasuhisa Fujii. Renal function after bladder-preserving therapy for patients with muscle-invasive bladder cancer: Results of selective bladder-preserving tetramodality therapy consisting of maximal transurethral resection, induction chemoradiotherapy and partial cystectomy. *Int. J. Urol.*. 2019.10; 26(10); 1010-1012
25. Rebecca A Campbell, Molly E DeWitt-Foy, Hajime Tanaka, Yun-Lin Ye, Yanbo Wang, Jeffrey Reese, Venkatesh Krishnamurthi, Wen Dong, Steven C Campbell. Functional Recovery From Prolonged Warm Ischemia: Compelling Case Scenarios. *Urology*. 2019.10; 132; 22-27
26. Hiroshi Fukushima, Kazutaka Saito, Yosuke Yasuda, Hajime Tanaka, Dattatraya Patil, Brittney H. Cotta, Sunil H. Patel, Viraj A. Master, Ithaar H. Derweesh, Yasuhisa Fujii. Female sex predicts favorable prognosis in non-metastatic clear cell renal cell carcinoma patients undergoing curative surgery: results from the International Marker Consortium for Renal Cancer (INMARC) 2019.11;
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28. Toshiki Kijima, Hajime Tanaka, Sho Uehara, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Clinical Outcomes of Patients With Histologic Variants of Urothelial Carcinoma Treated With Selective Tetramodal Bladder-preservation Therapy Incorporating Consolidative Partial Cystectomy 2019.12;
29. Soichiro Yoshida, Taro Takahara, Chikako Ishii, Yuki Arita, Yuma Waseda, Toshiki Kijima, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii. METastasis Reporting and Data System for Prostate Cancer as a Prognostic Imaging Marker in Castration-resistant Prostate Cancer 2019.12;
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[Conference Activities & Talks]

1. Kijima T., Fukuda S., Fukushima H., Moriyama S., Uehara S., Yasuda Y. Yoshida S., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Fujii Y.. Clinical outcomes of muscle-invasive bladder cancer patients with hydronephrosis treated with tetramodality bladder sparing therapy incorporating consolidative partial cystectomy.. *Genitourinary Cancers Symposium* 2019.02.15 San Francisco, USA
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3. M.Kobayashi,H.Msuda,M,Ito,Y.Waseda,Y.Fujii. 787:Artificial urinary sphincter implantation improves several storage and voiding symptoms in addition to urinary incontinence. 2019.03
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Gastrointestinal Surgery

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(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]**

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[Books etc]

1. Tomohiro Yamaguchi and Yusuke Kinugasa. Recent Advances in the Treatment of Colorectal cancer. Springer Nature Singapore, 2019.01 (ISBN : 978-981-13-3049-0)

[Conference Activities & Talks]

1. Mikito Inokuchi, Masatoshi Nakagawa, Toshiro Tanioka, Emi Kanemoto,Yuya Umebayashi, Toshifumi Saito, Ryosuke Fukuyo, Yasuaki Nakajima, Yusuke Kinugasa, Kazuyuki Kojima. Robotic gastrectomy using an ultrasonically activated device for gastric cancer. 91st Annual Meeting of the Japanese Gastric Cancer Association 2019.02.28 Numazu
2. Toshiro Tanioka, Kazuyuki Kojima, Ryosuke Fukuyo, YuyaUmebayashi, Toshifumi Saito, Emi Kanemoto, Kenta Kobayashi, Masatoshi Nakagawa, Takatoshi Matsuyama, Mikito Inokuchi, Yasuaki Nakajima, Yusuke Kinugasa. Comparing short-term outcomes between robotic and laparoscopic gastrectomy. 91st Annual Meeting of the Japanese Gastric Cancer Association 2019.03.01 Numazu
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4. Emi Kanemoto, Kazuyuki Kojima, Masatoshi Nakagawa, Mikito Inokuchi, Kenta Kobayashi, Toshiro Tanioka, Kentaro Gokita, Keisuke Okuno, Takatoshi Matsuyama, Yasuaki Nakajima, Yusuke Kinugasa. Implications of less impact of obesity on laparoscopic VS open approach. 91st Annual Meeting of the Japanese Gastric Cancer Association 2019.03.01 Numazu
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8. Masatoshi Nakagawa, Yuya Umebayashi, Toshifumi Saito, Ryosuke Fukuyo, Emi Kanemoto, Troshiro Tanioka, Kenta Kobayashi, Takatoshi Matsuyama, Yasuaki Nakajima, Mikito Inokuchi, Yusuke Kinugasa, Kazuyuki Kojima. Strategy for minimizing intraoperative troubles and trouble-shooting in laparoscopic gastrectomy. 91st Annual Meeting of the Japanese Gastric Cancer Association 2019.03.01 Numazu
9. Shinichi Yamauchi, Yasuko Aoyagi, Yudai Yamamoto, Ayumi Takaoka, Hironobu Baba, Akifumi Kikuchi, Satoshi Okazaki, Takatoshi Matsuyama, Toshiaki Ishikawa, Yasuaki Nakajima, Kazuyuki Kojima, Hiroyuki Uetake, Yusuke Kinugasa, Kenichi Sugihara. Clinical significance of extended lateral lymph node dissection for patients with lower rectal cancer: A propensity score analysis in a multicenter retrospective study. SSO 2019 Annual Cancer Symposium (72nd Annual Cancer Symposium of the Society of Surgical Oncology) 2019.03.29 San Diego(USA)
10. Takahiro Kinoshita, Masanori Tokunaga, Akio Kaitou, Takeo Fujita, Hisashi Fujiwara, Akiko Tonouchi, Akira Kameyama, Eigo Akimoto, Takeshi Ono, Hiroyuki Daikou. Clinical outcomes and perspectives of laparoscopic surgery for advanced gastric cancer. The 119th Annual Congress of Japan Surgical Society 2019.04.19 Osaka
11. Mikito Inokuchi, Masatoshi Nakagawa, Toshiro Tanioka, Kenta Kobayashi, Emi Kanemoto, Yuya Umebayashi, Toshifumi Saito, Ryosuke Fukuyo, Yasuaki Nakajima, Yusuke Kinugasa, Kazuyuki Kojima. Knacks of the assistant operator in laparoscopic gastrectomy with D2 lymphadenectomy. The 119th Annual Congress of Japan Surgical Society 2019.04.19 Osaka
12. Yusuke Kinugasa. The surgical technique and outcome of robotic rectal cancer surgery. FIS2019(2019 Annual meeting Focus in Surgery Beijing) 2019.04.26 Beijing
13. Masanori Tokunaga, Yukinori Kurokawa, Yuichiro Doki, Ryunosuke Machida, Shuji Takiguchi, Yuya Sato, Hitoshi Katai, Norimasa Fukushima, Yasunori Nishida, Haruhiko Cho, Takanobu Yamada, Masahide Kaji, Junya Fujita, Narikazu Boku, Takaki Yoshikawa, Masanori Terashima. The Impact of postoperative complications on survival outcomes in patients with cT3/4a gastric cancer. 2019 ASCO Annual Meeting 2019.06.03 Chicago
14. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Akihiro Hoshino, Takuya Okada, Tairo Ryotokuji, Kazuya Yamaguchi, Kagami Nagai, Tatsuyuki Kawano, Yusuke Kinugasa. A feasibility study of mediastinoscopic radical esophagectomy for thoracic esophageal cancer. The 73d Annual Meeting of the Japan Esophageal Society 2019.06.07 Fukuoka
15. Yusuke Kinugasa. Can MRI help detect enlarged lateral lymph nodes?. 12th Russian School of Colorectal Surgery Conference 2019.06.07 Moscow
16. Yusuke Kinugasa. Rectal cancer surgery based on anatomy. 12th Russian School of Colorectal Surgery Conference 2019.06.08 Moscow
17. Yusuke Kinugasa. Robotic. 12th Russian School of Colorectal Surgery Conference 2019.06.09 Moscow
18. Yusuke Kinugasa. Robotic surgery for locally advanced low rectal cancer. The 15th Shanghai International Colorectal Cancer Symposium 2019.06.16 Shanghai
19. Yusuke Kinugasa. Robotic surgery for colorectal cancer in Japan. TMDU International Summer Program 2019 2019.07.09 Tokyo
20. Yusuke Kinugasa. The surgical technique and outcome of robotic rectal cancer surgery. IASGO-CME(International Association of Surgeons, Gastroenterologists and Oncologists) Continuing Medical Education: Advanced Post-Graduate Course in Tokyo 2019 2019.07.10 Tokyo
21. Yusuke Kinugasa. Surgical Technique and the Related Anatomical Study of Robotic Transabdominal Intersphincteric Resection for Distal Rectal Cancer. Minimally Invasive Surgery and Multidisciplinary Treatment for Colorectal Cancer 2019.09.07 Taipei
22. Kenro Kawada, Yasuaki Nakajima, Yutaka Tokairin, Akihiro Hoshino, Takuya Okada, Toshihiro Matsui, Kazuya Yamaguchi, Yusuke Kinugasa. The accuracy of the preoperative diagnosis of lymph node metastasis using computed tomography for T1B esophageal cancer patients receiving esophagectomy after endoscopic treatment. UEG Week 2019(United European Gastroenterology) 2019.10.21 Barcelona

23. Kazuya Yamaguchi, Kenro Kawada, Kazuharu Aoyama, Toshihiro Matsui, Takuya Okada, Akihiro Hoshino, Yutaka Tokairin, Yasuaki Nakajima, Yusuke Kinugasa, Youichi Kumagai, Tomohiro Tada. The application of artificial intelligence using a convolutional neural network for detecting head and neck cancer in endoscopic images. UEG Week 2019(United European Gastroenterology) 2019.10.21 Barcelona
24. Toshiro Tanioka, Akihiro Hoshino, Takatoshi Matsuyama, Yusuke Kinugasa. Usefulness of Self-Made Instruction Manual for Laparoscopic Surgery. American College of Surgeons Clinical Congress 2019 2019.10.29 San Francisco
25. Yusuke Kinugasa. Laparoscopic (Robotic) D3 LN Dissection for Right Colon Cancer. Annual congress of KSS 2020 2019.11.02 Seoul
26. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Masafumi Okuda, Taichi Ogo, Katsumasa Saito, Naoto Fujiwara, Tairou Ryoutokuji, Takuya Okada, Yutaka Miyawaki, Youichi Kumagai, Kagami Nagai, Tatsuyuki Kawano. . Efficacy of endoscopy for evaluating esophago-gastric anastomosis on post-esophagectomy day 1. . 14th World Congress of the International Society for Diseases of the Esophagus

Thoracic Surgery

Professor Kenichi Okubo
 Junior Associate Professor Hironori Ishibashi
 Assistant Professor Masashi Kobayashi
 Hospital assistant professor Sachiko Imai
 Graduate Student Akiko Sugawara
 Graduate Student Ken Takahashi
 Graduate Student Katsutoshi Seto
 Graduate Student Ryo Wakejima
 Graduate Student Syunichi Baba
 Graduate Student Yasuhiro Nakashima
 Graduate Student Ayaka Asakawa
 Graduate Student Yuya Ishikawa
 Graduate Student Mariko Takemura

(1) Outline

Department of Thoracic Surgery deal with clinical management, basic and clinical research, and education of thoracic surgery, which includes surgical diagnosis and treatment of respiratory diseases.

(2) Research

- Minimally invasive surgery for lung cancer
- Multimodal treatments for thoracic malignancies
- Surgery for metastatic lung tumors
- Clinico-pathological studies on lung cancer

(3) Education

Department of Thoracic Surgery has a mission to educate medical post-graduates for expert thoracic surgeons. Thoracic surgeon requires the Board of Surgery and the Board of Thoracic Surgery to perform clinical cares as a specialist. We provide clinical specialty course for thoracic surgery and graduate course for thoracic surgery, and support to obtain the boards.

(4) Clinical Services & Other Works

Out-patient Clinic: Tuesday, Thursday, Friday
 Operative Day: Monday, Wednesday, Thursday, Friday
 Clinical Conference: Monday
 Chest Conference : Monday
 Clinico-pathological Conference: Wednesday
 Medical Round: every morning
 Professor's Round: Tuesday
 Journal Club: Tuesday (every other week)

Mortality & Morbidity Conference: Tuesday (every other week)

Lab Meeting: Tuesday (monthly)

Scientific Meeting: Japan Surgical Society, Japanese Association for Chest Surgery, Japanese Association for Thoracic Surgery, Japan Lung Cancer Society, Japan Society for Respiratory Endoscopy

(5) Clinical Performances

Thoracic Surgery deal with surgical treatment for lung, mediastinum, pleura and chest wall. We provide high-grade medical care as a university hospital. We offer less invasive surgery for early-stage lung cancers or benign diseases, and multimodality treatment for locally advanced thoracic malignancies.

(6) Publications

[Original Articles]

1. Masashi Kobayashi, Hironori Ishibashi, Chihiro Takasaki, Sachiko Imai, Susumu Kirimura, Kenichi Okubo.. Pathological evaluation of the visceral pleura in the radical pleurectomy/decortication for malignant pleural mesothelioma patients. *Journal of Thoracic Disease*. 2019.03; 11(3); 717-723
2. Horinouchi H, Asano F, Okubo K, Okada Y, Ohsaki Y, Komase Y, Hashizume T, Kohno M, Aoe M.. Current status of diagnostic and therapeutic bronchoscopy in Japan: 2016 National survey of bronchoscopy. *Respiratory Investigation*. 2019.05; 57(3); 238-244
3. Ayaka Asakawa, Hirotooshi Horio, Takashi Yamamichi, Masayuki Okui, Masahiko Harada.. Clinical features of HIV-infected patients with non-small-cell lung cancer after lung resection General Thoracic and Cardiovascular Surgery. *General Thoracic and Cardiovascular Surgery* [First Online: 31 May 2019] . 2019.05;
4. Masaaki Sato, Kazuhiro Nagayama, Masashi Kobayashi, Jun Nakajima.. Virtual-assisted lung mapping 2.0: preoperative bronchoscopic three-dimensional lung mapping. *The Annals of thoracic surgery*. *The Annals of Thoracic Surgery*. 2019.07; 108(1); 269-273
5. Mikubo M, Seto K, Kitamura A, Nakaguro M, Hattori Y, Maeda N, Miyazaki T, Watanabe K, Murakami H, Tsukamoto T, Yamada T, Fujita S, Masago K, Ramkissoon S, Ross JS, Elvin J, Yatabe Y.. Calculating the Tumor Nuclei Content for Comprehensive Cancer Panel Testing. *Journal of Thoracic Oncology*. [Epub ahead of print 2019 Oct 9] . 2019.10;
6. Ryo Wakejima, Kentaro Inamura, Hironori Ninomiya, Hiroko Nagano, Mingyon Mun, Sakae Okumura, Kenichi Okubo, Yuichi Ishikawa.. Mucinous lung adenocarcinoma, articularly referring to EGFR-mutated mucinous adenocarcinoma. *Pathology international*. 10 November 2019 [In press] . 2019.11;

[Others]

1. Bilateral cardiac sympathetic denervation of a recurrent refractory ventricular tachycardia occurring after catheter ablation of atrial fibrillation and outflow tract premature ventricular contractions., 2019.01 *Journal of Arrhythmia*. 2019;Jan 30; 35(2): 287-289. Atsuhiko Yagishita, Masahiko Goya, Yoshihide Takahashi, Hironori Ishibashi, Kikou Akiyoshi, Masahiro Sekigawa, Shingo Maeda, Mihoko Kawabata, Kenichi Okubo, Kenzo Hirao.
2. Successful Excision of Endobronchial Cellular Schwannoma With Right Lower Sleeve Lobectomy., 2019.03 *The Annals of Thoracic Surgery* March 2019.Volume 107,e203-5. Hironori Ishibashi, Ryo Wakejima, Chihiro Takasaki, Kenichi Okubo.
3. Successful excision of epithelioid hemangioendothelioma of the superior vena cava., 2019.08 *The Annals of Thoracic Surgery*. Available online 28 August 2019. Hironori Ishibashi, Chihiro Takasaki, Takumi Akashi, Kenichi Okubo.

Igakuken Disease-oriented Molecular Biology

Visiting Professor Takahiko Hara

Visiting Professor Makoto Arai

Visiting Professor Masato Hasegawa

Visiting Professor Haruo Okado

Associate Visiting Professor Takashi Shichita

Associate Visiting Professor Yuichiro Mitaoka

Graduate Student Takuya Yagi, Eiji Katada,
Yuki Mizuoka, Chihiro Nakata (April~), Miho
Nakagawa (April~), Miyu Tanikawa (April~),
Kaho Ishige (April~), Mai Asakura (April~),
Akari Nakamura (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.

[Makoto Arai] 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.

[Takashi Shichita] To develop the therapeutic method for stroke and dementia, we will clarify the cellular and molecular mechanisms underlying sterile inflammation and tissue repair after brain tissue injury. In addition to the classical method of molecular biology and biochemistry, the latest analysis methods of immunology, neuroscience, and epigenetics are applied to our research.

[Yuichiro Miyaoka] Our goal is to develop new therapeutic approaches for genetic disorders by using genome editing in human iPS cells. We introduce causative mutations of heart and liver diseases into human iPS cells to study the pathogenic mechanism by analyzing these cells with cellular and molecular biology techniques such as PCR and immuno-staining. We also seek for ways to improve genome editing technologies including CRISPR/Cas9 to achieve precise genome editing.

(2) Education

We will educate students for the purpose that they could investigate molecular mechanisms of life-threatening diseases such as cancer, diabetes, schizophrenia, amyotrophic lateral sclerosis, and brain malformations. Trained students will eventually help us to develop novel therapeutic strategies against them. In addition, they must learn the importance of good animal models (including genetically engineered mice), which faithfully reproduce symptom and progression of the diseases.

(3) Publications

[Original Articles]

1. M. Nakajima, T. Suzuki, T. Hara, and K. Kitajima. In vitro differentiation of mouse T cell-derived hybrid cells obtained through cell fusion with embryonic stem cells. *Biochem. Biophys. Res. Commun.*, 513: 701-707, 2019.
2. H. Tabata, T. Hara, and K. Kitajima. Inhibitory action of an ERK1/2 inhibitor on primitive endoderm cell differentiation from mouse embryonic stem cells. *Biochem. Biophys. Res. Commun.*, 512: 399-404, 2019.

3. N. Yokote, M. Y. Suzuki-Kosaka, T. Michiue, T. Hara, and K. Tanegashima. Latrophilin2 is involved in neural crest cell migration and placode patterning in *Xenopus laevis*. *Int. J. Dev. Biol.*, 63: 29-35, 2019.
4. R. Mizutani, R. Saiga, A. Takeuchi, K. Uesugi, Y. Terada, Y. Suzuki, V. De Andrade, F. De Carlo, S. Takekoshi, C. Inomoto, N. Nakamura, I. Kushima, S. Iritani, N. Ozaki, S. Ide, K. Ikeda, K. Oshima, M. Itokawa, and M. Arai. Three-dimensional alteration of neurites in schizophrenia. *Transl. Psychiatry*, 9: 85, 2019.
5. A. Shimozawa, Y. Fujita, H. Kondo, Y. Takimoto, M. Terada, M. Sunagi, S. Hisanaga, and M. Hasegawa. Effect of L-DOPA/benserazide on propagation of pathological α -synuclein. *Front. Neurosci.*, 13: 595, 2019.
6. J. Y. Vargas, F. Loria, Y. J. Wu, G. Córdova, T. Nonaka, S. Bellow, S. Syan, M. Hasegawa, G. M. van Woerden, C. Trollet, and C. Zurzolo. The Wnt/ Ca^{2+} pathway is involved in interneuronal communication mediated by tunneling nanotubes. *EMBO J.* 38: e101230, 2019.
7. A. Mori, T. Hatano, T. Inoshita, K. Shiba-Fukushima, T. Koinuma, H. Meng, S. I. Kubo, S. Spratt, C. Cui, C. Yamashita, Y. Miki, K. Yamamoto, T. Hirabayashi, M. Murakami, Y. Takahashi, H. Shindou, T. Nonaka, M. Hasegawa, A. Okuzumi, Y. Imai, and N. Hattori. Parkinson's disease-associated iPLA2-VIA/PLA2G6 regulates neuronal functions and α -synuclein stability through membrane remodeling. *Proc. Natl. Acad. Sci. U. S. A.*, 116: 20689-20699, 2019.
8. M. Sanchez-Valpuesta, Y. Suzuki, Y. Shibata, N. Toji, Y. Ji, N. Afrin, C. N. Asogwa, I. Kojima, D. Mizuguchi, S. Kojima, K. Okanoya, H. Okado, K. Kobayashi, and K. Wada. Corticobasal ganglia projecting neurons are required for juvenile vocal learning but not for adult vocal plasticity in songbirds. *Proc. Natl. Acad. Sci. U. S. A.*, 116: 22833-22843, 2019.
9. S. Yamasaki, S. Ando, M. Richards, S. L. Hatch, S. Koike, S. Fujikawa, S. Kanata, K. Endo, Y. Morimoto, M. Arai, H. Okado, S. Usami, T. A. Furukawa, M. Hiraiwa-Hasegawa, K. Kasai, and A. Nishida. Maternal diabetes in early pregnancy, and psychotic experiences and depressive symptoms in 10-year-old offspring: A population-based birth cohort study. *Schizophr. Res.*, 206: 52-57, 2019.
10. M. Kita, J. Nakae, Y. Kawano, H. Asahara, H. Takemori, H. Okado, and H. Itoh. Zfp238 regulates the thermogenic program in cooperation with Foxo1. *iScience*, 12: 87-101, 2019.

[Review Articles]

1. T. Nonaka and M. Hasegawa. Prion-like properties of assembled TDP-43. *Curr. Opin. Neurobiol.*, 61: 23-28, 2019.
2. I. Kawakami, T. Arai, and M. Hasegawa. The basis of clinicopathological heterogeneity in TDP-43 proteinopathy. *Acta Neuropathol.*, 138: 751-770, 2019.
3. H. Okado H. Regulation of brain development and brain function by the transcriptional repressor RP58. *Brain Res.*, 1705: 15-23, 2019.
4. K. Nakamura and T. Shichita. Cellular and molecular mechanisms of sterile inflammation in ischemic stroke. *J. Biochem.*, 165: 459-464, 2019.

[Books]

1. M. Hasegawa. Structure of NFT: Biochemical Approach. *Adv. Exp. Med. Biol.*, 1184: 23-34, 2019.

[Conference Activities & Talks]

1. M. Hasegawa. α -SYNUCLEIN - CAN IT FORM PRIONS ? World Congress of Neurology 2019 (WCN2019). 2019.10.30, Dubai.
2. T. Tanaka, S. Hirai, M. Hosokawa, T. Saito, T. Saido, M. Hasegawa, and H. Okado, Induction of Alzheimer's disease pathology by early life stress, 6th Congress of Asian College of Neuropsychopharmacology, 2019.10.11-13, Fukuoka.
3. S. Hirai, H. Miwa, T. Tanaka, Y. Kunii, M. Arai, and H. Okado. Novel schizophrenia phenotype that is found a created mouse model caused by nutritional environment. 6thAsCNP 2019, 2019.10.10-12, Fukuoka.
4. S. Hirai, M. Arai, Y. Kunii, H. Miwa, and H. Okado. Creating a novel schizophrenia model mouse caused by a combination of nutritional environment and genetic risk and characterization of the onset mechanism. 14th World Congress of Biological Psychiatry. 2019.6.4, Vancouver.
5. T. Tanaka and H. Okado. Mechanism for the maintenance of cognitive function. Neuro2019, 2019.7.25-28, Niigata.
6. T. Shichita. Damage-associated molecular patterns in ischemic stroke. 2019 Brain&Brain PET international meeting. 2019.7.6, Yokohama.
7. G. Takahashi, H. Mori, S. Ishiguro, N. Yachie, and Y. Miyaoka. Precise Deletion Mutagenesis by Dual Cas12a DNA Cleavage. Frontiers in Genome Engineering 2019, 2019.11.26, Kobe.

Clinical Anatomy

Professor : Keiichi AKITA

Associate Professor : Akimoto NIMURA (Department of Functional Joint Anatomy)

Junior Associate Professor : Kumiko YAMAGUCHI (Department of Professional Development in Health Science)

Assistant Professor : Masayo HARADA, Hisayo NASU, Shirou SUZUKI (Department of Functional Joint Anatomy)

Specally Appointed Assistant Professor : Satoru MURO(April ~)

Parttime Lecturer : Kenji IBUKURO, Itsuko OKUDA, Sachiyuki TSUKADA, Masataka NAKAZAWA,

Kaoru KITSUKAWA, Tomoyuki YANO(April ~), Kenro CHIKAZAWA(April ~)

Graduate Student : Satoru MURO(~ March), Kentaro AMAHA(~ March), Yasunori TATARA(~ March),

Shota HOSHIKA(~ March), Phichaya BARAMEE(~ March), Kazuhito SEKIZAWA(~ March),

Eiichirou KAGAWA, Kohtaro EGUCHI, Saya HORIUCHI, Yusuke UEDA, Atsuhiko OCHI,

Souichi HATTORI, Koh MIWA, Suriyut JANARUK, Syuusaku HOSONO, Haruka EISHI,

Masahiro TSUTSUMI, Wachirawit SIRIRAT, Shouko MOUE, Ming Yan HE,

Areeya JIAMJUNYASIRI, Atsuhiko FUKAI(April ~), Tharnmanularp SUTHASINEE(Sept ~),

Affiliated Researcher : Johann ZWIRNER(Oct ~ Jan)

Research Student : Mamiko SUZUKI

(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. Tsutsumi M, Nimura A, Akita K. The Gluteus Medius Tendon and Its Insertion Sites: An Anatomical Study with Possible Implications for Gluteus Medius Tears. *The Journal of bone and joint surgery. American volume*. 2019.01; 101(2); 177-184
2. Kentaro Amaha, Akimoto Nimura, Reiko Yamaguchi, Natnicha Kampan, Atsushi Tasaki, Kumiko Yamaguchi, Ryuichi Kato, Keiichi Akita. Anatomic study of the medial side of the ankle base on the joint capsule: an alternative description of the deltoid and spring ligament. *J Exp Orthop*. 2019.01; 6(1); 2
3. Itsuko Okuda, Naoki Yoshioka, Yukio Shirakabe, Keiichi Akita. Basic analysis of facial ageing: The relationship between the superficial musculoaponeurotic system and age. *Exp. Dermatol.*. 2019.02; 28 Suppl 1; 38-42
4. Takuya Higashino, Mutsumi Okazaki, Hiroki Mori, Kumiko Yamaguchi, Keiichi Akita. Reply: Microanatomy of Sensory Nerves in the Upper Eyelid: A Cadaveric Anatomical Study. *Plast. Reconstr. Surg.*. 2019.02; 143(2); 437e-438e
5. Koji Fujita, Kenji Kimori, Akimoto Nimura, Atsushi Okawa, Yoshikazu Ikuta. MRI analysis of carpal tunnel syndrome in hemodialysis patients versus non-hemodialysis patients: a multicenter case-control study. *J Orthop Surg Res*. 2019.03; 14(1); 91
6. Hisayo Nasu, Phichaya Baramée, Natnicha Kampan, Akimoto Nimura, Keiichi Akita. An anatomic study on the origin of the long head of the triceps brachii. *JSES Open Access*. 2019.03; 3(1); 5-11
7. Yoshie Tanabe, Kazunori Yasuda, Eiji Kondo, Yasuyuki Kawaguchi, Keiichi Akita, Tomonori Yagi. Comparison of Graft Length Changes During Knee Motion Among 5 Different Anatomic Single-Bundle Anterior Cruciate Ligament Reconstruction Approaches: A Biomechanical Study. *Orthop J Sports Med*. 2019.03; 7(3); 2325967119834933
8. Shota Hoshika, Akimoto Nimura, Reiko Yamaguchi, Hisayo Nasu, Kumiko Yamaguchi, Hiroyuki Sugaya, Keiichi Akita. Medial elbow anatomy: A paradigm shift for UCL injury prevention and management. *Clin Anat*. 2019.04; 32(3); 379-389
9. Muro S., Tsukada Y., Harada M., Ito M., Akita K.. Anatomy of the smooth muscle structure in the female anorectal anterior wall: convergence and anterior extension of the internal anal sphincter and longitudinal muscle *COLORECTAL DISEASE*. 2019.04; 21(4); 472-480
10. Asumi Midorikawa, Liangcheng Wang, Tomoyuki Kuwata, Yoshie Taniguchi, Isao Horiuchi, Chikako Matsushita, Kenro Chikazawa, Kenjiro Takagi. Management of pregnancy complicated by ankylosing spondylitis: A case report and literature review. *Clin Case Rep*. 2019.04; 7(4); 766-769

11. Sachiya Tsukada, Kenji Kurosaka, Tetsuyuki Maeda, Akihiro Iida, Masahiro Nishino, Naoyuki Hirasawa. Early stage periarticular injection during total knee arthroplasty may provide a better postoperative pain relief than late-stage periarticular injection: a randomized-controlled trial. *Knee Surg Sports Traumatol Arthrosc.* 2019.04; 27(4); 1124-1131
12. Tomoyuki Kuroiwa, Megumi Matsumoto, Ryuji Kato, Akimoto Nimura, Toshitaka Yoshii, Atsushi Okawa, Koji Fujita. Activation of cancer-related and mitogen-activated protein kinase signaling pathways in human mature osteoblasts isolated from patients with type 2 diabetes. *Bone Rep.* 2019.06; 10; 100199
13. Natnicha Kampan, Keiichi Akita, Pasuk Mahakkanukrauh. The malaris muscle concept reconsidered. *Anat Cell Biol.* 2019.06; 52(2); 134-139
14. Masayoshi Saito, Sachiya Tsukada, Nobuko Fujita, Mahbubur Rahman, Wataru Morita, Nobuto Kitamura, Atsushi Tasaki. Post-operative pain control following arthroscopic rotator cuff repair: peri-articular injection versus interscalene brachial plexus block. *Int Orthop.* 2019.06; 43(6); 1435-1441
15. Yasunori Tatara, Hisayo Nasu, Masahiro Tsutsumi, Keiichi Akita. Origins, Courses, and Distributions of the Lumbar Arterial Branches in Relation to the Spinal Nerves: An Anatomical Study. *Spine.* 2019.07; 44(14); E808-E814
16. Kenji Ibukuro, Masaya Mori, Keiichi Akita. The hepatic capsular arteries: imaging features and clinical significance. *Abdom Radiol (NY).* 2019.08; 44(8); 2729-2739
17. Ken Imai, Kenro Chikazawa, Liangcheng Wang, Tomoyuki Kuwata. A Gauze-tying Trocar Technique for Laparoscopic Hysterectomy Procedures Involving Large Uteri. *Gynecol Minim Invasive Ther.* 2019.08; 8(3); 138-139
18. Tsutsumi M, Nimura A, Honda E, Utsunomiya H, Uchida S, Akita K. An Anatomical Study of the Anterosuperior Capsular Attachment Site on the Acetabulum. *The Journal of bone and joint surgery. American volume.* 2019.09; 101(17); 1554-1562
19. Fujita Koji, Watanabe Takuro, Kuroiwa Tomoyuki, Sasaki Toni, Nimura Akimoto, Sugiura Yuta. A Tablet-Based App for Carpal Tunnel Syndrome Screening: Diagnostic Case-Control Study *JMIR MHEALTH AND UHEALTH.* 2019.09; 7(9); e14172
20. Tomoyuki Kuroiwa, Akimoto Nimura, Shiro Suzuki, Toru Sasaki, Atsushi Okawa, Koji Fujita. Measurement of thumb pronation and palmar abduction angles with a small motion sensor: a comparison with Kapandji scores. *J Hand Surg Eur Vol.* 2019.09; 44(7); 728-733
21. Shiho Oide, Tomoyuki Kuwata, Liangcheng Wang, Ken Imai, Kenro Chikazawa, Isao Horiuchi, Kenjiro Takagi, Ryo Konno. Incidence of residual bacterial contamination of transvaginal ultrasound probes. *J Med Ultrason (2001).* 2019.10; 46(4); 475-479
22. Kohtaro Eguchi, Toshihiro Matsui, Masayoshi Mukai, Taro Sugimoto. Prediction of the depth of invasion in superficial pharyngeal cancer: Microvessel morphological evaluation with narrowband imaging. *Head Neck.* 2019.11; 41(11); 3970-3975
23. Kohtaro Eguchi, Jason Y K Chan, Ichiro Tateya, Akira Shimizu, F Christopher Holsinger, Taro Sugimoto. Curved Laryngopharyngoscope With Flexible Next-Generation Robotic Surgical System for Transoral Hypopharyngeal Surgery: A Preclinical Evaluation. *Ann. Otol. Rhinol. Laryngol.* 2019.11; 128(11); 1023-1029
24. Shiho Oide, Tomoyuki Kuwata, Liangcheng Wang, Ken Imai, Kenro Chikazawa, Kenjiro Takagi. Placental mesenchymal dysplasia with a good outcome: A case report. *J. Obstet. Gynaecol. Res.* 2019.11; 45(11); 2284-2288
25. Toru Sasaki, Shigenori Kawabata, Yuko Hoshino, Kensuke Sekihara, Yoshiaki Adachi, Miho Akaza, Isamu Ozaki, Koji Fujita, Akimoto Nimura, Toshitaka Yoshii, Yuki Miyano, Yuki Mitani, Taishi Watanabe, Shinji Sato, Sukchan Kim, Atsushi Okawa. Visualization of electrophysiological activity at the carpal tunnel area using magnetoneurography. *Clin Neurophysiol.* 2019.12;

[Books etc]

1. Akimoto Nimura, Keiichi Akita, Hiroyuki Sugaya. *DISORDERS OF THE ROTATOR CUFF AND BICEPS TENDON.* ELSEVIER, 2019.10 (ISBN : 978-0-323-28784-5)

[Conference Activities & Talks]

1. Keiichi Akita. Clinical Anatomy of Anus and Rectum. Song-Do International Proctology Symposium 2019.04.20 Soul, Korea
2. Keiko Fukino, Masahiro Tsutsumi, Akimoto Nimura, Jose Sanudo, Takashi Ono, Keiichi Akita. Spatial distribution of the palatopharyngeus in consideration of the role of the swallowing. International Congress of Anatomia Clinica 2019.06.24 Madrid, Spain
3. Keiichi Akita. Recent Works of Pelvic Floor Anatomy: Spatial Distributions of Skeletal and Smooth Muscular Tissues. International Congress of Anatomia Clinica 2019.06.24 Madrid, Spain
4. Haruka Eishi, Kumiko Yamaguchi, Yoshihiro Hiramatsu, Keiichi Akita. Intramural distribution of the arteries in the stomach Demonstrated by X-ray examination with barium contrast medium injected. International Congress of Anatomia Clinica 2019.06.24 Madrid, Spain
5. Satoru Muro, Maika Habu, Hiromasa Ka, Ryuzaburo Kagawa, Masayo Harada, Keiichi Akita. Coexistence of dense and sparse areas in longitudinal smooth muscle of the anal canal inspired by MRI. International Congress of Anatomia Clinica 2019.06.25 Madrid, Spain
6. Masahiro Tsutsumi, Akimoto Nimura, Eisaburo Honda, Hajime Utsunomiya, Soshi Uchida, Keiichi Akita. Morphological analysis of the hip capsular attachment on the anterosuperior acetabular margin. International Congress of Anatomia Clinica 2019.06.26 Madrid, Spain
7. Akimoto Nimura, Masahiro Tsutsumi, Satoru Muro, Keiichi Akita . Anatomical relationship between the morphology of the styloid process of the ulna and Radioulnar ligament attachment. International Congress of Anatomia Clinica 2019.06.26 Madrid, Spain
8. Kumiko Yamaguchi, Nobutoshi Nawa, Keiichi Akita. Utilization and effects of learning materials in human anatomy course. International Congress of Anatomia Clinica 2019.06.26 Madrid, Spain
9. Sritara Sasin, Masahiro Tsutsumi, Keiko Fukino, Takashi Ono, Keiichi Akita. Morphological analysis of the lateral pterygoid muscle inserting into the medial surface of the condylar process. The 6th Asian Academy congress for TMJ 2019.07.27 Tokyo, Japan
10. Hisayo Nasu, Akimoto Nimura, Keiichi Akita. Supporting structures in the lateral side of the knee. The 19th congress of the International Federation of Associations of Anatomists 2019.08.09 London, UK
11. Mina Nakagawa, Kanako Noritake, Kumiko Yamaguchi, Janelle Moross, Jun Tsuruta, Keiichi Akita. Introduction of Clinical Exchange Training for Medical and Dental Students. The Association for Medical Education in Europe 2019 2019.08.26 Vienna, Austria
12. Keiichi Akita. Clinical Anatomy of Masticatory muscles and Pharyngeal muscles. Lecture for Department of Otolaryngology (ENT) 2019.08.26 Bangkok, Thailand
13. Keiichi Akita. Clinical Anatomy of Pelvic Floor Muscles and Anorectal Canal. Lecture for OB & GYN doctors 2019.08.26 Bangkok, Thailand
14. Kumiko Yamaguchi, Nobutoshi Nawa, Chiharu Kawakami, Mina Nakagawa, Jun Tsuruta, Keiichi Akita. How other disciplines influence team members during multi-disciplinary decision making. The Association for Medical Education in Europe 2019 2019.08.27 Vienna, Austria
15. Chiharu Kawakami, Kumiko Yamaguchi, Nobutoshi Nawa, Mina Nakagawa, Jun Tsuruta, Keiichi Akita. Promoting student contribution at Interprofessional Education workshops - differences among eight health professions. The Association for Medical Education in Europe 2019 2019.08.27 Vienna, Austria
16. Nobutoshi Nawa, Kumiko Yamaguchi, Chiharu Kawakami, Mina Nakagawa, Jun Tsuruta, Keiichi Akita. Differences in effects of interprofessional education workshops by students' discipline and gender among medical and dental students. The Association for Medical Education in Europe 2019 2019.08.27 Vienna, Austria
17. Keiichi Akita. Introduction to Anatomy Such Importance Basic for Doctor. Lecture at Faculty of Science 2019.08.27 Bangkok, Thailand

18. Keiichi Akita. Clinical Anatomy of Shoulder joint with special reference to Rotator cuff muscles Femoral and Tibial Attachments of ACL and PCL. Lecture at Department of Orthopedics 2019.08.27 Bangkok, Thailand
19. Keiichi Akita. Surgical Anatomy of Anorectal region. Lecture for General Surgery residents and Medical students 2019.08.28 Bangkok, Thailand
20. Satoru Muro, Keiichi Akita. Anatomy of the smooth muscle structure in the region anterior to the anorectum in male. Standard Surgical Treatment of Colorectal Cancer Workshop 2019.11.09 Seoul, Korea
21. Satoru Muro, Keiichi Akita. Anatomical concept specific to the anorectum: proximity and association of smooth and skeletal muscles. Standard Surgical Treatment of Colorectal Cancer Workshop 2019.11.09 Seoul, Korea
22. Akimoto Nimura. Shoulder Anatomy. 2nd Asia-Pacific Shoulder and Elbow Symposium 2019.11.30 Bunkyo-ku, Tokyo

Systems BioMedicine

Professor Hiroshi ASAHARA

Assistant Professor Tomoki CHIBA, Takahide MATSUSHIMA, Ryouta KURIMOTO

Kensuke KATAOKA

Graduate Students Yuki YANO, Hiroto YAMAMOTO, Hiroki TSUTSUMI, Maiko INOTSUME, Lin LIU, Takayuki MIYAZAKI, Kaho TAKADA, Ken KUROIWA, Risa TERAOKA, Kaduki ICHIKAWA, Haruka HOSOGAI, Yutaro Uchida, Mari MATSUNAGA, Haruto Yoshida

(1) Research

Screening with an RNA binding protein library identified new regulators of microRNA.

We identified novel regulators of tumor suppressor microRNAs.

The function of the epigenome on bone morphogenesis was analyzed using micro-CT.

We have been shown that the tendons/ligaments specific transcription factor Mohawk is essential for the development and homeostasis processes in tendons and ligaments.

We have been developed completely automated ChIP system using LabDroid “Maholo” .

Search for novel regulator of microRNA by high throughput screening.

Revealed the molecular mechanism by which osteocytes regulate bone homeostasis.

The Screening of novel Damage-associated molecular patterns proteins

Protein localization analysis by High-throughput microscope system

MiRNA which regulates cartilage homeostasis was identified.

We developed screening system for miRNA target genes using reporter vector library.

MicroRNA KO mice were generated using CRISPR/Cas9 system, and its function in skeletal pattern formation was analyzed.

Molecular mechanisms and in vivo roles of RNA-binding proteins and long non-coding RNAs in the context of inflammatory response

(2) Education

Under Graduate:

Conducting “Molecular Genetics” , which is a series of lectures to understand the gene expression machinery and human genetics and their application to current medicine and biology. Under graduate students can join the lab works to learn the skills for molecular biology and pathology.

Graduate School:

Organizing “Development and Regeneration” lecture series to understand the basis for regenerative medicine and reproduction at the level of molecular genetics.

Students can join the Lab to perform researches using various experimental techniques, such as microarray, cell-based high throughput screening etc. Using these techniques, core molecular network for tissue development and inflammatory diseases will be examined, which forms the basis of systems biomedicine.

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

1. Kita M, Nakae J, Kawano Y, Asahara H, Takemori H, Okado H, Itoh H. Zfp238 Regulates the Thermogenic Program in Cooperation with Foxo1. *iScience*. 2019.02; 12; 87-101
2. Takayoshi Sasako, Mitsuru Ohsugi, Naoto Kubota, Shinsuke Itoh, Yukiko Okazaki, Ai Terai, Tetsuya Kubota, Satoshi Yamashita, Kunio Nakatsukasa, Takumi Kamura, Kaito Iwayama, Kumpei Tokuyama, Hiroshi Kiyonari, Yasuhide Furuta, Junji Shibahara, Masashi Fukayama, Kenichiro Enooku, Kazuya Okushin, Takeya Tsutsumi, Ryosuke Tateishi, Kazuyuki Tobe, Hiroshi Asahara, Kazuhiko Koike, Takashi Kadowaki, Kohjiro Ueki. Hepatic Sdf2l1 controls feeding-induced ER stress and regulates metabolism. *Nat Commun*. 2019.02; 10(1); 947
3. Sho Mokuda, Ryo Nakamichi, Tokio Matsuzaki, Yoshiaki Ito, Tempei Sato, Kohei Miyata, Masafumi Inui, Merissa Olmer, Eiji Sugiyama, Martin Lotz, Hiroshi Asahara. Wwp2 maintains cartilage homeostasis through regulation of Adamts5. *Nat Commun*.. 2019.06; 10(1); 2429
4. Yamashita Satoshi, Kataoka Kensuke, Yamamoto Hiroto, Kato Tomoko, Hara Satoshi, Yamaguchi Katsushi, Renard-Guillet Claire, Katou Yuki, Shirahige Katsuhiko, Ochi Haruki, Ogino Hajime, Uchida Tokujiro, Inui Masafumi, Takada Shuji, Shigenobu Shuji, Asahara Hiroshi. Comparative analysis demonstrates cell type-specific conservation of SOX9 targets between mouse and chicken *SCIENTIFIC REPORTS*. 2019.08; 9(1); 12560
5. Kurimoto Ryota, Tsutsumi Hiroki, Uchida Yutaro, Asahara Hiroshi. New regulatory mechanism of tumor suppressor microRNA let-7s (comprehensive approach for tumor suppressors in vitro) *ANNALS OF ONCOLOGY*. 2019.10; 30;
6. Uchida Yutaro, Chiba Tomoki, Kurimoto Ryota, Asahara Hiroshi. Post-transcriptional regulation of inflammation by RNA-binding proteins via cis-elements of mRNAs(和訳中) *The Journal of Biochemistry*. 2019.11; 166(5); 375-382
7. Carmen Adriaens, Florian Rambow, Greet Bervoets, Toomas Silla, Mari Mito, Tomoki Chiba, Hiroshi Asahara, Tetsuro Hirose, Shinichi Nakagawa, Torben Heick Jensen, Jean-Christophe Marine. The long noncoding RNA NEAT1.1 is seemingly dispensable for normal tissue homeostasis and cancer cell growth. *RNA*. 2019.12; 25(12); 1681-1695
8. Momo Isobe, Hikaru Toya, Mari Mito, Tomoki Chiba, Hiroshi Asahara, Tetsuro Hirose, Shinichi Nakagawa. Forced isoform switching of Neat1.1 to Neat1.2 leads to the loss of Neat1.1 and the hyperformation of paraspeckles but does not affect the development and growth of mice. *RNA*. 2019.12;

[Books etc]

1. Hiroki Tsutsumi, Ryota Kurimoto. Symptoms / disease classification Clinical laboratory test value Complete guide. *Jihou*, 2019.01
2. Mokuda Sho, Olmer Merissa, Lotz Martin K., Sugiyama Eiji, Asahara Hiroshi . 骨と軟骨の生物学 WWドメイン含有タンパク質 2(Wwp2) は miR-140 と協働して軟骨の恒常性を維持する (Bone and Cartilage Biology WW domain-containing protein 2(Wwp2) maintains cartilage homeostasis in coordination with miR-140) . (一社) 日本リウマチ学会, 2019.03

[Misc]

1. Yutaro Uchida, Tomoki Chiba, Ryota Kurimoto, Hiroshi Asahara. Post-transcriptional regulation of inflammation by RNA-binding proteins via cis-elements of mRNAs. *J. Biochem*.. 2019.11; 166(5); 375-382

[Conference Activities & Talks]

1. Hiroshi Asahara. miRNAs in arthritis pathogenesis and therapy. The 20th Takeda Science Foundation Symposium on BioSciences 2019.02.01

2. Hiroshi Asahara. Genome dynamics for chondrogenesis and miRNAs for cartilage homeostasis via Sox9. Cartilage GRC 2019 2019.03.21
3. 浅原弘嗣. 腱・靱帯のメカノプロパティを応用した再生医療. FAOPS2019 2019.03.31
4. Hiroshi Asahara. miRNAs in arthritis pathogenesis and therapy. 2019 Keystone Symposia Conference 2019.04.17
5. Hiroshi Asahara, Sho Mokuda, Yoshiaki Ito, Masafumi Inui, Ryo Nakamichi, Tomoki Chiba, Ryota Kurimoto, Takahide Matsushima. miRNAs in arthritis pathogenesis and therapy. The 24th Annual Meeting of the RNA Society 2019.06.14
6. 浅原弘嗣、茂久田翔、伊藤義晃、中道亮、杉山英二、松崎時夫. Wwp2 maintains cartilage homeostasis through regulation of Adamts5. 第5回日本骨免疫学会 2019.06.26
7. Ryota Kurimoto, Hiroki Tsutsumi, Yutaro Uchida, Hiroshi Asahara. 腫瘍抑制 microRNA let-7 family の新たな制御機構の解明. 第17回日本臨床腫瘍学会 2019.07.19
8. Ryota Kurimoto, Hiroki Tsutsumi, Maiko Inotsume, Hiroshi Asahara. New regulatory mechanism of tumor suppressor microRNA let-7s. 16thn Bone Biology Forum 2019.08.16 Makuhari, Chiba, Japan
9. 浅原弘嗣. Lecture I “Cartilage homeostasis and arthritis pathogenesis via RNA regulation”. 16th Meeting of Bone Biology Forum 2019.08.16
10. Ryota Kurimoto, Hiroki Tsutsumi, Hiroshi Asahara. New regulatory mechanism of tumor suppressor microRNA let-7s (comprehensive approach for tumor suppressors in vitro) . 16th Meeting of Bone Biology Forum 2019.08.16
11. Hiroshi Asahara. Characterization of a novel Sox9 enhancer and down-stream targets with implications in Arthritis parthenogenesis and therapeutics.. SOX meeting2019 2019.10.01
12. 浅原弘嗣. Homeostasis of tendons and ligaments connecting musculoskeletal system. Japan Bone Academy2019 2019.12.15

Comprehensive Pathology

Professor
Masanobu KITAGAWA
Junior associate Professor
Morito KURATA
Assistant Professor
Kouhei YAMAMOTO, Ichiro ONISHI
Laboratory Technician
Miori INOUE
Technical Assistant
Sachiko ISHIBASHI, Masumi IKEDA,
Graduate Students
Masae YANAI, Ryoko KATO, Naoko YAMADA, Keisuke Sugita,
Towako TAGUCHI, Yuta TSUGENO, Jyunko KUNIEDA, Yuko MATSUKI
Genji KAWADE, Masanori MATSUDA, Tan Wang, Akiko YAMAMOTO,
Miyaka UEMORI, Jyunichiro SATO, Masahiro KAWADA,
Noriaki FUKUHARA, Tomohiro YOKOUCHI, Shigeo TODA,
Jyunnosuke HAYASAKA, Jyunpei KAWAMURA, Azusa TERAOKA

(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-pathology research

Surgical materials, biopsy materials, and various organs obtained by pathological dissection are subjected to immunohistological, electron microscopic, and molecular pathological research in addition to the usual morphological methods. The concept and diagnosis of disease to establish new concepts for treatment.

(2) Experimental pathological study

In vivo and in vitro using mice as experimental models, immunohistological, virological, biochemical and molecular biological analyses of cells of the blood system are performed.

1. Analysis of the mechanism of retrovirus-induced leukemia and development of its therapeutic model

The function of host T cells plays an important role in the onset of tumors by Friend Leukemia Virus. We are analyzing what signaling mechanisms are activated by virus infection and how T cell functions are controlled.

2. Apoptosis induction using retrovirus-derived proteins and its application to gene therapy. Gp70 from Friend Leukemia Virus activates the pro-apoptotic pathway for DNA damage signals, highlighting host-derived genes. Using this system, we are applying it to treatments including gene therapy.

3. Molecular and pathological study on the mechanism of Myelodysplastic syndromes (MDS) onset. MDS is a disease that occurs in relatively elderly people, and causes peripheral blood cytopenias due to the frequent apoptosis in the bone marrow. We are analyzing the expression and regulation of molecules that cause apoptosis in MDS bone marrow cells from both hematopoietic cells and stromal cells.

4. Study on drug resistance of various hematopoietic diseases

Analysis of drug resistance genes of various hematopoietic diseases and the movement of related molecules.

5. Comprehensive study on the mechanism of immune system formation and its breakdown with age. The formation of the immune system progresses rapidly after birth, reaches a peak during puberty, and then declines with age. As a result, it is not uncommon for elderly people after the age of 70 to have markedly reduced immune function, and are susceptible to infectious diseases, similar to AIDS. In order to elucidate the mechanism of such age-related changes in the immune system, the age-related changes in the thymus, T cells, and the neuroendocrine immune system are analyzed at the molecular level.

6. Molecular pathological study on cancer growth and progression.

We mainly use human pathological tissue of the digestive system to analyze various substances related to the growth and progression of cancer using molecular pathological techniques.

(3) Education

Undergraduate education: Education is provided throughout the four years from the first grade to the fourth grade of specialized courses through the general pathology, each theory practice, PBL, block type learning, comprehensive diagnostics practice, BSL, and the like. The program is implemented in cooperation with the human pathology department, hospital pathology department, molecular pathology department, difficult research neuropathology department, and dentistry oral pathology course. At the case study meeting, CPE, which is held at the end of each discussion practice, a small number of students are in charge of one case, give presentations, and promote understanding of pathology through case experience.

(4) Lectures & Courses

Post-graduate education: Training of pathological, anatomy and surgical pathology for the purpose of acquiring the qualification of a pathological society-certified physician, as well as training in related hospitals. Through CPC and case study meetings with clinical departments, the aim is to deepen their understanding of clinical medicine. Regarding research, in addition to the usual pathological methods, we will use them according to the theme of each person such as immunopathology, virology, biochemistry and molecular biology methods, so that we can conduct advanced research.

(5) Publications

[Original Articles]

1. Nagatsuma Misako, Takasawa Kei, Yamauchi Takeru, Nakagawa Ryuichi, Mizuno Tomoko, Tanaka Eriko, Yamamoto Kouhei, Uemura Noriko, Kashimada Kenichi, Morio Tomohiro. 脂肪腫症、腎血管性高血圧および糖尿病を呈する Schimmelpenning 症候群患者における接合後の KRAS 変異 (A postzygotic KRAS mutation in a patient with Schimmelpenning syndrome presenting with lipomatosis, renovascular hypertension, and diabetes mellitus) Journal of Human Genetics. 2019.02; 64(2); 177-181
2. Kawamoto A., Nagata S., Anzai S., Takahashi J., Kawai M., Hama M., Nogawa D., Yamamoto K., Kuno R., Suzuki K., Shimizu H., Hiraguri Y., Yui S., Oshima S., Tsuchiya K., Nakamura T., Ohtsuka K., Kitagawa M., Okamoto R., Watanabe M.. Synergy of Notch signalling and TNF-alpha in the inflamed intestinal epithelia of IBD patients leads to up-regulation of UBD, a ubiquitin-like protein JOURNAL OF CROHNS & COLITIS. 2019.03; 13; S91

3. Nagaishi T, Yamada D, Suzuki K, Fukuyo R, Saito E, Fukuda M, Watabe T, Tsugawa N, Takeuchi K, Yamamoto K, Arai A, Ohtsuka K, Watanabe M. Indolent T cell lymphoproliferative disorder with villous atrophy in small intestine diagnosed by single-balloon enteroscopy. *Clinical journal of gastroenterology*. 2019.04;
4. 野川 大地, グリニサ・アヒマティ, 山本 阿紀子, 立澤 杏奈, 峰尾 竜徳, 大西 威一郎, 倉田 盛人, 宮坂 尚幸, 山本 浩平, 北川 昌伸. 卵巣癌における MCM2 タンパクの細胞内局在に着目した臨床病理学的検討 (Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma) *日本病理学会会誌*. 2019.04; 108(1); 410
5. Mio Mori, Tomoyuki Fujioka, Leona Katsuta, Junichi Tsuchiya, Kazunori Kubota, Mai Kasahara, Goshi Oda, Tsuyoshi Nakagawa, Ichiroh Onishi, Ukihide Tateishi. Diagnostic performance of time-of-flight PET/CT for evaluating nodal metastasis of the axilla in breast cancer. *Nucl Med Commun*. 2019.07;
6. Kouhei Yamamoto, Shinya Abe, Ayaka Honda, Jun Hashimoto, Yuuki Aizawa, Sachiko Ishibashi, Taro Takemura, Nobutaka Hanagata, Masahide Yamamoto, Osamu Miura, Morito Kurata, Masanobu Kitagawa. Fatty acid beta oxidation enzyme HADHA is a novel potential therapeutic target in malignant lymphoma. *Lab. Invest.*. 2019.09;
7. 野川 大地, グリニサ・アヒマティ, 山本 阿紀子, 大西 威一郎, 倉田 盛人, 宮坂 尚幸, 山本 浩平, 北川 昌伸. 卵巣癌における MCM2 タンパクの細胞内局在に着目した臨床病理学的検討 (Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma) *日本癌学会総会記事*. 2019.09; 78 回; P-1151
8. Nagaishi Takashi, Yamada Daiki, Suzuki Kohei, Fukuyo Ryosuke, Saito Eiko, Fukuda Masayoshi, Watabe Taro, Tsugawa Naoya, Takeuchi Kengo, Yamamoto Kouhei, Arai Ayako, Ohtsuka Kazuo, Watanabe Mamoru. シングルバルーン小腸内視鏡検査で診断された小腸の絨毛萎縮を伴う、緩徐進行性 T 細胞リンパ増殖性疾患 (Indolent T cell lymphoproliferative disorder with villous atrophy in small intestine diagnosed by single-balloon enteroscopy) *Clinical Journal of Gastroenterology*. 2019.10; 12(5); 434-440
9. Kitagawa M, Kurata M, Onishi I, Yamamoto K. Bone marrow niches in myeloid neoplasms. *Pathology international*. 2019.11;

[Conference Activities & Talks]

1. 山本 浩平, 阿部 晋也, 本田 彩華, 山本 正英, 三浦 修, 倉田 盛人, 北川 昌伸. ラノラジンは難治性悪性リンパ腫に対する有望な抗腫瘍薬としての可能性を有する (Ranolazine is a potential anti-tumor reagent against refractory cases in malignant lymphoma). *日本病理学会会誌* 2019.04.01
2. 野川 大地, グリニサ・アヒマティ, 山本 阿紀子, 立澤 杏奈, 峰尾 竜徳, 大西 威一郎, 倉田 盛人, 宮坂 尚幸, 山本 浩平, 北川 昌伸. 卵巣癌における MCM2 タンパクの細胞内局在に着目した臨床病理学的検討 (Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma). *日本病理学会会誌* 2019.04.01
3. 倉田 盛人, 山本 浩平, 北川 昌伸. PI3K 変異型乳癌における新規協調癌遺伝子とシグナル探索 (Discovery of cancer genes and pathways operative in PI3K activated mammary cancer). *日本癌学会総会記事* 2019.09.01
4. 山本 浩平, 阿部 晋也, 倉田 盛人, 本田 彩華, 山本 正英, 北川 昌伸. ラノラジンは難治性悪性リンパ腫に対する有望な抗腫瘍薬としての可能性を有する (Ranolazine is a potential anti-tumor reagent against refractory cases in malignant lymphoma). *日本癌学会総会記事* 2019.09.01
5. 野川 大地, グリニサ・アヒマティ, 山本 阿紀子, 大西 威一郎, 倉田 盛人, 宮坂 尚幸, 山本 浩平, 北川 昌伸. 卵巣癌における MCM2 タンパクの細胞内局在に着目した臨床病理学的検討 (Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma). *日本癌学会総会記事* 2019.09.01

Molecular Oncology

Professor: Shinji TANAKA
Associate Professor: Yoshimitsu AKIYAMA
Assistant Professor: Shu SHIMADA
Assistant Professor: Ayano NIIBE
Laboratory Technician: Hiromi NAGASAKI
Graduate Student: Yuna TAKAGI

(1) Outline

To understand the molecular mechanisms underlying carcinogenesis and malignant progression for clinical application of cancer prevention, diagnosis and treatment.

(2) Research

1. Molecular analysis of refractory malignancies including liver, pancreatic and scirrhous gastric cancers
2. Development of molecularly targeted therapy for refractory malignancies
3. Cancer epigenetics/epigenomics and clinical application in refractory malignancies
4. Research of cancer stem cells and targeted therapy
5. Development of regenerative medicine using stem cell research

(3) Education

Hygiene is our charge. The undergraduate curriculum of hygiene includes lectures, and laboratory studies. Topics of lectures consist of environmental pollution and human health, world-wide environmental problems, carcinogen and occupational cancer, smoking-related diseases, infectious diseases including AIDS and hepatitis, food poisoning, anoxia and heat-related diseases.

(4) Lectures & Courses

The graduate students pursue their own projects associated with one of researches being in progress in the division. Every student can learn the basic scientific techniques, such as genetic engineering, cell culture and biochemical procedures. There are also many special lectures on cancer, gene, cell biology and biochemistry for the graduate students. On weekly seminars, the students present their own research data and introduce important papers from newly-arrived journals. Once the students get new findings, they are encouraged to present them at the domestic or international meeting and write manuscripts.

(5) Publications

[Original Articles]

1. Shu Shimada, Kaoru Mogushi, Yoshimitsu Akiyama, Takaki Furuyama, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shigeki Arii, Minoru Tan-

- abe, Jack R Wands, Shinji Tanaka. Comprehensive molecular and immunological characterization of hepatocellular carcinoma. *EBioMedicine*. 2019.02; 40; 457-470
2. Hiroshi Fukamachi, Seon-Kyu Kim, Jiwon Koh, Hye Seung Lee, Yasushi Sasaki, Kentaro Yamashita, Taketo Nishikawaji, Shu Shimada, Yoshimitsu Akiyama, Sun-Ju Byeon, Dong-Hyuck Bae, Keisuke Okuno, Masatoshi Nakagawa, Toshiro Tanioka, Mikito Inokuchi, Hiroshi Kawachi, Kiichiro Tsuchiya, Kazuyuki Kojima, Takashi Tokino, Yoshinobu Eishi, Yong Sung Kim, Woo Ho Kim, Yasuhito Yuasa, Shinji Tanaka. A subset of diffuse-type gastric cancer is susceptible to mTOR inhibitors and checkpoint inhibitors. *J. Exp. Clin. Cancer Res*. 2019.03; 38(1); 127
 3. Shimada S, Tanaka S. A new era for understanding genetic evolution of multistep carcinogenesis. *Journal of gastroenterology*. 2019.07; 54(7); 667-668
 4. Jun Yoshino, Daisuke Ban, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka & Minoru Tanabe. The Clinical Implications of Peripancreatic Fluid Collection After Distal Pancreatectomy *World Journal of Surgery*. 2019.08; 43(8); 2069-2076
 5. Guo Q, Furuta K, Lucien F, Sanchez LHG, Hirsova P, Krishnan A, Kabashima A, Pavelko KD, Madden B, Alhuwaish H, Gao Y, Revzin A, Ibrahim SH. Integrin $\beta < \text{sub}> 1< / \text{sub}>$ -enriched Extracellular Vesicles Mediate Monocyte Adhesion and Promote Liver Inflammation in Murine NASH. *Journal of hepatology*. 2019.08;
 6. Matsui S, Kudo A, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Tanaka S, Tanabe M.. Does sunitinib have a patient-specific dose without diminishing its antitumor effect on advanced pancreatic neuroendocrine neoplasms? *Journal of Cancer Research and Clinical Oncology*. 2019.08; 145(8); 2097-2104
 7. Bo Liu, Atsushi Kudo, Yuko Kinowaki, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Takumi Akashi, Minoru Tanabe. A simple and practical index predicting the prognoses of the patients with well-differentiated pancreatic neuroendocrine neoplasms *The Japanese Society of Gastroenterology*. 2019.09; 54(9); 819-828
 8. Liu B, Kudo A, Kinowaki Y, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Tanaka S, Akashi T, Tanabe M.. A simple and practical index predicting the prognoses of the patients with well-differentiated pancreatic neuroendocrine neoplasms *Journal of Gastroenterology*. 2019.09; 54(9); 819-828
 9. Yoshino J, Akiyama Y, Shimada S, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Yamaoka S, Tanabe M, Tanaka S.. Loss of ARID1A induces a stemness gene ALDH1A1 expression with histone acetylation in the malignant subtype of cholangiocarcinoma. *Carcinogenesis*. 2019.10;
 10. Matsui S, Ogura T, Ban D, Ogawa K, Ono H, Mitsunori Y, Kudo A, Tanaka S, Tanabe M.. Position of the Pancreas Division Line and Postoperative Outcomes After Distal Pancreatectomy. *World Journal of Surgery*. 2019.11;

[Books etc]

1. CANCER BIOLOGY ILLUSTRATED. 2019.09

[Conference Activities & Talks]

1. Asymmetric dimethylation at histone H3 arginine 2 by PRMT6 in gastric cancer progression. 2019.05.28
2. Takeshi Ishii, Toshiro Ogura, Yoshiki Murase, Toshitaka Sugawara, Masahumi Akasu, Tomotaka Kato, Jun Yoshino, Shuichi Watanabe, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Surgery for obese patients with hepatocellular carcinoma. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.13 Takamatsu
3. Toshitaka Sugawara, Daisuke Ban, Takeshi Ishii, Satoshi Matsui, Masahumi Akasu, Tomotaka Kato, Daisuke Asano, Jun Yoshino, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Preoperative factors for early recurrence of resected pancreatic ductal adenocarcinoma. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.14 Takamatsu

4. Shuichi Watanabe, Daisuke Ban, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The analysis of the treatment for the metachronous solitary metastasis after curative surgery in pancreatic cancer. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.14 Takamatsu
5. Shu Shimada, Yoshimitsu Akiyama, Shinji Tanaka. Comprehensive molecular and immunological characterization of hepatocellular carcinoma. The 78th Annual Meeting of the Japanese Cancer Association 2019.09.26 Kyoto
6. Yoshimitsu Akiyama, Shu Shimada, Shinji Tanaka. Overexpression of histone arginine methyltransferase PRMT6 contributes to prognosis and malignancy of gastric cancer. The 78th Annual Meeting of the Japanese Cancer Association 2019.09.27 Kyoto
7. Shinji Tanaka, Shuichi Watanabe, Minoru Tanabe.. Novel genetic and immunological classification of hepatocellular carcinoma for the subtype-specific precision immunotherapy. JAPAN DIGESTIVE DISEASE WEEK 2019 2019.11.22 Kobe

[Patents]

1. Dominant negative mutants of IRS-1 and uses thereof (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

Associate Professor: Takumi AKASHI

Assistant Professor: Susumu KIRIMURA, Shohei TOMII, Yuko KINOWAKI, Hiroshi Shintaku

Project Assistant Professor: 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) Development of novel markers significant for histopathological diagnosis
- 3) Clinico-pathological analysis of malignant mesothelioma
- 4) Clinico-pathological analysis of inflammatory bowel disease
- 5) Clinico-pathological analysis of glomerular disease
- 6) Clinico-pathological analysis of pancreatic neuroendocrine tumor
- 7) Clinico-pathological analysis of neuronal degenerative disease

(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 (40 case in a year), cytopathology services (8,696 cases in a year) and surgical pathology (11,670 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 2019.

(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. Hiroshi Watanabe, Hajime Tanaka, Yasuhisa Fujii, Makoto Kodama, Takumi Akashi, Tomoyuki Fujioka, Kazunori Kubota, Yukihisa Saida, Ukihide Tateishi. A case of immunoglobulin G4-related inflammatory pseudotumor mimicking renal cell carcinoma. *Abdom Radiol (NY)*. 2019.01;
2. Masashi Kobayashi, Hironori Ishibashi, Chihiro Takasaki, Sachiko Imai, Susumu Kirimura, Kenichi Okubo. Pathological evaluation of the visceral pleura in the radical P/D for MPM patients *Journal of Thoracic Disease*. 2019.01;
3. Okada R, Ito T, Nomura F, Kirimura S, Cho Y, Sekine M, Tateishi Y, Ariizumi Y, Asakage T. The quantitative analysis of the human papillomavirus DNA load in submandibular gland lesions with droplet digital polymerase chain reaction. *Acta oto-laryngologica*. 2019.02; 1-6
4. Omigawa Chika, Namiki Takeshi, Ueno Makiko, Ugajin Tsukasa, Miura Keiko, Yokozeki Hiroo. Case of Wells' syndrome: A rare association with the clinical course of chronic lymphocytic leukemia *JOURNAL OF DERMATOLOGY*. 2019.02; 46(2); E57-E59
5. Hiroki Arakawa, Keiji Tanese, Keiko Miura, Satoshi Ebata, Daisuke Yamada, Yuri Masui, Masaru Tanaka, Toshiaki Saida, Shin-Ichi Ansai. Poromas with large lumens histopathologically mimicking syringocystadenoma papilliferum: Report of three cases. *Australas. J. Dermatol.*. 2019.02; 60(1); e51-e55
6. Namiki T, Hsieh M, Iwamoto Y, Ugajin T, Tanaka K, Mori H, Miura K, Yokozeki H. Subcutaneous ossifying fibromyxoid tumor of the scalp: a potential importance of CT, MRI, and PET/CT on the diagnosis. *International journal of dermatology*. 2019.03;
7. Kobayashi Masashi, Ishibashi Hironori, Takasaki Chihiro, Imai Sachiko, Kirimura Susumu, Okubo Kenichi. Pathological evaluation of the visceral pleura in the radical pleurectomy/decortication for malignant pleural mesothelioma patients *JOURNAL OF THORACIC DISEASE*. 2019.03; 11(3); 717-723
8. Yujiro Nakano, Takanobu Yoshimoto, Ryo Watanabe, Masanori Murakami, Tatsuya Fukuda, Kazutaka Saito, Yasuhisa Fujii, Takumi Akashi, Toshihiro Tanaka, Tetsuya Yamada, Mitsuhide Naruse, Yoshihiro Ogawa. miRNA299 involvement in CYP11B2 expression in aldosterone-producing adenoma. *Eur. J. Endocrinol.*. 2019.05;
9. Yamamoto Kurara, Uchida Keisuke, Furukawa Asuka, Tamura Tomoki, Ishige Yuki, Negi Mariko, Kobayashi Daisuke, Ito Takashi, Kakegawa Tomoya, Hebisawa Akira, Awano Nobuyasu, Takemura Tamiko, Amano Tomonari, Akashi Takumi, Eishi Yoshinobu. Catalase expression of *Propionibacterium acnes* may contribute to intracellular persistence of the bacterium in sinus macrophages of lymph nodes affected by sarcoidosis *IMMUNOLOGIC RESEARCH*. 2019.06; 67(2-3); 182-193

10. Minghsiu Hsieh, Shown Tokoro, Tsukasa Ugajin, Takeshi Namiki, Keiko Miura, Hiroo Yokozeki. Ultrasonography as an auxiliary diagnostic tool for morphea profunda: A case report. *J. Dermatol.*. 2019.07; 46(7); 626-630
11. Yujiro Nakano, Takanobu Yoshimoto, Ryo Watanabe, Masanori Murakami, Tatsuya Fukuda, Kazutaka Saito, Yasuhisa Fujii, Takumi Akashi, Toshihiro Tanaka, Tetsuya Yamada, Mitsuhide Naruse, Yoshihiro Ogawa. miRNA299 involvement in CYP11B2 expression in aldosterone-producing adenoma. *Eur. J. Endocrinol.*. 2019.07; 181(1); 69-78
12. Hironori Ishibashi, Chihiro Takasaki, Takumi Akashi, Kenichi Okubo. Successful excision of epithelioid hemangioendothelioma of the superior vena cava. *Ann. Thorac. Surg.*. 2019.08;
13. Iijima Y, Tateishi T, Tsuchiya K, Sumi Y, Akashi T, Miyazaki Y. A Case of Pneumoconiosis Caused by Inhalation of Metallic Titanium Grindings. *Internal medicine (Tokyo, Japan)*. 2019.10;
14. Nakashima Y., Inamura K., Ninomiya H., Kirimura S., Kobayashi M., Okubo K., Ishikawa Y.. Overlapping Immunophenotypes Between Mesothelioma and Angiosarcoma: Usefulness of Claudin-5 in the Differential Diagnosis *JOURNAL OF THORACIC ONCOLOGY*. 2019.10; 14(10); S482
15. Shown Tokoro, Takeshi Namiki, Tsukasa Ugajin, Keiko Miura, Masaru Tanaka, Hiroo Yokozeki. Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber's disease): detailed assessment of skin lesions by dermoscopy and ultrasound. *Int. J. Dermatol.*. 2019.11; 58(11); e224-e226
16. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Emi Inoue-Shinomiya, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Minoru Tanabe, Emiko Sugawara, Akira Takemoto, Hidenori Ojima, Michiie Sakamoto, Masaru Muraoka, Shinichi Takano, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive genetic analysis of cholangiolocellular carcinoma with a coexistent hepatocellular carcinoma-like area and metachronous hepatocellular carcinoma. *Hepatol Res.* 2019.12; 49(12); 1466-1474

[Conference Activities & Talks]

1. A subcutaneous nodule of the right lower eyelid. 2019.04.20

[Social Contribution]

1. The Japanese Society of Diagnostic Dermatopathology, Department of Diagnostic Pathology, Saitama Medical University International Medical Center, 2005.04.17 - Now
2. Ochanomizu Study Meeting of Dermatopathology, 2009.04 - Now

Experimental Animal Model for Human Disease

Professor
Junior Associate Professor
Assistant Professor

Masami Kanai-Azuma
Yoshikazu Hirate
Hikaru Ito

(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)Effect of maternal stress during pregnancy.

(2) Publications

[Original Articles]

1. Miura K, Harikae K, Nakaguch M, Imaimatsu K, Hiramatsu R, Tomita A, Hirate Y, Kanai-Azuma M, Kurohmaru M, Ogura A, Kanai Y. Molecular and genetic characterization of partial masculinization in embryonic ovaries grafted into male nude mice. PLoS ONE. 2019; 14(3); e0212367
2. Risa Nomura, Kenichi Kashimada, Hitomi Suzuki, Liang Zhao, Atsumi Tsuji-Hosokawa, Hideo Yagita, Masatoshi Takagi, Yoshiakira Kanai, Josephine Bowles, Peter Koopman, Masami Kanai-Azuma, Tomohiro Morio. Nr5a1 suppression during the murine fetal period optimizes ovarian development by fine-tuning Notch signaling. J. Cell. Sci.. 2019.04; 132(8);
3. Hirate Yoshikazu, Nakano Yuki, Yoshida Tatsumi, Ito Hikaru, Uemura Mami, Kanai Yoshiakira, Kanai-Azuma Masami. 子宮内膜上皮移植に対する、TRECK に基づいたアプローチ法の確立 (Establishment of a TRECK-based approach for replacement of uterine endometrial epithelium) Experimental Animals. 2019.07; 68(Suppl.); S66
4. Takahashi Hitomi, Hirate Yoshikazu, Li Jinling, Ito Yoshiaki, Otsuka Chiho, Anezaki Mayumi, Asahara Hirosh, Chen-Tsai Ruby Yanru, Kanai-Azuma Masami. 試験管内授精マウス胚における TARGATT ノックインシステムを用いた部位特異的遺伝子導入 (Site-specific transgenesis using TARGATT knock-in system in in vitro fertilized mouse embryos) Experimental Animals. 2019.07; 68(Suppl.); S219
5. Rie Saba, Keiko Kitajima, Lucille Rainbow, Silvia Engert, Mami Uemura, Hidekazu Ishida, Ioannis Kokkinopoulos, Yasunori Shintani, Shigeru Miyagawa, Yoshiakira Kanai, Masami Kanai-Azuma, Peter Koopman, Chikara Meno, John Kenny, Heiko Lickert, Yumiko Saga, Ken Suzuki, Yoshiki Sawa, Kenta Yashiro. Endocardium differentiation through Sox17 expression in endocardium precursor cells regulates heart development in mice. Sci Rep. 2019.08; 9(1); 11953

[Conference Activities & Talks]

1. Yoshikazu Hirate, Hitomi Takahashi, Yoshiaki Ito, Jilnling Li, Chiho Ohtsuka, Hiroshi Asahara, Ruby Yanru Chen-tsai, Masami Kanai-Azuma. Site-directed transgenic mice production using TARGATTtmKnock-in technology in TMDU. 15th TRANSGENIC TECHNOLOGY MEETING 2019.04.07 神戸国際会議場
2. Yoshikazu Hirate, Hitomi Takahashi, Yoshiaki Ito, Jinling Li, Chiho Otsuka, Hiroshi Asahara, Ruby Yanru Chen-Tsai, Masami Kanai-Azuma. Site-directed transgenic mice production using TARGATTTMknock-in technology in TMDU. The 15th Transgenic Technology Meeting (TT2019) 2019.04.08 Kobe, Hyogo, Japan
3. Yoshikazu Hirate, Yuki Nakano, Tatsumi Yoshida, Hikaru Ito, Mami Uemura, Yoshiakira Kanai, and Masami Kanai-Azuma. Establishment of a TRECK-based approach for replacement of uterine endometrial epithelium. The 66th Annual Meeting of Japanese Association for Laboratory Animal Science 2019.05.16 Fukuoka, Japan
4. Yoshikazu Hirate, Yuki Nakano, Tatsumi Yoshida, Dania Badran, Hikaru Ito, Mami Uemura, Yoshiakira Kanai, and Masami Kanai-Azuma. Attempt for uterine epithelial replacement by TRECK-induced selective cell death and cell transplantation. The 32nd Molossinus colloquium 2019.06.27 Chiba, Japan
5. Masami Kanai-Azuma. Mouse model of human female infertility. 第8回日本・中国・韓国マウスリソースワークショップ 2019.08.26 つくば（理化学研究所バイオリソース研究センター内）

Signal Gene Regulation

Professor (Bio-Matrix, Medical Biochemistry) HATA Yutaka
Associate Professor FUNATO Noriko

(1) Research

1. Genetic regulators of craniofacial and bone development.
2. Molecular control of cleft lip and/or palate.
3. Study of wound healing and tissue regeneration.

(2) Education

Lecture

Goals/Outline:

Students will learn the basics in life sciences by understanding the regulation of signal transduction involved in cell proliferation, differentiation, and death.

Practice

Goals/Outline:

Students will learn to handle recombinant DNA molecules and analyze the data obtained from experiments.

Lab

Goals/Outline:

Students will learn basic molecular biology and genetic engineering techniques by observing and/or performing biochemical experiments using cultured cells and gene-engineered mice.

(3) Lectures & Courses

The aim of Research Core is to provide laboratory equipments, 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 and histology.

(4) Publications

[Conference Activities & Talks]

1. Noriko Funato. Craniofacial Development: Using Computational Data for Generating Experimental Data. Frontier Meeting 2019.02.15 Tokyo Medical and Dental University, Tokyo, Japan

Molecular Cytogenetics

Professor Johji Inazawa M.D., Ph.D.
 Associate professor Jun Inoue Ph.D.
 Assistant Professor Gen Yasuyuki Ph.D.
 Assistant Professor Tomoki Muramatsu Ph.D.
 Assistant Professor DanielaTiaki Uehara 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. Kikuchi-Koike R, Nagasaka K, Tsuda H, Ishii Y, Sakamoto M, Kikuchi Y, Fukui S, Miyagawa Y, Hiraike H, Kobayashi T, Kinoshita T, Kanai Y, Shibata T, Imoto I, Inazawa J, Matsubara O, Ayabe T. Array comparative genomic hybridization analysis discloses chromosome copy number alterations as indicators of patient outcome in lymph node-negative breast cancer. BMC cancer. 2019.05; 19(1); 521
2. Akatsu Y, Takahashi N, Yoshimatsu Y, Kimuro S, Muramatsu T, Katsura A, Maishi N, Suzuki HI, Inazawa J, Hida K, Miyazono K, Watabe T. Fibroblast growth factor signals regulate transforming growth factor- β -induced endothelial-to-myofibroblast transition of tumor endothelial cells via Elk1. Mol. Oncol.. 2019.08; 13(8); 1706-1724

3. Takata R, Takahashi A, Fujita M, Momozawa Y, Saunders EJ, Yamada H, Maejima K, Nakano K, Nishida Y, Hishida A, Matsuo K, Wakai K, Yamaji T, Sawada N, Iwasaki M, Tsugane S, Sasaki M, Shimizu A, Tanno K, Minegishi N, Suzuki K, Matsuda K, Kubo M, Inazawa J, Egawa S, Haiman CA, Ogawa O, Obara W, Kamatani Y, Akamatsu S, Nakagawa H. 12 new susceptibility loci for prostate cancer identified by genome-wide association study in Japanese population. *Nature communications*. 2019.09; 10(1); 4422
4. Kousuke Tanimoto, Tomoki Muramatsu, Johji Inazawa. Massive computational identification of somatic variants in exonic splicing enhancers using The Cancer Genome Atlas. *Cancer Med*. 2019.10;
5. Hirabayashi K, Uehara DT, Abe H, Ishii A, Moriyama K, Hirose S, Inazawa J. Copy number variation analysis in 83 children with early-onset developmental and epileptic encephalopathy after targeted resequencing of a 109-epilepsy gene panel. *Journal of human genetics*. 2019.11; 64(11); 1097-1106
6. Low SK, Chin YM, Ito H, Matsuo K, Tanikawa C, Matsuda K, Saito H, Sakurai-Yageta M, Nakaya N, Shimizu A, Nishizuka SS, Yamaji T, Sawada N, Iwasaki M, Tsugane S, Takezaki T, Suzuki S, Naito M, Wakai K, Kamatani Y, Momozawa Y, Murakami Y, Inazawa J, Nakamura Y, Kubo M, Katagiri T, Miki Y. Identification of two novel breast cancer loci through large-scale genome-wide association study in the Japanese population. *Scientific reports*. 2019.11; 9(1); 17332
7. Hirabayashi Kyoko, Uehara Daniela Tiaki, Abe Hidetoshi, Ishii Atsushi, Moriyama Keiji, Hirose Shinichi, Inazawa Johji. Copy number variation analysis in 83 children with early-onset developmental and epileptic encephalopathy after targeted resequencing of a 109-epilepsy gene panel(和訳中) *Journal of Human Genetics*. 2019.11; 64(11); 1097-1106

[Conference Activities & Talks]

1. Furusawa A, Inoue J, Miyamoto M, Takano M, Tsuda H, Song YS, Aoki D, Miyasaka N, Inazawa J. Ovarian cancer therapeutic potential of glutamine depletion based on GS expression. . The 3rd International Symposium of International Society of Precision Cancer Medicine 2019. 2019.03.12 Seoul, Korea
2. Inoue J, Gokita K, Kojima K, Inazawa J. Therapeutic potential of LNP-mediated delivery of miR-634 for cancer therapy. The 3rd International Symposium of International Society of Precision Cancer Medicine 2019. 2019.03.12 Seoul, Korea
3. Kishikawa M, Inoue J, Asakage T, Inazawa J. Therapeutic potential of the topical treatment of miR-634 ointment for skin cancer. The 3rd International Symposium of International Society of Precision Cancer Medicine 2019. 2019.03.12 Seoul, Korea
4. Gen Y, Inoue J, Inazawa J. The exploration of novel tumor suppressive miRNAs using function-based miRNA screening. The 3rd International Symposium of International Society of Precision Cancer Medicine 2019. 2019.03.12 Seoul, Korea
5. 1. Takagawa Y, Gen Y, Muramatsu T, Harada H, Inazawa J. xploring novel tumor suppressive microRNAs in OSCC. The 3rd International Symposium of International Society of Precision Cancer Medicine 2019. 2019.03.12 Seoul, Korea
6. Inazawa J. Exploring novel cancer-related microRNAs and their diagnostic and therapeutic potentials in Personalized Cancer Medicine (PCM). The 3rd International Symposium of International Society of Precision Cancer Medicine 2019. 2019.03.13 Seoul, Korea
7. 劉 暢, 玄 泰行, 稲澤 譲治. miR-3140 は BRD4-MYCN 経路を標的とし、神経芽腫細胞の増殖を抑制する (miR-3140 suppressed tumor cell growth in neuroblastoma by targeting BRD4-MYCN pathway). 日本癌学会総会記事 2019.09.01
8. 村松 智輝, 佐藤 拓, 田邊 稔, 稲澤 譲治. 循環腫瘍細胞亜株 (Panc-1-CTC) の発現解析から見出した TGFBI の機能解析 (Identification and characterization of TGFBI in circulating tumor cell subline from pancreatic cancer cell line). 日本癌学会総会記事 2019.09.01
9. 徐 博, 村松 智輝, 稲澤 譲治. 扁平上皮がん細胞においてピタバスタチンは AKT、ERK の抑制を介して細胞増殖を阻害する (Pitavastatin inhibits the cell growth through the downregulation of AKT and ERK in squamous cell carcinoma). 日本癌学会総会記事 2019.09.01

10. 玄 泰行, 村松 智輝, 井上 純, 稲澤 譲治. 新規癌抑制型 miRNA による MYC 標的核酸抗癌治療の可能性 (Oligonucleotide therapeutics using a novel tumor-suppressive microRNA targeting MYC pathway). 日本癌学会総会記事 2019.09.01
11. 高川 祐希, 玄 泰行, 村松 智輝, 原田 浩之, 稲澤 譲治. 機能的 miRNA ライブラリースクリーニングによる、BRD4 を標的とする新規癌抑制型 miRNA の同定 (Function-based microRNA library screening identified novel tumor suppressive microRNAs targeting BRD4). 日本癌学会総会記事 2019.09.01
12. 岸川 正大, 井上 純, 濱本 英利, 小林 勝則, 朝蔭 孝宏, 稲澤 譲治. 甲状腺未分化癌に対する miR-634 を用いた核酸抗癌剤の開発 (Development of miRNA-formulation using miR-634 for anaplastic thyroid cancer therapy). 日本癌学会総会記事 2019.09.01
13. 井上 純, 岸川 正大, 濱本 英利, 小林 勝則, 藤原 恭子, 稲澤 譲治. 皮膚扁平上皮癌における miR-634 軟膏による抗腫瘍効果 (Therapeutic potential of the topical treatment of miR-634 ointment for cutaneous squamous cell carcinoma). 日本癌学会総会記事 2019.09.01
14. 内藤 諒, 村松 智輝, 谷本 幸介, 稲澤 譲治. 統合的 mRNA, miRNA 発現情報を基盤とした独自のマイクロ RNA 標的遺伝子予測データベースの構築 (Construction of an in-house microRNA-target prediction database based on an integrative mRNA-microRNA expression data). 日本癌学会総会記事 2019.09.01
15. 吉松 康裕, 赤津 裕一, 高橋 直也, 紀室 志織, 村松 智輝, 桂 彰宏, 間石 奈湖, 鈴木 洋, 稲澤 譲治, 樋田 京子, 宮園 浩平, 渡部 徹郎. 線維芽細胞増殖因子 (FGF2) は腫瘍血管内皮細胞において TGF- β によって誘導される内皮-筋線維芽移行を制御する (Fibroblast growth factor 2 regulates TGF- β -induced endothelial-to-myofibroblast transition of tumor endothelial cells). 日本癌学会総会記事 2019.09.01

Hematology

Professor Osamu Miura

Professor(Immunotherapy for Hematopoietic Disorders) Norihiko Kawamata

Junior Associate Professor Masahide Yamamoto

Assistant Professor Toshikage Nagao, Yoshihiro Umezawa, Keigo Okada

Project Assistant Professor Chizuko Sakashita

Assistant Professor (Department of Clinical Laboratory) Ayako Nogami

Senior Resident Youtarou Motomura, Junichi Mukae, Akihiko Nishijima

Graduate Student Daisuke Watanabe, Sunichiro Yasuda, Satoru Aoyama

(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

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. Research focusing on Myeloproliferative Neoplasms (MPN): Tumorigenesis, Chemo-resistance, new drugs.
3. Signal transduction mechanisms from cytokine/growth factor receptors regulating proliferation, survival, and adhesion of hematopoietic cells including leukemia and lymphoma cells.
4. Molecular analysis of Chronic Myeloid Leukemia (CML): rare variants, chemo-resistance, target therapy.
5. Development of novel CAR-T technology: Chimeric Antigen Receptor T-cell targeting leukemia.

The Department is also actively involved in a variety of clinical studies for treatment of various leukemias, lymphomas, and multiple myeloma.

(3) Education

The Department of hematology is responsible for teaching basic and clinical hematology to the 3rd and 4th grade students in the integrated hematology course and the hematology and oncology united block course. The Department is also responsible for teaching the 5th and 6th grade students in clinical clerkship to obtain basic knowledge and problem-solving abilities in hematology as well as general internal medicine. The Department is also actively involved in training about 24 junior residents every year to acquire clinical skills in hematology and internal medicine and about 4 senior residents to practice diagnosis and treatment of various hematological disorders and to obtain the certificate for hematology specialist. As a division in the Graduate School of Medical and Dental Sciences, the Department is actively involved in education of 6 to 8 graduate students, who participate in the research projects listed above, to obtain the Ph. D. degree in medicine.

(4) Lectures & Courses

The major objective of the course is to understand the pathophysiology of blood cells, blood cell-forming organs, and hemostasis to provide a basis for rational diagnosis and treatment of their disorders.

(5) Clinical Services & Other Works

The Department of Hematology provides diagnosis and treatment for hematological diseases, such as leukemia, malignant lymphoma, anemia, and thrombocythemia, with chemotherapeutics, molecularly-targeted drugs, immunosuppressive agents, and hematopoietic cell trans-plantation.

(6) Clinical Performances

We provide the highest quality of patient care for a wide spectrum of blood diseases and cancers.

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

1. Makoto Nakagawa, Shuhei Fujita, Takuo Katsumoto, Kazutsune Yamagata, Yoko Ogawara, Ayuna Hattori, Yuki Kagiya, Daisuke Honma, Kazushi Araki, Tatsuya Inoue, Ayako Kato, Koichiro Inaki, Chisa Wada, Yoshimasa Ono, Masahide Yamamoto, Osamu Miura, Yasuharu Nakashima, Issay Kitabayashi. Dual inhibition of enhancer of zeste homolog 1/2 overactivates WNT signaling to deplete cancer stem cells in multiple myeloma. *Cancer Sci.* 2019.01; 110(1); 194-208
2. Junichi Tsuchiya, Masahide Yamamoto, Hyeyeol Bae, Takumi Oshima, Tomohiro Yoneyama, Osamu Miura, Ukihide Tateishi. Tumor Identification of Less Aggressive or Indolent Lymphoma With Whole-Body 11C-Acetate PET/CT. *Clin Nucl Med.* 2019.01;
3. Ayako Nogami, Keigo Okada, Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Osamu Miura. Inhibition of the STAT5/Pim Kinase Axis Enhances Cytotoxic Effects of Proteasome Inhibitors on FLT3-ITD-Positive AML Cells by Cooperatively Inhibiting the mTORC1/4EBP1/S6K/Mcl-1 Pathway. *Transl Oncol.* 2019.02; 12(2); 336-349
4. Keisuke Tanaka, Shigeo Toyota, Megumi Akiyama, Naoki Wakimoto, Yuichi Nakamura, Yuho Najima, Noriko Doki, Kazuhiko Kakihana, Aiko Igarashi, Takeshi Kobayashi, Kazuteru Ohashi, Daisuke Kudo, Atsushi Shinagawa, Hina Takano, Takayuki Fujio, Yasushi Okoshi, Mitsuo Hori, Takashi Kumagai, Tatsuya Saito, Junichi Mukae, Koh Yamamoto, Ikuyo Tsutsumi, Takuya Komeno, Chikashi Yoshida, Masahide Yamamoto, Hiroshi Kojima, . Efficacy and Safety of a Weekly Cyclophosphamide-Bortezomib-Dexamethasone Regimen as Induction Therapy Prior to Autologous Stem Cell Transplantation in Japanese Patients with Newly Diagnosed Multiple Myeloma: A Phase 2 Multicenter Trial. *Acta Haematol.* 2019.02; 141(2); 111-118
5. Hiroki Akiyama, Yoshihiro Umezawa, Shinya Ishida, Keigo Okada, Ayako Nogami, Osamu Miura. Inhibition of USP9X induces apoptosis in FLT3-ITD-positive AML cells cooperatively by inhibiting the mutant kinase through aggresomal translocation and inducing oxidative stress. *Cancer Lett.* 2019.04; 453; 84-94

6. Emi Uchida, Shihoko Suwa, Ryoto Yoshimoto, Ken Watanabe, Takeshi Kasama, Osamu Miura, Tetsuya Fukuda. TOPK is regulated by PP2A and BCR/ABL in leukemia and enhances cell proliferation. *Int. J. Oncol.*. 2019.05;
7. Norihiko Kawamata, Ryohei Watanabe. Molecular analysis of the BCR-ABL1 fusion gene in a chronic myeloid leukemia patient with BCR-ABL1 International Scale-undetectable disease. *The Japanese journal of clinical hematology*. 2019.07; 60(7); 767-772
8. Herrmann A, Nagao T, Zhang C, Lahtz C, Li YJ, Yue C, Mülthart R, Yu H. An effective cell-penetrating antibody delivery platform. *JCI insight*. 2019.07; 4(14);
9. Kota Yoshifuji, Yoshihiro Umezawa, Ayako Ichikawa, Ken Watanabe, Osamu Miura, Masahide Yamamoto. Methotrexate-associated Classical Hodgkin Lymphoma Shows Distinct Clinicopathological Features but Comparable Clinical Outcomes With Sporadic Cases. *In Vivo*. 2019.09; 33(5); 1599-1604
10. Masahide Yamamoto, Keisuke Tanaka, Yoshihiro Umezawa, Toshikage Nagao, Shigeo Toyota, Osamu Miura. Soluble Interleukin-2 Receptor Level at Diagnosis Predicts Prognosis of Patients With Follicular Lymphoma Irrespective of Initial Management Strategy. *Anticancer Res.*. 2019.09; 39(9); 5115-5122
11. Kouhei Yamamoto, Shinya Abe, Ayaka Honda, Jun Hashimoto, Yuuki Aizawa, Sachiko Ishibashi, Taro Takemura, Nobutaka Hanagata, Masahide Yamamoto, Osamu Miura, Morito Kurata, Masanobu Kitagawa. Fatty acid beta oxidation enzyme HADHA is a novel potential therapeutic target in malignant lymphoma. *Lab. Invest.*. 2019.09;
12. Takashi Ikeda, Keita Mori, Koji Kawamura, Takehiko Mori, Shotaro Hagiwara, Yasunori Ueda, Kaoru Kahata, Naoyuki Uchida, Nobuhiro Tsukada, Satoshi Murakami, Masahide Yamamoto, Tsutomu Takahashi, Tatsuo Ichinohe, Makoto Onizuka, Yoshiko Atsuta, Yoshinobu Kanda, Shinichiro Okamoto, Kazutaka Sunami, Hiroyuki Takamatsu. Comparison between autologous and allogeneic stem cell transplantation as salvage therapy for multiple myeloma relapsing/progressing after autologous stem cell transplantation. *Hematol Oncol*. 2019.10;
13. Daisuke Watanabe, Ayako Nogami, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Osamu Miura. FLT3-ITD Activates RSK1 to Enhance Proliferation and Survival of AML Cells by Activating mTORC1 and eIF4B Cooperatively with PIM or PI3K and by Inhibiting Bad and BIM. *Cancers (Basel)*. 2019.11; 11(12);

[Misc]

1. Umezawa Y, Kawamata N. Novel therapies for acute myeloid leukemia based on genomic aberrations *The Japanese journal of clinical hematology*. 2019; 60(6); 594-599

[Conference Activities & Talks]

1. Satoru Aoyama, Shunichiro Yasuda, Daisuke Watanabe, Yoshihiro Umezawa, Osamu Miura, Norihiko Kawamata. A Multi-antigen Recognition CAR-T Cell System Using Protease Mediated Protein Cleavage.. The 10th JSH International Symposium 2019.05.17 Mie, Japan
2. Shunichiro Yasuda, Satoru Aoyama, Ryouto Yoshimoto, Daisuke Watanabe, Kouhei Yamamoto, Marito Araki , Norio Komatsu, and Norihiko Kawamata. MPL Overexpression Is a Mechanism of Ruxolitinib-Resistance in CALR mutant Cells. The 10th JSH international symposium 2019.05.17 Mie, Japan
3. Shunichiro Yasuda, Satoru Aoyama, Ryoto Yoshimoto, Daisuke Watanabe, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Ayako Nogami, Kouhei Yamamoto, Takeo Fujiwara , Yoko Eda, Marito Araki , Norio Komatsu , Tetsuya Fukuda, Ayako Arai, Osamu Miura, and Norihiko Kawamata. Overexpression of MPL causes ruxolitinib-resistance in myeloproliferative neoplasms with CALR frame-shift mutations. . The 81st annual meeting of the Japanese society of hematology 2019.10.11 Tokyo
4. Toshikage Nagao, Tohru Aoyama, Ayako Nogami, Yoshihiro Umezawa, Masahide Yamamoto, Norihiko Kawamata, Osamu Miura. Establishment of TNET-1, a novel cell line derived from triple negative essential thrombocythemia. The 81st annual meeting of the Japanese society of hematology 2019.10.11 Tokyo
5. Toshikage Nagao, Ayako Nogami, Yoshihiro Umezawa, Ken Watanabe, Osamu Miura. Establishment and characterization of the new ABC-type DLBCL cell line TMD12. The 81st annual meeting of Japanese society of hematology 2019.10.11 Tokyo

6. Kosuke Arai, Keisuke Tanaka, Yoshihiro Umezawa, Toshikage Nagao, Shigeo Toyota, Osamu Miura, Masahide Yamamoto. Soluble interleukin-2 receptor predicts prognosis in newly diagnosed follicular lymphoma patients. The 81st annual meeting of the Japanese society of hematology 2019.10.12 Tokyo
7. Satoru Aoyama, Shunichiro Yasuda, Daisuke Watanabe, Yoshihiro Umezawa, Osamu Miura, Norihiko Kawamata. A multi-antigen recognition system for CAR-T technology using a protein cleavage method.. The 81st Annual Meeting of the Japanese Society of Hematology 2019.10.12 Tokyo, Japan
8. Ayako Nogami, Watanabe Daisuke, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Toshikage Nagao, Shuji Tohdaand Osamu Miura. FLT3-ITD Enhances Proliferation and Survival of AML Cells through Activation of RSK1 to Upregulate the mTORC1/eIF4F Pathway Cooperatively with PIM or PI3K and to Inhibit Bad and Bim. 60th ASH Annual Meeting and Exposition 2019.12.01 FL, Orange County Convention Center
9. Satoru Aoyama, Shunichiro Yasuda, Daisuke Watanabe, Hiroki Akiyama, Yoshihiro Umezawa, Ayako Nogami, Osamu Miura, Norihiko Kawamata. A Novel Protease-Mediated Chimeric Antigen Receptor (CAR) Double-Arm” CAR-T cell system Improves Target Specificity of CAR-T Cell Therapy. The 61st ASH Annual Meeting and Exposition 2019.12.07 Orlando, FL
10. Shunichiro Yasuda, Satoru Aoyama, Ryoto Yoshimoto, Daisuke Watanabe, Keigo Okada, Hiroki Akiyama, YoshihiroUmezawa, Ayako Nogami, Kouhei Yamamoto, Takeo Fujiwara , Yoko Edahiro, Marito Araki , Norio Komatsu , Tetsuya Fukuda, Ayako Arai, Osamu Miura, and Norihiko Kawamata. Overexpression of MPL Causes Ruxolitinib-Resistance in Myeloproliferative Neoplasms with Calreticulin Frame-Shift Mutations. The 61st American Society of Hematology Annual Meeting & Exposition 2019.12.07 Orlando, FL

Molecular Endocrinology and Metabolism

Professor: Tetsuya Yamada

Associate Professor: Kenji Ikeda, Hajime Izumiyama

Assistant Professor: Chikara Komiya, Kazutaka Tsujimoto, Kumiko Shiba

Clinical Fellow: Takeshi Kakei, Taito Miyoshi, Shoko Mori, Chang Ching Houn

Resident: Sohei Matsushita

Project Assistant Professor: Xunmei Yuan, Mitsuyuki Numasawa

Graduate Students (Doctor's course): Yujiro Nakano, Tatsuya Fukuda, Nozomi Hanzawa, Masahiro Asakawa, Yoshihiro

(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 diabetes, 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) Mechanisms and development of new therapeutic strategies of diabetes and metabolic syndrome
- 2) Thermogenesis and energy metabolism
- 3) Induced molecular mechanism of thermogenic fat
- 4) Role of epigenetic regulation in metabolism
- 5) Mechanism of pathogenesis in endocrine tumors

3. Clinical Services

Comprehensive inpatient and outpatient services in the area of endocrine and metabolic disorders, including:

- 1) diabetes mellitus, diabetic complications, metabolic syndrome, and obesity
- 2) diseases of the thyroid, pituitary and adrenal glands.
- 3) primary and secondary hypertension
- 4) disorders of calcium metabolism

(2) Publications

[Original Articles]

1. Nakano Y, Hashimoto K, Ohkiba N, Okuma H, Minami I, Takahashi H, Tanaka Y, Yoshimoto T, Yamada T. A Case of Refractory Hypothyroidism due to Poor Compliance Treated with the Weekly Intravenous and Oral Levothyroxine Administration. *Case reports in endocrinology*. 2019; 2019; 5986014
2. Kaneko Keizo, Satake Chihiro, Izumi Tomohito, Tanaka Mamiko, Yamamoto Junpei, Asai Yoichiro, Sawada Shojiro, Imai Junta, Yamada Tetsuya, Katagiri Hideki. Enhancement of postprandial endogenous

- insulin secretion rather than exogenous insulin injection ameliorated insulin antibody-induced unstable diabetes: a case report *BMC ENDOCRINE DISORDERS*. 2019.01; 19(1); 5
3. Chen Yong, Ikeda Kenji, Yoneshiro Takeshi, Scaramozza Annarita, Tajima Kazuki, Wang Qiang, Kim Kyeongkyu, Shinoda Kosaku, Sponton Carlos Henrique, Brown Zachary, Brack Andrew, Kajimura Shingo. Thermal stress induces glycolytic beige fat formation via a myogenic state *NATURE*. 2019.01; 565(7738); 180-+
 4. Niitsu Y, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Satou F, Tsujino M, Ota K, Kudo A, Tanabe M, Yamada T, Ogawa Y. Clinical outcomes of 20 Japanese patients with insulinoma treated with diazoxide. *Endocrine journal*. 2019.02; 66(2); 149-155
 5. Nakatsu Yusuke, Matsunaga Yasuka, Yamamotoya Takeshi, Ueda Koji, Inoue Masa-ki, Mizuno Yu, Nakanishi Mikako, Sano Tomomi, Yamawaki Yosuke, Kushiya Akifumi, Sakoda Hideyuki, Fujishiro Midori, Ryo Akihito, Ono Hiraku, Minamino Tohru, Takahashi Shin-ichiro, Ohno Haruya, Yoneda Masayasu, Takahashi Kei, Ishihara Hisamitsu, Katagiri Hideki, Nishimura Fusanori, Kanematsu Takashi, Yamada Tetsuya, Asano Tomoichiro. Prolyl Isomerase Pin1 Suppresses Thermogenic Programs in Adipocytes by Promoting Degradation of Transcriptional Co-activator PRDM16 *CELL REPORTS*. 2019.03; 26(12); 3221-3230
 6. Takeda Y, Umakoshi H, Takeda Y, Yoneda T, Kurihara I, Katabami T, Ichijo T, Wada N, Yoshimoto T, Ogawa Y, Kawashima J, Sone M, Takahashi K, Watanabe M, Matsuda Y, Kobayashi H, Shibata H, Kamemura K, Otsuki M, Fujii Y, Yamamoto K, Ogo A, Yanase T, Suzuki T, Naruse M, JPAS Study Group.. Impact of adrenocorticotrophic hormone stimulation during adrenal venous sampling on outcomes of primary aldosteronism. *Journal of hypertension*. 2019.05; 37(5); 1077-1082
 7. Yujiro Nakano, Takanobu Yoshimoto, Ryo Watanabe, Masanori Murakami, Tatsuya Fukuda, Kazutaka Saito, Yasuhisa Fujii, Takumi Akashi, Toshihiro Tanaka, Tetsuya Yamada, Mitsuhide Naruse, Yoshihiro Ogawa. miRNA299 involvement in CYP11B2 expression in aldosterone-producing adenoma. *Eur. J. Endocrinol.* 2019.05;
 8. KanakoToda, Koji Mizutani, Isao Minami, Ming Ye, Takahiro Arakawa, Kohji Mitsubayashi, Yoshihiro Ogawa, Kouji Araki, Kayoko Shinada. Effects of oral health instructions on glycemic control and oral health status of periodontitis patients with type 2 diabetes mellitus: A preliminary observation *Journal of Dental Sciences*. 2019.06; 14(2); 171-177
 9. Mori K, Tsuchiya K, Nakamura S, Miyachi Y, Shiba K, Ogawa Y, Kitamura K. Ipragliflozin-induced adipose expansion inhibits cuff-induced vascular remodeling in mice. *Cardiovascular diabetology*. 2019.06; 18(1); 83
 10. Mori Kentaro, Tsuchiya Kyoichiro, Nakamura Suguru, Shiba Kumiko, Miyachi Yasutaka, Ogawa Yoshihiro, Kitamura Kenichiro. Molecular Mechanisms of Obesity-Associated Vascular Vulnerability via Signals of Appetite Regulation *DIABETES*. 2019.06; 68;
 11. Yoneshiro Takeshi, Wang Qiang, Tajima Kazuki, Matsushita Mami, Maki Hiroko, Igarashi Kaori, Dai Zhipeng, White Phillip J., McGarrah Robert W., Ilkayeva Olga R., Deleze Yann, Oguri Yasuo, Kuroda Mito, Ikeda Kenji, Li Huixia, Ueno Ayano, Ohishi Maki, Ishikawa Takamasa, Kim Kyeongkyu, Chen Yong, Sponton Carlos Henrique, Pradhan Rachana N., Majd Homa, Greiner Vanille Juliette, Yoneshiro Momoko, Brown Zachary, Chondronikola Maria, Takahashi Haruya, Goto Tsuyoshi, Kawada Teruo, Sidossis Labros, Szoka Francis C., McManus Michael T., Saito Masayuki, Soga Tomoyoshi, Kajimura Shingo. BCAA catabolism in brown fat controls energy homeostasis through SLC25A44 *NATURE*. 2019.08; 572(7771); 614-+
 12. Kazuki Tajima, Kenji Ikeda, Hsin-Yi Chang, Chih-Hsiang Chang, Takeshi Yoneshiro, Yasuo Oguri, Heejin Jun, Jun Wu, Yasushi Ishihama, Shingo Kajimura. Mitochondrial lipoylation integrates age-associated decline in brown fat thermogenesis *Nature Metabolism*. 2019.09; 1; 886-898
 13. Fukuda T., Bouchi R., Asakawa M., Takeuchi T., Shiba K., Tsujimoto K., Komiya C., Yoshimoto T., Ogawa Y., Yamada T.. Sarcopenic obesity is associated with a faster decline in renal function in people with type 2 diabetes *DIABETIC MEDICINE*. 2019.10;
 14. Hayashi R, Minami I, Sasahara Y, Izumiyama H, Yoshimoto T, Kishino M, Kudo A, Tateishi U, Tanabe M, Yamada T. Diagnostic accuracy of selective arterial calcium injection test for localization of gastrinoma. *Endocrine journal*. 2019.12;

15. Asakawa M, Itoh M, Suganami T, Sakai T, Kanai S, Shirakawa I, Yuan X, Hatayama T, Shimada S, Akiyama Y, Fujiu K, Inagaki Y, Manabe I, Yamaoka S, Yamada T, Tanaka S, Ogawa Y. Upregulation of cancer-associated gene expression in activated fibroblasts in a mouse model of non-alcoholic steatohepatitis. *Scientific reports*. 2019.12; 9(1); 19601

[Conference Activities & Talks]

1. Xunmei Yuan, Koshi Hashimoto, Yoshihiro Ogawa. Epigenetic regulation of genes related to energy metabolism in perinatal mouse liver and its long-term effects in adulthood. 2019 神戸
2. Xunmei Yuan, Koshi Hashimoto, Nozomi Hanzawa, Miho Hamaguchi, Kazutaka Tsujimoto, Tetsuya Yamada and Yoshihiro Ogawa. Genome-wide DNA methylation analysis of PGC1 α -deficient mice. 2019
3. Takahashi K, Yamada T, Sugisawa T, Kawata K, Asai Y, Munakata Y, Kodama S, Sawada S, Imai J, Inada M, Katagiri H.. Systemic glucose oxidation is enhanced in acquired liver and muscle insulin receptor knockout mice.. The 9th Federation of Asian and Oceanian Physiological Societies Congress 2019.03.29
4. Adachi Y, Ota K, Ishi R, Cho K, Hiramatsu Y, Masuda S, Koseki S, Hayashi T, Komatsu N, Mizoguchi Y, Minami I, Yamada T, Watanabe T.. Lower Insulin Secretion Is Associated with Parahippocampal Gyrus Atrophy in Elderly Patients with Type 2 Diabetes Mellitus.. 79th Scientific Sessions American Diabetes Association 2019.06.09

Hepatobiliary and Pancreatic Surgery

Director & Professor

Minoru Tanabe MD, PhD

Associate Professor

Atsushi Kudo MD, PhD

Lecturer

Daisuke Ban MD, PhD

Assistant Professor

Yusuke Mitsunori MD, PhD (until March)

Hiroaki Ono MD, PhD

Kosuke Ogawa MD, PhD

Toshiro Ogura MD, PhD (until September)

Keiichi Akahoshi MD, PhD (from April)

Shuichi Watanabe MD, PhD (from October)

Yoshiya Ishikawa MD, PhD (from October)

Graduate School Students

Bo Liu MD (until September)

Shuichi Watanabe MD (until September)

Jun Yoshino MD (until March)

Daisuke Asano MD (until March)

Masafumi Akasu MD

Tomotaka Kato MD

Toshitaka Sugawara MD

Takeshi Ishii MD

Satoshi Matsui MD (until March)

Yoshiki Murase MD

Aya Maekawa MD (from April)

Kouhei Yagi MD (from 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 and pancreatic cancers
- Liver transplantation and organ preservation
- Treatments for neuroendocrine tumor
- Innovation of imaging modality for hepatobiliary and pancreatic cancers
- Establishment of PDX model in hepatobiliary and pancreatic cancer

(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) Lectures & Courses

Undergraduate education: Educate and acquire knowledge as a surgeon in general and basic knowledge, then more practical knowledge and stages, in accordance with the actual case as much as possible in a one-on-one system with a supervising doctor. At the same time, they will teach you how to be a doctor and learn morals according to specific cases such as how to treat patients and issues of illness notification. Basic surgical procedures will be entrusted to postgraduate education, but the aim is to gain many clinical experiences by assisting many patients with hepatobiliary and pancreatic surgery as high-assistance surgery.

Post-graduate education: The primary purpose is to develop surgeons with a high level of consulting skills in cooperation with related hospitals. Instruct students to have a viewpoint. We want to not only provide surgeons and gastroenterologists with training that can be obtained, but also motivate internationally competitive specialists and surgical researchers to make a leap forward.

(5) Clinical Services & Other Works

Diseases of hepatobiliary, pancreatic, and splenic areas are the targets of our department, and we mainly focus on multidisciplinary treatments for malignant tumors centering on surgical treatment. The mission of the university is to push the limits of surgical indications for highly advanced and refractory cancers, using preoperative simulation using a workstation and resection / reconstruction with vascular complications. In addition, arthroscopic surgery will be developed as a minimally invasive treatment. As an important treatment option for patients with end-stage liver disease, we also make indications for living donor liver transplantation. In laparoscopic surgery, we will develop new surgical instruments and procedures to promote safer, reduced port surgery that minimizes abdominal wall destruction, and expand the indication of minimally invasive operations.

(6) 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: 74 cases, pancreatectomy: 81 cases) were performed in 2019, placing

one of the top high volume medical centers in the country for hepatobiliary pancreatic surgery. More than 600 patients with neuroendocrine tumors were treated in 2019. We have treated the largest number of the patients with NENs in Japan.

(7) Publications

[Original Articles]

1. Shu Shimada, Kaoru Mogushi, Yoshimitsu Akiyama, Takaki Furuyama, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shigeki Ariei, Minoru Tanabe, Jack R. Wands, Shinji Tanaka. Comprehensive molecular and immunological characterization of hepatocellular carcinoma EBioMedicine published by the lancet. 2019.02; 40; 457-470
2. Watanabe S, Shimada S, Akiyama Y, Ishikawa Y, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Loss of KDM6A characterizes a poor prognostic subtype of human pancreatic cancer and potentiates HDAC inhibitor lethality. International Journal of Cancer. 2019.07; 145(1); 192-205
3. Asano D, Nara S, Kishi Y, Esaki M, Hiraoka N, Tanabe M, Shimada K. A Single-Institution Validation Study of Lymph Node Staging By the AJCC 8th Edition for Patients with Pancreatic Head Cancer: A Proposal to Subdivide the N2 Category. Annals of Surgical Oncology. 2019.07; 26(7); 2112-2120
4. Jun Yoshino, Daisuke Ban, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The Clinical Implications of Peripancreatic Fluid Collection After Distal Pancreatectomy World Journal of Surgery. 2019.08; 43(8); 2069-2076
5. Ariizumi S, Ban D, Abe Y, Kumamoto T, Koizumi S, Tanabe M, Shinoda M, Endo I, Otsubo T, Yamamoto M. High-signal-intensity MR Image in the Hepatobiliary Phase Predicts Long-term Survival in Patients With Hepatocellular Carcinoma Anticancer Reserch. 2019.08; 39; 4219-4225
6. Matsui S, Kudo A, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Tanaka S, Tanabe M. Does sunitinib have a patient-specific dose without diminishing its antitumor effect on advanced pancreatic neuroendocrine neoplasms? Journal of Cancer Research and Clinical Oncology. 2019.08; 145(8); 2097-2104
7. Liu B, Kudo A, Kinowaki Y, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Tanaka S, Akashi T, Tanabe M. A simple and practical index predicting the prognoses of the patients with well-differentiated pancreatic neuroendocrine neoplasms The Japanese Society of Gastroenterology. 2019.09; 54(9); 819-828
8. Taiga Wakabayashi, Taizo Hibi, Godai Yoneda, Yasuhito Iwao, Yu Sawada, Hiroyuki Hoshino, Shuichiro Uemura, Daisuke Ban, Atsushi Kudo, Yusuke Takemura, Kohei Mishima, Masahiro Shinoda, Osamu Itano, Takehito Otsubo, Itaru Endo, Yuko Kitagawa, Minoru Tanabe, Hiroto Egawa, Masakazu Yamamoto. Predictive model for survival after liver resection for noncolorectal liver metastases in the modern era: a Japanese multicenter analysis. Journal of Hepato-Biliary-Pancreatic Sciences. 2019.10; 26(10); 441-448
9. Ohtsuka T, Nagakawa Y, Toyama H, Takeda Y, Maeda A, Kumamoto Y, Nakamura Y, Hashida K, Honda G, Fukuzawa K, Toyoda E, Tanabe M, Gotohda N, Matsumoto I, Ryu T, Uyama I, Kojima T, Unno M, Ichikawa D, Inoue Y, Matsukawa H, Sudo T, Takaori K, Yamaue H, Eguchi S, Tahara M, Shinzeki M, Eguchi H, Kurata M, Morimoto M, Hayashi H, Marubashi S, Inomata M, Kimura K, Amaya K, Sho M, Yoshida R, Murata A, Yoshitomi H, Hakamada K, Yasunaga M, Abe N, Hioki M, Tsuchiya M, Misawa T, Seyama Y, Noshiro H, Sakamoto E, Hasegawa K, Kawabata Y, Uchida Y, Kameyama S, Ko S, Takao T, Kitahara K, Nakahira S, Baba H, Watanabe M, Yamamoto M, Nakamura M. A multicenter prospective registration study on laparoscopic pancreatectomy in Japan: report on the assessment of 1,429 patients. Journal of Hepato-Biliary-Pancreatic Sciences. 2019.10;
10. Yoshino J, Akiyama Y, Shimada S, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Loss of ARID1A induces a stemness gene ALDH1A1 expression with histone acetylation in the malignant subtype of cholangiocarcinoma. Carcinogenesis. 2019.10;
11. Matsui S, Ogura T, Ban D, Ogawa K, Ono H, Mitsunori Y, Kudo A, Tanaka S, Tanabe M. Position of the Pancreas Division Line and Postoperative Outcomes After Distal Pancreatectomy. World Journal of Surgery. 2019.11;

12. Kato T, Ban D, Tateishi U, Ogura T, Ogawa K, Ono H, Mitsunori Y, Kudo A, Tanaka S, Tanabe M. Reticular Pattern around SMA in CT Imaging Predicting Poor Prognosis of Pancreatic Head Cancer. *Journal of Hepato-Biliary-Pancreatic Sciences*. 2019.11;
13. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Emi Inoue-Shinomiya, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Minoru Tanabe, Emiko Sugawara, Akira Takemoto, Hidenori Ojima, Michiie Sakamoto, Masaru Muraoka, Shinichi Takano, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive genetic analysis of cholangiolocellular carcinoma with a coexistent hepatocellular carcinoma-like area and metachronous hepatocellular carcinoma. *Hepatol Res*. 2019.12; 49(12); 1466-1474
14. Hayashi R, Minami I, Sasahara Y, Izumiyama H, Yoshimoto T, Kishino M, Kudo A, Tateishi U, Tanabe M, Yamada T. Diagnostic accuracy of selective arterial calcium injection test for localization of gastrinoma. *Endocrine Journal*. 2019.12;
15. Ono H, Kudo A, Akahoshi K, Ogura T, Ogawa K, Ban D, Tanaka S, Tanabe M. Combination of weekly streptozocin and oral S-1 treatment for patients of unresectable or metastatic pancreatic neuroendocrine neoplasms. *Journal of Cancer Research and Clinical Oncology*. 2019.12;
16. Kosuke Ogawa, Qiushi Lin, Le Li, Xuewei Bai, Xuesong Chen, Hua Chen, Rui Kong, Yongwei Wang, Hong Zhu, Fuliang He, Qinggang Xu, Lianxin Liu, Min Li, Songhua Zhang, Katsuya Nagaoka, Rolf Carlson, Howard Safran, Kevin Charpentier, Bei Sun, Jack Wands. Aspartate β -hydroxylase promotes pancreatic ductal adenocarcinoma metastasis through activation of SRC signaling pathway *Journal of Hematology & Oncology*. 2019.12; 12(1); 144

[Conference Activities & Talks]

1. Daisuke Ban. Key techniques of laparoscopic right posterior sectionectomy. China-Japan-Korea Laparoscopic Hepatectomy Summit Forum 2019.03.22 China· GuangZhou
2. MINORU TANABE. SILS Laparoscopic cholecystectomy. ASIA IRCAD Advanced Course in Hepatobiliary and Pancreatic surgery 2019.04.25 Taiwan
3. MINORU TANABE. Prerecorded LIVE case : Single Port laparoscopic cholecystectomy. ASIA IRCAD Advanced Course in Hepatobiliary and Pancreatic surgery 2019.04.25 Taiwan
4. D. Ban, T. Ishii, Y. Murase, A. Maekawa, T. Sugawara, S. Matsui, T. Kato, J. Yoshino, T. Ogura, K. Ogawa, H. Ono, A. Kudo, M. Tanabe. Image guided laparoscopic liver resection with real-time reference and simulation by tablet device. The 2nd World Congress of the International Laparoscopic Liver Society 2019.05.09 Tokyo
5. Yasuhisa Mori, Yuichiro Otsuka, Yoshihiro Miyasaka, Daisuke Ban, Yukio Iwashita, Hironori Kaneko, Minoru Tanabe, Go Wakabayashi. Development of New guidelines for laparoscopic liver resection; A program of Japanese Society for Endoscopic Surgery. The 2nd World Congress of the International Laparoscopic Liver Society 2019.05.09 Tokyo
6. Yasuhisa Mori, Yuichiro Otsuka, Yoshihiro Miyasaka, Daisuke Ban, Yukio Iwashita, Hironori Kaneko, Minoru Tanabe, Go Wakabayashi. Development of New guidelines for laparoscopic liver resection; A program of Japanese Society for Endoscopic Surgery. The 2nd World Congress of the International Laparoscopic Liver Society 2019.05.09 Tokyo
7. Minoru Tanabe. Safe diffusion of laparoscopic liver resection in Japan: An analysis of National Clinical Database. The 2nd World Congress of the International Laparoscopic Liver Society 2019.05.11 Tokyo
8. D Ban, T Sugawara, T Kato, A Kdo, M Tanabe. THE IMPLICATION OF INDUCTION CHEMOTHERAPY FOLLOWED BY CHEMORADIOTHERAPY FOR LOCALLY ADVANCED PANCREATIC CANCER, INTENDED CONVERSION SURGERY. 53rd ANNUAL MEETING of Pancreas Club 2019.05.18 San Diego
9. T Kato, D Ban, T Ogura, K Ogawa, H Ono, Y Mistunori, A Kudo, M Tanabe. WHERE IS THE APPROPRIATE BORDERLINE? - THE POOR PROGNOSIS IN RESECTABLE PANCREATIC CANCER WITH HAZY DENSITY. 53rd ANNUAL MEETING of Pancreas Club 2019.05.18 San Diego

10. K Akahoshi, H Ono, M Akasu, D Ban, A Kudo, A Konta, S Tanaka, M Tanabe. RAPID GROWTH SPEED OF CYSTS CAN PREDICT MALIGNANT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS. 53rd ANNUAL MEETING of Pancreas Club 2019.05.18 San Diego
11. T Sugawara, D Ban, S Watanabe, T Ogura, K Ogawa, H Ono, Y Mitsunori, A Kudo, M Tanabe. PREOPERATIVE FACTORS FOR EARLY RECURRENCE OF RESECTED PANCREATIC DUCTAL ADENOCARCINOMA. 53rd ANNUAL MEETING of Pancreas Club 2019.05.18 San Diego
12. T Ohtsuka, D Ban, Y Nakamura, Y Nakagawa, M Tanabe, Y Gotoh, VVDM Velasquez, K Nakata, Y Sahara, K Takaori, G Honda, T Misawa, M Kawai, H Yamaue, T Morikawa, T Kuroki, Y Mou, WJ Lee, SV Shrikhande, CN Tang, C Conrad, HS Han, C Palanivelu, HJ Asbun, DA Koo. DIFFICULTY SCORING SYSTEM IN LAPAROSCOPIC DISTAL PANCREATECTOMY. 53rd ANNUAL MEETING of Pancreas Club 2019.05.18 San Diego
13. T Ohtsuka, D Ban, Y Nakamura, Y Nakagawa, M Tanabe, Y Gotoh, VVDM Velasquez, K Nakata, Y Sahara, K Takaori, G Honda, T Misawa, M Kawai, H Yamaue, T Morikawa, T Kuroki, Y Mou, WJ Lee, SV Shrikhande, CN Tang, C Conrad, HS Han, C Palanivelu, HJ Asbun, DA Koo. DIFFICULTY SCORING SYSTEM IN LAPAROSCOPIC DISTAL PANCREATECTOMY. 53rd ANNUAL MEETING of Pancreas Club 2019.05.18 San Diego
14. Daisuke Ban . Safe Techniques of Liver Parenchyma Dissection - Excavation. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.13 Takamatsu
15. Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Roadmap to the qualified laparoscopic HBP surgeon. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.13 Takamatsu
16. Takeshi Ishii, Toshiro Ogura, Yoshiki Murase, Toshitaka Sugawara, Masahumi Akasu, Tomotaka Kato, Jun Yoshino, Shuichi Watanabe, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Surgery for obese patients with hepatocellular carcinoma. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.13 Takamatsu
17. Toshiro Ogura, Daisuke Ban, Satoshi Matsui, Takeshi Ishii, Toshitaka Sugawara, Tomotaka Kato, Masahumi Akasu, Daisuke Asano, Jun Yoshino, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Laparoscopic anatomical hepatectomy approaching the hepatic vein first. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.13 Takamatsu
18. Toshitaka Sugawara, Daisuke Ban, Takeshi Ishii, Satoshi Matsui, Masahumi Akasu, Tomotaka Kato, Daisuke Asano, Jun Yoshino, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Preoperative factors for early recurrence of resected pancreatic ductal adenocarcinoma. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.14 Takamatsu
19. Keiichi Akahoshi, Satoshi Nara, Shinsuke Hiraoka, Yogi Kishi, Minoru Esaki, Kazuaki Shimada. Recurrence patterns and optimal lymph node discussion for intrahepatic cholangiocarcinoma. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.14 Takamatsu
20. Shuichi Watanabe, Daisuke Ban, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The analysis of the treatment for the metachronous solitary metastasis after curative surgery in pancreatic cancer. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.14 Takamatsu
21. Tomotaka Kato, Hiroaki Ono, Toshiro Ogura, Kosuke Ogawa, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Minoru Tanabe. Functional analysis of RRM1 gene related to cell proliferation and gemcitabine resistance in pancreatic cancer cells. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.14 Takamatsu
22. Atsushi Kudo, Yoshiki Murase, Daisuke Asano, Toshitaka Sugawara, Takeshi Ishii, Satoshi Matsui, Tomotaka Kato, Masahumi Akasu, Jun Yoshino, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Minoru Tanabe. Biomarker and Treatment strategy for pancreatic neuroendocrine tumors. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.15 Takamatsu

23. Kosuke Ogawa, Atsushi Kudo, Toshiro Ogura, Yusuke Mitsunori, Hiroaki Ono, Daisuke Ban, Minoru Tanabe. Strategy for liver metastases of pancreatic neuroendocrine tumor. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.15 Takamatsu
24. Masahumi Akasu, Atsushi Kudo, Tomotaka Kato, Daisuke Asano, Jun Yoshino, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Minoru Tanabe. The effect of venous invasion and recurrence in Neuroendocrine tumor. The effect of venous invasion and recurrence in Neuroendocrine tumor 2019.06.15 Takamatsu
25. Hiroaki Ono, Atsushi Kudo, Kosuke Ogawa, Toshiro Ogura, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. Evaluation of the management for advanced P-NET with liver metastasis. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.15 Takamatsu
26. Yoshiki Murase, Atsushi Kudo, Toshitaka Sugawara, Satoshi Matsui, Takeshi Ishii, Tomotaka Kato, Masahumi Akasu, Daisuke Asano, Jun Yoshino, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Minoru Tanabe. The index to decide PFS after lanreotide administration for patients with neuroendocrine tumor. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.15 Takamatsu
27. Daisuke Ban, Yoshiki Murase, Satoru Murao, Satoshi Matsui, Takeshi Ishii, Toshitaka Sugawara, Masahumi Akasu, Tomotaka Kato, Jun Yoshino, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Daisuke Asano, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Keiichi Akita, Minoru Tanabe. Current topics of the surgical anatomy concerning Pancreatoduodenectomy. The 31st Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2019.06.15 Takamatsu
28. Daisuke Ban. The efficacy of induction chemotherapy for locally advanced pancreatic cancer, intended conversion surgery. The 65th annual congress of international college of surgeons Japan section 2019.06.22 Tokyo
29. David Gerber, Minoru Tanabe. TRANSPLANT VS. LIVER RESECTION FOR PRIMARY HCC (DEBATE). 48th World Congress of Surgery 2019.08.14
30. Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Minoru Tanabe. NON-VIRAL HEPATOCELLULAR CARCINOMA AND LIFESTYLE RELATED DISEASES AS ITS RISK FACTORS. 48th World Congress of Surgery 2019.08.14 Krakow
31. Hiroaki Ono, Atsushi Kudo, Kosuke Ogawa, Toshiro Ogura, Yusuke Mitsunori, Daisuke Ban, Minoru Tanabe. EVALUATION OF MULTIDISCIPLINARY TREATMENT FOR ADVANCED PANCREATIC NEUROENDOCRINE TUMOR. 48th World Congress of Surgery 2019.08.14 Krakow
32. Minoru Tanabe. Standardization and Safe Dissemination of Laparoscopic Liver Resection in Japan. IASGO2019 2019.10.05 Bangkok
33. Daisuke Ban. Current status of laparoscopic liver resection in Japan - the development and our position. Lietuvos chirurgu asociacijos suvaziavimas 2019 2019.10.11 Lithuania
34. Hiroaki Ono, Sadakatsu Ikeda, Kosuke Ogawa, Toshiro Ogura, Daisuke Ban, Atsushi Kudo, Satoshi Miyake, Shinji Tanaka, Minoru Tanabe. Genomic sequencing in HBP malignancies. JAPAN DIGESTIVE DISEASE WEEK 2019 2019.11.22 Kobe
35. Shinji Tanaka, Shuichi Watanabe, Minoru Tanabe.. Novel genetic and immunological classification of hepatocellular carcinoma for the subtype-specific precision immunotherapy. JAPAN DIGESTIVE DISEASE WEEK 2019 2019.11.22 Kobe

[Patents]

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

Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa
Associate Professor: Toshitaka Yoshii
Junior Associate Professor: Hiroyuki Inose
Assistant Professor: Yuko Segawa, Hirotaka Koyanagi,
Koji Fujita, Takashi Hirai, Masato Yuasa
Specially Appointed Assistant Professor: Masanobu Hirao, Hiroaki Onuma

「Department of Orthopaedic and Trauma Research」
Specially Appointed Associate Professor: Yoshinori Asou
Junior Associate Professor: Yoto Oh
Assistant Professor: Hiroki Ochi
Specially Appointed Assistant Professor: Ryohei Takada

「Joint Research Department of Advanced Technology in Medicine」
Joint Research Professor: Shigenori Kawabata
Specially Appointed Junior Associate Professor: Yuko Hoshino

(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 especially 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.

(3) Education

Our department has several regular programs such as "Bedside Professor Round" at Monday 14:30-16:30, "Clinical Conference" at Monday 7:30-9:00, and "Journal Clubs 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 up-dated knowledge of clinical medicine through regularly-held journal clubs and research meetings.

(4) Lectures & Courses

Japanese orthopaedic research is characterized by the fact that surgeon himself participates in experiments while he is working as a clinician. A lot of new knowledge concerning bone, cartilage and nerve were discovered by this so-called "surgeon scientist".

We have already taken a new artificial bone developed in our section to the market and have been preparing a revolutionary device for measuring spinal magnetic signals. We think it very important that research by a surgeon should be based on clinical problems even when methodology of molecular biology is used.

Our graduate students learn basic technique of orthopaedic research and also acquire the ability of life-continuing attitude for clinical studies.

(5) Clinical Services & Other Works

Our orthopaedic department consists of two graduate school Sections, the Orthopaedic and Spinal Surgery and the Joint Surgery and Sports Medicine. We deal with all kinds of orthopaedic diseases such as spine, hand, hip, knee, and musculoskeletal tumor. More than twenty registered orthopaedic surgeons belong to our department. We also organized 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 collagen, using to fill large bone defect.

(7) Publications

[Original Articles]

1. Hiroyuki Inose, Yutaka Kobayashi, Masato Yuasa, Takashi Hirai, Toshitaka Yoshii, Atsushi Okawa. Post-operative lymphocyte percentage and neutrophil-lymphocyte ratio are useful markers for the early prediction of surgical site infection in spinal decompression surgery *Journal of Orthopaedic Surgery*. 2019;
2. Koji Fujita. Elucidation of the mechanism of the promotion of bone fracture healing by mature osteoblast transplantation and its application to development of novel therapeutic methods. *Impact..* 2019; 2019(4); 54-56
3. Shimura H, Sato T, Nimura A, Wakabayashi Y, Fujita K. Surgical Repair of Dorsal Capsulo-Ligamentous Complex for Dislocation of the Thumb Carpometacarpal Joint. *Open Journal of Orthopedics..* 2019; 9(08); 145
4. Shuta Ushio, Yuko Hoshino, Shigenori Kawabata, Yoshiaki Adachi, Kensuke Sekihara, Satoshi Sumiya, Dai Ukegawa, Kyohei Sakaki, Taishi Watanabe, Yuki Hasegawa, Atsushi Okawa. Visualization of the electrical activity of the cauda equina using a magnetospinography system in healthy subjects. *Clin Neurophysiol*. 2019.01; 130(1); 1-11
5. Toshitaka Yoshii, Takashi Hirai, Akio Iwanami, Narihito Nagoshi, Kazuhiro Takeuchi, Kanji Mori, Tsuyoshi Yamada, Shoji Seki, Takashi Tsuji, Kanehiro Fujiyoshi, Mitsuru Furukawa, Soraya Nishimura, Kanichiro Wada, Masao Koda, Takeo Furuya, Yukihiro Matsuyama, Tomohiko Hasegawa, Katsushi Takeshita, Atsushi Kimura, Masahiko Abematsu, Hirotaka Haro, Tetsuro Ohba, Masahiko Watanabe, Hiroyuki Katoh, Kei Watanabe, Hiroshi Ozawa, Haruo Kanno, Shiro Imagama, Kei Ando, Shunsuke Fujibayashi, Morio Matsumoto, Masaya Nakamura, Masashi Yamazaki, Atsushi Okawa, Yoshiharu Kawaguchi. Co-existence of ossification of the nuchal ligament is associated with severity of ossification in the whole spine in patients

- with cervical ossification of the posterior longitudinal ligament -A multi-center CT study. *J Orthop Sci.* 2019.01; 24(1); 35-41
6. Yoto Oh, Yoshiro Kurosa, Atsushi Okawa. Staged internal plate fixation of severe lower extremity fractures that use a temporary external fixator for the initial treatment as an intraoperative retention tool: a technical note. *Arch Orthop Trauma Surg.* 2019.01; 139(1); 53-59
 7. Yasuhiro Shirai, Kenzo Hirao, Tomohiko Shibuya, Shuichi Okawa, Yuki Hasegawa, Yoshiaki Adachi, Kensuke Sekihara, Shigenori Kawabata. Magnetocardiography Using a Magnetoresistive Sensor Array. *Int Heart J.* 2019.01; 60(1); 50-54
 8. Takashi Hirai, Takashi Taniyama, Toshitaka Yoshii, Koichi Mizuno, Mikio Okamoto, Hiroyuki Inose, Masato Yuasa, Kazuyuki Otani, Shigeo Shindo, Osamu Nakai, Atsushi Okawa. Clinical Outcomes of Surgical Treatment for Arachnoid Web: A Case Series. *Spine Surg Relat Res.* 2019.01; 3(1); 43-48
 9. Tsuyoshi Kato, Hiroyuki Inose, Shoichi Ichimura, Yasuaki Tokuhashi, Hiroaki Nakamura, Masatoshi Hoshino, Daisuke Togawa, Toru Hirano, Hirotaka Haro, Tetsuro Ohba, Takashi Tsuji, Kimiaki Sato, Yutaka Sasao, Masahiko Takahata, Koji Otani, Suketaka Momoshima, Ukihide Tateishi, Makoto Tomita, Ryuichi Takemasa, Masato Yuasa, Takashi Hirai, Toshitaka Yoshii, Atsushi Okawa. Comparison of Rigid and Soft-Brace Treatments for Acute Osteoporotic Vertebral Compression Fracture: A Prospective, Randomized, Multicenter Study. *J Clin Med.* 2019.02; 8(2);
 10. Tsuyoshi Yamada, Toshitaka Yoshii, Yu Matsukura, Takuya Oyaizu, Masato Yuasa, Takashi Hirai, Kyohei Sakaki, Hiroyuki Inose, Ichiro Torigoe, Kenichiro Sakai, Atsushi Okawa, Yoshiyasu Arai. Retrospective analysis of surgical outcomes for atlantoaxial subluxation. *J Orthop Surg Res.* 2019.03; 14(1); 75
 11. Kei Watanabe, Keiichi Katsumi, Masayuki Ohashi, Yohei Shibuya, Tomohiro Izumi, Toru Hirano, Naoto Endo, Takashi Kaito, Tomoya Yamashita, Hiroyasu Fujiwara, Yukitaka Nagamoto, Yuji Matsuoka, Hidekazu Suzuki, Hirosuke Nishimura, Hidetomi Terai, Koji Tamai, Atsushi Tagami, Syuta Yamada, Shinji Adachi, Toshitaka Yoshii, Shuta Ushio, Katsumi Harimaya, Kenichi Kawaguchi, Nobuhiko Yokoyama, Hidekazu Oishi, Toshiro Doi, Atsushi Kimura, Hirokazu Inoue, Gen Inoue, Masayuki Miyagi, Wataru Saito, Atsushi Nakano, Daisuke Sakai, Tadashi Nukaga, Shota Ikegami, Masayuki Shimizu, Toshimasa Futatsugi, Seiji Ohtori, Takeo Furuya, Sumihisa Orita, Shiro Imagama, Kei Ando, Kazuyoshi Kobayashi, Katsuhito Kiyasu, Hideki Murakami, Katsuhito Yoshioka, Shoji Seki, Michio Hongo, Kenichiro Kakutani, Takashi Yurube, Yasuchika Aoki, Masashi Oshima, Masahiko Takahata, Akira Iwata, Hirooki Endo, Tetsuya Abe, Toshinori Tsukanishi, Kazuyoshi Nakanishi, Kota Watanabe, Tomohiro Hikata, Satoshi Suzuki, Norihiro Isogai, Eijiro Okada, Haruki Funao, Seiji Ueda, Yuta Shiono, Kenya Nojiri, Naobumi Hosogane, Ken Ishii. Surgical outcomes of spinal fusion for osteoporotic thoracolumbar vertebral fractures in patients with Parkinson's disease: what is the impact of Parkinson's disease on surgical outcome? *BMC Musculoskelet Disord.* 2019.03; 20(1); 103
 12. Sopak Supakul, Kenta Yao, Hiroki Ochi, Tomohito Shimada, Kyoko Hashimoto, Satoko Sunamura, Yo Mabuchi, Miwa Tanaka, Chihiro Akazawa, Takuro Nakamura, Atsushi Okawa, Shu Takeda, Shingo Sato. Pericytes as a Source of Osteogenic Cells in Bone Fracture Healing. *Int J Mol Sci.* 2019.03; 20(5);
 13. Toshitaka Yoshii, Satoru Egawa, Takashi Hirai, Takashi Kaito, Kanji Mori, Masao Koda, Hirotaka Chikuda, Tomohiko Hasegawa, Shiro Imagama, Masahiro Yoshida, Motoki Iwasaki, Atsushi Okawa, Yoshiharu Kawaguchi. A systematic review and meta-analysis comparing anterior decompression with fusion and posterior laminoplasty for cervical ossification of the posterior longitudinal ligament. *J Orthop Sci.* 2019.03;
 14. Koji Fujita, Kenji Kimori, Akimoto Nimura, Atsushi Okawa, Yoshikazu Ikuta. MRI analysis of carpal tunnel syndrome in hemodialysis patients versus non-hemodialysis patients: a multicenter case-control study. *J Orthop Surg Res.* 2019.03; 14(1); 91
 15. Fujita K., Kaburagi H., Nimura A., Miyamoto T., Wakabayashi Y., Seki Y., Aoyama H., Shimura H., Kato R., Okawa A.. Lower grip strength and dynamic body balance in women with distal radial fractures (vol 30, 2019) *OSTEOPOROSIS INTERNATIONAL.* 2019.03; 30(3); 697
 16. Naobumi Hosogane, Kenya Nojiri, Satoshi Suzuki, Haruki Funao, Eijiro Okada, Norihiro Isogai, Seiji Ueda, Tomohiro Hikata, Yuta Shiono, Kota Watanabe, Kei Watanabe, Takashi Kaito, Tomoya Yamashita, Hiroyasu Fujiwara, Yukitaka Nagamoto, Hidetomi Terai, Koji Tamai, Yuji Matsuoka, Hidekazu Suzuki,

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17. Shingo Morishita, Toshitaka Yoshii, Atsushi Okawa, Kiyohide Fushimi, Takeo Fujiwara. Perioperative complications of anterior decompression with fusion versus laminoplasty for the treatment of cervical ossification of the posterior longitudinal ligament: propensity score matching analysis using a nation-wide inpatient database. *Spine J.* 2019.04; 19(4); 610-616
 18. Shuta Ushio, Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masahito Yuasa, Shigenori Kawabata, Atsushi Okawa. Preoperative Risk Factors for Adjacent Segment Degeneration after Two-Level Floating Posterior Fusion at L3-L5. *Spine Surg Relat Res.* 2019.04; 4(1); 43-49
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[Conference Activities & Talks]

1. Koji Fujita, Takuro Watanabe, Yuta Sugiura, Akimoto Nimura, Atsushi Okawa. Developing a tablet-based application for postoperative rehabilitation of patients with carpal tunnel syndrome . American Association for Hand Surgery, Annual Meeting 2019.01.31 Palm Desert, USA
2. Takashi Hirai, Yoshiharu Kawaguchi, Toshitaka Yoshii, Narihito Nagoshi, Kazuhiro Takeuchi, Kanji Mori, Atsushi Okawa. Prevalence of ossified spinal lesions in patients with ossification of the posterior longitudinal ligament (OPLL) and sex differences in distribution of OPLL: A multicenter cross-sectional study. Orthopaedic Research Society 2019 Annual Meeting 2019.02.02 Austin, TX USA
3. Satoru Egawa, Keigo Hirai, Rempei Matsumoto, Toshitaka Yoshii, Atsushi Okawa, Shinichi Sotome. Therapeutic Effect of Antibiotic-loaded Hydroxyapatite Collagen (HAp/Col) Composite on Acute, Bone-Destructive Osteomyelitis in Rats . Orthopaedic Research Society 2019 Annual Meeting 2019.02.02 Austin, TX, USA
4. Shuta Ushio, Shigenori Kawabata, Kensuke Sekihara, Deguchi Hiroshi, Yoshiaki Adachi, Atsushi Okawa. Visualization of neural activity of thoracic spinal cord by magnetospinography system. ACNS 2019 2019.02.06 Las Vegas, USA
5. Ryohei Takada, Sarah Whitehouse, Matthew Hubble, Matthew Wilson, Jonathan Howell, John Timperley, Al-Amin Kassam. Does varus or valgus alignment of the Exeter stem influence survival or patient outcome in total hip arthroplasty? A review of 4126 cases with a minimum follow up of 5 years.. British Hip Society Annual Scientific Meeting 2019.02.27 Nottingham
6. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Atsushi Okawa. Accuracy of cup positioning of supine vs. lateral position in total hip arthroplasty using anterolateral approach: A prospective, randomized, controlled trial.. American Academy of Orthopaedic Surgeons 2019 2019.03.12 Las Vegas, USA

7. Shuta Ushio, Toshitaka Yoshii, Takashi Hirai, Hiroyuki Inose, Masato Yuasa, Shigenori Kawabata, Atsushi Okawa. Investigation on factors related to outcomes in of surgical procedures for proximal type of cervical spondylotic amyotroph. 10th CSRS-AP 2019 2019.03.14 Yokohama
8. Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Shuta Ushio, Shigenori Kawabata, Atsushi Okawa, Kenichiro Sakai. Increase of fusion segment height may impact on postoperative dislodgement of strut after anterior cervical corpectomy with fusion for multilevel OPLL. 10th CSRS-AP 2019 2019.03.14 Yokohama
9. Toshitaka Yoshii, Shingo Morishita, Takashi Hirai, Kenichiro Sakai, Atsushi Okawa. Perioperative complications of anterior decompression with fusion vs posterior decompression with fusion for the treatment of cervical ossification of the posterior longitudinal ligament: Propensity score matching analysis using a national inpatient database . CSRS-AP 2019 2019.03.14 Yokohama
10. Hiroaki Onuma, Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Atsuyuki Kawabata, Atsushi Okawa . Influence of Segmental Fusion on Postoperative Outcomes of Bone Grafted and Non-bone grafted Double-door Laminoplasty for Treatment of Cervical Spondylotic Myelopathy . 10th CSRS-AP 2019 2019.03.14 Yokohama
11. Yuko Segawa, Kyoko Hoshino, Kazue Kimura, Yuri Nagao, Masaharu Hayashi, Atsushi Okawa. Histories of visits to orthopaedics in patients with Segawa disease. 12th Combined meeting of Asia Pacific spine society & asia pacific paediatric orthopaedic society 2019.04.04 Incheon, Korea
12. Yoto Oh. Surgical treatment of atypical femoral fracture based on the subtype classification. 45th annual meeting of the Korean Fracture Society 2019.04.26 Busan, Korea
13. Oh Y, Tano A, Kaku T, Okawa A. Ankle arthrodesis using the Masquelet technique for open ankle fracture with substantial . 20th European Congress of Trauma & Emergency Surgery 2019.05.05 Praha, Czech
14. Kaku T, Miyatake K, Oh Y, Tano A, Jinno T, Okawa A. Can total hip arthroplasty be indicated for elderly patients with displaced femoral neck fractures?. 20th European Congress of Trauma & Emergency Surgery 2019.05.05 Praha, Czech
15. Kaku T, Oh Y, Kurosa Y, Okawa A. External iliac arterial injury by open pelvic ring fracture: a case report. 20th European Congress of Trauma & Emergency Surgery 2019.05.05 Praha, Czech
16. Toshifumi Watanabe, Hideyuki Koga, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Takeshi Muneta, Ichiro Sekiya, Tetsuya Jinno, Atsushi Okawa. Joint laxity affects clinical outcomes in posterior-stabilized total knee arthroplasty. 92nd Annual Meeting of the Japanese Orthopaedic Association 2019.05.09 Yokohama
17. Miho Akaza, Shigenori Kawabata, Taishi watanabe, Yuki Hasegawa, Iida Shintaro, Toru Sasaki, Yoshiaki Adachi, Kensuke Sekihara, Tadashi Kanouchi, Yuki Sumi, Atsushi Ohkawa, Takanori Yokota. Diagnosis of C8 radiculopathy by magnetospinogram. 60th Annual Meeting of the Japanese Society of Neurology 2019.05.24 Osaka
18. Yoto Oh. Validation of novel classification for atypical femoral fractures. 4th AOTrauma Asia Pacific Scientific Congress 2019.05.24 Taipei Taiwan
19. Oh Y, Yamamoto K, Fujita K, Hashimoto J, Wakabayashi Y, Fukushima K, Kurosa Y, Kitagawa M, Okawa A. Biological activity in mid-shaft stress fracture of the bowed femoral shaft is not suppressed as in atypical subtrochanteric femoral fracture: validation of newly devised subtype classification for atypical femoral fracture. 4th AOTrauma Asia Pacific Scientific Congress 2019.05.24 Taipei Taiwan
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21. Koji Fujita, Hirotaka Iijima, Hidetoshi Kaburagi, Akimoto Nimura, Atsushi Okawa. Gait Analysis Of Patients With Distal Radius Fracture Using A Novel Laser-tug System. The 2019 American College of Sports Medicine 2019.05.30 Orlando, USA
22. Takashi Hirai, Toshitaka Yoshii, Tomoyuki Yokoyama, Atsushi Okawa. 3' UTR alternative splicing of mRNAs may contribute to the mechanisms of peripheral neuropathy.. 46Th ISSLS 2019.06.03 Kyoto

23. Tsuyoshi Kato, Hiroyuki Inose, Toshitaka Yoshii, Atsushi Okawa. Development of a guide for the conservative treatment for acute OVF according to a prospective, randomized, multicenter study by the comparison of hard and soft-brace treatments. 46TH ISSLS 2019.06.06 Kyoto
24. Shuta Ushio, Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Shigenori Kawabata, Atsushi Okawa. Preoperative risk factor of adjacent segment degeneration after two-levels floating posterior fusion at L2-L4 or L3-L5 levels. 46th ISSLS 2019.06.07 Kyoto
25. Naoki Yamamoto, Tomoko Sakai, Dai Ukegawa, Chisato Hoshino, Jinno Tetsuya, Atsushi Okawa. Earlier mobility with T-cane after total knee arthroplasty influences long-term mobility . 13th International Spcoety of Physical and Rehabilitation medicine World Congress 2019 2019.06.09 Kobe, Japan
26. Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Shuta Ushio, Hiroaki Onuma, Atsuyuki Kawabata, Atsushi Okawa. Surgical outcomes of thoracic arachnoid web: a case series . ICORS 2019 2019.06.19 Montreal, Canada
27. Hiroaki Onuma, Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Shuta Ushio, Atsuyuki Kawabata, Atsushi Okawa. Influence of Segmental Fusion on Postoperative Outcomes of Bone Grafted and Non-Bone Grafted Double-Door Laminoplasty, the Modified Kirita-Miyazaki Method, for Treatment of Cervical Spondylotic Myelopathy . ICORS 2019 2019.06.19 Montreal, Canada
28. Atsuyuki Kawabata, Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Hiroaki Onuma, Shuta Ushio, Atsushi Okawa. Identification of Predictive Factors for Mechanical Complications after Adult Spinal Deformity Surgery; A MultiInsti-tutional Retrospective Study . ICORS 2019 2019.06.19 Montreal, Canada
29. Koji Fujita, Tomoyuki Kuroiwa, Akimoto Nimura, Atsushi Okawa. Development of method for measuring the thumb pronation and palmar abduction angles during opposition movement using a three-axis gyroscope. 14th IFSSH & 11th IFSHT Triennial Congress with combined FESSH Congress 2019.06.21 Berlin, Germany
30. Naoki Yamamoto, Takuya Oyaizu, Masaki Horie, Mitsuhiro Enomoto, Masato Yuasa, Ryohei Takada, Kazuyoshi Yagishita. Hyperbalic Oxygen treatment promotes muscle regeneration via angiogenesis by triggering increased RNS in acute skeletal muscle injury . 52th Undersea & Hyperbaric Medical Society Annual scientific meeting 2019 2019.06.27 Kobe, Japan
31. Hiroyuki Inose, Tsuyoshi Kato, Toshitaka Yoshii, Atsushi Okawa. A Prospective, Randomized, Multi-center Study of Brace Treatments for Acute Osteoporotic Vertebral Compression Fracture. NASS2019 Summer Spine Meeting 2019.07.31 Honolulu, Hawaii
32. Oh Y, Yamamoto K, Hashimoto J, Fujita K, Yoshii T, Fukushima K, Kurosa Y, Wakabayashi Y, Kitagawa M, Okawa A. Validation of newly devised subtype classification for atypical femoral fracture. 8th Fragility Fracture Network Global Congress 2019 2019.08.28 Oxford England
33. Kaku T, Oh Y, Miyatake K, Yoshii T, Okawa A. Trial of geriatrician-led treatment system for elderly patients with hip fractures. 8th FFN Global Congress 2019.08.28 Oxford England
34. Hirotaka Koyanagi, Toshitaka Yoshii, Takashi Hirai, Shingo Sato, Atsushi Okawa. Experience of successful surgical treatment for lumbar giant cell tumour. ISOLS 2019 Meeting Athens 2019.09.11 Greece
35. Hiroyuki Inose, Atsushi Okawa. Predictors of surgical site infection after spinal instrumentation surgery: A consecutive series. Eurospine 2019 2019.10.16 HELSINKI, FINLAND
36. Hiroyuki Inose. Comparison of decompression, decompression plus fusion, and decompression plus stabilization for degenerative spondylolisthesis. Joa Visiting RCOST 2019 2019.10.20 THAI, PATAYA
37. Toshitaka Yoshii. Minimally invasive reconstruction of osteoporotic vertebral fracture and collapse . Sino-Japanese MIS t Symposium 2019 2019.10.25 Beijing China
38. Naoki Yamamoto, Takuya Oyaizu, Masaki Horie, Mitsuhiro Enomoto, Masato Yuasa, Ryohei Takada, Kazuyoshi Yagishita. Hyperbaric oxygen therapy promotes muscle regeneration via angiogenesis by reactive nitrogen species in muscle contusion injury of rat.. The 4th conference of Asia-pasific Undersea and Hyperbaric Medical Society 2019.10.25 nakatsu, Oita Japan

39. Mio Norose, Akimoto Nimura, Takashi Miyamoto, Shiro Suzuki, Koji Fujita. Arthroscopic bankart repair for recurrent shoudlder dislocation in the skeletally immature patient:a case report. The 46th Annual Meeting of the Japan Shoulder Society 2019.10.25 Nagano
40. Jun Hashimoto,Shigenori Kawabata, Toru Sasaki, Yuko Hoshino, Kensuke Sekihara, Yoshiaki Adachi, Taishi Watanabe, Yuki Miyano, Shinji Sato, Yuki Mitani, Sukchan Kim, Atsushi Okawa. Magnetospinography is a noninvasive and useful modality to visualize electrophysiological activities in the lumbar radiculopathy. 24th World Congress of Neurology 2019.10.30 Dubai
41. S. Kim,S. Kawabata, M. Akaza, K. Sekihara, Y. Hoshino, T. Sasaki, T. Watanabe, Y. Miyano, S. Sato, Y. Mitani, T. Yamaga, Y. Adachi, A. Okawa. VISUALIZATION OF NEURAL ACTIVITIES IN LUMBAR SPINE IN RESPONSE TO THE SCIATIC NERVE STIMULATION BY MAGNETONEUROGRAPHY. 24th World Congress of Neurology 2019.10.30 Dubai
42. Saeri Kaminaka,Miho Akaza, Shigenori Kawabata, Taishi watanabe, Yuki Hasegawa, Iida Shintaro, Toru Sasaki, Yoshiaki Adachi, Kensuke Sekihara, Tadashi Kanouchi, Yuki Sumi, Atsushi Okawa, Takanori Yokota. Diagnosis of C8 radiculopathy by magnetospinogram. 24th World Congress of Neurology 2019.10.30 Dubai
43. Satoshi Sumiya,Shigenori Kawabata, Shuta Ushio, Yuko Hoshino, Kensuke Sekihara, Taishi Watanabe, Yuki Miyano, Sukchan Kim, Yoshiaki Adachi, Atsushi Okawa. Visualization of electrophysiological activity in the cervical spinal cord using Magnetospinography. 24th World Congress of Neurology 2019.10.30 Dubai
44. Satoshi Sumiya,Shigenori Kawabata, Shuta Ushio, Toshitaka Yoshii, Atsushi Okawa. Cervical spinal cord injury associated with neck flexion in posterior cervical decompression -Verification by intraoperative spinal cord monitoring-. 24th World Congress of Neurology 2019.10.30 Dubai
45. Shigenori Kawabata,Toru Sasaki, Yuko Hoshino, Kensuke Sekihara, Yoshiaki Adachi, Taishi Watanabe, Yuki Miyano, Atsushi Okawa. Diagnosis of conduction block in cervical myelopathy patients by non-invasive magnetospinography. 24th World Congress of Neurology 2019.10.30 Dubai
46. Taishi Watanabe,Shigenori Kawabata, Yuko Hoshino, Yuki Miyano, Toru Sasaki, Shuta Ushio, Yoshiaki Adachi, Isamu Ozaki, Kensuke Sekihara, Atsushi Okawa. VISUALIZATION OF NERVE ACTIVITIES ALONG THE BRACHIAL PLEXUS AFTER MEDIAN / ULNAR NERVE STIMULATION USING A MAGNETONEUROGRAPHY SYSTEM. 24th World Congress of Neurology 2019.10.30 Dubai
47. Toru Sasaki,Shigenori Kawabata, Yuko Hoshino, Kensuke Sekihara, Miho Akaza, Yoshiaki Adachi, Taishi Watanabe, Yuki Hasegawa, Shinji Sato, Yuki Mitani, Sukchan Kim, Atsushi Okawa. Visualization of electrophysiological activity in patients with carpal tunnel syndrome using magnetoneurography. 24th World Congress of Neurology 2019.10.30 Dubai

[Awards & Honors]

1. Undersea & Hyperbaric Medical Society 2019 Annual Scientific meeting - President's award: Best Resident/Trainee Oral Presentation (Naoki Yamamoto), Undersea & Hyperbaric Medical Society, 2019.06
2. ASBMR2019 Annual Meeting :Award of Poster(AOBULIKASIMU AIKEBAIER), American Society for Bone and Mineral Research , 2019.09
3. ASBMR2019 Annual Meeting :Young Investigator Travel Grant (AIDEHAMU AIHEMAITI), 2019.09
4. ASBMR2019 Annual Meeting :Symposiast Special Symposium (AIDEHAMU AIHEMAITI), American Society for Bone and Mineral Research , 2019.09

Diagnostic Radiology and Nuclear Medicine

Professor Ukihide Tateishi

Project Professor Yukihsa Saida

Associate Professors Ichiro Yamada,

Yoshio Kitazume(Department of medical informatics associate professor)

Lecturers Mitsuhiro Kishino, Tomoyuki Fujioka(Jun. ~)

Research Associates Makiko Honda, Syuichiro Nakaminato,
Junichi Tsuchiya, Jun Oyama, Mio Mori, Marie Takahashi(Apr. ~),
Ryosuke Watanabe(Dec. ~), Kota Yokoyama(Jun. ~)

Hospital Staff members Sayumi Tsuyuzaki,

Kouichiro Kimura(Apr. ~), Kenji Nishida, Momo Wakui,

Resident Ayumi Yamada(~ Mar.), Yurika Hashimoto(~ Mar.),
Leona Katsuta(~ Mar.)

Wu Xiaotong(Apr. ~),

Tsubasa Okazaki(Apr. ~ Sep.), Yuuki Yokoi(Oct. ~)

Graduate Students

Takuya Adachi, Takumi Ooshima, Takehiro Tamura, Hyeyel Bae,

Ryo Miyazawa, Ken Yamagiwa, Syuichi Yanai, Li Runan, Mirai Kawano

(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. Texture analysis and AI imaging are applied to both of anatomic and functional imaging modalities. We investigate from first order (kurtosis) to high order (NGLCM, NGTDM, GLSZM). The faculty is also formulating scan protocols that obtain images over time with 3D PET/CT, as a minimally invasive technique of extracting in vivo metabolic data. Known tracers include ^{18}F -FDG (glucose metabolism), ^{11}C -choline (lipid metabolism), ^{11}C -acetate (lipid metabolism), ^{18}F -FAZA (hypoxia), ^{18}F -FACBC (amino acid metabolism), $^{62/64}\text{Cu}$ -ATSM (redox), ^{18}F -FLT (DNA synthesis), ^{18}F -NaF (bone metabolism), ^{68}Ga -DOTATATE (somatostatin receptor), and ^{18}F -Fluorobetapir (Amyloid), ^{18}F -Flutemetamol (Amyloid). The usefulness of multiple tracers in the discipline of oncology has been observed

in numerous carcinomas. ^{177}Lu -DOTATATE PRRT started as the first domestic Phase I study. 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: TACE 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 17 PET examinations per day, mainly for malignant tumor, as well as eight to 10 general radioisotope examinations per day, mainly brain and myocardial SPECT. PET/CT for radiation planning and C-11 acetate PET/CT F-18 FLT PET/CT for malignancies were introduced in 2016.

(6) Clinical Performances

Being a core diagnosis and treatment department, diagnostic radiology and nuclear medicine is a department that engages in inter-disciplinary clinical practice forming strong partnerships to meet the needs of its internal client departments and works to resolve issues faced by the university hospital, bearing its responsibility to unswervingly fulfill its mission from a global perspective. Diagnostic radiology and nuclear medicine is equipped with the capabilities to process large volumes of imaging information, it develops problem presentation, technical skill acquisition, and collaboration with all departments, and possesses the characteristics to go on conscientiously tackling new modalities, probes and contrasts as well as clinical trials.

(7) Publications

[Original Articles]

1. Nukui Y, Yamana T, Masuo M, Tateishi T, Kishino M, Tateishi U, Tomita M, Hasegawa T, Aritsu T, Miyazaki Y. Serum CXCL9 and CCL17 as biomarkers of declining pulmonary function in chronic bird-related hypersensitivity pneumonitis. *PloS one*. 2019; 14(8); e0220462

2. Yoshio Kitazume, Tomoyuki Fujioka, Kento Takenaka, Jun Oyama, Kazuo Ohtsuka, Toshimitsu Fujii, Ukihide Tateishi. Crohn Disease: A 5-Point MR Enterocolonography Classification Using Enteroscopic Findings. *AJR Am J Roentgenol.* 2019.01; 212(1); 67-76
3. Hiroshi Watanabe, Hajime Tanaka, Yasuhisa Fujii, Makoto Kodama, Takumi Akashi, Tomoyuki Fujioka, Kazunori Kubota, Yukihisa Saida, Ukihide Tateishi. A case of immunoglobulin G4-related inflammatory pseudotumor mimicking renal cell carcinoma. *Abdom Radiol (NY).* 2019.01;
4. Nukui Y, Miyazaki Y, Masuo M, Okamoto T, Furusawa H, Tateishi T, Kishino M, Tateishi U, Ono J, Ohta S, Izuhara K, Inase N. Periostin as a predictor of prognosis in chronic bird-related hypersensitivity pneumonitis. *Allergology international : official journal of the Japanese Society of Allergology.* 2019.03;
5. Fujioka T, Kubota K, Mori M, Kikuchi Y, Katsuta L, Kasahara M, Oda G, Ishiba T, Nakagawa T, Tateishi U. Distinction between benign and malignant breast masses at breast ultrasound using deep learning method with convolutional neural network. *Japanese journal of radiology.* 2019.03;
6. Mio Mori, Hideyuki Hayashi, Minoru Fukuda, Sumihisa Honda, Takeshi Kitazaki, Kazuto Shigematsu, Naohiro Matsuyama, Mayumi Otsubo, Takeshi Nagayasu, Mikiko Hashisako, Kazuhiro Tabata, Masataka Uetani, Kazuto Ashizawa. Clinical and computed tomography characteristics of non-small cell lung cancer with ALK gene rearrangement: Comparison with EGFR mutation and ALK/EGFR-negative lung cancer. *Thorac Cancer.* 2019.04; 10(4); 872-879
7. Fujioka T, Mori M, Kubota K, Kikuchi Y, Katsuta L, Kasahara M, Oda G, Ishiba T, Nakagawa T, Tateishi U. Simultaneous comparison between strain and shear wave elastography of breast masses for the differentiation of benign and malignant lesions by qualitative and quantitative assessments. *Breast cancer (Tokyo, Japan).* 2019.06;
8. Mio Mori, Tomoyuki Fujioka, Leona Katsuta, Junichi Tsuchiya, Kazunori Kubota, Mai Kasahara, Goshi Oda, Tsuyoshi Nakagawa, Ichiroh Onishi, Ukihide Tateishi. Diagnostic performance of time-of-flight PET/CT for evaluating nodal metastasis of the axilla in breast cancer. *Nucl Med Commun.* 2019.07;
9. Tamura T, Shiwaku H, Jitoku D, Kurumaji A. Effect of Tandospirone, a Partial Agonist of the 5-HT1A Receptor, in a Patient With Chronic Poststroke Emotional Incontinence With Anxiousness. *The primary care companion for CNS disorders.* 2019.09; 21(5);
10. Yamada I, Miyasaka N, Kobayashi D, Wakana K, Oshima N, Wakabayashi A, Sakamoto J, Saida Y, Tateishi U, Eishi Y. Endometrial carcinoma: texture analysis of apparent diffusion coefficient maps and its correlation with histopathologic findings and prognosis. *Radiology: Imaging Cancer.* 2019.11; 1(2); e190054
11. Tomoyuki Fujioka, Mio Mori, Kazunori Kubota, Yuka Kikuchi, Leona Katsuta, Mio Adachi, Goshi Oda, Tsuyoshi Nakagawa, Yoshio Kitazume, Ukihide Tateishi. Breast Ultrasound Image Synthesis using Deep Convolutional Generative Adversarial Networks. *Diagnostics (Basel).* 2019.11; 9(4);

[Books etc]

1. Mori M, Fujioka T, Tateishi U. Diagnostic imaging of large / medium vessel vasculitis. Gakken Medical Shujunsha Co.,Ltd., 2019.02

[Conference Activities & Talks]

1. Tomoyuki Fujioka. Challenge for distinction between benign and malignant breast masses at breast ultrasound using deep learning method with convolutional neural network.. The 28 Annual Meeting of the Japanese Society of Breast Cancer Imaging 2019.02.10
2. T. Fujioka, K. Kubota, M. Mori, K. Nomura, Y. Yashima, L. Katsuta, U. Tateishi. The technique of how to approach MR detected suspicious breast lesions. European Congress of Radiology 2019 2019.03.01
3. Kishino M, Kume H, Uchiyama H, Nishida K, Mori K, Yamashita Y, Kudo T, Saida Y, Tateishi U. The imaging features of paravesical space arteriovenous malformation as a new subgroup of pelvic vascular anomaly. The 78th Annual Meeting of the Japan Radiological Society 2019.04.11

4. Tomoyuki Fujioka, Kazunori Kubota, Mio Mori, Yuka Kikuchi, Kyoko Nomura, Leona Katsusta, Ukihide Tateishi . Distinction between benign and malignant breast masses at breast ultrasound using deep learning method with convolutional neural network. 2019.04.12 Yokohama
5. Shuichiro Nakaminato , Mitsuhiro Kishino, Marie Takahashi, Koichiro Kimura, Ayumi Yamada, Yoshio Kitazume , Ukihide Tateishi. Transcatheter arterial embolization for recurrent hemarthrosis after arthroplasty. The 48th Annual Meeting of the Japanese Society of Interventional Radiology 2019.05.30 Fukuoka
6. Kishino M, Nakaminato S, Kitazume Y, Takahashi M, Kimura K, Nishida K, Takeguchi T, Takeguchi Y, Yanai S, Saida Y, Tateishi U. Is the improvement of liver function post B-RTO associated with liver volume increase? . The 48th Annual Meeting of the Japanese Society of Interventional Radiology 2019.05.30 Fukuoka
7. Y.Saida. Future of general health check by imaging diagnosis. 2019.08.31
8. Kishino M, Nakaminato S, Kitazume Y, Takahashi M, Kimura K, Nishida K, Takeguchi T, Takeguchi Y, Yanai S, Saida Y, Tateishi U. Clinical significance of liver volume change after portal vein embolization and hepatofugal collateral obliteration — The bigger the better?. CIRSE 2019 2019.09.07

Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka
Assistant Professor, Ryo Watanabe

(1) Research

- 1) Elucidation of genetic architecture of human metabolic diseases using genome and meta-genome information
- 2) Identification of biomarkers for personalized medicine
- 3) Pharmacogenomics
- 4) Functional genomics
- 5) Statistical genetics and genome drug discovery

(2) Lectures & Courses

As we say “Every human is different” , human genetic diversity has essential impacts on clinical fields, e.g. disease risk, clinical efficacy, and drug responses. Our laboratory aims to elucidate the diversity of human being through comprehensive research activities including genome and epi-genome analyses of human diseases, methodological development of statistical genetics, and human resources cultivation to achieve personalized medicine.

(3) Publications

[Original Articles]

1. Wataru Shimizu, Hisaki Makimoto, Kenichiro Yamagata, Tsukasa Kamakura, Mitsuru Wada, Koji Miyamoto, Yuko Inoue-Yamada, Hideo Okamura, Kohei Ishibashi, Takashi Noda, Satoshi Nagase, Aya Miyazaki, Heima Sakaguchi, Isao Shiraishi, Takeru Makiyama, Seiko Ohno, Hideki Itoh, Hiroshi Watanabe, Ken-shi Hayashi, Masakazu Yamagishi, Hiroshi Morita, Masao Yoshinaga, Yoshiyasu Aizawa, Kengo Kusano, Yoshihiro Miyamoto, Shiro Kamakura, Satoshi Yasuda, Hisao Ogawa, Toshihiro Tanaka, Naotaka Sumitomo, Nobuhisa Hagiwara, Keiichi Fukuda, Satoshi Ogawa, Yoshifusa Aizawa, Naomasa Makita, Tohru Ohe, Minoru Horie, Takeshi Aiba. Association of Genetic and Clinical Aspects of Congenital Long QT Syndrome With Life-Threatening Arrhythmias in Japanese Patients. *JAMA Cardiol.* 2019.03; 4(3); 246-254
2. Yujiro Nakano, Takanobu Yoshimoto, Ryo Watanabe, Masanori Murakami, Tatsuya Fukuda, Kazutaka Saito, Yasuhisa Fujii, Takumi Akashi, Toshihiro Tanaka, Tetsuya Yamada, Mitsuhide Naruse, Yoshihiro Ogawa. miRNA299 involvement in CYP11B2 expression in aldosterone-producing adenoma. *Eur. J. Endocrinol.* 2019.05;
3. Kyaw Thiha, Yoichi Mashimo, Hiroyuki Suzuki, Hiromichi Hamada, Akira Hata, Toshiro Hara, Toshihiro Tanaka, Kaoru Ito, Yoshihiro Onouchi, . Investigation of novel variations of ORAI1 gene and their association with Kawasaki disease. *J. Hum. Genet.* 2019.06; 64(6); 511-519
4. Yusuke Ebana, Yihan Sun, Xiaoxi Yang, Taiju Watanabe, Satoru Makita, Kouichi Ozaki, Toshihiro Tanaka, Hirokuni Arai, Tetsushi Furukawa. Pathway analysis with genome-wide association study (GWAS)

data detected the association of atrial fibrillation with the mTOR signaling pathway. *Int J Cardiol Heart Vasc.* 2019.09; 24; 100383

5. Chisato Shimizu, Jihoon Kim, Hariklia Eleftherohorinou, Victoria J Wright, Long T Hoang, Adriana H Tremoulet, Alessandra Franco, Martin L Hibberd, Atsushi Takahashi, Michiaki Kubo, Kaoru Ito, Toshihiro Tanaka, Yoshihiro Onouchi, Lachlan J M Coin, Michael Levin, Jane C Burns, Hiroko Shike, . HLA-C variants associated with amino acid substitutions in the peptide binding groove influence susceptibility to Kawasaki disease. *Hum. Immunol.* 2019.09; 80(9); 731-738

[Conference Activities & Talks]

1. Ryo Watanabe, Yasuhiro Maejima, Takashi Nakaoka, Tetsuo Sasano, Mitsuaki Isobe, Toshihiro Tanaka. Exploration of novel biomarkers for cardiac sarcoidosis by expression analysis of circulating exosomal microRNAs. The 3rd JCS Council Forum on Basic CardioVascular Research 2019.09.06 Tokyo

Applied Regenerative Medicine

Professor: Ichiro SEKIYA

Assistant Professor: Koji OTABE, Hisako KATANO

Project Assistant Professor: Nobutake OZEKI, Mitsuru MIZUNO,
Yuji KONO

Project Researcher : Keiichiro KOMORI, Kentaro ENDO

Graduate Student: Naoto WATANABE, Yoshihisa KUSHIDA, So SUZUKI, Akinobu HYODO, Hayato AOKI,
Kiyotaka HORIUCHI, Rei KUBOTA, Shunichi FUJII, Ryota FUJISAWA

Specially Appointed Researcher : Kimiko TAKANASHI,

Assistant Researcher: Mika WATANABE, Kaoru KOMORIYA,

Technical Assistant : Emi KODA, Junko TAKEBE, Hiroko HATANO

Assistant Clerk: Hitomi SEKI

(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 the cell and regenerative therapy.
- 3) Establishment of safety test for regenerative medicine.
- 4) Translational research.
- 5) Development of software for 3D analysis of knee MRI.

(3) Clinical Services & Other Works

Our purpose is to establish a new treatment for knee osteoarthritis. So far, we have shown that synovial stem cells have a high ability to differentiate into cartilage and that they promote the natural healing process by transplantation. We have also developed a technique for performing cell transplantation in minimally invasive arthroscopic surgery. After these basic researches and two clinical studies, in August 2017, we started a “doctor-initiated clinical trial for meniscal injury of autologous synovial stem cells”. We signed a patent license agreement with a company in March 2019 and consulted PMDA after the trial in June. In addition, with the support of the AMED Regenerative Medicine Practical Research Project (Principal Investigator: Ichiro Sekiya), a clinical study “Intra-articular injection of synovial stem cells for osteoarthritis of the knee” was started in December 2017 and ended the observation period for all study subjects in March 2019. Furthermore, through joint research with a company, the company developed MRI 3D analysis software that can automatically display cartilage thickness in the knee joint and was launched as a new volume analyzer in 2019.

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

1. Tomomasa Nakamura, Hideyuki Koga, Koji Otabe, Masafumi Horie, Toshifumi Watanabe, Kazuyoshi Yagishita, Ichiro Sekiya, Takeshi Muneta. Comparison of three approaches for femoral tunnel during double-bundle anterior cruciate ligament reconstruction: A case controlled study. *J Orthop Sci.* 2019.01; 24(1); 147-152
2. Inomata Kei, Tsuji Kunilazu, Onuma Hroaki, Hoshino Takashi, Udo Mio, Akiyama Masako, Nakagawa Yusuke, Katagiri Hiroki, Miyatake Kazumasa, Sekiya Ichiro, Muneta Takeshi, Koga Hideyuki. Time course analyses of structural changes in the infrapatellar fat pad and synovial membrane during inflammation-induced persistent pain development in rat knee joint *BMC Musculoskelet Disord.* 2019.01; 20(8);
3. Mai Katakura, Masafumi Horie, Toshifumi Watanabe, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Kenta Katagiri, Hiroko Ueki, Stefano Zaffagnini, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Effect of meniscus repair on pivot-shift during anterior cruciate ligament reconstruction: Objective evaluation using triaxial accelerometer. *Knee.* 2019.01; 26(1); 124-131
4. Watanabe Toshifumi, Aoki Akino, Hoshi Kenji, Muneta Takeshi, Sekiya Ichiro, Koga Hideyuki. Anterior Tibial Post Impingement during Stair Climbing: A Kinematic Analysis and Clinical Outcome *J Arthroplasty.* 2019.02; 34(2); 379-384
5. Nobutake Ozeki, Hideyuki Koga, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Tomoyuki Saito, Takeshi Muneta, Ichiro Sekiya. Biomechanical analysis of the centralization procedure for extruded lateral menisci with posterior root deficiency in a porcine model. *J Orthop Sci.* 2019.03; S0949-2658(19); 30064-30068
6. Noda S, Kawashima N, Yamamoto M, Hashimoto K, Nara K, Sekiya I, Okiji T. Effect of cell culture density on dental pulp-derived mesenchymal stem cells with reference to osteogenic differentiation. *Scientific Reports.* 2019.04; 9(1); 5430
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8. Ryota Fujisawa, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Cryopreservation in 95% serum with 5% DMSO maintains colony formation and chondrogenic abilities in human synovial mesenchymal stem cells. *BMC Musculoskelet Disord.* 2019.07; 20(1); 316
9. Ueki Hiroko, Katagiri Hiroki, Otabe Koji, Nakagawa Yusuke, Ohara Toshiyuki, Shioda Mikio, Kohno Yuji, Hoshino Takashi, Sekiya Ichiro, Koga Hideyuki. Contribution of Additional Anterolateral Structure Augmentation to Controlling Pivot Shift in Anterior Cruciate Ligament Reconstruction *AMERICAN JOURNAL OF SPORTS MEDICINE.* 2019.07; 47(9); 2093-2101
10. Shimpei Kondo, Yusuke Nakagawa, Mitsuru Mizuno, Kenta Katagiri, Kunikazu Tsuji, Shinji Kiuchi, Hideo Ono, Takeshi Muneta, Hideyuki Koga, Ichiro Sekiya. Transplantation of Aggregates of Autologous Synovial Mesenchymal Stem Cells for Treatment of Cartilage Defects in the Femoral Condyle and the Femoral Groove in Microminipigs. *Am J Sports Med.* 2019.08; 47(10); 2338-2347
11. Yusuke Nakagawa, Toshifumi Watanabe, Yusuke Amano, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Benefit of subcutaneous patient controlled analgesia after total knee arthroplasty. *Asia Pac J Sports Med Arthrosc Rehabil Technol.* 2019.10; 18; 18-22
12. Katakura M, Nakamura K, Watanabe T, Horie M, Nakamura T, Katagiri H, Otabe K, Nakagawa Y, Ohara T, Sekiya I, Muneta T, Koga H. Risk factors for residual anterolateral rotational instability after double bundle anterior cruciate ligament reconstruction: Evaluation by quantitative assessment of the pivot shift phenomenon using triaxial accelerometer. *The Knee.* 2019.10;

13. Akinobu Hyodo, Nobutake Ozeki, Yuji Kohno, So Suzuki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Makoto Tomita, Yusuke Nakagawa, Hideyuki Koga, Shinji Kiuchi, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Ichiro Sekiya. Projected Cartilage Area Ratio Determined by 3-Dimensional MRI Analysis: Validation of a Novel Technique to Evaluate Articular Cartilage. *JB JS Open Access*. 2019.10; 4(4); e0010
14. Mitsuru Mizuno, Hisako Katano, Yuri Shimozaaki, Sho Sanami, Nobutake Ozeki, Hideyuki Koga, Ichiro Sekiya. Time-lapse image analysis for whole colony growth curves and daily distribution of the cell number per colony during the expansion of mesenchymal stem cells. *Sci Rep*. 2019.11; 9(1); 16835
15. Naoto Watanabe, Mitsuru Mizuno, Junpei Matsuda, Naoko Nakamura, Koji Otabe, Hisako Katano, Nobutake Ozeki, Yuji Kohno, Tsuyoshi Kimura, Kunikazu Tsuji, Hideyuki Koga, Akio Kishida, Ichiro Sekiya. Comparison of High-Hydrostatic-Pressure Decellularized Versus Freeze-Thawed Porcine Menisci. *J. Orthop. Res.*. 2019.11; 37(11); 2466-2475
16. Ichiro Sekiya, Hideyuki Koga, Koji Otabe, Yusuke Nakagawa, Hisako Katano, Nobutake Ozeki, Mitsuru Mizuno, Masafumi Horie, Yuji Kohno, Kenta Katagiri, Naoto Watanabe, Takeshi Muneta. Additional Use of Synovial Mesenchymal Stem Cell Transplantation Following Surgical Repair of a Complex Degenerative Tear of the Medial Meniscus of the Knee: A Case Report. *Cell Transplant*. 2019.11; 28(11); 1445-1454
17. Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Ichiro Sekiya, Hideyuki Koga. The effect of a longitudinal tear of the medial meniscus on medial meniscal extrusion in anterior cruciate ligament injury patients. *Knee*. 2019.12; 26(6); 1292-1298

[Misc]

1. Akari Sasaki, Mitsuru Mizuno, Manabu Mochizuki, Ichiro Sekiya. Mesenchymal stem cells for cartilage regeneration in dogs. *World J Stem Cells*. 2019.05; 11(5); 254-269

[Conference Activities & Talks]

1. Akinobu Hyodo, Nobutake Ozeki, So Suzuki, Hayato Aoki, Naoto Watanabe, Yoshihisa Kushida, Yuji Kohno, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya.. "Projected Cartilage Area Ratio" By Mri 3d Analysis Detects Decrease Of Cartilage Amount In Several Months In Patients Complaining Knee Pain.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.02 Austin,USA
2. Rei Kubota, Hideyuki Koga, Nobutake Ozeki, Yuji Kohno, Junpei Matsuda, Yoshihisa Kushida, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Ichiro Sekiya.. Influence Of Knee Flexion Angle On The Biomechanical Effect Of Centralization For Extruded Lateral Meniscus. Orthopaedic Research Society 2019 Annual Meeting 2019.02.02 Austin,USA
3. Kiyotaka Horiuchi, Hideyuki Koga, Mitsuru Mizuno, Hisako Katano, Keiichiro Komori, Koji Otabe, Shizuka Fujii, Nobutake Ozeki, Tsujii Kunikazu, Ichiro Sekiya.. Determining The Optimum Initial Cell Density That Yields The Highest Number Of Mesenchymal Stem Cells Per Dish.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.03 Austin,USA
4. Hayato Aoki, Nobutake Ozeki, Akinobu Hyodo, So Suzuki, Yoshihisa Kushida, Naoto Watanabe, Yuji Kohno, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya.. Whole Image Of Discoid Lateral Meniscus Analyzed By 3d Mri.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.03 Austin,USA
5. So Suzuki, Nobutake Ozeki, Yuji Kohno, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya.. Medial Meniscus Extrusion (MME) Area And MME Volume Determined By 3D-MRI Are More Sensitive Than MME Distance Determined By 2D-MRI For Evaluating Cartilage Loss In Knees With Medial Meniscus Degenerative Tears.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.03 Austin,USA
6. Ryota Fujisawa, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Shizuka Fujii, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Cryopreservation In 95% Serum With 5% DmsO Maintained Colony Formation And Chondrogenic Abilities In Human Synovial Mesenchymal Stem Cells.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.03 Austin,USA

7. So Suzuki, Mitsuru Mizuno, Yoshihisa Kushida, Yuji Kohno, Nobutake Ozeki, Koji Otabe, Shizuko Ichinose, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Morphological Alterations Of Synovial Mesenchymal Stem Cells During Adhesion To The Meniscus.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.05 Austin,USA
8. Mitsuru Mizuno, Hisako Katano, Yuri Shimozaeki, Sho Sanami, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Time Lapse Imaging Analysis On Colony Proliferation Process Of Primary Synovial Mscs.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.05 Austin,USA
9. Naoto Watanabe, Mitsuru Mizuno, Junpei Matsuda, Naoko Nakamura, Koji Otabe, Hisako Katano, Nobutake Ozeki, Yuji Kohno, Tsuyoshi Kimura, Kunikazu Tsuji, Hideyuki Koga, Akio Kishida, Ichiro Sekiya.. Comparison Of Decellularized Meniscus By High Hydrostatic Pressure With Freeze-thawed Meniscus.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.05 Austin,USA
10. Naoto Watanabe, Nobutake Ozeki, Mitsuru Mizuno, Keiichiro Komori, Yuji Kohno, Hisako Katano, Koji Otabe, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Quantitative Analysis Of Mesenchymal Stem Cells (MSCs) In Synovial Fluid Two Weeks After Synovial Removal And Meniscus Repair, Followed By Transplantation Of Synovial MSCs.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.05 Austin,USA
11. Yuji Kohno, Mitsuru Mizuno, Otabe Koji, Nobutake Ozeki, Hisako Katano, Keiichiro Komori, Kunikazu Tsuji, Mikio Matsumoto, Haruka Kaneko, Yuji Takazawa, Hideyuki Kog, Ichiro Sekiya.. Yields Of MSCs From Synovial Fluid Reflect Yields Of MSCs From The Synovium Of RA Knees.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.05 Austin,USA
12. Yoshihisa Kushida, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Use Of 3D MRI And 3D T2 Mapping Images For Evaluation Of The Natural Course Of Cartilage Repair In The Knees Of Micromini Pigs.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.05 Austin,USA
13. Yoshihisa Kushida, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Quantification Of Cartilage Volume By 3D Color Optical Coherence Tomography In A Meniscectomized Rat Model.. Orthopaedic Research Society 2019 Annual Meeting 2019.02.05 Austin,USA
14. Akinobu Hyodo,Nobutake Ozeki, Yuji Kohno, So Suzuki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Makoto Tomita, Yusuke Nakagawa, Hideyuki Koga, Shinji Kiuchi, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Ichiro Sekiya.. Projected cartilage area ratio determined by 3D MRI analysis: a validation of a novel technique to evaluate articular cartilage.. 13th International Workshop on Osteoarthritis Imaging 2019.06.26 Charlottetown, Canada
15. Hayato Aoki, Nobutake Ozeki, Akinobu Hyodo, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Ichiro Sekiya.. Learning times and segmentation accuracy of U-Net Convolutional Neural Networks on automatic segmentation for MRI of knee.. 13th International Workshop on Osteoarthritis Imaging 2019.06.26 Charlottetown, Canada
16. Nobutake Ozeki, Hideyuki Koga, Hayato Aoki, Akinobu Hyodo, Kenji Suzuki, Yoshinori Itai, Jun Masumoto, Ichiro Sekiya. . 3D MRI analysis for cartilage in anterior cruciate ligament injured knees.. 13th International Workshop on Osteoarthritis Imaging 2019.06.26 Charlottetown, Canada
17. Ichiro Sekiya. Regeneration of Degenerated Meniscus by Synovial Stem Cells : Evaluation by 3D MRI. The Koret Foundation Lecture 2019.11.05 Davis,USA

JFCR Cancer Biology

Professor Takuro NAKAMURA

Professor Noriko Saitoh

Professor Kiyotaka SHIBA

Professor Kengo TAKEUCHI

Professor Akihiro TOMIDA

Professor Toru HIROTA

Graduate Student Yoshiharu Kusama, Yasuyo
Teramura, Ayumi Fujimoto

(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. Understanding of molecular mechanisms for epigenetic regulation in breast cancer (Saitoh)
3. Application of nanobiotechnology in cancer diagnostics (Shiba)
4. Pathological and genetic analysis of human cancer such as malignant lymphoma and lung cancer (Takeuchi)
5. Strategy for innovative drug therapy based on cancer biology (Tomida)
6. To understand how chromosomes are assembled and segregated in mitosis, and to elucidate the pathology underlying chromosomal instability in cancers (Hirota)

(3) Publications

[Original Articles]

1. Matsumura, S., Minamisawa, T., Suga, K., Kishita, H., Akagi, T., Ichiki, T., Ichikawa, Y. and Shiba, K. (2019). Subtypes of tumour cell-derived small extracellular vesicles having differently externalized phosphatidylserine. *J Extracell Vesicles* 8, 1579541.
2. Suzuki, Y., Kobayashi, K., Wakisaka, Y., Deng, D., Tanaka, S., Huang, C.J., Lei, C., Sun, C.W., Liu, H., Fujiwaki, Y., Lee, S., Isozaki, A., Kasai, Y., Hayakawa, T., Sakuma, S., Arai, F.,

- Koizumi, K., Tezuka, H., Inaba, M., Hiraki, K., Ito, T., Hase, M., Matsusaka, S., Shiba, K., Suga, K., Nishikawa, M., Jona, M., Yatomi, Y., Yalikun, Y., Tanaka, Y., Sugimura, T., Nitta, N., Goda, K. and Ozeki, Y. (2019). Label-free chemical imaging flow cytometry by high-speed multicolor stimulated Raman scattering. *Proc Natl Acad Sci U S A* 116, 15842-15848.
3. Inoue S, Hirota Y, Ueno T, Fukui Y, Yoshida E, Hayashi T, Kojima S, Takeyama R, Hashimoto T, Kiyono T, Ikemura M, Taguchi A, Tanaka T, Tanaka Y, Sakata S, Takeuchi K, Muraoka A, Osuka S, Saito T, Oda K, Osuga Y, Terao Y, Kawazu M, Mano H. Uterine adenomyosis is an oligoclonal disorder associated with KRAS mutations. *Nat Commun*. 2019;10:5785.
4. Kim SJ, Yoon DH, Kang HJ, Hong JY, Lee HS, Oh SY, Shin HJ, Kong JH, Yi JH, Sakamoto K, Ko YH, Huh J, Lee SS, Takeuchi K, Shin DY, Suh C, Kim WS. Ruxolitinib shows activity against Hodgkin lymphoma but not primary mediastinal large B-cell lymphoma. *BMC Cancer*. 2019;19:1080.
5. Teramura Y, Yamazaki Y, Tanaka M, Sugiura Y, Takazawa Y, Takeuchi K, Nakayama T, Kaneko T, Musha Y, Funauchi Y, Ae K, Matsumoto S, Nakamura T. Case of mesenchymal tumor with the PPP6R3-USP6 fusion, possible nodular fasciitis with malignant transformation. *Pathol Int*. 2019;69:706-709.
6. Takamatsu M, Yamamoto N, Kawachi H, Chino A, Saito S, Ueno M, Ishikawa Y, Takazawa Y, Takeuchi K. Prediction of early colorectal cancer metastasis by machine learning using digital slide images. *Comput Methods Programs Biomed*. 2019;178:155-161.
7. Matsue K, Abe Y, Narita K, Kobayashi H, Kitadate A, Takeuchi M, Miura D, Takeuchi K. Diagnosis of intravascular large B cell lymphoma: novel insights into clinicopathological features from 42 patients at a single institution over 20 years. *Br J Haematol*. 2019;187:328-336.
8. Yorita K, Togashi Y, Nakagawa H, Miyazaki K, Sakata S, Baba S, Takeuchi K, Hayashi Y, Murakami I, Kuroda N, Oda Y, Kohashi K, Yamada Y, Kiyozawa D, Michal M, Michal M. Vocal cord inflammatory myofibroblastic tumor with mucoid deposits harboring TIMP3-ALK fusion: A potential diagnostic pitfall. *Pathol Int*. 2019;69:366-371.
9. Watatani Y, Sato Y, Miyoshi H, Sakamoto K, Nishida K, Gion Y, Nagata Y, Shiraishi Y, Chiba K, Tanaka H, Zhao L, Ochi Y, Takeuchi Y, Takeda J, Ueno H, Kogure Y, Shiozawa Y, Kakiuchi N, Yoshizato T, Nakagawa MM, Nanya Y, Yoshida K, Makishima H, Sanada M, Sakata-Yanagimoto M, Chiba S, Matsuoka R, Noguchi M, Hiramoto N, Ishikawa T, Kitagawa J, Nakamura N, Tsurumi H, Miyazaki T, Kito Y, Miyano S, Shimoda K, Takeuchi K, Ohshima K, Yoshino T, Ogawa S, Kataoka K. Molecular heterogeneity in peripheral

- T-cell lymphoma, not otherwise specified revealed by comprehensive genetic profiling. *Leukemia*. 2019;33:2867-2883.
10. Nagaishi T, Yamada D, Suzuki K, Fukuyo R, Saito E, Fukuda M, Watabe T, Tsugawa N, Takeuchi K, Yamamoto K, Arai A, Ohtsuka K, Watanabe M. Indolent T cell lymphoproliferative disorder with villous atrophy in small intestine diagnosed by single-balloon enteroscopy. *Clin J Gastroenterol*. 2019;12:434-440.
 11. Takeuchi K. Discovery Stories of RET Fusions in Lung Cancer: A Mini-Review. *Front Physiol*. 2019;10:216.
 12. Hanawa Y, Higashiyama M, Horiuchi K, Ayaki K, Ito S, Mizoguchi A, Nishii S, Wada A, Inaba K, Sugihara N, Furuhashi H, Takajo T, Shirakabe K, Watanabe C, Tomita K, Komoto S, Nagao S, Miura S, Shimazaki H, Takeuchi K, Ueno H, Hokari R. Crohn's Disease Accompanied with Small Intestinal Extramedullary Plasmacytoma. *Intern Med*. 2019;58:2019-2023.
 13. Gong B, Kiyotani K, Sakata S, Nagano S, Kumehara S, Baba S, Besse B, Yanagitani N, Fribolet L, Nishio M, Takeuchi K, Kawamoto H, Fujita N, Katayama R. Secreted PD-L1 variants mediate resistance to PD-L1 blockade therapy in non-small cell lung cancer. *J Exp Med*. 2019;216:982-1000.
 14. Osumi H, Kawachi H, Yoshio T, Ida S, Yamamoto N, Horiuchi Y, Ishiyama A, Hirasawa T, Tsuchida T, Hiki N, Takeuchi K, Fujisaki J. Epstein-Barr virus status is a promising biomarker for endoscopic resection in early gastric cancer: proposal of a novel therapeutic strategy. *J Gastroenterol*. 2019;54:774-783.
 15. Nakayama I, Shinozaki E, Sakata S, Yamamoto N, Fujisaki J, Muramatsu Y, Hirota T, Takeuchi K, Takahashi S, Yamaguchi K, Noda T. Enrichment of CLDN18-ARHGAP fusion gene in gastric cancers in young adults. *Cancer Sci*. 2019;110:1352-1363.
 16. Fukuda K, Takeuchi S, Arai S, Katayama R, Nanjo S, Tanimoto A, Nishiyama A, Nakagawa T, Taniguchi H, Suzuki T, Yamada T, Nishihara H, Ninomiya H, Ishikawa Y, Baba S, Takeuchi K, Horiike A, Yanagitani N, Nishio M, Yano S. Epithelial-to-Mesenchymal Transition Is a Mechanism of ALK Inhibitor Resistance in Lung Cancer Independent of ALK Mutation Status. *Cancer Res*. 2019;79:1658-1670.
 17. Kataoka K, Miyoshi H, Sakata S, Dobashi A, Couronne L, Kogure Y, Sato Y, Nishida K, Gion Y, Shiraishi Y, Tanaka H, Chiba K, Watatani Y, Kakiuchi N, Shiozawa Y, Yoshizato T, Yoshida K, Makishima H, Sanada M, Onozawa M, Teshima T, Yoshiki Y, Ishida T, Suzuki K, Shimada K, Tomita A, Kato M, Ota Y, Izutsu K, Demachi-Okamura A, Akatsuka Y, Miyano S, Yoshino T, Gaulard P, Hermine O, Takeuchi K, Ohshima K, Ogawa S. Frequent structural variations involving programmed death ligands in Epstein-Barr virus-associated lymphomas. *Leukemia*. 2019;33:1687-1699.

18. Haga Y, Uemura M, Baba S, Inamura K, Takeuchi K, Nonomura N, Ueda K. Identification of Multisialylated LacdiNAc Structures as Highly Prostate Cancer Specific Glycan Signatures on PSA. *Anal Chem*. 2019;91:2247-2254.
19. Matsue K, Abe Y, Kitadate A, Miura D, Narita K, Kobayashi H, Takeuchi M, Enzan N, Tanaka A, Takeuchi K. Sensitivity and specificity of incisional random skin biopsy for diagnosis of intravascular large B-cell lymphoma. *Blood*. 2019;133:1257-1259.
20. Tsuyama N, Yokoyama M, Fujisaki J, Oguchi M, Terui Y, Takeuchi K. Villous colonization (glove balloon sign): A histopathological diagnostic marker for follicular lymphomas with duodenal involvement including duodenal-type follicular lymphoma. *Pathol Int*. 2019;69:48-50.
21. Chang KC, Yu-Yun Lee J, Sakamoto K, Baba S, Takeuchi K. Blastic plasmacytoid dendritic cell neoplasm with immunoblastoid morphology and MYC rearrangement and overexpression. *Pathology*. 2019;51:100-102.
22. Abdalla, M.O.A., Yamamoto, T., Machara, K., Ohkawa, Y., Miura, H., Hiratani, I., Nakayama, H., Nakao, M., Saitoh, N. (2019). The Eleanor ncRNAs activate the topological domain of the ESR1 locus to balance against apoptosis. *Nat. Commun*, 10(1), 3778. doi:10.1038/s41467-019-11378-4
23. Okamoto Y, Saito T, Tani Y, Toki T, Hasebe A, Koido M, Tomida A. (2020) The kinase PERK represses translation of the G-protein-coupled receptor LGR5 and receptor tyrosine kinase ERBB3 during ER stress in cancer cells. *J Biol Chem*. 295:4591-4603.
24. Fujimura A, Hayashi Y, Kato K, Kogure Y, Kameyama M, Shimamoto H, Daitoku H, Fukamizu A, Hirota T, Kimura, K. Identification of a novel nucleolar protein complex required for mitotic chromosome segregation through centromeric accumulation of Aurora B. *Nucleic Acids Res*, 48:6583-6596, 2020.
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26. Nishimura K., Johmura Y, Deguchi K, Jiang Z, Uchida KSK, Suzuki N, Shimada M, Chiba Y, Hirota T, Yoshimura SH, Kono K, Nakanish M. Cdk1-mediated DIAPH1 phosphorylation maintains metaphase cortical tension and inactivates the spindle assembly checkpoint at anaphase. *Nat Commun*. 10:981-993, 2019.
27. Nakayama I, Shinozaki E, Sakata S, Yamamoto N, Fujisaki J, Muramatsu Y, Hirota T, Takeuchi K, Takahashi S, Yamaguchi K, Noda T. Enrichment of CLDN18-ARHGAP fusion gene in gastric cancers in young adults. *Cancer Sci*. 110:1352-1363, 2019.
28. Supakul S, Yao K, Ochi H, Shimada T, Hashimoto K, Sunamura S, Mabuchi Y, Tanaka M, Akazawa C, Nakamura T, Okawa A, Takeda S, Sato S. Pericytes as a source of osteogenic

cells in bone fracture healing. **Int J Mol Sci**, 20:1079, 2019.

29. Teramura Y, Yamazaki Y, Tanaka M, Sugiura Y, Takazawa Y, Takeuchi K, Nakayama T, Kaneko T, Musha Y, Funauchi Y, Ae K, Matsumoto S, Nakamura T. Case of mesenchymal tumor with the PPP6R3-USP6 fusion, possible nodular fasciitis with malignant transformation. **Pathol Int**, 69:706-709, 2019.

[Review Articles]

1. Yamamoto, T., Saitoh, N. (2019). Non-coding RNAs and chromatin domains. *Curr Opin Cell Biol*. 58, 26-33, 2019. doi:10.1016/j.ceb.2018.12.005
2. Takahashi M, Hirota T. Folding the genome into mitotic chromosomes. *Curr Opin Cell Biol*, 60:19-26, 2019.

[Conference Activities & Talks]

1. Noriko Saitoh. Non-coding RNAs delineate the 3D genome architecture in endocrine-therapy resistant breast cancer. Riken IMS Cancer Immunology Seminar Series, Oct 11, 2019 (Riken, Yokohama, Kanagawa)
2. Yamamoto, T., Ichikawa, Y., Ohkawa, Y., Hiratani, I., Nakao, M., Saitoh, N. Non-coding RNAs that define the active chromatin domain in endocrine therapy-resistant breast cancer cells. International Symposium for Female Researchers in Chromatin Biology. June 23, 2019. Riken CDB
3. Toru Hirota. A robust control of mitotic transitions prevents chromosome missegregation. International Symposium Cancer Etiology. Tohoku Forum for Creativity. Tohoku Univ, Sep 24, 2019.
4. Jo Minji, Oltea Sampetrean, Hideyuki Saya, Toru Hirota. Possible contribution of chromosomal instability in cancer progression. The 78th Annual meeting of the Japanese Cancer Association. Kyoto, Sept 27, 2018.
5. Toru Hirota: Spatial control of Aurora B activity at centromeres in mitosis. Symposium. The 42nd Annual meeting of the Molecular Biology Society of Japan. Fukuoka, Dec 4, 2019.
6. Toru Hirota. How activity of Aurora B is controlled at centromeres in mitosis. Seminar. Okinawa Institute of Science and Technology, Feb 5, 2020.

Medical Science Mathematics

Professor: Tatsuhiko Tsunoda, Junior Associate Professor: Fuyuki Miya,
Assistant Professor: Jo Nishino, Assistant Professor: Takashi Kamatani

(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. Daichi Shigemizu, Shintaro Akiyama, Yuya Asanomi, Keith A Boroevich, Alok Sharma, Tatsuhiko Tsunoda, Kana Matsukuma, Makiko Ichikawa, Hiroko Sudo, Satoko Takizawa, Takashi Sakurai, Kouichi Ozaki, Takahiro Ochiya, Shumpei Niida. Risk prediction models for dementia constructed by supervised principal component analysis using miRNA expression data. *Commun Biol.* 2019; 2; 77
2. Takahiro Otani, Hisashi Noma, Shonosuke Sugawara, Aya Kuchiba, Atsushi Goto, Taiki Yamaji, Yuta Kochi, Motoki Iwasaki, Shigeyuki Matsui, Tatsuhiko Tsunoda. Exploring predictive biomarkers from clinical genome-wide association studies via multidimensional hierarchical mixture models. *Eur. J. Hum. Genet.* 2019.01; 27(1); 140-149
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4. Hamendra Manhar Reddy, Alok Sharma, Abdollah Dehzangi, Daichi Shigemizu, Abel Avitesh Chandra, Tatsuhiko Tsunoda. GlyStruct: glycation prediction using structural properties of amino acid residues. *BMC Bioinformatics.* 2019.02; 19(Suppl 13); 547
5. Ronesh Sharma, Alok Sharma, Ashwini Patil, Tatsuhiko Tsunoda. Discovering MoRFs by trisecting intrinsically disordered protein sequence into terminals and middle regions. *BMC Bioinformatics.* 2019.02; 19(Suppl 13); 378
6. Alok Sharma, Artem Lysenko, Yosvany López, Abdollah Dehzangi, Ronesh Sharma, Hamendra Reddy, Abdul Sattar, Tatsuhiko Tsunoda. HseSUMO: Sumoylation site prediction using half-sphere exposures of amino acids residues. *BMC Genomics.* 2019.04; 19(Suppl 9); 982

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15. Daichi Shigemizu, Shintaro Akiyama, Yuya Asanomi, Keith A Boroevich, Alok Sharma, Tatsuhiko Tsunoda, Takashi Sakurai, Kouichi Ozaki, Takahiro Ochiya, Shumpei Niida. A comparison of machine learning classifiers for dementia with Lewy bodies using miRNA expression data. *BMC Med Genomics*. 2019.10; 12(1); 150
16. Abel Chandra, Alok Sharma, Abdollah Dehzangi, Daichi Shigemizu, Tatsuhiko Tsunoda. Bigram-PGK: phosphoglycerylation prediction using the technique of bigram probabilities of position specific scoring matrix. *BMC Mol Cell Biol*. 2019.12; 20(Suppl 2); 57

[Books etc]

1. Singh V, Sharma A, Chandra A, Dehzangi A, Shigemizu D, Tsunoda T. Computational Prediction of Lysine Pupylation Sites in Prokaryotic Proteins Using Position Specific Scoring Matrix into Bigram for Feature Extraction. In: Nayak A., Sharma A. (eds) *PRICAI 2019: Trends in Artificial Intelligence*. *PRICAI 2019. Lecture Notes in Computer Science*. Springer, 2019.08 (ISBN : 978-3-030-29893-7)
2. Vans E., Sharma A., Patil A., Shigemizu D., Tsunoda T. Clustering of Small-Sample Single-Cell RNA-Seq Data via Feature Clustering and Selection. In: Nayak A., Sharma A. (eds) *PRICAI 2019: Trends in Artificial Intelligence*. *PRICAI 2019. Lecture Notes in Computer Science*. Springer, 2019.08

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4. Tatsuhiko Tsunoda, Toshihiro Tanaka, Yusuke Nakamura (Eds.). Genome-Wide Association Studies. Springer Nature, 2019.11 (ISBN : 978-9811381768)

[Misc]

1. Mansoor Saqi, Artem Lysenko, Yi-Ke Guo, Tatsuhiko Tsunoda, Charles Auffray. Navigating the disease landscape: knowledge representations for contextualizing molecular signatures. Brief. Bioinformatics. 2019.03; 20(2); 609-623

[Conference Activities & Talks]

1. Tatsuhiko Tsunoda. Cancer heterogeneity and immunology for precision medicine. CREST International Symposium on Big Data Application 2019.01.15 Tokyo, Japan
2. Tatsuhiko Tsunoda. Medical Big Data Analysis for Precision Medicine. CREST Joint International Symposium for Big Data 2019.03.12 Kyoto, Japan
3. Exome sequencing data shows multicellular colonization in tumor metastasis. 2019.09.11
4. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. 2019.09.25
5. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. CREST Joint International Symposium on Big Data 2019.12.17
6. Tatsuhiko Tsunoda. Data-driven Medical Sciences with Omic Analysis. Moonshot International Symposium 2019.12.18 Tokyo

[Patents]

1. METHOD FOR SELECTING IPS CELL CLONE, AND METHOD FOR SELECTING GENE USED IN METHOD FOR SELECTING SAME, Announcement Number : WO 2012/115270

[Works]

1. DeepInsight: Package of DeepInsight methodology, Software, 2019.08

Genomic Function and Diversity

Professor Yuta Kochi

Associate Professor Satomi Mitsuhashi

Collaborative Researcher Kensuke Yamaguchi

Collaborative Researcher Kyoko Kobayashi

Assistant Administrative Staff Asako Yuasa

(1) Outline

Complex diseases such as immunological diseases, metabolic diseases and cancer diseases are caused by both genetic and environmental factors, with varying combinations in different individuals. Genome-wide association studies (GWAS) have led to the discovery of thousands of risk variants involved in these diseases, but the precise mechanisms of the diseases are not fully understood. Our laboratory aims to elucidate the disease etiology by dissecting the diversity of genomic function among individuals. To this end, we integrate bioinformatic approaches with molecular biology techniques in the analysis of genetic variants such as expression QTL and splicing QTL mapping. We will also establish to predict each individual's pathophysiology (disease severity, drug response, etc.) based on the individual's genome information to bring precision medicine into clinical practice.

(2) Research

1. To dissect pathological mechanism of complex traits, we integrated the disease GWAS data with expression QTL and splicing QTL data, and we comprehensively identified disease-associated alternative isoforms.
2. By re-sequencing the GWAS genes in rheumatoid arthritis patients, we identified accumulation of rare coding variants in TYK2 gene that influenced inflammatory cytokine signals.
3. To further seek disease susceptible loci for systemic lupus erythematosus, we are performing GWAS meta-analysis in world-wide collaboration.

(3) Publications

[Original Articles]

1. Takahiro Otani, Hisashi Noma, Shonosuke Sugawara, Aya Kuchiba, Atsushi Goto, Taiki Yamaji, Yuta Kochi, Motoki Iwasaki, Shigeyuki Matsui, Tatsuhiko Tsunoda. Exploring predictive biomarkers from clinical genome-wide association studies via multidimensional hierarchical mixture models. *Eur. J. Hum. Genet.* 2019.01; 27(1); 140-149
2. Hatano Hiroaki, Ota Mineto, Takeshima Yusuke, Iwasaki Yukiko, Nagafuchi Yasuo, Kochi Yuta, Shoda Hirofumi, Okamura Tomohisa, Fujio Keishi, Yamamoto Kazuhiko. 遺伝学 全身性エリテマトーデス (SLE)

と関節リウマチ (RA) 患者の末梢血単核球細胞 (PBMCs) の多様な免疫細胞サブセットにおける splicing quantitative trait loci(sQTL) の影響に関する包括的研究 (Genetics A comprehensive study of splicing quantitative trait loci(sQTL) effects in various immune cell subsets in peripheral blood mononuclear cells(PBMCs) of systemic lupus erythematosus(SLE) and rheumatoid arthritis(RA) patients) 日本リウマチ学会総会・学術集会プログラム・抄録集. 2019.03; 63 回; 325

3. Molineros JE, Looger LL, Kim K, Okada Y, Terao C, Sun C, Zhou XJ, Raj P, Kochi Y, Suzuki A, Akizuki S, Nakabo S, Bang SY, Lee HS, Kang YM, Suh CH, Chung WT, Park YB, Choe JY, Shim SC, Lee SS, Zuo X, Yamamoto K, Li QZ, Shen N, Porter LL, Harley JB, Chua KH, Zhang H, Wakeland EK, Tsao BP, Bae SC, Nath SK. Amino acid signatures of HLA Class-I and II molecules are strongly associated with SLE susceptibility and autoantibody production in Eastern Asians. *PLoS genetics*. 2019.04; 15(4); e1008092
4. Okada Y, Eyre S, Suzuki A, Kochi Y, Yamamoto K. Genetics of rheumatoid arthritis: 2018 status. *Annals of the rheumatic diseases*. 2019.04; 78(4); 446-453
5. Akizuki S, Ishigaki K, Kochi Y, Law SM, Matsuo K, Ohmura K, Suzuki A, Nakayama M, Iizuka Y, Koseki H, Ohara O, Hirata J, Kamatani Y, Matsuda F, Sumida T, Yamamoto K, Okada Y, Mimori T, Terao C. PLD4 is a genetic determinant to systemic lupus erythematosus and involved in murine autoimmune phenotypes. *Annals of the rheumatic diseases*. 2019.04; 78(4); 509-518
6. Motegi T, Kochi Y, Matsuda K, Kubo M, Yamamoto K, Momozawa Y. Identification of rare coding variants in *TYK2* protective for rheumatoid arthritis in the Japanese population and their effects on cytokine signalling. *Annals of the rheumatic diseases*. 2019.08; 78(8); 1062-1069
7. Ono Chisato, Kochi Yuta, Tanaka Shinya, Yamamoto Kazuhiko, Baba Yoshihiro. Systemic lupus erythematosus and other systemic autoimmune diseases Role of *Fcrl5* in B cell immune response and peripheral tolerance(和訳中) 日本免疫学会総会・学術集会記録. 2019.11; 48(Proceedings); 2-B

Organogenesis and Neogenesis

Takanori Takebe, MD, PhD, Professor
 Yosuke Yoneyama, PhD, Assistant Professor
 Hirokazu Kawaguchi, PhD, Assistant Professor
 Norikazu Saiki, PhD, Project Assistant Professor
 Rie Ouchi-Koike, PhD, Project Researcher
 Mari Maezawa, Research Assistant
 Kanae Ohtsu, Research Assistant
 Yoko Sekinami, Technical Assistant
 Michiko Mori, Administrative Assistant

(1) Outline

The Takebe Lab enjoys developing new technology and implementing fresh outlooks on discoveries that may be ignored, under-appreciated and overlooked by the traditional scientific community. The Takebe Lab takes a creative lead for the exploitation and dissemination of unpredictable, extraordinary and crazy paradigm by integrating discovery and technology, eventually revolutionizing science, and medico-health-care paradigm. The Takebe Lab is also lending its support to commercial execution to move forward.

The self-organizing tissue-based approach coupled with induced pluripotent stem cell (iPSC) technology has just begun as a promising field for designing a miniature organ, aka an organoid, in culture and is expected to achieve valuable outcomes in ‘(re-) generative medicine’ and ‘drug development’. However, how the complex but stereotyped tissue shapes self-organize still remains largely unknown. To understand such complex self-organizing mechanisms, Dr Takebe’s lab proposes to take a ‘reverse reductionism approach’ for a holistic mechanistic understanding of the dynamic nature of a self-developing system. We also seek to translate knowledge of living systems into a revolutionary technology platform towards practical biomedical use in clinics.

(2) Research

Organoids are multicellular structures that can be derived from adult organs or pluripotent stem cells. Early versions of organoids range from simple epithelial structures to complex, disorganized tissues with large cellular diversity. The current challenge is to engineer cellular complexity into organoids in a controlled manner that results in organized assembly and acquisition of tissue function. These efforts have relied on studies of organ assembly during embryonic development and have resulted in development of organoids with multilayer tissue complexity and higher order functions. To advance the field forward, Takebe Lab would like to achieve three interactive and complementary goals:

1. The deductive development of a complex human organoid model
2. The multidisciplinary dissection of self-driven mechanisms of organogenesis
3. The technology prototyping towards biomedical applications

Our early efforts are being made on liver organoid (liver bud or miniature liver) systems using human iPSC. For example, we have demonstrated successful integration of endothelial cells (Nature, 2013), mesenchymal

cells (Cell Stem Cell, 2015) and macrophages (Cell Metab, 2019) into human liver organoids, allowing for the study of drug testing and transplant applications. More recently, we showed the inter-coordinated specification and invagination of the human hepato-biliary-pancreatic system from human pluripotent stem cells, thereby, connecting multi-organ systems in a dish (Nature, 2019). Thus we are tackling the questions how the next generation of organoids can be designed by utilizing an engineering-based narrative design, and what promise and impact will be brought towards future biomedical applications (Science, 2019). Our interested expertise includes cell biology, mathematics, bioinformatics, morphogenesis, genomics, bioengineering, chemistry or biomechanics. In a longer term, we seek to realize “organoid medicine” applications through human implementation of extracorporeal device, precision medicine, drug discovery and organ replacement therapy. We are accelerating such biomedical applications of organoids by collaborating with international and diverse industry collaborators, such as the Cincinnati Children’s Hospital and the Takeda-CiRA program.

(3) Publications

[Original Articles]

1. Liu T, Zhou L, Yang K, Iwasawa K, Kadekaro AL, Takebe T, Andl T, Zhang Y. The β -catenin/YAP signaling axis is a key regulator of melanoma-associated fibroblasts. *Signal transduction and targeted therapy*. 2019; 4; 63
2. Ouchi R, Togo S, Kimura M, Shinozawa T, Koido M, Koike H, Thompson W, Karns RA, Mayhew CN, McGrath PS, McCauley HA, Zhang RR, Lewis K, Hakozaiki S, Ferguson A, Saiki N, Yoneyama Y, Takeuchi I, Mabuchi Y, Akazawa C, Yoshikawa HY, Wells JM, Takebe T. Modeling Steatohepatitis in Humans with Pluripotent Stem Cell-Derived Organoids. *Cell metabolism*. 2019.05;
3. Takebe T. Creativity for a cure. *Nature medicine*. 2019.06; 25(6); 868
4. Takebe T, Wells JM. Organoids by design. *Science (New York, N.Y.)*. 2019.06; 364(6444); 956-959
5. Koike H, Iwasawa K, Ouchi R, Maezawa M, Giesbrecht K, Saiki N, Ferguson A, Kimura M, Thompson WL, Wells JM, Zorn AM, Takebe T. Modelling human hepato-biliary-pancreatic organogenesis from the foregut-midgut boundary. *Nature*. 2019.10; 574(7776); 112-116
6. Ogawa-Ochiai K, Yoshimura K, Takebe T, Iwahashi M, Shirai A, Tsuda M, Ogawa M, Ishikawa H. The effect of contact needle therapy on fatigue in patients with cancer in palliative care: A study protocol for a randomized controlled trial. *Medicine*. 2019.11; 98(44); e17809
7. Fang H, Yao S, Chen Q, Liu C, Cai Y, Geng S, Bai Y, Tian Z, Zacharias AL, Takebe T, Chen Y, Guo Z, He W, Diao J. De Novo-Designed Near-Infrared Nanoaggregates for Super-Resolution Monitoring of Lysosomes in Cells, in Whole Organoids, and in Vivo. *ACS nano*. 2019.12; 13(12); 14426-14436

[Conference Activities & Talks]

1. Takebe T. Next-Gen Organoids from Pluripotency. *Keystone Symposia* 2019.01.29
2. Takebe T. The Era of Organoid Medicine. *日本再生医療学会 International Symposium* 2019.03.22
3. Takebe T. Organoid by design. *ISSCR Annual Mtg* 2019.06.27 Los Angeles
4. Takebe T. Making Organoids More Complex Towards Medicine. *3rd HY Indang Symposium* 2019.09.25 Seoul
5. Takebe T. Organoid Medicine for Liver Disorders. *ISSCR/KSSCR International Symposium* 2019.09.26 Seoul
6. Takebe T. The promise of organoid, medicine -from screen to therapeutics. *2019 Taiwan-TMDU Joint Symposium* 2019.10.05 台湾
7. Takebe T. Directing Complex Organogenesis from Human iPSC towards Therapy. *CiRA 国際シンポジウム* 2019.11.29 京都
8. Takebe T. Designer’s Organoids by Narrative Engineering. *第42回日本分子生物学会年会* 2019.12.06 福岡

Bioelectronics

Staff

Yuji Miyahara (Professor)
 Akira Matsumoto (Associate Professor)
 Tatsuro goda (Assistant Professor)
 Miyuki Tabata (tenure track Assistant Professor)
 Yukichi Horiguchi (Assistant Professor)
 Taiki Miyazawa (Project Assistant Professor)
 Siyuan Chen (Collaborative Researcher)
 Michiko Ito (Collaborative Researcher)
 Takuya Miyazaki (Collaborative Researcher)
 Hiroko Matsumoto (Technical Assistant)
 Yuki Morooka (Technical Assistant)
 Chiharu Mizoi (Technical Assistant)
 Sayo Kotaki (Technical Assistant)
 Ulala Minamibata (Staff Assistant)

Graduate student

Chindanai RATANAPORNCHAROEN, Hideki Fujisaki, Hiroaki Hatano, Chattarika KHAMHANGLIT,
 Maki Shikatani, Ayumu Tsuchiya, Xinyue Liu, Ayano Mukaida

(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. Chen Siyuan, Matsumoto Hiroko, Moro-oka Yuki, Tanaka Miyako, Miyahara Yuji, Suganami Takayoshi, Matsumoto Akira. Microneedle-Array Patch Fabricated with Enzyme-Free Polymeric Components Capable of On-Demand Insulin Delivery ADVANCED FUNCTIONAL MATERIALS. 2019.02; 29(7);
2. Hatano H, Goda T, Matsumoto A, Miyahara Y. Induced Proton Perturbation for Sensitive and Selective Detection of Tight Junction Breakdown. Analytical chemistry. 2019.03; 91(5); 3525-3532
3. Taiki Miyazawa, Akira Matsumoto, Yuji Miyahara. Determination of cellular vitamin C dynamics by HPLC-DAD Analyst. 2019.03;
4. Mayuko Itaya, Taiki Miyazawa, Jean-Marc Zingg, Takahiro Eitsuka, Angelo Azzi, Mohsen Meydani, Teruo Miyazawa, Kiyotaka Nakagawa. The differential cellular uptake of curcuminoids in vitro depends dominantly on albumin interaction Phytomedicine. 2019.03;
5. Yoshizumi Toshihiro, Goda Tatsuro, Yatabe Rui, Oki Akio, Matsumoto Akira, Oka Hiroaki, Washio Takashi, Toko Kiyoshi, Miyahara Yuji. Field-effect transistor array modified by a stationary phase to generate informative signal patterns for machine learning-assisted recognition of gas-phase chemicals MOLECULAR SYSTEMS DESIGN & ENGINEERING. 2019.04; 4(2); 386-389
6. Ratanaporncharoen Chindanai, Tabata Miyuki, Goda Tatsuro, Matsumoto Akira, Miyahara Yuji, Ishihara Noboru, Masu Kazuya, Sriyudthsak Mana. Dental caries evaluation using wireless pH sensor: Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, Chindanai(和訳中) 生体医歯工学共同研究拠点成果報告書. 2019.04; 平成 30 年度; 119
7. Khamhanglit Chattarika, Tabata Miyuki, Goda Tatsuro, Matsumoto Akira, Miyahara Yuji, Kul-eung Pornnapat, Sriyudthsak Mana, Nakajima Anri. ISFET ゲート表面の機能化による pH 感度への影響 (Effect of functionalization of ISFET gate surface on pH sensitivity) 生体医歯工学共同研究拠点成果報告書. 2019.04; 平成 30 年度; 165

8. Goda T, Imaizumi Y, Hatano H, Matsumoto A, Ishihara K, Miyahara Y. Translocation Mechanisms of Cell-Penetrating Polymers Identified by Induced Proton Dynamics. *Langmuir : the ACS journal of surfaces and colloids*. 2019.06; 35(24); 8167-8173
9. Miyuki Tabata, Yuji Miyahara. Label-free nucleic acid amplification detection using electrochemical sensors for liquid biopsy *Journal of Photopolymer Science and Technology*. 2019.06; 32;
10. Siyuan Chen, Hiroko Matsumoto, Yuki Moro-oka, Miyako Tanaka, Yuji Miyahara, Takayoshi Suganami, Akira Matsumoto. Smart Microneedle Fabricated with Silk Fibroin Combined Semi-interpenetrating Network Hydrogel for Glucose-Responsive Insulin Delivery *ACS Biomaterials Science & Engineering*. 2019.07;
11. Taiki Miyazawa, Akira Matsumoto, Yuji Miyahara. Determination of intra- and extra-cellular vitamin C dynamics; the simplest-ever and label-free chromatographic technique *GIT laboratory journal*. 2019.09;
12. Chen Siyuan, Matsumoto Hiroko, Moro-oka Yuki, Tanaka Miyako, Miyahara Yuji, Suganami Takayoshi, Matsumoto Akira. Smart Microneedle Fabricated with Silk Fibroin Combined Semi interpenetrating Network Hydrogel for Glucose-Responsive Insulin Delivery *ACS BIOMATERIALS SCIENCE & ENGINEERING*. 2019.11; 5(11); 5781-5789
13. Hatano H, Goda T, Matsumoto A, Miyahara Y. Induced Proton Dynamics on Semiconductor Surfaces for Sensing Tight Junction Formation Enhanced by an Extracellular Matrix and Drug. *ACS sensors*. 2019.12;

[Books etc]

1. Miyuki Tabata, Yuji Miyahara. *Biosensors based on field-effect transistors*. Springer, 2019.08 (ISBN : 978-981-13-7611-5)

[Misc]

1. Taiki Miyazawa, Gregor C. Burdeos, Mayuko Itaya, Kiyotaka Nakagawa, Teruo Miyazawa. Vitamin E: Regulatory Redox Interactions *IUBMB life*. 2019.01; 71(4); 430-441
2. Taiki Miyazawa, Akira Matsumoto, Yuji Miyahara . Determination of Intra- and Extra-cellular Vitamin C Dynamics *GIT Laboratory Journal*. 2019.09;
3. Miyuki Tabata, Yuji Miyahara. Liquid Biopsy in Combination with Solid-state Electrochemical Sensors and Nucleic Acid Amplification *Journal of Materials Chemistry B*. 2019.09;

[Conference Activities & Talks]

1. Tatsuro Goda. Conducting Polymers with Target Recognition Element for Biosensing Applications. International Conference on BioSensors, BioElectronics, BioMedical Devices, BioMEMS/NEMS & Applications (Bio4Apps 2018/2019) 2019.01.06 Harbin
2. Tatsuro Goda. Conducting Polymers with Recognizable Units for Biosensing Applications. Seminar at Inner Mongolia University for Nationalities 2019.01.09
3. Miyuki Tabata, Chindanai Ratanaporncharoen, Yuichi Kitasako, Masaomi Ikeda, Junji Tabami, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Micro Ir/IrOx pH sensor for quantitative dental caries detection. 3rd International Symposium of the Network-type Joint Usage/Research Center for Radiation Disaster Medical Science 2019.01.13 Celecton Fukushima
4. Miyuki Tabata, Chindanai Ratanaporncharoen, Yuichi Kitasako, Masaomi Ikeda, Junji Tabami, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Micro Ir/IrOx pH sensor for quantitative dental caries detection. The 3rd International Symposium of the Network-type Joint Usage/Research Center for Radiation Disaster Medical Science 2019.01.13
5. Miyuki Tabata, Chindanai Ratanaporncharoen, Yuichi Kitasako, Masaomi Ikeda, Junji Tabami, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Micro Ir/IrOx pH sensor for quantitative dental caries detection. The 3rd International Symposium of the Network-type Joint Usage/Research Center for Radiation Disaster Medical Science 2019.01.13

6. Tatsuro Goda. Conducting Polymers for Biosensing Applications. 5th Joint Symposium between IBB/TMDU and Chulalongkorn University on Biomedical Materials and Engineering 2019.01.17
7. Tatsuro Goda. Biorecognizable Conducting Polymers for Biosensing. Symposium: Crossing Borders in Medical Nanoscience and Biomaterials 2019.03.08
8. Taiki Miyazawa, Akira Matsumoto, Yuji Miyahara. Determination of Vitamin C kinetics of cancer cells by HPLC-DAD. 日本化学会 第 99 春季年会 2019.03.17 甲南大学 岡本キャンパス
9. Taiki Miyazawa, Akira Matsumoto, Yuji Miyahara. Determination of Vitamin C kinetics of cancer cells by HPLC-DAD. 日本化学会第 99 春季年会 2019.03.17
10. Siyuan Chen, Hiroko Matsumoto, Yuki Moro-oka, Kozue Ochi, Miyako Tanaka, Yuji Miyahara, Takayoshi Suganami, Akira Matsumoto. Enzyme-Free and Nanoparticle Free Polymeric Microneedle-Array Patch Serves as On-Skin Pancreas for Sustained On-Demand Insulin Delivery. 第 68 回高分子学会年次大会 2019.05.29
11. Miyuki Tabata, Yuji Miyahara. Biosensors detecting cancer biomarkers for liquid biopsy. Matrafured2019 2019.06.16
12. Akira Matsumoto. Borono-lectin” based polymer engineering for smart drug delivery systems. 2019 US-Japan Polymer Symposium:- Macromolecules: Challenges and Opportunities for the 21st Century- 2019.06.21
13. Miyuki Tabata, Yuji Miyahara. Label-free nucleic acid amplification detection using electrochemical sensors for liquid biopsy. The 36th International Conference of Photopolymer Science and Technology 2019.06.24
14. Specific Detection of Human Influenza Virus Using Resistive Pulse Sensing with Nanoparticle-based Molecular Recognition. 10th International Conference on Molecular Electronics & BioElectronics (MBE10) 2019.06.25
15. Hiroaki Hatano, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Ultrasensitive assays for epithelial tight junction formation by monitoring proton leaks using ISFET. 10th International Conference on Molecular Electronics and Bioelectronics (M&BE10) 2019.06.25 Nara
16. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Specific Detection of Human Influenza Virus Using Resistive Pulse Sensing with Nanoparticle-based Molecular Recognition. 10th International Conference on Molecular Electronics and Bioelectronics (M&BE10) 2019.06.25 Nara
17. Tatsuro Goda, Yuji Miyahara. Development of Influenza Virus-Recognizable Conducting Polymers for Bioelectronic Applications. 10th International Conference on Molecular Electronics and Bioelectronics (M&BE10) 2019.06.25 Nara
18. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Specific Detection of Human Influenza Virus Using Resistive Pulse Sensing with Nanoparticle-based Molecular Recognition. 10th International Conference on Molecular Electronics and Bioelectronics (M&BE10) 2019.06.25
19. Hiroaki Hatano, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Ultrasensitive assays for epithelial tight junction formation by monitoring proton leaks using ISFET. The 10th International Conference on Molecular Electronics and Bioelectronics (M&BE10) 2019.06.25
20. Tatsuro Goda, Hideki Fujisaki, Wenfeng Hai, Masahiro Toya, Akira Matsumoto, Yuji Miyahara. Sugar-tethered and Zwitterionic PEDOTs for Virus Detections and Antifouling Biosensing. 12th International Symposium on Flexible Organic Electronics (ISFOE19) 2019.07.01 Thessaloniki
21. Tatsuro Goda, Hideki Fujisaki, Wenfeng Hai, Masahiro Toya, Akira Matsumoto, Yuji Miyahara. Sugar-tethered and Zwitterionic PEDOTs for Virus Detections and Antifouling Biosensing. 12th International Symposium on Flexible Organic Electronics (ISFOE19) 2019.07.01
22. Miyuki Tabata, Yuji Miyahara. Electrical/Electrochemical detection of small nucleic acids for liquid biopsy. EMN Barcelona Meeting 2019 2019.08.19

23. Investigation of Virus Detection System Using Molecular Recognition Surface on Polymer Layer and AI Technology. 2019.09.25
24. Taiki Miyazawa, Akira Matsumoto, Yuji Miyahara. Using nutrients and nanomaterials for therapeutic purpose. OKINAWA COLLOIDS 2019: An International Conference on Colloid & Surface Science Celebrating the 70th Anniversary of the Divisional Meeting of Division of Colloid and Surface Chemistry 2019.11.04 Bankoku Shinryokan
25. Chattarika Khamhanglit, Miyuki Tabata, Pornnapat Kul-eung, Mana Sriyudthsak, Tatsuro Goda, Akira Matsumoto, Tetsuo Tabei, Anri Nakajima, Yuji Miyahara. The effect of chemical modification on gate surface to pH response of ISFET,. The 3rd International Symposium on Biomedical Engineering 2019.11.08

[Awards & Honors]

1. Most Impressive Presentation Award, 2019.11

Material-Based Medical Engineering

Prof. Akio Kishida
Assoc. Prof. Tsuyoshi Kimura
Assist. Prof. Yoshihide Hashimoto
Secretary Naomi Hiwatari

Doctor Course Student
Masaki Watanabe
Takuya Konishi
Mako Kobayashi

(1) Outline

In our laboratory, we have treated many research topics from the fundamental study of biomaterials in terms of material engineering to the application study of the medical devices. The keywords of our policy are "contribution to medical care" and "exploration of basic scientific principles".

(2) Research

In order to develop technologies that contribute to the medical and dental care, there is a need for systems 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 researches aimed at specific clinical applications using cell engineering and genetic engineering techniques. Target fields are development of novel medical material, regenerative medicine, gene therapy, and treatment engineering.

(1) Regenerative medicine using decellularized biological tissue

For removing immunogenicity, biological tissues are decellularized using a novel processing method, high hydrostatic pressure (HHP) method. We have demonstrated that decellularized biological tissues are promising materials in tissue engineering and regenerative medicine fields.

(2) Molecular assembly by the high hydrostatic pressure technique

We found that hydrogen bonds form molecular aggregates under high pressure condition. Using the HHP processing of more than 6,000 atm, we prepare the nucleic acid assembly and apply it as a gene delivery system.

(3) Extracellular matrices remodeling

We have conducted researches on tissue remodeling using artificially reconstructed extracellular matrix. Specifically, we are aiming at the application as artificial skin and cornea by designing well-organized extracellular matrix structure.

(4) Immune control systems: technology of specific cell capture and release

In cancer immunotherapy, by removing regulatory T cells (Treg) that negatively regulate immune reactions, anti-tumor immune responses can be enhanced. We are developing novel biomaterials and technologies to capture and release Treg using interfacial science.

(3) Education

Our laboratory is in charge of lectures on " Medical Materials Engineering", " Applied Biomaterials", and " Medical, Dental and Pharmaceutical Industrial Engineering" in the graduate school, and " Biomedical Engineering " in the faculty.

Through these lectures, we will explain from the basic knowledge of various materials to the molecular design theory required for device development.

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

1. K. Iwasaki, K. Akazawa, M. Nagata, M. Komaki, I. Honda, C. Morioka, N. Yokoyama, H. Ayame, K. Yamaki, Y. Tanaka, T. Kimura, A. Kishida, T. Watabe, I. Morita. The fate of transplanted periodontal ligament stem cells in surgically created periodontal defects in rats *Int J Mol Sci.* 2019.01; 20(1); 192
2. T. Kimura, M. Kondo, Y. Hashimoto, T. Fujisato, N. Nakamura, A. Kishida. Surface topography of PDMS replica transferred from various decellularized aortic lumens affects cellular orientation *ACS Biomater Sci Eng.* 2019.04; 5(11); 5721-5726
3. P. Wu, N. Nakamura, H. Morita, K. Nam, T. Fujisato, T. Kimura, A. Kishida. A hybrid small - diameter tube fabricated from decellularized aortic intima - media and electrospun fiber for artificial small - diameter blood vessel *J Biomed Mater Res Part A.* 2019.05; 107(5); 1064-1070
4. N. Watanabe, M. Mizuno, J. Matsuda, N. Nakamura, K. Otabe, H. Katano, N. Ozeki, Y. Kohno, T. Kimura, K. Tsuji, H. Koga, A. Kishida, I. Sekiya. Comparison of high - hydrostatic - pressure decellularized versus freeze - thawed porcine menisci *J Orthop Res.* 2019.06; 37(11); 2466-2475
5. N. Nakamura, A. Ito, T. Kimura, A. Kishida. Extracellular matrix induces periodontal ligament reconstruction in vivo *Int J Mol Sci.* 2019.07; 20(13); 3277
6. M. Funasaki, C. Minato, M. Nonaka, M. Ozawa, A. Kishida, A. Ohsaki. New friedelane triterpenes from *Anchietea Pyrifolia* *Phytochem Lett.* 2019.08; 32; 42-46
7. Y. Hashimoto, S. Funamoto, S. Sasaki, J. Negishi, S. Hattori, T. Honda, T. Kimura, H. Kobayashi, A. Kishida. Re-epithelialization and remodeling of decellularized corneal matrix in a rabbit corneal epithelial wound model *Mater Sci Eng C-Mater Biol App.* 2019.09; 102; 238-246
8. J. Negishi, S. Funamoto, Y. Hashimoto, K. Yanagisawa. PLA-collagen composite scaffold fabrication by vacuum pressure impregnation *Tissue Eng Part C: Methods.* 2019.12; 25(12); 742-747

[Books etc]

1. Y. Hashimoto, S. Funamoto, S. Sasaki, T. Kimura, H. Kobayashi, A. Kishida. Decellularized matrix for corneal tissue engineering: Recent advances in development and clinical potential. RSC publishing, 2019.12 (ISBN : 978-1-78801-467-0)

[Conference Activities & Talks]

1. N. Nakamura, H. Harukaze, R. Ohira, M. Yamada, T. Fujisato, T. Kimura, A. Kishida. Integration of decellularized ligament and artificial material through recellularization for periodontal reconstruction. SFB 2019 2019.04.03 Seattle, USA
2. T. Kimura, M. Kobayashi, Y. Hashimoto, T. Fujisato, N. Nakamura, A. Kishida. A synthetic replica having surface morphology of decellularized tissue regulated orientation and shape of cells. SFB 2019 2019.04.03 Seattle, USA
3. M. Kobayashi, M. Kondo, A. Tamura, Y. Hashimoto, T. Fujisato, T. Kimura, A. Kishida. The effect of decellularization method on cell behavior on the decellularized aorta. SFB 2019 2019.04.03 Seattle, USA
4. A. Kishida. Frontiers of biomaterials: Cell separation and biological tissue hybrids. XLVI ESAO Congress 2019.09.03 Hanover, Germany

5. A. Kishida, R. Tokunaga, Y. Hashimoto, N. Nakamura, T. Kimura. Development of an antibody-immobilized filter for capturing target cells. ESB 2019 2019.09.09 Dresden, Germany
6. T. Kimura, Y. Yoshida, S. Anzai, H. Takahashi, T. Shimizu, N. Nakamura, A. Kishida. Cell culture on various decellularized pericardia. iLIM-4 2019.10.03 Miyagi, Japan
7. T. Kimura, J. Kadota, N. Nakamura, Y. Hashimoto, A. Kishida. Network formation of endothelial cells on hydrogels derived from decellularized matrices. TERMIS-AP 2019 2019.10.14 Brisbane, Australia
8. T. Kimura, R. Tokunaga, Y. Hashimoto, N. Nakamura, A. Kishida. Development of an immunomodulatory biomaterial for cancer. ICMaSS 2019 2019.11.02 Nagoya, Japan
9. N. Nakamura, H. Harukaze, Y. Kato, T. Kimura, A. Kishida. Preparation of decellularized ligament and tendon sheets for reconstruction of periodontal ligament. IFAO 2019 2019.11.13 Osaka, Japan
10. T. Kimura, R. Tokunaga, Y. Hashimoto, N. Nakamura, A. Kishida. Development of an implantable immunomodulatory material based on cell moving for cancer treatment. IFAO 2019 2019.11.13 Osaka, Japan
11. S. Kurokawa, H. Masumoto, Y. Hashimoto, S. Funamoto, T. Ikeda, A. Kishida, K. Minatoya. Evaluation for patency and recellularization of decellularized vascular grafts with high hydrostatic pressure method in a xeno-transplantation animal model. AHA 2019 2019.11.16 Philadelphia, USA
12. Y. Yoshida, M. Suzuki, S. Anzai, N. Nakamura, T. Kimura, A. Kishida. Preparation of ligament-like tissue using decellularized pericardium. 2nd G'Lowing Polymer Symposium in KANTO 2019.11.30 Tokyo, Japan
13. A. Kishida, J. Kadota, N. Nakamura, Y. Hashimoto, T. Kimura. Network formation of endothelial cells on hydrogels derived from decellularized matrices. TERMIS-AM 2019 2019.12.02 Orland, USA
14. M. Kobayashi, M. Ohara, Y. Hashimoto, N. Nakamura, T. Fujisato, T. Kimura, A. Kishida. Effect of basement membrane structure on cell behavior and function on decellularized aorta. TERMIS-AM 2019 2019.12.02 Orland, USA
15. T. Kimura, J. Kadota, N. Nakamura, Y. Hashimoto, A. Kishida. Network formation of endothelial cells on decellularized ECM hydrogels. MRM 2019 2019.12.10 Kanagawa, Japan

Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Suguru YOSHIDA
Assistant Professor	Yoshitake NISHIYAMA
Assistant Professor	Junpei TAGUCHI
Associate Professor	Yasunori MINAMI
Assistant Professor	Kazuya KANEMOTO
Assistant Professor	Yuki SAKATA
Technical Assistant	Yuki HAZAMA, Haruka HIRAYAMA, Satomi TOMITA
Graduate Students	Yu NAKAMURA, Tsubasa MATSUZAWA, Tsuneyuki KOBAYASHI, Norikazu TERASHIMA, Mai IKEDA, Daisuke KORI, Takahiro AIMI, Rika IDOGAWA, Akihiro KOBAYASHI, Kazuya SUGIYAMA, Hinano TAKEMURA, Mai MINOSHIMA
Collaborator	Minori SUZUKI

(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 chemical modification methods of biomolecules by strained alkynes.
3. Target protein identification of bioactive compounds based on radioisotope-free (non-RI) photoaffinity labeling based on diazido probe strategy.
4. Development of new methods to efficiently connect multiple molecules based on the characteristic features of azido group.
5. Design and synthesis of efficient substrates for bioluminescence reactions and fluorescent probes for bioimaging and diagnosis of diseases.
6. Development of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

(3) Publications

[Original Articles]

1. Toyoda Y, Morimoto K, Suno R, Horita S, Yamashita K, Hirata K, Sekiguchi Y, Yasuda S, Shiroishi M, Shimizu T, Urushibata Y, Kajiwara Y, Inazumi T, Hotta Y, Asada H, Nakane T, Shiimura Y, Nakagita T, Tsuge K, Yoshida S, Kuribara T, Hosoya T, Sugimoto Y, Nomura N, Sato M, Hirokawa T, Kinoshita M, Murata T, Takayama K, Yamamoto M, Narumiya S, Iwata S, Kobayashi T. Ligand binding to human prostaglandin E receptor EP4 at the lipid-bilayer interface. *Nat Chem Biol.* 2019.01; 15(1); 18-26

- Yoshida S, Kuribara T, Ito H, Meguro T, Nishiyama Y, Karaki F, Hatakeyama Y, Koike Y, Kii I, Hosoya T. A facile preparation of functional cycloalkynes via an azide-to-cycloalkyne switching approach. *Chem Commun.* 2019.03; 55(24); 3556-3559
- Kanemoto K, Yoshida S, Hosoya T. Synthesis of Alkynyl Sulfides by Copper-Catalyzed Thiolation of Terminal Alkynes Using Thiosulfonates. *Org Lett.* 2019.04; 21(9); 3172-3177
- Nishiyama Y, Misawa Y, Hazama Y, Oya K, Yoshida S, Hosoya T. Synthesis of Diverse 3-Azido-5-(azidomethyl)benzene Derivatives via Formal C–H Azidation and Functional Group-Selective Transformations. *Heterocycles.* 2019.06; 99(2); 1053-1072
- Watanabe K, Tsuda J, Ochiai H, Niwa T, Hosoya T. Divergent Synthesis of Photoaffinity Probe Candidates by Click Reactions of Azido-Substituted Aryltrifluoromethyldiazirines. *Heterocycles.* 2019.06; 99(2); 1366-1387
- Meguro T, Chen S, Kanemoto K, Yoshida S, Hosoya T. Modular Synthesis of Unsymmetrical Doubly-ring-fused Benzene Derivatives Based on a Sequential Ring Construction Strategy Using Oxadiazinones as a Platform Molecule. *Chem Lett.* 2019.06; 48(6); 582-585
- Yoshida S, Hazama Y, Kanemoto K, Nakamura Y, Hosoya T. Facile Synthesis of Diverse *o*-Iodoaryl Triflates from *o*-Silylaryl Triflates by Aluminum-mediated Desilyliodination. *Chem Lett.* 2019.07; 48(7); 742-745
- Uetake Y, Isoda M, Niwa T, Hosoya T. Synthesis of (2,2-Diborylvinyl)arenes by Rhodium-Catalyzed Desulfanylation *gem*-Diborylation of 2-Arylviny Sulfides. *Org Lett.* 2019.07; 21(13); 4933-4938
- Nakamura Y, Miyata Y, Uchida K, Yoshida S, Hosoya T. 3-Thioaryne Intermediates for the Synthesis of Diverse Thioarenes. *Org Lett.* 2019.07; 21(13); 5252-5258
- Yoshida S, Goto S, Nishiyama Y, Hazama Y, Kondo M, Matsushita T, Hosoya T. Effect of Resonance on the Clickability of Alkenyl Azides in the Strain-promoted Cycloaddition with Dibenzo-fused Cyclooctynes. *Chem Lett.* 2019.09; 48(9); 1038-1041
- Nakamura Y, Ozawa S, Yoshida S, Hosoya T. Facile Synthesis of Diverse 2,6-Disubstituted Arylsilanes via Silylamination and Silylsulfanylation of Aryne Intermediates Generated from *o*-Iodoaryl Triflates. *Chem Lett.* 2019.11; 48(11); 1296-1299
- Uchida K, Minami Y, Yoshida S, Hosoya T. Synthesis of Diverse γ -Aryl- β -ketoesters via Aryne Intermediates Generated by C–C Bond Cleavage. *Org Lett.* 2019.11; 21(22); 9019-9023
- Kitakaze K, Taniuchi S, Kawano E, Hamada Y, Miyake M, Oyadomari M, Kojima H, Kosako H, Kuribara T, Yoshida S, Hosoya T, Oyadomari S. Cell-based HTS identifies a chemical chaperone for preventing ER protein aggregation and proteotoxicity. *eLife.* 2019.12; 8; e43302

[Misc]

- Yoshida S, Hosoya T. Target Identification of Bioactive Compounds by Photoaffinity Labeling Using Diazido Probes. *Cutting-Edge Organic Synthesis and Chemical Biology of Bioactive Molecules – The Shape of Organic Synthesis to Come.* 2019.06; 335-355
- Nakamura Y, Yoshida S, Hosoya T. Recent Advances in Synthetic Hetaryne Chemistry. *Heterocycles.* 2019.12; 98(12); 1623-1677

[Conference Activities & Talks]

- Nakamura Y, Yoshida S, Hosoya T. FACILE SYNTHESIS OF DIVERSE BENZOPYRAN DERIVATIVES VIA GOLD-CATALYZED CYCLIZATION AND GENERATION OF ARYNES. *European Symposium on Organic Chemistry (ESOC2019)* 2019.07.15 Vienna, Austria
- Yoshida S, Shimomori K, Kim Y, Kanemoto K, Hosoya T. SINGLE C–F BOND CLEAVAGE OF TRIFLUOROMETHYLARENES WITH A LATENTLY TRANSFORMABLE ORTHO-SILYL GROUP. *European Symposium on Organic Chemistry (ESOC2019)* 2019.07.15 Vienna, Austria

3. Matsuzawa T, Uchida K, Yoshida S, Hosoya T. SYNTHESIS OF DIVERSE BENZOTHIOPHENES VIA REACTION OF ARYNES WITH ALKYNYL SULFIDES. European Symposium on Organic Chemistry (ESOC2019) 2019.07.16 Vienna, Austria
4. Niwa T, Isoda M, Uetake Y, Hosoya T. Cu-Catalyzed Defluoroborylation for Facile Synthesis of Fluoroalkenes. 20th IUPAC International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis (OMCOS 20) 2019.07.22 Heidelberg, Germany
5. Niwa T, Isoda M, Uetake Y, Hosoya T. Convergent synthesis of fluoroalkenes using a bis-reactive unit. 19th European Symposium on Fluorine Chemistry 2019.08.30 Warsaw, Poland
6. Nakamura Y, Yoshida S, Hosoya T. Synthesis of Diverse Heterocyclic Compounds via Au-Catalyzed Cyclization and Generation of Arynes. 27th International Society of Heterocyclic Chemistry Congress (27th ISHC Congress 2019) 2019.09.03 Kyoto
7. Matsuzawa T, Yoshida S, Hosoya T. Facile Synthesis of *N*-Arylphenothiazines by Rearrangement of *o*-Sulfanylanilines. 27th International Society of Heterocyclic Chemistry Congress (27th ISHC Congress 2019) 2019.09.03 Kyoto
8. Yoshida S, Uchida K, Minami Y, Hosoya T. Synthesis of Diverse Arenes via Aryne Intermediates Generated by C–C Bond Cleavage. 2019.11.09 Chino

Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D.
Associate Professor Wataru NOMURA, Ph.D.
Assistant Professor Kohei TSUJI, Ph.D.
Assistant Professor Takuya KOBAYAKAWA, Ph.D.
Technical Assistant Ami MASUDA
Assistant Tomoe KAMEI

Graduate students
D4 Maxwell Mamfe Sakyamah
D3 Kiju KONNO, Yuzuna HONDA, Daisuke MATSUMOTO, Daisuke MIYAKI
D2 Kento EBIHARA, Kofi Baffour-Awuah Owusu
M2 Tsukasa HASHIMOTO, Tomoki KISHI, Shunsuke SAWAMURA, Kohei TAKAHASHI, Takumi KAMIMURA,
Masaki KURAKAMI, Yuki WATANABE, WANG RONGYI, LIU YISHAN
M1 Chika AZUMA, Takahiro ISHII, Miyuki NAKAYAMA, Sayaka BOKU, LIU YIJIE, YANG TINGTING

Internal Collaborators
YANG TINGTING

(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 proteins, TALEN and CRISPR-Cas9 for gene therapy and nanotechnology.
Utilizing DNA sequence-specific recognition of zinc finger proteins, TALEN and CRISPR-Cas9, 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: Third laboratory 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. Kouki Matsuda, Takuya Kobayakawa, Kiyoto Tsuchiya, Shin-Ichiro Hattori, Wataru Nomura, Hiroyuki Gatanaga, Kazuhisa Yoshimura, Shinichi Oka, Yasuyuki Endo, Hirokazu Tamamura, Hiroaki Mitsuya, Kenji Maeda. Benzolactam-related compounds promote apoptosis of HIV-infected human cells via protein kinase C-induced HIV latency reversal. *J. Biol. Chem.* 2019.01; 294(1); 116-129
2. Akinobu Z. Suzuki, Ryota Sekine, Shiori Takeda, Ryosuke Aikawa, Yukiko Shiraishi, Tomomi Hamaguchi, Hiroyuki Okuno, Tamamura Hirokazu, Furuta Toshiaki. A clickable caging group as a new platform for modular caged compounds with improved photochemical properties *CHEMICAL COMMUNICATIONS*. 2019.01; 55(4); 451-454
3. Takuya Kobayakawa, Kiju Konno, Nami Ohashi, Kohei Takahashi, Ami Masuda, Kazuhisa Yoshimura, Shigeyoshi Harada, Hirokazu Tamamura. Soluble-type small-molecule CD4 mimics as HIV entry inhibitors *BIOORGANIC & MEDICINAL CHEMISTRY LETTERS*. 2019.03; 29(5); 719-723

4. Maxwell M. Sakyiamah, Takuya Kobayakawa, Masayuki Fujino, Makoto Konno, Tetsuo Narumi, Tomohiro Tanaka, Wataru Nomura, Naoki Yamamoto, Tsutomu Murakami, Hirokazu Tamamura. Design, synthesis and biological evaluation of low molecular weight CXCR4 ligands BIOORGANIC & MEDICINAL CHEMISTRY. 2019.03; 27(6); 1130-1138
5. Maxwell M Sakyiamah, Wataru Nomura, Takuya Kobayakawa, Hirokazu Tamamura. Development of a NanoBRET-Based Sensitive Screening Method for CXCR4 Ligands. Bioconjug. Chem.. 2019.05; 30(5); 1442-1450
6. Takuya Kobayakawa, Kento Ebihara, Yuzuna Honda, Masayuki Fujino, Wataru Nomura, Naoki Yamamoto, Tsutomu Murakami, Hirokazu Tamamura. Dimeric C34 Derivatives Linked through Disulfide Bridges as New HIV-1 Fusion Inhibitors. Chembiochem. 2019.08; 20(16); 2101-2108
7. Mohammad Mamun Alam, Takeo Kuwata, Kazuki Tanaka, Muntasir Alam, Shokichi Takahama, Kazuya Shimura, Masao Matsuoka, Natsuki Fukuda, Hiroshi Morioka, Hirokazu Tamamura, Shuzo Matsushita. Synergistic Inhibition of Cell-to-cell HIV-1 Infection by Combinations of Single Chain Variable Fragments and Fusion Inhibitors Biochem Biophys Rep.. 2019.09; 20; 100687

[Books etc]

1. The Frontier of Peptide Drug Discovery. 2019.05 (ISBN : 978-4-7813-1417-4)

[Misc]

1. Kenji Maeda, Debananda Das, Takuya Kobayakawa, Hirokazu Tamamura, Hiroaki Takeuchi. Discovery and Development of anti-HIV Therapeutic Agents: Progress Towards Improved HIV Medication. Current topics in medicinal chemistry. 2019.07; 19(18); 1621-1649
2. Takuya Kobayakawa. Development for peptidomimetic chemistry utilizing the oxetanyl structure Journal of Synthetic Organic Chemistry, Japan; Review de Debut. 2019.07; 77(7); 720-721
3. Takuya Kobayakawa, Hirokazu Tamamura. Development for peptidomimetic chemistry based on chloroalkene structures Journal of Synthetic Organic Chemistry, Japan. 2019.09; 77(9); 904-911

[Conference Activities & Talks]

1. Maxwell M. Sakyiamah, Wataru Nomura, Takuya Kobayakawa, Hirokazu Tamamura. Development of a NanoBRET-based sensitive screening method for CXCR4 ligands . The 14th Annual Meeting of Japanese Society for Chemical Biology 2019.06.10 Aichi
2. Hirokazu Tamamura. Development of bivalent ligands of GPCR and their application to molecular probes for cancer cells and anti-cancer agents. 7th Modern Solid Phase Synthesis & Its Applications Symposium 2019.09.07 Palm Cove, Australia
3. Hirokazu Tamamura. Elucidation of a dimerization state of a GPCR and its application to molecular probes for cancer cells. The 2019 International Conference on Molecular Imaging and Minimally Invasive Therapy (2019 MIMIT) 2019.10.18 Beijing, China
4. Takuya Kobayakawa, Hirokazu Tamamura. Development of chemical synthesis for peptidomimetic based on a chloroalkene dipeptide isostere and its application to a cyclic peptide. The 56th Japanese Peptide Symposium 2019.10.23 Tokyo
5. Masaki Kurakami, Takuya Kobayakawa, Masaru Yokoyama, Tsutomu Murakami, Moemi Kaneko, Osamu Kotani, Hironori Sato, Hirokazu Tamamura. Structure-activity relationship studies of small molecular anti-HIV-1 compounds targeting a dipeptide site of HIV-1 capsid proteins. The 56th Japanese Peptide Symposium 2019.10.23 Tokyo
6. Kento Ebihara, Yuzuna Honda, Takuya Kobayakawa, Tsutomu Murakami, Hirokazu Tamamura. Development of HIV-1 fusion inhibitors based on the C34 dimer derived from an HIV-1 envelope protein gp41. The 56th Japanese Peptide Symposium 2019.10.23 Tokyo
7. Yuki Watanabe, Takuya Kobayakawa, Atsuhiko Taniguchi, Yoshio Hayashi, Hirokazu Tamamura. Development of peptidomimetic inhibitors for aggregation of amyloid beta. The 56th Japanese Peptide Symposium 2019.10.23 Tokyo

8. Rongyi Wang, Takuya Kobayakawa, Moemi Kaneko, Kofi Owusu, Tsutomu Murakami, Hirokazu Tamamura. Development of cell-permeable anti-HIV peptides based on capsid proteins. The 56th Japanese Peptide Symposium 2019.10.25 Tokyo
9. Maxwell M. Sakyiamah, Wataru Nomura, Takuya Kobayakawa, Hirokazu Tamamura. Development of a nanoBRET-based sensitive screening method to search for chemokine receptor CXCR4 ligands. The 56th Japanese Peptide Symposium 2019.10.25 Tokyo
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11. Tsutomu Murakami, Kento Ebihara, Takuya Kobayakawa, Masayuki Fujino, Eiichi Kodama, Hirokazu Tamamura. Elucidation of mechanism of HIV-1 fusion inhibitors developed by dimerization strategy. The 67th Annual Meeting of the Japanese Society for Virology 2019.10.29 Tokyo
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Metallic Biomaterials

Takao HANAWA Prof
Yusuke TSUTSUMI Senior Assoc Prof
Maki ASHIDA Assist Prof
Peng CHEN Assist Prof
Hisashi DOI Assist Prof
Akira UMISE Assist Prof
Shukan OKANO Technical Support Staff
Noriko NAKAISHI Technical Support Staff
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 minimize metal allergy

Countermeasure techniques for metal ion release from metallic biomaterials which causes metal allergy are investigated. Novel reagents of patch testing for the detection of sensitization to metal ions are developed.

(2) Lectures & Courses

Metallic biomaterials play an important role as medical devices. Our laboratory mainly deals with effects of crystal structure, process, and thermal treatment on mechanical properties (e.g. strength or toughness). We also focus on structure and property of nanometer-scaled surface phenomena: Formation of living tissue on metals, especially, reactions between biomolecules or cells and metals, changes in surface oxide layers in living tissues, and electrochemical property of metallic biomaterials. The aim of the education is perfect understanding of metallic biomaterials, enabling students to select a proper material for medical treatments or researches.

(3) Publications

[Original Articles]

1. Sun SH, Ishimoto T, Hagihara K, Tsutsumi Y, Hanawa T, Nakano T. Excellent mechanical and corrosion properties of austenitic stainless steel with a unique crystallographic lamellarmicrostructure via selective laser melting Scr. Mater.. 2019.01; 159(15); 89-93

2. Takahashi H, Ishimoto T, Inoue T, Kimura H, Uetsuki K, Okuda N, Nakanishi Y, Oh JY, Ito M, Nakashima Y, Hanawa T, Nakano T. Effects of autogenous bone graft on mass and quality of trabecular bone in Ti-6Al-4V spinal cage fabricated with electron beam melting Mater. Trans.. 2019.01; 60(1); 144-148
3. Goto K, Umise A, Tahara M, Hosoda H. Compressive deformation behavior and magnetic susceptibility of Au₂CuAl biomedical shape memory alloys Mater. Trans.. 2019.03; 60(5); 662-665
4. Shimabukuro M, Tsutsumi Y, Yamada R, Ashida M, Chen P, Doi H, Nozaki K, Nagai A, Hanawa T. Investigation of realizing both antibacterial property and osteogenic cell compatibility on titanium surface by simple electrochemical treatment ACS Biomater. Sci. Eng.. 2019.03; 5(11); 5623-5630
5. Lee DH, Hanawa T, Jang SH, Lee HJ, Hong MH, Min BK, Kwon TY. Effect of post-sintering conditions on the mechanical properties of a new Co-Cr alloy produced by new subtractive manufacturing J. Nanosci. Nanotechnol.. 2019.04; 19(4); 2395-2398
6. Oishi M, Tsutsumi Y, Chen P, Nakaishi M, Ashida M, Doi H, Hanawa T. Surface characterization of commercially available yttria-stabilized tetragonal zirconia polycrystalline in water and Hanks' solution using X-ray photoelectron spectroscopy Dent. Mater. J.. 2019.06; 38(3); 496-504
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8. Park JW, Hanawa T, Chung JH. The relative effects of Ca and Mg ions on MSC osteogenesis in the surface modification of microrough Ti implants Int. J. Nanomed.. 2019.07; 14; 5697-5711
9. Watanabe K, Ashida M, Masuda T, Kral P, Takizawa Y, Yumoto M, Otagiri Y, Sklenicka V, Hanawa T, Horita Z. Production of superplastic Ti-6Al-7Nb alloy using high-pressure sliding process Mater. Trans.. 2019.07; 60(9); 1785-1791
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11. Kittikundecha N, Kajima Y, Takaichi A, Wai Cho HH, Htat HL, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Fatigue properties of removable partial denture clasps fabricated by selective laser melting followed by heat treatment J. Mech. Behav. Biomed. Mater.. 2019.10; 98; 79-89
12. Shimabukuro M, Ito H, Tsutsumi Y, Nozaki K, Chen P, Yamada R, Ashida M, Nagai A, Hanawa T. The effects of various metallic surfaces on cellular and bacterial adhesion Metals. 2019.10; 9(11); 1145
13. Shimabukuro M, Tsutsumi Y, Nozaki K, Chen P, Yamada R, Ashida M, Doi H, Nagai A, Hanawa T. Chemical and biological roles of zinc in a porous titanium dioxide layer formed by micro-arc oxidation Coatings. 2019.10; 9(11); 705
14. Sun X, Liu D, Zhou W, Nomura N, Doi H, Tsutsumi Y, Hanawa T. Effects of quenching process on microstructure, mechanical properties and magnetic susceptibility in Zr-1Mo alloy fabricated by powder bed fusion process Mater. Des.. 2019.11; 187; 108356
15. Isoshima K, Ueno T, Arai Y, Saito H, Chen P, Tsutsumi Y, Hanawa T, Wakabayashi N. The change of surface charge by lithium ion coating enhances protein adsorption on titanium J. Mech. Behav. Biomed. Mater.. 2019.12; 100; 103393

[Books etc]

1. Chen P, Tsukamoto M. Surface modification with femtosecond laser. In: Novel Structured Metallic and Inorganic Materials, Eds, Setsuhara Y, Kamiya T, Yamaura S. Springer Nature, Singapore, 2019.09 (ISBN : 978-981-13-7610-8)
2. Hanawa T. Current and future hard materials for medical field. In: Novel Structured Metallic and Inorganic Materials, Eds, Setsuhara Y, Kamiya T, Yamaura S. Springer Nature, Singapore, 2019.09 (ISBN : 978-981-13-7610-8)

[Misc]

1. Hanawa T. Titanium-tissue interface reaction and its control with surface treatment Front. Bioeng. Biotechnol.. 2019.07; 7; 170

[Conference Activities & Talks]

1. Hanawa T. Biofunctionalization of metals with electrochemical surface modification. Twelfth International Symposium on Advances in Electrochemical Science and Technology (iSAEST-12) 2019.01.08 Chennai, India
2. Rajan ST, Thampi VVA, Hanawa T, Chen P, Subramanian B. In-vitro investigations of assimilation inhibition on Ti with Zirconium based thin films. Twelfth International Symposium on Advances in Electrochemical Science and Technology (iSAEST-12) 2019.01.08 Chennai, India
3. Shimabukuro M, Hanawa T. Dual functionalization of titanium surface with micro-arc oxidation. The 5th Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2019.01.17 Bangkok, Thailand
4. Chen P, Takenaka K, Tsukamoto M, Ashida M, Tsutsumi Y, Doi H, Hanawa T. Promoted osteoconductivity of titanium with chessboard-patterned surface nano topography fabricated by femtosecond laser irradiation. Society for Biomaterials 2019 Annual Meeting and Exposition (SFB2019) 2019.04.03 Seattle, USA
5. Chen P. Nanotechnology for intelligent surface designing of metallic implants. International Young Scholars Forum 2019.05.20 Chengdu, China
6. Ashida M, Hanawa T, Chen P, Tsutsumi Y, Horita Z. Strengthening of Ti-6Al-7Nb alloy by high-pressure torsion processing. The 14th World Conference on Titanium (Ti-2019) 2019.06.10 Nantes, France
7. Kajima Y, Takaichi A, Oishi T, Kittikundecha N, Tsutsumi Y, Hanawa T, Wakabayashi N. Enhanced mechanical properties and corrosion resistance of SLM-processed CoCrMo alloys. 97th General Session of the IADR 2019.06.20 Vancouver, Canada
8. Takaichi A, Kittikundecha N, Kajima Y, Takahashi H, Hanawa T, Wakabayashi N. Enhanced fatigue strength of SLMed Co-Cr-Mo clasp by post-heat treatment clasp . 97th General Session & Exhibition of the IADR 2019.06.22 Vancouver, Canada
9. Hanawa T. Characterization and control of surface states of metals and ceramics. 4th International Conference on Innovations in Biomaterials, Biomanufacturing and Biotechnologies (Bio-4) 2019.07.21 Toronto, Canada
10. Chen P, Takenaka K, Tsukamoto M, Ashida M, Tsutsumi Y, Hanawa T. Promotion of osteoconductivity of titanium with multi-scaled hierarchical patterned topography fabricated by femtosecond laser irradiation. The 10th Pacific Rim International Conference on Advanced Materials and Processing (PRICM10) 2019.08.18 Xi'an, China
11. Nomura N, Sun X, Zhou W, Kikuchi K, Tsutsumi Y, Hanawa T, Kawasaki A. Microstructure and mechanical properties of low magnetic Zr-1Mo alloy for biomedical applications. The 10th Pacific Rim International Conference on Advanced Materials and Processing (PRICM10) 2019.08.18 Xi'an, China
12. Hanawa T. Biofunctionalization of metals with development of new alloy, manufacturing process and surface modification. The 10th Pacific Rim International Conference on Advanced Materials and Processing (PRICM10) 2019.08.18 Xi'an, China
13. Hanawa T, Ashida M, Tsutsumi Y, Chen P. New zirconium alloy with large strength to decrease MRI artifact. The 10th Pacific Rim International Conference on Advanced Materials and Processing (PRICM10) 2019.08.18 Xi'an, China
14. Toriyabe A, Goto K, Umise A, Hanawa T, Hosoda H. Suppression of intergranular fracture of Au-Cu-Al biomedical shape memory alloys. 1st Tokyo Tech-NCTU Joint Symposium on Advanced Materials 2019.09.02 Tokyo, Japan

15. Shimabukuro M, Tsutsumi Y, Nozaki K, Chen P, Ashida M, Doi H, Hanawa T. Antibacterial property of Ag, Cu, Zn, and Ga incorporated to Ti surface by micro-arc oxidation treatment. 30th Annual Conference of the European Society for Biomaterials (ESB2019) 2019.09.09 Dresden, Germany
16. Umise A, Goto K, Chang TFM, Tahara M, Sone M, Hanawa T, Hosoda H. Deformation behavior of Au-28Cu-22Al biomedical shape memory alloy micropillars. 30th Annual Conference of the European Society for Biomaterials (ESB2019) 2019.09.09 Dresden, Germany
17. Liu H, Nagira T, Fujii H, Niinomi M, Chen P, Hanawa T. Dissimilar friction welding of Ti-6Al-4V alloy and SUS316L stainless steel for biomedical application. The 4th International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-4) 2019.10.03 Sendai, Japan
18. Chen P, Shinohara N, Shinonaga T, Tsukamoto M, Ashida M, Tsutsumi Y, Hanawa T. Regulation of preosteoblast behaviors by multi-scaled hierarchical patterned titanium surface fabricated with femtosecond laser irradiation. The 4th International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-4) 2019.10.03 Sendai, Japan
19. Umise A, Goto K, Tahara M, Tsutsumi Y, Kanetaka H, Hanawa T, Hosoda H. Effect Fe additions on mechanical properties and corrosion behavior of AuCuAl based biomedical shape memory alloys. The 4th International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-4) 2019.10.04 Sendai, Japan
20. Hanawa T. Chemical and topographical modification of materials surface to add biofunction. Turku Biomaterials Days and JSPS ACF Activity Seminar 2019 2019.10.25 Turku, Finland
21. Umise A, Yamaji K, Goto K, Tahara M, Kanetaka H, Hanawa T, Hosoda H. Mechanical property improvement of AuCuAl biomedical superelastic alloys containing α phase. International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development Satellite (iLIM-s) 2019.11.01 Nagoya, Japan
22. Shimabukuro M, Tsutsumi Y, Nozaki K, Chen P, Hanawa T. Comparison of antibacterial property of Ag, Cu, Zn and Ga incorporated to Ti surface. International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development Satellite (iLIM-s) 2019.11.02 Nagoya, Japan
23. Shimabukuro M, Tsutsumi Y, Nozaki K, Chen P, Hanawa T. Optimization of Ag concentration on Ti surface for realizing dual function. International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development Satellite (iLIM-s) 2019.11.02 Nagoya, Japan
24. Chen P, Shinohara N, Shinonaga T, Tsukamoto M, Ashida M, Tsutsumi Y, Hanawa T. Calcification promotion of preosteoblast by titanium with chessboard-patterned nano surface topography produced with femtosecond laser irradiation. International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development Satellite (iLIM-s) 2019.11.02 Nagoya, Japan
25. Chen P, Hanawa T. Regulation of stem cell behaviors by titanium with multiscaled topography surface design using femtosecond laser. International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development Satellite (iLIM-s) 2019.11.02 Nagoya, Japan
26. Hanawa T. Biofunctionalisation of metallic materials for regenerative medicine. KI-NTU-Oral Health ACP Joint Research Conference 2019.11.04 Singapore
27. Umise A, Goto K, Tahara M, Chang TFM, Sone M, Hanawa T, Hosoda H. Deformation behavior of Au-CuAl biomedical superelastic alloys by micro-compression tests. The 4th International Symposium on Biomedical Engineering (ISBE2019) 2019.11.14 Hamamatsu, Japan
28. Miyoshi M, Umise A, Tahara M, Goto K, Hanawa T, Hosoda H. Effect of C and Y additions on microstructure and mechanical properties in AuTiCo biomedical shape memory alloy. The 4th International Symposium on Biomedical Engineering (ISBE2019) 2019.11.14 Hamamatsu, Japan
29. Hanawa T. Electrodeposition mechanism of biofunctional molecules to titanium surface. TACT2019 2019.11.17 Taipei, Taiwan

30. Kajima Y, Takaichi A, Oishi T, Kittikundecha N, Htat H, Hanawa T, Wakabayashi N, Yoneyama T. Effect of various heat treatments on the microstructure, texture and mechanical anisotropy of CoCrMo alloys produced by selective laser melting. 8th international conference on mechanics of biomaterials and tissues 2019.12.18 Hawaii, USA

Organic Biomaterials

Professor: Nobuhiko YUI
 Associate Professor: Atsushi TAMURA
 Assistant Professor: Yoshinori ARISAKA
 Researcher: Masahiko TERAUCHI
 Secretary: Nanae NISHI
 Part-time Lecturer : Satoshi YAMAGUCHI

(1) Research

1. Design of Polyrotaxane-based Surfaces and Three-dimensional Architectures

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. In addition, Polyrotaxane-based three-dimensional architectures such as hydrogels, scaffolds, and resins are developed for biologically active supramolecular biomaterials. The mobility and stimuli-responsively dissociative character of polyrotaxanes are integrated to the three-dimensional architectures to demonstrate novel functions in the Biomaterials.

2. Stimuli-labile Polyrotaxanes as a Therapeutic Agent for Intractable Diseases

Stimuli-labile polyrotaxanes that release threaded cyclodextrins under intracellular environments are developed and evaluated their activity in the treatment of various intractable diseases including lysosomal storage disorders.

3. Supramolecular Complexes for Bioactive Molecules for Enhancing Biological Activities

Supramolecular polyelectrolyte complexes of biomolecules, such as nucleic acid and protein, with polyrotaxanes are designed to enhance stability and biological activities, and their therapeutic efficacies are evaluated in vitro and in vivo.

4. Detachable Dental Adhesives Based on Photo-degradable Supermolecular Cross-linkers

Photo-degradable polyrotaxanes are developed as a component of detachable dental adhesive, cement, and resin. By the irradiation of light, the mechanical strength of the polyrotaxane-containing dental materials are found to decrease. Therefore, the photo-degradable polyrotaxanes-containing dental materials would be applied as detachable dental materials.

(2) Publications

[Original Articles]

1. Masahiko Terauchi, Mari Shibata, Akane Wada, Yasuyuki Michi, Satoshi Yamaguchi, Tetsuya Yoda. Second primary squamous cell carcinoma in an oral cavity free flap: a case report and review of the literature Oral and Maxillofacial Surgery Cases. 2019;
2. 4. Masahiko Terauchi, Atsushi Tamura, Asato Tonegawa, Satoshi Yamaguchi, Tetsuya Yoda, Nobuhiko Yui. Polyelectrolyte Complexes between Polycarboxylates and BMP-2 for Enhancing Osteogenic Differ-

- entiation: Effect of Chemical Structure of Polycarboxylates. *Polymers*. 2019;
3. Jian Seo, Nobuhiko Yui, Ji-Hun Seo. Development of a supramolecular accelerator simultaneously to increase the cross-linking density and ductility of an epoxy resin *Chemical Engineering Journal*. 2019.01; 356(15); 303-311
 4. Hyodo K, Arisaka Y, Yamaguchi S, Yoda T, Yui N. Stimulation of Microvascular Networks on Sulfonated Polyrotaxane Surfaces with Immobilized Vascular Endothelial Growth Factor. *Macromolecular bioscience*. 2019.01; e1800346
 5. Kai Shibaguchi, Atsushi Tamura, Masahiko Terauchi, Mitsuaki Matsumura, Hiroyuki Miura, Nobuhiko Yui. Mannosylated polyrotaxanes for increasing cellular uptake efficiency in macrophages via receptor-mediated endocytosis. *Molecules*. 2019.01; 24(3); 439
 6. Yoshinori Arisaka, Nobuhiko Yui. Engineering molecularly mobile polyrotaxane surfaces with heparin-binding EGF-like growth factors for improving hepatocyte functions. *Journal of Biomedical Materials Research Part A*. 2019.02; 107(5); 1080-1085
 7. Arun Kumar Rajendan, Yoshinori Arisaka, Sachiko Iseki, Nobuhiko Yui. Sulfonated polyrotaxane surfaces with basic fibroblast growth factor alters the osteogenic potential of human mesenchymal stem cells in short-term culture *ACS Biomaterials Science and Engineering*. 2019.02; 5(11); 5652-5659
 8. Masahiko Terauchi, Satoshi Akiya, Junya Kumagai, Yoshio Ohyama, Satoshi Yamaguchi. An Analysis of Dentigerous Cysts Developed around a Mandibular Third Molar by Panoramic Radiographs. *Dent J (Basel)*. 2019.02; 7(1);
 9. Yuma Yamada, Shinnosuke Daikuhara, Atsushi Tamura, Kei Nishida, Nobuhiko Yui, Hideyoshi Harashima. Enhanced autophagy induction via the mitochondrial delivery of methylated β -cyclodextrins-threaded polyrotaxanes by a MITO-Porter. *Chemical Communications*. 2019.06; 55(50); 7203-7206
 10. Asato Tonegawa, Atsushi Tamura, Nobuhiko Yui. Emerging nanoassembly of polyrotaxanes comprising acetylated α -cyclodextrins and high-molecular-weight axle polymer. *ACS Macro Letters*. 2019.07; 8(7); 826-834
 11. Taishi Higashi, Kentaro Morita, Xia Song, Jingling Zhu, Atsushi Tamura, Nobuhiko Yui, Keiichi Motoyama, Hidetoshi Arima, Jun Li. One-pot synthesis of cyclodextrin-based radial poly[n] catenanes. *Communications Chemistry*. 2019.07; 2; 78
 12. Masahiko Terauchi, Atsushi Tamura, Asato Tonegawa, Satoshi Yamaguchi, Tetsuya Yoda, Nobuhiko Yui. Polyelectrolyte complexes between polycarboxylates and BMP-2 for enhancing osteogenic differentiation: effect of chemical structure of polycarboxylates *Polymers*. 2019.08; 11(8); 1327
 13. Yoshinori Arisaka, Nobuhiko Yui. Investigating How Organic Solvents Affect Tissue Culture Polystyrene Surfaces through Responses of Mesenchymal Stem Cells. *Macromolecular bioscience*. 2019.08; e1900165
 14. Yoshinori Arisaka, Nobuhiko Yui. Suspending Polyrotaxane Dissociation via Photo-Reversible Capping of Terminals. *Macromolecular rapid communications*. 2019.08; 40(20); 1900323
 15. Alsandi Q, Ikeda M, Nikaido T, Tsuchida Y, Sadr A, Yui N, Suzuki T, Tagami J. Evaluation of mechanical properties of new elastomer material applicable for dental 3D printer. *J Mech Behav Biomed Mater*. 2019.08; 100; 103390
 16. Dae Hoon Lee, Atsushi Tamura, Yoshinori Arisaka, Ji-Hun Seo, Nobuhiko Yui. Mechanically reinforced gelatin hydrogels by introducing slidable supramolecular cross-linkers *Polymers*. 2019.11; 11(11); 1787
 17. Dae Hoon Lee, Yoshinori Arisaka, Asato Tonegawa, Tae Woong Kang, Atsushi Tamura, Nobuhiko Yui. Cellular orientation on repeatedly stretching gelatin hydrogels with supramolecular cross-linkers. *Polymers*. 2019.12; 11(12); 2095

[Misc]

1. Yoshinori Arisaka, Nobuhiko Yui. Polyrotaxane-based biointerfaces with dynamic biomaterial functions. *Journal of Materials Chemistry B*. 2019.02; 7(13); 2123-2129

[Conference Activities & Talks]

1. Yoshinori Arisaka, Nobuhiko Yui. Combination of molecular mobility of sulfonated-polyrotaxane and growth factors for improving hepatocyte functions. The Society For Biomaterials, 2019 Annual Meeting and Exposition 2019.04.04 Seattle, the United States
2. Preparation of stretchable gelatin hydrogels chemically cross-linked by polyrotaxanes. 2019.05.29
3. Satomi Matsunaga, Tomohiro Takagaki, Nanako Matsui, Masaomi Ikeda, Yoshinori Arisaka, Atsushi Tamura, Nobuhiko Yui, Toru Nikaido, Junji Tagami. Development of "reversible-adhesion" resin cement with a UV-cleavable PRX cross-linker. IADR/AADR/CADR General Session & Exhibition 2019.06.22
4. Atsushi Tamura, Kei Nishida, Nobuhiko Yui. Coacervate droplets formation of methylated β -cyclodextrin-threaded polyrotaxanes in aqueous media and their applications as an injectable protein carrier. ACS National Meeting & Expositions 2019.08.25 San Diego Convention Center, San Diego, CA, USA
5. Yoshinori Arisaka, Nobuhiko Yui. Effects of wettability and roughness of conventional culture-substrates on differentiation of mesenchymal stem cells. 4th International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-4) 2019.10.03
6. Atsushi Tamura, Nobuhiko Yui. Acid-degradable polyrotaxanes prevent LPS-induced fulminant hepatitis. Tissue Engineering & Regenerative Medicine International Society - AP Chapter and the 7th Asian Biomaterials Congress (TERMIS-AP + ABMC7 2019) 2019.10.16 Brisbane Convention & Exhibition Center, Brisbane, Australia
7. Dae Hoon Lee, Yoshinori Arisaka, Atsushi Tamura, Nobuhiko Yui. Improving mechanical properties of gelatin by polyrotaxane crosslinkers. Tissue Engineering & Regenerative Medicine International Society - AP Chapter and the 7th Asian Biomaterials Congress (TERMIS-AP + ABMC7 2019) 2019.10.17 Brisbane Convention & Exhibition Center, Brisbane, Australia
8. Yoshinori Arisaka, Nobuhiko Yui. The effect of sulfonated polyrotaxane-surfaces on hepatic responses. International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development Satellite (iLIM-s) 2019.11.02 Aichi
9. 3. Masahiko Terauchi, Atsushi Tamura Satoshi Yamaguchi, Tetsuya Yoda, Nobuhiko Yui. Bone regeneration with bone morphogenetic protein-2 amplified by supramolecular sulfonated polyrotaxane. 日韓若手アワードシンポジウム 2019.11.25
10. Masahiko Terauchi, Eriko Marukawa, Shintaro Yamazaki, Zhu Hongfei, Narumi Oshibe, Aoi Kaneko, Tranminh Cuomng, Tetsuya Yoda. Comparative evaluation of the various bone substitutes for bone regeneration at peri-implant defects in dogs.. 8th International Conference on Mechanics of Biomaterials and Tissues 2019.12.15
11. Shintaro Yamazaki, Eriko Marukawa, Masahiko Terauchi, Zhu Hongfei, Narumi Oshibe, Aoi Kaneko, Tranminh Cuomng, Tetsuya Yoda. The effectiveness of various bone substitutes for the alveolar ridge preservation after tooth extraction in canine models. . . 8th International Conference on Mechanics of Biomaterials and Tissues. 2019.12.15

Molecular Cell Biology

Professor Hiroshi Shibuya
Associate Professor Toshiyasu Goto
Assistant Professor Masahiro Shimizu

(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. Shimizu M, Tanaka N. IL-8-induced O-GlcNAc modification via GLUT3 and GFAT regulates cancer stem cell-like properties in colon and lung cancer cells. *Oncogene*. 2019.02; 38(9); 1520-1533

[Conference Activities & Talks]

1. Michiru Nishita, Koki Kamizaki, Ikumi Nishikaku, Hiroshi Shibuya, Kunio Matsumoto, Yasuhiro Minami. Ror1 signaling through Dvl and Rif promotes invasion of lung adenocarcinoma cells.. ASCB (米国細胞生物学会) 2019.12

Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D.
 Lecturer Kengo Homma, Ph.D.
 Lecturer Satoshi Kofuji, Ph.D.
 Assistant Professor Erika Ishihara, Ph.D.
 Junior Assistant Professor Yukari Mori, Ph.D.
 Secretary Kazuko Tanaka

(1) Outline

Our goal is to define the molecular basis for the mechanism of organ formation and regeneration using knockout mice and mutant fishes. To accomplish this goal, we have focused on defining signaling molecules and pathways that regulate liver formation and stress responses. Moreover, we are trying to establish a cell therapy for intractable diseases such as liver failures using self-bone marrow cells. Our study will provide new insights into understanding the precise molecular mechanisms that underlie organ failures found in human disease and will lead to the development of new rational therapy for the diseases.

(2) Research

1. Studies on vertebrate early embryogenesis
2. Studies on vertebrate organogenesis
3. Studies on organ homeostasis
4. Studies on behavioral rhythm

(3) Publications

[Original Articles]

1. Yoshino H, Yin G, Kawaguchi R, Popov KI, Temple B, Sasaki M, Kofuji S, Wolfe K, Kofuji K, Okumura K, Randhawa J, Malhotra A, Majd N, Ikeda Y, Shimada H, Kahoud ER, Haviv S, Iwase S, Asara JM, Campbell SL, Sasaki AT. Correction: Identification of lysine methylation in the core GTPase domain by GoMADScan. *PloS one*. 2019; 14(10); e0224443
2. Yoshino H, Yin G, Kawaguchi R, Popov KI, Temple B, Sasaki M, Kofuji S, Wolfe K, Kofuji K, Okumura K, Randhawa J, Malhotra A, Majd N, Ikeda Y, Shimada H, Kahoud ER, Haviv S, Iwase S, Asara JM, Campbell SL, Sasaki AT. Identification of lysine methylation in the core GTPase domain by GoMADScan. *PloS one*. 2019; 14(8); e0219436
3. Nigorikawa K, Matsumura T, Sakamoto H, Morioka S, Kofuji S, Takasuga S, Hazeki K. Sac1 Phosphoinositide Phosphatase Regulates Foam Cell Formation by Modulating SR-A Expression in Macrophages. *Biological & pharmaceutical bulletin*. 2019; 42(6); 923-928

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6. Isobe Y, Nigorikawa K, Tsurumi G, Takemasu S, Takasuga S, Kofuji S, Hazeki K. PIKfyve accelerates phagosome acidification through activation of TRPML1 while arrests aberrant vacuolation independent of the Ca²⁺ channel. *Journal of biochemistry*. 2019.01; 165(1); 75-84
7. Takemasu S, Ito M, Morioka S, Nigorikawa K, Kofuji S, Takasuga S, Eguchi S, Nakanishi H, Matsuoka I, Sasaki J, Sasaki T, Hazeki K. Lysophosphatidylinositol-acyltransferase-1 is involved in cytosolic Ca²⁺ oscillations in macrophages. *Genes to cells : devoted to molecular & cellular mechanisms*. 2019.03;
8. Kofuji S, Hirayama A, Eberhardt AO, Kawaguchi R, Sugiura Y, Sampetean O, Ikeda Y, Warren M, Sakamoto N, Kitahara S, Yoshino H, Yamashita D, Sumita K, Wolfe K, Lange L, Ikeda S, Shimada H, Minami N, Malhotra A, Morioka S, Ban Y, Asano M, Flanary VL, Ramkissoon A, Chow LML, Kiyokawa J, Mashimo T, Lucey G, Mareninov S, Ozawa T, Onishi N, Okumura K, Terakawa J, Daikoku T, Wise-Draper T, Majd N, Kofuji K, Sasaki M, Mori M, Kanemura Y, Smith EP, Anastasiou D, Wakimoto H, Holland EC, Yong WH, Horbinski C, Nakano I, DeBerardinis RJ, Bachoo RM, Mischel PS, Yasui W, Suematsu M, Saya H, Soga T, Grummt I, Bierhoff H, Sasaki AT. IMP dehydrogenase-2 drives aberrant nucleolar activity and promotes tumorigenesis in glioblastoma. *Nature cell biology*. 2019.08; 21(8); 1003-1014
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10. Takemasu S, Nigorikawa K, Yamada M, Tsurumi G, Kofuji S, Takasuga S, Hazeki K. Phosphorylation of TMEM55B by Erk/MAPK regulates lysosomal positioning. *Journal of biochemistry*. 2019.08; 166(2); 175-185
11. Naffouje R, Grover P, Yu H, Sendilnathan A, Wolfe K, Majd N, Smith EP, Takeuchi K, Senda T, Kofuji S, Sasaki AT. Anti-Tumor Potential of IMP Dehydrogenase Inhibitors: A Century-Long Story. *Cancers*. 2019.09; 11(9);
12. Takuro Nagoya, Kenya Kamimura, Ryo Goto, Yoko Shinagawa-Kobayashi, Yusuke Niwa, Atsushi Kimura, Norihiro Sakai, Masayoshi Ko, Hiroshi Nishina, Shuji Terai. Inhibition of sodium-glucose cotransporter 2 ameliorates renal injury in a novel medaka model of nonalcoholic steatohepatitis-related kidney disease. *FEBS Open Bio*. 2019.12; 9(12); 2016-2024
13. Ryo Goto, Kenya Kamimura, Yoko Shinagawa-Kobayashi, Norihiro Sakai, Takuro Nagoya, Yusuke Niwa, Masayoshi Ko, Kohei Ogawa, Ryosuke Inoue, Takeshi Yokoo, Akira Sakamaki, Hiroteru Kamimura, Satoshi Abe, Hiroshi Nishina, Shuji Terai. Inhibition of sodium glucose cotransporter 2 (SGLT2) delays liver fibrosis in a medaka model of nonalcoholic steatohepatitis (NASH). *FEBS Open Bio*. 2019.12; 9(4); 643-652

[Conference Activities & Talks]

1. 小藤智史, 佐々木敦朗. GTP-metabolic reprogramming that regulates the nucleolar activity and tumorigenesis . 第 42 回日本分子生物学会年会 2019.12.04

Immunology

Professor: Takeshi TSUBATA, M.D., Ph.D.
 Associate Professor: Takahiro ADACHI, Ph.D.
 Assistant Professor: Chizuru AKATSU, Ph.D.
 Project Assistant Professor: Shuichi KINPAPA, Ph.D.
 Lecturer: Ji-Yang WANG, Ph.D.
 Project Researcher: Nazim MEDZHIDOV, Ph.D., Yang-Yang FENG, Ph.D.
 Technical Assistant: Yuko TERAMOTO, Emi HAGIUDA
 Staff Assistant: Chikako SAWADA
 Graduate Students: Amin ALBORZIAN DE SHEIKH,
 Graduate Students: Yuki ANBE, Kyoko NISHIDA, Wang LONG
 Graduate Students: Hongrui YANG, Xuexin LI,
 Graduate Students: Yuming HUANG,
 Graduate Students: Akio KATO, Shinji KUNITAKE
 Graduate Research Students: Masato SUZUKI, Yang CUI, Yi DING
 Research Students: Yuya SUZUKI, Ayaka OOKAME, Orla Williams
 Collaborative Researcher: Wataru TAKASHIMA

(1) Research

Immune responses to non-protein antigens play crucial roles in host defense against pathogens, and autoimmune diseases. The mechanisms for immune responses to non-protein antigens are distinct from those to protein antigens, but are largely unknown. The aims of our research are to elucidate the mechanisms for antibody responses to non-protein antigens, and to develop novel drugs for autoimmune diseases and cancer immunotherapy by regulating antibody responses. Followings are our research subjects.

- 1) Elucidation of the mechanisms for humoral immune responses to polysaccharide antigens.
- 2) Elucidation of the mechanisms for autoantibody production in lupus and immuno-neurological disorders.
- 3) Elucidation of the role of glycan signals in the regulation of B lymphocyte (B cell) activation
- 4) Elucidation of the role of endosomal signaling in B cell activation
- 5) Development of novel drugs for autoimmune diseases by regulating regulatory B cells.
- 6) Development of therapeutic vaccines that substitute for therapeutic antibodies

(2) Education

Our department is responsible for the education on immunology provided by the PhD Program in Biomedical Sciences and Engineering, and the Master's Program in Medical and Dental Science and Technology.

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.

Lecture course on immunology at the Master's Program aims at giving the students basic ideas how immune

system recognizes and responds to the antigens, and how immune system efficiently removes pathogens without responding to self-antigens or environmental antigens. In the lecture course on molecular pathophysiology at the PhD Program, lectures on immune responses and pathophysiology of immunological diseases are given so that the students are introduced with the current topics in the field of humoral immune responses and immunological diseases.

(3) Publications

[Original Articles]

1. Hong Rongjian, Lai Nannan, Xiong Ermeng, Ouchida Rika, Sun Jiping, Zhou Yang, Tang Yue, Hikida Masaki, Tsubata Takeshi, Tagawa Masatoshi, Wang Yanqing, Wang Ji-Yang. Distinct roles of BCNP1 in B-cell development and activation *International Immunology*. 2019; 32(1); 17-26
2. Adachi Takahiro, Yoshikawa Soichiro, Tezuka Hiroyuki, Tsuji Noriko M., Ohteki Toshiaki, Karasuyama Hajime, Kumazawa Toshihiko. Propolis induces Ca²⁺ signaling in immune cells *BIOSCIENCE OF MICROBIOTA FOOD AND HEALTH*. 2019; 38(4); 141-149
3. Isobe, J., Maeda, S., Obata, Y., Iizuka, K., Nakamura, Y., Fujimura, Y., Kimizuka, T., Hattori, K., Kim, YG., Morita, T., Kimura, I., Offermanns, S., Adachi, T., Nakao, A., Kiyono, H., Takahashi, D., Hase, K.. Commensal-bacteria-derived butyrate promotes the T cell-independent IgA response in the colon. *Int Immunol.* 2019; dxz078
4. Hong R, Lai N, Ouchida R, Xiong E, Zhou Y, Min Q, Liu J, Tang Y, Hikida M, Tsubata T, Wang Y, Wang JY. The B cell novel protein 1 (BCNP1) regulates BCR signaling and B cell apoptosis. *European journal of immunology*. 2019.03; 49; 911-917
5. Yoshikawa Soichiro, Oh-hora Masatsugu, Hashimoto Ryota, Nagao Toshihisa, Peters Louis, Egawa Mayumi, Ohta Takuya, Miyake Kensuke, Adachi Takahiro, Kawano Yohei, Yamanishi Yoshinori, Karasuyama Hajime. Pivotal role of STIM2, but not STIM1, in IL-4 production by IL-3-stimulated murine basophils *SCIENCE SIGNALING*. 2019.04; 12(576);
6. Feng Yang-Yang, Tang Miao, Suzuki Mitsuhiro, Gunasekara Chinthika, Anbe Yuki, Hiraoka Yuichi, Liu Jun, Grasberger Helmut, Ohkita Mamoru, Matsumura Yasuo, Wang Ji-Yang, Tsubata Takeshi. Essential Role of NADPH Oxidase-Dependent Production of Reactive Oxygen Species in Maintenance of Sustained B Cell Receptor Signaling and B Cell Proliferation *JOURNAL OF IMMUNOLOGY*. 2019.05; 202(9); 2546-2557
7. Xiong Ermeng, Li Yingqian, Min Qing, Cui Chaoqun, Liu Jun, Hong Rongjian, Lai Nannan, Wang Ying, Sun Jiping, Matsumoto Ryohtaroh, Takahashi Daisuke, Hase Koji, Shinkura Reiko, Tsubata Takeshi, Wang Ji-Yang. MZB1 promotes the secretion of J-chain-containing dimeric IgA and is critical for the suppression of gut inflammation *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*. 2019.07; 116(27); 13480-13489
8. Fujii Yasuyuki, Suzuki Kenta, Adachi Takahiro, Taira Shu, Osakabe Naomi. Corticotropin-releasing hormone is significantly upregulated in the mouse paraventricular nucleus following a single oral dose of cinnamtannin A2 as an (-)-epicatechin tetramer *JOURNAL OF CLINICAL BIOCHEMISTRY AND NUTRITION*. 2019.07; 65(1); 29-33

[Books etc]

1. Takeshi Tsubata. Development of Siglec Regulators. In “Glycoscience: Basic Science to Applications” (ed. by Naoyuki Taniguchi, Tamao Endo, Jun Hirabayashi, Shoko Nishihara, Kenji Kadomatsu, Kazunari Akiyoshi and Kiyoko F. Aoki-Kinoshita). Springer, 2019.09 (ISBN : 9811358559)

[Misc]

1. Tsubata T. CD72 is a Negative Regulator of B Cell Responses to Nuclear Lupus Self-antigens and Development of Systemic Lupus Erythematosus. *Immune network*. 2019.02; 19(1); e1

2. Tsubata Takeshi. Inhibitory B cell co-receptors and autoimmune diseases Immunological Medicine. 2019.09; 42(3); 108-116

[Conference Activities & Talks]

1. Long Wang, Endo Ayaka, Takematsu Hiromu, Fedder Thomas, Tsubata Takeshi. Development of anti-CD22 antibody that inhibits ligand binding of CD22. The Regular Meeting of the Japanese Biochemical Society Kanto Branch 2019.06.22 Yokohama, KANAGAWA
2. Yang-Yang Feng, Miao Tang, Mitsuhiro Suzuki, Chinthika Gunasekara, Yuki Anbe, Yuichi Hiraoka, Jun Liu, Helmut Grasberger, Mamoru Ohkita, Yasuo Matsumura, Ji-Yang Wang, and Takeshi Tsubata. Essential role of NADPH oxidase-dependent production of reactive oxygen species in maintenance of sustained B cell receptor signaling and B cell proliferation. The 28th Annual Meeting of the Japanese Society for Cell Death Research 2019.07.13 TOKYO
3. Daiki Yamada, Takashi Nagaishi, Taro Watabe, Naoya Tsugawa, Yudai Kojima, Takahiro Adachi, Mamoru Watanabe. Analysis of Ileocecal Immune Response in an Animal Model of Colitis. ICMI2019 2019.07.17 Brisbane (Australia)
4. YangYang Feng, Miao Tang, Mitsuhiro Suzuki, Chinthika Gunasekara, Yuki Anbe, Yuichi Hiraoka, Jun Liu, JiYang Wang, Takeshi Tsubata. Essential role of NOX3-mediated endosomal production of ROS in maintenance of sustained B cell receptor signaling and B cell proliferation. The 92nd Annual Meeting of the Japanese Biochemical Society 2019.09.18 Yokohama, KANAGAWA
5. Takeshi Tsubata. Inhibitory B cell co-receptors and autoimmune diseases. Mini-symposium on Protein Structure and Function 2019.10.03 Taipei, TAIWAN
6. Takeshi Tsubata. SHP-1 (PTPN6) regulates development of SLE through CD72. The 4th Taiwan-Japan Bilateral Conference on Protein Phosphatase 2019.11.15 Taipei, TAIWAN
7. Takeshi Tsubata. Regulation of the immune response to nucleic acids and systemic lupus erythematosus. The 1st “Wuxi talents” Symposium of Experimental Research Center of the First People’s Hospital of Huaihua 2019.11.29 Huaihua, CHINA
8. Fukuda, Y., Osakabe, N., Adachi, T.. Elucidation of recognition mechanism of dorsal root ganglion for food factors. The international conference on food factors(ICoFF2019) 2019.12.03 Kobe
9. Naoya Tsugawa, Takashi Nagaishi, Daiki Yamada, Toshimitsu Fujii, Yudai Kojima, Arisa Tokai, Taro Watabe, Shuang Wang, Michio Onizawa, Takahiro Adachi, Mamoru Watanabe. BCR signaling in the activated B cells may be regulated by the long isoform of Ceacam1. The 48th Annual Meeting of the Japanese Society for Immunology 2019.12.11 Hamamatsu (Japan)
10. Kyoko Nishida, Akihiro Kimura, Takeshi Tsubata, Harumi Suzuki. The anti-oxidative enzyme NAD(P)H quinone oxidoreductase1 promotes Th17 cells differentiation by protecting oxidative stress. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.12 Hamamatsu, SHIZUOKA
11. Ying Wang, Jun Liu, Ermeng Xiong, Chizuru Akatsu, Takeshi Tsubata, Ji-Yang Wang. LAPTM5 mediates anti-IgM-induced apoptosis in immature B cells. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.12 Hamamatsu, SHIZUOKA
12. Yang-Yang Feng, Jun Liu, Ji-Yang Wang, Takeshi Tsubata. Essential role of late redoxosome in BCR ligation-induced B cell activation. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.12 Hamamatsu, SHIZUOKA
13. Chizuru Akatsu, Quan-Zhen Li, Hideharu Sekine, Teizo Fujita, Takeshi Tsubata. The inhibitory B cell co-receptor CD72 recognizes various lupus self-antigens including C1q and inhibits B cell responses to these self-antigen. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.12 Hamamatsu, SHIZUOKA
14. Liu, J., Qian, J., Xiong, E., Zhang, L., Wang, Y., Chu, Y., Tsubata, T. and Wang, J.-Y.. Role of the IgM Fc receptor in marginal zone B cell development and function. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.12 Hamamatsu, SHIZUOKA

15. Xiong, E., Cui, C., Min, Q., Liu, J., Lai, N., Wang, Y., Matsumoto, R., Takahashi, D., Hase, K., Shinkura, R., Tsubata, T. and Wang, J.-Y.. MZB1 promotes the secretion of J chain-containing IgA and is critical for the suppression of gut inflammation. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.12 Hamamatsu, SHIZUOKA
16. Tang, Y., Lai, N., Xiong, E., Ouchida, R., Sun, J., Hikida, M., Tsubata, T., Wang, Y. and Wang, J.-Y.. Distinct roles of B cell novel protein 1 in B cell development and activation. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.12 Hamamatsu, SHIZUOKA
17. Takeshi Tsubata. Regulation of B cells and autoimmune diseases. The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.13 Hamamatsu, SHIZUOKA
18. Adachi, T., Watabe, T., Nagaishi, T., Watanabe, M., Karasuyama, H., Yoshikawa, S.. IgA deficiency causes spontaneous enteritis . The 48th Annual Meeting of the Japanese Society for Immunology (JSI) 2019.12.13 Hamamatsu, SHIZUOKA

Structural Biology

Professor Nobutoshi ITO
Associate Professor Teikichi IKURA
Assistant Professor Nobutaka NUMOTO

(1) Outline

The advance of genome science and proteomic analysis has produced a large amount of information about the primary structure of proteins and their spatial and temporal distributions. On the other hand, most of the proteins only function when they take certain three dimensional structures. As obviously seen in so-called prion diseases, proteins which are chemically correct but structurally incorrect not only fail to function properly but also can harm cells. Our laboratory aims to understand the function of biological macromolecules at atomic level through structure analysis and other methods of physical chemistry, in the hope that accumulation of such knowledge will eventually lead to development of drugs. We are also involved in providing database of such structural data to scientists through the activities of Protein Data Bank Japan.

(2) Research

Collaborating with groups within and outside of the university, we are engaged in various research projects including;

- 1) Structural analyses of B-cell coreceptors
- 2) Physicochemical analysis on the mechanism of the signal transduction for activation of T cells
- 3) Structural analyses of potential drug targets of nuclear receptors
- 4) Analysis of interactions between tau protein and Pin1
- 5) Molecular mechanism of the sero-specificity of dengue virus
- 6) Rational design of PDZ domain inhibitors involved in regulation of intracellular signaling
- 7) Structural basis of giant hemoglobins
- 8) Molecular basis of suppression of HIV-1
- 9) Structure based drug design for protein kinases
- 10) 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. Teikichi Ikura, Yasushige Yonezawa, Nobutoshi Ito. Mutational effects of Cys113 on structural dynamics of Pin1 Biophysics and Physicobiology. 2019;
2. Yurina Miyashita, Nobutaka Numoto, Sundaram Arulmozhiraja, Shogo Nakano, Naoya Matsuo, Kanade Shimizu, Osamu Shibahara, Michiko Fujihara, Hiroki Kakuta, Sohei Ito, Teikichi Ikura, Nobutoshi Ito, Hiroaki Tokiwa. Dual conformation of the ligand induces the partial agonistic activity of retinoid X receptor α (RXR α). FEBS Lett.. 2019.01; 593(2); 242-250
3. Yuhi Hosoe, Nobutaka Numoto, Satomi Inaba, Shuhei Ogawa, Hisayuki Morii, Ryo Abe, Nobutoshi Ito, Masayuki Oda. Structural and functional properties of Grb2 SH2 dimer in CD28 binding. Biophys Physicobiol. 2019.02; 16; 80-88
4. Nakayama S, Shimonaka S, Elahi M, Nishioka K, Oji Y, Matsumoto SE, Li Y, Yoshino H, Mogushi K, Hatano T, Sato T, Ikura T, Ito N, Motoi Y, Hattori N. Tau aggregation and seeding analyses of two novel MAPT variants found in patients with motor neuron disease and progressive parkinsonism. Neurobiology of aging. 2019.03;
5. Masuno Hiroyuki, Kazui Yuko, Tanatani Aya, Fujii Shinya, Kawachi Emiko, Ikura Teikichi, Ito Nobutoshi, Yamamoto Keiko, Kagechika Hiroyuki. Development of novel lithocholic acid derivatives as vitamin D receptor agonists BIOORGANIC & MEDICINAL CHEMISTRY. 2019.08; 27(16); 3674-3681
6. Akihiro Nishiguchi, Nobutaka Numoto, Nobutoshi Ito, Takachika Azuma, Masayuki Oda. Three-dimensional structure of a high affinity anti-(4-hydroxy-3-nitrophenyl)acetyl antibody possessing a glycine residue at position 95 of the heavy chain. Mol. Immunol.. 2019.10; 114; 545-552
7. Teikichi Ikura, Yasushige Yonezawa, Nobutoshi Ito. Mutational effects of Cys113 on structural dynamics of Pin1 Biophysics and Physicobiology. 2019.11; 16; 452-465

[Conference Activities & Talks]

1. Syotaro Yasukouchi, Nobutaka Numoto, Natsuko Tenno, Takeshi Tenno, Nobutoshi Ito, Hidekazu Hiroaki. Novel interaction mode in the crystal structure of hDvl1 PDZ. Wnt Workshop 2018-2019 2019.02.02 Osaka
2. Teikichi Ikura. Hierarchical aspects in protein function. 2019.02.14 Kyoto
3. Nobutaka Numoto. Structural changes during the enzymatic reaction revealed by the substrate-bound crystal structure of cutinase. The 2019 Annual Meeting of the Japan Society for Bioscience, Biotechnology, and Agrochemistry 2019.03.27 Tokyo
4. Akihiro Nishiguchi, Nobutaka Numoto, Nobutoshi Ito, Takachika Azuma, Masayuki Oda. Structural basis of antigen recognition changes during affinity maturation of anti-nitrophenyl antibodies. The 508th meeting of Kansai branch, The Japan Society for Bioscience, Biotechnology, and Agrochemistry 2019.06.01 Kyoto
5. Nobutaka Numoto, Yoshihiro Fukumori, Kunio Miki, Nobutoshi Ito. Transitions of oxygen occupancy of each subunit in the allosteric intermediates of giant hemoglobin. Joint Annual Meeting of 71st JSCB & 19th PSSJ 2019.06.24 Kobe
6. Teikichi Ikura, Yasushige Yonezawa and Nobutoshi Ito. A single mutation C113A caused drastic change in the dynamic of Pin1. Joint Annual Meeting of 71st JSCB & 19th PSSJ 2019.06.25 Kobe City
7. Akihiro Nishiguchi, Nobutaka Numoto, Nobutoshi Ito, Takachika Azuma, Masayuki Oda. Antigen recognition mechanism of an affinity-matured single chain Fv antibody against anti-(4-hydroxy-3-nitrophenyl)acetyl. The 92nd Annual Meeting of the Japanese Biochemical Society 2019.09.18 Yokohama
8. Nobutaka Numoto, Yoshihiro Fukumori, Kunio Miki, Nobutoshi Ito. Time-resolved structure analysis of allosteric intermediate of the giant hemoglobin. The 57th Annual Meeting of the BSJ 2019.09.24 Miyazaki
9. Shotaro Yasukochi, Nobutaka Numoto, Kiminori Hori, Natsuko Tenno, Takeshi Tenno, Nobutoshi Ito, Hidekazu Hiroaki. Crystal structure of human Dishevelled1 PDZ with its inhibitor. The 57th Annual Meeting of the BSJ 2019.09.24 Miyazaki

10. Teikichi Ikura, Nobutoshi Ito. Micronization of a protease derived from Pin1. The 57th annual meeting of the Biophysical Society of Japan 2019.09.25
11. Nobutaka Numoto, Yoshihiro Fukumori, Kunio Miki, Nobutoshi Ito. Allosteric structural change of giant hemoglobin. Annual Meeting 2019 and General Assembly of Crystallographic Society of Japan 2019.11.20 Kanazawa
12. Daisuke Imai, Nobutaka Numoto, Sundaram Arulmozhiraja, Shogo Masuda, Hiroki Kakuta, Hiroaki Tokiwa, Nobutoshi Ito. Structural analysis of NEt-3IB/NEt-4IB-bound Retinoid X Receptor α . 16th Conference of the Asian Crystallographic Association 2019.12.18 Singapore

Neuroscience

Professor Kohichi Tanaka
Assistant Professor Saeko Ishida
Assistant Professor Yuichi Hiraoka

Graduate Student (doctor course)
Takehisa Handa
Bi Haining

Graduate Student (master course)
Haruna Aikawa
Yuuta Sawada
Zhao Di
Ryo Matsuura
Minami Kato

Technical Staff
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. Human genetic studies have suggested that de novo mutations in GLAST (EAAT1) is linked to schizophrenia. Consistent with this, GLAST null mice show phenotypes relevant to positive, negative and executive/cognitive symptoms of schizophrenia, including novelty-induced locomotor hyperactivity, abnormal social behavior characterized by reduced initiation of social interactions, poor nesting and impaired pairwise visual discrimination learning. Repeated phencyclidine (PCP) administration induces several schizophrenia-like psychobehavioral abnormalities and decreased extracellular glutamate levels, which are associated with increased expression of GLAST in the prefrontal cortex of mice. In this study, we investigated the functional roles of GLAST in the schizophrenia-like psychobehavioral abnormalities induced by repeated PCP administration using GLAST heterozygous (GLAST+/-) mice. PCP-administered GLAST wild-type (+/+) mice showed enhancement of immobility in a forced swimming test, impairments of visual recognition memory in a novel object recognition

test, decrease in high potassium (K⁺)-induced extracellular glutamate release, and overexpression of GLAST and S100 proteins in the PFC, compared to saline-administered GLAST^{+/+} mice. Such behavioral and neurochemical abnormalities were not observed in PCP-administered GLAST^{+/-} mice. These results clearly suggest that overexpression of GLAST and glial activation play important roles in the development of emotional and cognitive abnormalities in PCP-administered GLAST^{+/+} mice. It is therefore necessary to strictly regulate the expression of GLAST to maintain normal brain function. Studies targeting GLAST may lead to the development of medications for emotional (negative symptoms) and cognitive impairments in schizophrenia.

2. Elucidation of the effect of abnormalities in the GATOR1 complex on focal epilepsy

Epilepsy is characterized by recurrent seizures resulting from excessive neuronal discharge and presents a wide variety of clinical symptoms. Although epilepsy is a frequent neurological disorder that occurs in about 1% of the population, there is often no fundamental cure for it, forcing it to rely on symptomatic treatment with prolonged use of antiepileptic drugs. In addition, seizures in about 30% of patients fail to respond to the drugs. Therefore, the development of new treatment and prevention methods is urgent.

"Focal epilepsy", in which the site of abnormal neuronal firing is limited to a part of the cerebral hemisphere, accounts for half of adult epilepsy. Gap activity toward Rags 1 (GATOR1) complex abnormality is involved in about 10% of the onset of focal epilepsy. The GATOR1 complex is a complex composed of DEP domain-containing protein 5 (DEPDC5) and Nitrogen permease regulator 2 / 3-like protein (NPRL2, NPRL3). It suppresses the mechanical target of rapamycin complex1 (mTORC1) pathway that controls cell growth and proliferation (Fig.2). However, the function of the GATOR1 complex in the nervous system has not been clarified. We aim to elucidate the function of the GATOR1 complex and the role on epileptogenesis using mouse models.

Because conventional knockout (KO) of DEPDC5, NPRL2, and NPRL3 in mice results in embryonic lethal, it was impossible to analyze their functions in adults. In this year, we focused on the cerebral cortex where most seizure focus exist, and generated the conditional knockout (cKO) mice of each gene. Phenotypic analysis revealed that each cKO mouse exhibited spontaneous epileptic seizures and cerebral cortical dysplasia similarly to patients, indicating that they are useful as epilepsy model mice (Fig.3). Further analysis of these mice will promote our research on elucidation of the onset mechanism.

(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. Uchida Mizuki, Hida Hirotake, Mori Kentaro, Yoshimi Akira, Kitagaki Shinji, Yamada Kiyofumi, Hiraoka Yuichi, Aida Tomomi, Tanaka Kohichi, Ozaki Norio, Noda Yukihiro. Functional roles of the glial glutamate transporter (GLAST) in emotional and cognitive abnormalities of mice after repeated phencyclidine administration EUROPEAN NEUROPSYCHOPHARMACOLOGY. 2019.08; 29(8); 914-924

Epigenetic Epidemiology

Professor: Masaaki MURAMATSU

Associate Professor : Noriko SATO

Assistant Professor : Chihiro Imai

Adjunct Instructor : Sumio Sugano, Tomio Arai

Graduate Student: Hiroo Fujitani, Tadaaki Katsuta, Shilpa Pavethynath

Maidina Abudushataer, Ake Ko Ko Minn, Zong Yuan, Tong Daike

Research Student: Arisa Nakata, Kin Kin

(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: Medical Information

Noriko Sato: Biomedical Science

Noriko Sato: Molecular and Cellular Biology

Noriko Sato: Introduction to Human Molecular Genetics

Noriko Sato: Bioinformatics

(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. Fudono Ayako, Sato Noriko, Miyasaka Naoyuki. Trimester specific difference in exosomal microRNA expression(和訳中) 日本産科婦人科学会雑誌. 2019.02; 71(臨増); S-200
2. Pavethynath S, Imai C, Jin X, Hichiwa N, Takimoto H, Okamitsu M, Tarui I, Aoyama T, Yago S, Fudono A, Muramatsu M, Miyasaka N, Sato N. Metabolic and Immunological Shifts during Mid-to-Late Gestation Influence Maternal Blood Methylation of *CPT1A* and *SREBF1*. International journal of molecular sciences. 2019.03; 20(5);
3. Tay Zar Kyaw, Seiji Yamaguchi, Chihiro Imai, Marina Uematsu and Noriko Sato. The utility of post-test newborn blood spot screening cards for epigenetic association analyses: association between HIF3A methylation and birth weight for gestational age Journal of Human Genetics . 2019.05;
4. Sato N, Miyasaka N. Heterogeneity in fetal growth velocity. Scientific reports. 2019.08; 9(1); 11304
5. Sato N, Miyasaka N. Stratified analysis of the correlation between gestational weight gain and birth weight for gestational age: a retrospective single-center cohort study in Japan. BMC pregnancy and childbirth. 2019.11; 19(1); 402

[Conference Activities & Talks]

1. Ayako Fudono, Noriko Sato, Naoyuki Miyasaka. Trimester specific difference in exosomal microRNA expression. 第 71 回日本産科婦人科学会学術講演会 2019.04.12 名古屋
2. Pavethynath Shilpa, 今井千裕, JIN Xin, 飛知和尚美, 瀧本秀美, 岡光基子, 樽井依織, 青山友子, 矢郷哲志, 不殿絢子, 宮坂尚幸, 佐藤憲子. 妊娠後半期の末梢血における脂質関連遺伝子の DNA メチル化. 第 73 回日本栄養・食糧学会大会 2019.05.18
3. 不殿絢子, 佐藤憲子, 宮坂尚幸. 正常妊娠における PlGF 値と母児体格との関係. 第 8 回日本 DOHaD 学会学術集会 2019.08.09 東京
4. Sato N, Miyasaka N. Gestational Weight Gain and Birthweight-for-Gestational Age: TMDU Hospital Cohort Study. DOHAD 2019 Congress 2019.10.22 Melbourne, Australia
5. Imai C, Pavethynath S, Xin J, Hichiwa N, Takimoto H, Okamitsu M, Tarui I, Aoyama T, Yago S, Fudono A, Muramatsu M, Miyasaka N, Sato N. Intra- and Inter- individual Differences in CPT1A and SREBF1 Methylation of Maternal Leukocytes During Mid-to-Late Gestation. DOHAD 2019 Congress 2019.10.22 Melbourne, Australia
6. Fudono A, Sato N, Takimoto H, Okamitsu M, Imai C, Aoyama T, Yago S, Tarui I, Yomogita H, Miyasaka N. Trimester Specific Difference in Exosomal MicroRNA Expression. DOHAD 2019 Congress 2019.10.22 Melbourne, Australia

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RIKEN Molecular and Chemical Somatology

Visiting Professor	Soichi Kojima
Visiting Professor	Mikiko Sodeoka
Visiting Professor	Nobumoto Watanabe
Visiting Professor	Ichiro Taniuchi
Visiting Professor	Motomasa Tanaka
Visiting Professor	Katsunori Tanaka
Visiting Lecturer	Nobuhiko Miyasaka
Visiting Lecturer	Ambara R. Pradipta
Visiting Lecturer	Takeshi Nakano
Visiting Lecturer	Kosuke Dodo
Visiting Lecturer	Ryo Endo
Visiting Lecturer	Akiko Tane
Visiting Lecturer	Yutaka Furutani
Visiting Lecturer	Qin Xian-Yang
Visiting Lecturer	Sanae Sekihara
Visiting Lecturer	Vivian Saitou
Visiting Lecturer	Kai-Wan Hui
Graduate Students	D3 Chih-Hao Shen
	D2 Ziyu Liu
	D1 Nayan Suryawanshi
	(October~)

(1) Research

Molecular and Chemical Somatology is an interdisciplinary field for understanding of the basis of Bioorganic Chemistry, Chemical Biology, Structural Biology and Molecular Immunology and Molecular Neuroscience as well as their applications to Medicine and Biology by dealing with a variety of molecules that regulate cellular functions including low molecular weight organic compounds, proteins, sugars, and hormones. Students will learn and discuss about the outlines and/or the latest topics on discovery, structure, synthesis, biology, and management of the key molecules/factors, and deepen their understanding of this new research field.

(2) Education

- 1) Synthetic Organic Chemistry
 - Design and synthesis of bioactive molecules based on synthetic organic chemistry and chemical biology research.
- 2) Chemical Biology
 - Discovery, target identification and analyses of mechanism of action of bioactive compounds that regulate biological function.
- 3) Molecular Cellular Pathology
 - Clarification of pathogenesis of diseases at molecular and cellular levels utilizing bioprobes.
- 4) Molecular Immunology
 - Regulatory mechanisms for lymphocyte development
- 5) Molecular Neuropathology
 - Molecular basis of neurodegenerative disorders and psychiatric diseases

(3) Publications

[Original Articles]

1. Tenno, M., Wong, A., Ikegaya, M., Miyauchi, E., Seo, W., See, P., Kato, T., Taida, T., Ohno, H., Yoshida, H., Ginhoux, F., Taniuchi, I. Essential functions of Runx/Cbfb in conventional dendritic cells for priming Ror γ t⁺ Treg and Th17 cells in the gut. *Life Sci Alliance*. 3:e201900441 (2019).
2. Suvarna, K., Honda, K., Muroi, M., Kondoh, Y., Osada H., Watanabe, N. A small-molecule ligand of valosin-containing protein/p97 inhibits cancer cell-accelerated fibroblast migration. *J Biol. Chem.* 294 (9): 2988-2996 (2019).
3. Sugiyama, S., Tanaka., M. Distinct segregation patterns of yeast cell-peripheral proteins uncovered by a method for protein segregatome analysis. *Proc. Natl. Acad. Sci. U. S. A.*, 116, 8909-8918 (2019).
4. Hui, K.K., Takashima, N., Watanabe, A., Chater, T.E., Matsukawa, H., Nekooki-Machida, Y., Nilsson, P., Endo, R., Goda, Y., Saido, T.C., Yoshikawa, T., Tanaka., M. GABARAPs dysfunction by autophagy deficiency in adolescent brain

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- impairs GABA_A receptor trafficking and social behavior. *Science Adv.*, 5(4), eaau8237 (2019).
5. Vong, K., Eda, S., Kadota, Y., Nasibullin, I., Wakatake, T., Yokoshima, S., Shirasu, K., Tanaka, K., An artificial metalloenzyme biosensor can detect ethylene gas in fruits and Arabidopsis leaves. *Nature Commun.* 10, 5746 (2019).
 6. Eda, S., Nasibullin, I., Vong, K., Kudo, N., Yoshida, M., Kurbanalieva A., Tanaka, K., Biocompatibility and therapeutic potential of glycosylated albumin artificial metalloenzymes, *Nature Catal.* 2, 780-792 (2019).

[Review Articles]

1. Ebihara, T., Taniuchi, I. Exhausted-like group 2 innate lymphoid cells in chronic allergic inflammation. *Trend. Immunol.* 40:1095-11 (2019).
2. Hui, K.K., Chen, Y.*, Endo, R.*, Tanaka, M. Translation from the ribosome to the clinic: Implication in neurological disorders and new perspectives from recent advances. *Biomolecules*, 9(11), 680 (2019).
3. Hui, K.K., Tanaka, M. Autophagy links MTOR and GABA signaling in the brain. *Autophagy*, 15(10), 1848-1849 (2019).

[Books]

1. Tanaka, K., Glycoconjugates and Glyoclusters as New Drug Delivery Molecules for In Vivo Molecular Imaging and Therapeutics, In *Glycoscience: Basic Science to Applications*, Taniguchi, N., Endo, T., Hirabayashi, J., Nishihara, S., Kadomatsu, K., Akiyoshi, K., and Aoki-Kinoshita K. F. (eds), *Springer*. 56-57 (2019).

[Conference Activities & Talks]

1. Taniuchi, I. "Roles of Bcl11 proteins During Thymocyte Differentiation". IUIS 2019. 17th International Congress of Immunology. Oct 19, 2019. Beijing, China.
2. Suvarna, K., Honda, K., Muroi, M., Kondoh, Y., Osada H., Watanabe, N. "Target identification of a small-molecule inhibitor of cancer cell-accelerated fibroblast migration as valosin-containing protein/p97". The 4th URICAS Symposium 2019, Mar 6, 2019. Penang, Malaysia.
3. Suvarna, K., Honda, K., Muroi, M., Kondoh, Y., Osada H., Watanabe, N. "Small molecule inhibitors of cancer cell-accelerated fibroblast migration and their mechanism of action". RIKEN-Max Planck Joint Research Center for Systems Chemical Biology 7th Annual Symposium. Sep. 15-18, 2019. Schloss Ringberg, Kreuth, Germany.

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4. Tanaka, M., Short disordered protein segment regulates species barrier in prion transmission, International Symposium on Neurodegenerative Diseases, October 25, 2019, UT Southwestern, Dallas.
5. Tanaka, K., “Therapeutic in vivo synthetic chemistry”. The 18th Asian Chemical Congress and the 20th General Assembly of the Federation of Asian Chemical Societies. Dec 8, 2019. Taipei, Taiwan.

NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA
Visiting Professor	Kenkichi MASUTOMI
Visiting Professor	Ryuji HAMAMOTO
Visiting Associate Professor	Masahiro YASUNAGA
Visiting Associate Professor	Satoshi FUJII
Visiting Lecturer	Tohru KIYONO
Visiting Lecturer	Kazunori AOKI
Visiting Lecturer	Takashi KOHNO
Visiting Lecturer	Yasuhito UEZONO
Visiting Lecturer	Naoto TSUCHIYA
Visiting Lecturer	Hiroyoshi NISHIKAWA
Graduate Students	D3 Tomoko WATANABE
	D2 Kazuma KOBAYASHI
	Takahiro SHIRAI
	D1 Yamato OGIWARA
	Eri HASHIMOTO
	M2 Megumi KAMISHIMA
	Kurumi KISHIMOTO
	Yuma NOZUE
	M1 Masako TSUDUKIHASHI
	Ai SASAKI

(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. Tamanaha-Nakasone A, Uehara K, Tanabe Y, Ishikawa H, Yamakawa N, Toyoda Z, Kurima K, Kina S, Tsuneki M, Okubo Y, Yamaguchi S, Utsumi D, Takahashi K, Arakawa H, Arasaki A, Kinjo T. K1 gene transformation activities in AIDS-related and classic type Kaposi's sarcoma: Correlation with clinical presentation. *Sci.Rep.* 9: 6416. 2019.
2. Maishi N, Kikuchi H, Sato M, Nagao-Kitamoto H, Annan DA, Babe S, Hojo T, Yanagiya M, Ohba Y, Ishii G, Masutomi K, Shinohara N, Hida Y, Hida K. Development of Immortalized Human Tumor Endothelial Cells from Renal Cancer. *Int J mol Sci.* 20: 18. 2019.
3. Takahashi M, Miki S, Fujimoto K, Fukuoka K, Matsushita Y, Maida Y, Yasukawa M, Hayashi M, Shinkyō R, Kikuchi K, Mukasa A, Nishikawa R, Tamura K, Narita Y, Hamada A, Masutomi K, Ichimura K. Eribulin penetrates brain tumor tissue and prolongs survival of mice harboring Intracerebral glioblastoma xenografts. *Cancer Sci.* 110: 2247-2257. 2019.
4. Matsuno Y, Atsumi Y, Shimizu A, Katayama K, Fujimori H, Hyodo M, Minakawa Y, Nakatsu Y, Kaneko S, Hamamoto R, Shimamura T, Miyano S, Tsuzuki T, Hanaoka F, Yoshioka KI. Replication stress triggers microsatellite destabilization and hypermutation leading to clonal expansion in vitro. *Nat Commun.* 10: 3925. 2019.
5. Yamada M, Saito Y, Imaoka H, Saiko M, Yamada S, Kondo H, Takamaru H, Sakamoto T, Sese J, Kuchiba A, Shibata T, Hamamoto R. Development of a Real-Time Endoscopic

- Image Diagnosis Support System Using Deep Learning Technology in Colonoscopy. *Sci Rep.* 9: 14465. 2019.
6. Kobayashi K, Murakami N, Takahashi K, Inaba K, Igaki H, Hamamoto R, Itami J. A Population-based Statistical Model for Investigating Heterogeneous Intraprostatic Sensitivity to Radiation Toxicity After ¹²⁵I Seed Implantation. *In Vivo.* 33: 2103-2111. 2019.
 7. Kobayashi K, Murakami N, Takahashi K, Inaba K, Hamamoto R, Itami J. Local Radiotherapy or Chemotherapy for Oligo-recurrent Cervical Cancer in Patients With Prior Pelvic Irradiation. *In Vivo.* 33: 1659-1665. 2019.
 8. Tsumura R, Manabe S, Takashima H, Koga Y, Yasunaga M, Matsumura Y. Evaluation of the antitumor mechanism of antibody-drug conjugates against tissue factor in stroma-rich allograft models. *Cancer Sci.* 110: 3296-3305. 2019.
 9. Koganemaru S, Kuboki Y, Koga Y, Kojima T, Yamauchi M, Maeda N, Kagari T, Hirotani K, Yasunaga M, Matsumura Y, Doi T. U3-1402, a Novel HER3-Targeting Antibody-Drug Conjugate, for the Treatment of Colorectal Cancer. *Mol Cancer Ther.* 18: 2043-2050. 2019
 10. Yasunaga M, Saijou S, Hanaoka S, Anzai T, Matsumura Y. Significant antitumor effect of an antibody against TMEM180, a new colorectal cancer-specific molecule. *Cancer Sci.* 110: 761-770. 2019.
 11. Fujii S, Yoshino T, Yamazaki K, Muro K, Yamaguchi K, Nishina T, Yuki S, Shinozaki E, Shitara K, Bando H, Mimaki S, Nakai C, Matsushima K, Suzuki Y, Akagi K, Yamanaka T, Nomura S, Esumi H, Sugiyama M, Nishida N, Mizokami M, Koh Y, Abe Y, Ohtsu A, Tsuchihara K. Histopathological factors affecting the extraction of high quality genomic DNA from tissue sections for next-generation sequencing. *Biomed Rep.* 11: 171-180, 2019.
 12. Oki T, Aokage K, Ueda T, Sugano M, Tane K, Miyoshi T, Kojima M, Fujii S, Kuwata T, Ochiai A, Funai K, Tsuboi M, Ishii G. Proportion of goblet cell is associated with malignant potential in invasive mucinous adenocarcinoma of the lung. *Pathol Int.* 69: 526-535, 2019.
 13. Okada N, Daiko H, Kanamori J, Sato A, Horikiri Y, Sato T, Fujiwara H, Tomioka T, Fujita

- T, Kojima T, Fujii S. Impact of pathologically assessing extranodal extension in the thoracic field on the prognosis of esophageal squamous cell carcinoma. *Surgery*. 165: 1203-1210, 2019.
14. Suzuki J, Kojima M, Aokage K, Sakai T, Nakamura H, Ohara Y, Tane K, Miyoshi T, Sugano M, Fujii S, Kuwata T, Ochiai A, Ito M, Suzuki K, Tsuboi M, Ishii G. Clinicopathological characteristics associated with necrosis in pulmonary metastases from colorectal cancer. *Virchows Arch*. 474: 569-575, 2019.

[Reviews Articles]

None

[Conference Activities & Talks]

1. Yasuyuki Nakamura, Naoki Ikari, Hirofumi Arakawa. Degradation of cancer mitochondria by the mitochondria-eating protein induces iron-dependent cancer cell death. AACR Annual Meeting 2019, Atlanta (USA) , March 2019.
2. Naoki Ikari, Yasuyuki Nakamura, Hirofumi Arakawa. Involvement of unique endosomes in the Mieap-induced vacuoles formation during Mieap-mediated cancer cell death. AACR Annual Meeting 2019, Atlanta (USA) , March 2019.
3. Ryuji Hamamoto. Medical Applications of AI: AI Research in the Era of Precision Medicine. Taiwan-Japan Symposium on the Development of Smart Hospitals and Medical Industry through the Use of AI and IoT, Taipei (Taiwan), July 2019.
4. Ryuji Hamamoto. Application of A.I. in Cancer Research. The 2nd Korea-China-Japan Cancer Control Workshop, Seoul (South Korea), November 2019.
5. Yasunaga M. Development of Antibody-Drug Conjugate Utilizing DDS and Molecular Imaging, Antibody Engineering & Therapeutics Asia, Tokyo. February 2019.
6. Yasunaga M, Manabe S, Asano R, Matsumura Y. Development of a next-generation antibody therapeutics against cancer and autoimmune disease utilizing DDS and molecular imaging. Keystone Symposia: Antibodies as Drugs, Breckenridge (USA), April 2019.

7. Tomoko Watanabe, Takayuki Honda, Hirohiko Totsuka, Eri Arai, Yae Kanai, Kouya Shiraishi, Takashi Kohno. Gene panel based prediction of homologous recombination deficiency in adolescent and young adult breast cancers. American society of human genetics, Houston (USA), October 2019.
8. Tomoko Watanabe, Takayuki Honda, Hirohiko Totsuka, Eri Arai, Yae Kanai, Kouya Shiraishi, Takashi Kohno. Gene panel based prediction of homologous recombination deficiency in adolescent and young adult breast cancers. American society of human genetics, Salt Lake City (USA), November 2019.
9. Chie Kudo-Saito, Yukinori Ozaki, Keiichi Kinowaki, Hidetaka Kawabata, Yamato Ogiwara. A mode of treatment resistance of metastatic tumor cells: propagation exceeds elimination in number. AACR Annual Meeting 2019. Atlanta (USA), April 2019.

Cellular and Molecular Medicine

Associate Professor Junko Sasaki

(1) **Outline**

Phosphoinositides (PIPs) are the molecules that contain phosphatidylinositol, which has a glycerol backbone, two long-chain fatty acids, and an inositol head group. As a result of combinatorial phosphorylation of the hydroxyls of inositol ring, seven other PIPs classes can be generated. Each PIPs exhibits a unique stereochemistry and can bind to distinct cellular protein targets, thereby regulating a wide variety of cellular activities and responses. In terms of PIPs acyl chains, our knowledge about how much importance these hydrocarbon chains have is only limited, in contrast to the phosphorylation patterns. Our goal is to reveal the functions of each PIPs molecular species.

(2) **Research**

Recently, we revealed that the acyl profiles of phosphoinositides are altered in human prostate cancer tissues. Therefore we are currently studying the physiological and pathophysiological functions of each PIPs molecular species by three approaches.

1. Cellular analyses: We examine changes in PIPs molecular species regulating cellular responses, including cell migration, proliferation, and differentiation.
2. In vivo analyses: We examine changes in PIPs molecular species of diseased tissues from gene-targeted mice lacking PIPs metabolizing enzymes.
3. Molecular analyses: We find the binding proteins of each PIPs molecular species by developing new methods for studying lipid-protein interaction.

(3) **Education**

Topics of research for graduate student

1. Cancers and PIPs molecular species
2. Inflammations and PIPs molecular species
3. Disorders of sex development and PIPs molecular species

(4) **Lectures & Courses**

Each student has an independent research theme. Students are expected to have experimental science knowledge and skills.

The goal is to be able to plan, execute, and present original research in cooperation with other researchers.

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

1. Takemasu Shinya, Ito Masaki, Morioka Shin, Nigorikawa Kiyomi, Kofuji Satoshi, Takasuga Shunsuke, Eguchi Satoshi, Nakanishi Hiroki, Matsuoka Isao, Sasaki Junko, Sasaki Takehiko, Hazeki Kaoru. Lysophosphatidylinositol-acyltransferase-1 is involved in cytosolic Ca²⁺ oscillations in macrophages. *Genes to Cells*. 2019.03; 24(5); 366-376
2. Fujioka Y, Satoh AO, Horiuchi K, Fujioka M, Tsutsumi K, Sasaki J, Nepal P, Kashiwagi S, Paudel S, Nishide S, Nanbo A, Sasaki T, Ohba Y. A Peptide Derived from Phosphoinositide 3-kinase Inhibits Endocytosis and Influenza Virus Infection. *Cell structure and function*. 2019.04; 44(1); 61-74
3. Koizumi A, Narita S, Nakanishi H, Ishikawa M, Eguchi S, Kimura H, Takasuga S, Huang M, Inoue T, Sasaki J, Yoshioka T, Habuchi T & Sasaki T.. Increased fatty acyl saturation of phosphatidylinositol phosphates in prostate cancer progression. *Sci Rep*. 2019.09; 9(1); 13257
4. 1. Kawai T, Miyata H, Nakanishi H, Sakata S, Morioka S, Sasaki J, Watanabe M, Sakimura K, Fujimoto T, Sasaki T, Ikawa M & Okamura Y.. PtdIns(4,5)P₂ Distribution Mediated by a Voltage-Sensing Phosphatase (VSP) Regulates Sperm Motility. *Proc. Natl. Acad. Sci. USA*. 2019.12; 116(51); 26020-26028

[Conference Activities & Talks]

1. Junko Sasaki. Molecular mechanisms of phosphoinositide signaling. 9th FAOPS Congress 2019.03.29 Kobe Convention Center
2. 成田 伸太郎, 中西 広樹, 松田 芳教, 小泉 淳, 江口 賢史, 高須賀 俊輔, 黄 明国, 井上 高光, 佐々木 純子, 南条 博, 羽瀧 友則, 佐々木 雄彦. 腎癌におけるイノシトールリン脂質発現プロファイル (The expression profile of phosphatidylinositol phosphates in clinical renal cell carcinoma). *日本癌学会総会記事* 2019.09.01
3. 成田 伸太郎, 中西 広樹, 松田 芳教, 小泉 淳, 江口 賢史, 高須賀 俊輔, 黄 明国, 井上 高光, 佐々木 純子, 南条 博, 羽瀧 友則, 佐々木 雄彦. 腎癌におけるイノシトールリン脂質発現プロファイル. *日本癌学会総会* 2019.09.26

Department of Anatomical and Physiological Science

(1) Publications

[Original Articles]

1. S Virachith, M Saito, Y Watanabe, K Inoue, O Hoshi, T Kubota. Anti- β_2 -glycoprotein I antibody with DNA binding activity enters living monocytes via cell surface DNA and induces tissue factor expression. Clin. Exp. Immunol.. 2019.02; 195(2); 167-178

Department of Molecular and Cellular Biology

Nobuharu Suzuki, Associate Professor

(1) Outline

2019 is the 2nd year for our department, since it was started in 2018. The members were Assoc. Prof. Suzuki and 3 graduate students. Regarding our research, we have three main projects: 1) the molecular mechanism of myelination in the central nervous system, 2) the maintenance system of the stemness of somatic stem cells, and 3) the pericellular microenvironment organized by extracellular matrix molecules. In terms of education, we teach graduate and undergraduate students at lectures and laboratory classes of molecular biology and biochemistry, particularly related to medical tests/technologies. In addition, Suzuki is a member of the administrative offices of Lab Safety and of Open Innovation for Research and contributes to their activities.

(2) Research

1) Molecular mechanism of myelination in the central nervous system

In the central nervous system, myelin is formed by oligodendrocytes and is essential for rapid propagation of neuronal signal. In our department, we investigate its cellular and molecular mechanism using the mutant mouse line that develops hypomyelination in the central nervous system and expand the results of our research to application studies. In 2019, we published two original articles regarding the molecular mechanism of myelination in the central nervous system by the transmembrane protein teneurin-4 and the extracellular protein laminin, and two reviews including our recent research results. In addition, we gave 5 presentations of our recent data at international and domestic meetings.

2) Maintenance mechanism of the stemness of somatic stem cells

We particularly focus on skeletal muscle satellite cells and carry out collaborated works together with other groups.

3) Pericellular microenvironment organized by extracellular matrix molecules

In recent years, research of pericellular microenvironment by extracellular matrix molecules has become popular. In our department, we examine functions of extracellular matrix proteins in myelination in the central nervous system and in maintenance of skeletal muscle stem cells. In 2019, we published an original article that revealed a significance of the microenvironment in migration and survival of oligodendrocyte precursor cells. Moreover, we proceeded further investigation of the study and reported our recent data at the Molecular Biology Meeting.

(3) Education

For undergraduate students, we teach “Medical Genetics and Human Genome Science, Lecture” and “Biochemistry, Laboratory”, and parts of “Advanced Laboratory Sciences”, “Practice of Medical Science” and “General Medical Technology”.

For graduate students, we teach parts of “Medical Technology I” and “Study of Pathogenesis and Pathophysiology” (master course), and a part of “Development of Novel Technologies for Clinical Tests” (Ph.D. course).

(4) Lectures & Courses

At first, we well-explain the fundamental mechanism of phenomena in organisms to students at any classes, since we want them to have curiosity as much as possible. Based on that, we teach them more expertized knowledge and techniques that are essential for medical technologists in order to let them to achieve at a high level of acquisition. In laboratory, we teach students from fundamental to advanced parts of our research field at lectures, journal clubs, and discussions to let them understand the history and our position in the current research field. Finally, we make efforts for students to have high motivation with their research and study and to enjoy new findings.

(5) Clinical Services & Other Works

Suzuki is Special Volunteer at National Institutes of Health (NIH) and a visiting fellow at National Center of Neurology and Psychiatry (NCNP) and contributes to relationships between the research institutes and universities, internationally and domestically. Also, Suzuki is a member of Society for Neuroscience (SfN), The American Society for Cell Biology (ASCB), The Molecular Biology Society of Japan (MBSJ), The Japan Neuroscience Society (JNS), The Japanese Society for Neurochemistry (JSN), and The Japanese Society for Matrix Biology and Medicine (JSMBM) and contributes to their activities.

(6) Publications

[Original Articles]

1. Chikako Hayashi, Nobuharu Suzuki, Yo Mabuchi, Naomi Kikura, Yukina Hosoda, Susana de Vega, Chihiro Akazawa. The extracellular domain of teneurin-4 promotes cell adhesion for oligodendrocyte differentiation. *Biochem. Biophys. Res. Commun.* 2019; in press;
2. Nobuharu Suzuki, Mai Hyodo, Chikako Hayashi, Yo Mabuchi, Kaori Sekimoto, Chinami Onchi, Kiyotoshi Sekiguchi, Chihiro Akazawa. Laminin α 2, α 4, and α 5 Chains Positively Regulate Migration and Survival of Oligodendrocyte Precursor Cells. *Sci Rep.* 2019.12; 9(1); 19882

[Misc]

1. Chikako Hayashi, Nobuharu Suzuki. Morphological and Functional Diversity of Oligodendrocytes in the Central Nervous System *Seikagaku.* 2019.10; 91(5); 701-705
2. Chikako Hayashi, Nobuharu Suzuki. Heterogeneity of Oligodendrocytes and Their Precursor Cells. *Adv. Exp. Med. Biol.* 2019.11; 1190; 53-62

[Conference Activities & Talks]

1. Nobuharu Suzuki, Yoshihiko Yamada. Teneurin-4 Is a Positive Regulator of CNS Myelination through Oligodendrocyte Process Formation. XIV European Meeting on Glial Cells in Health and Disease 2019.07.11
2. Chikako Hayashi, Nobuharu Suzuki, Naomi Kikura, Yukina Hosoda, Yo Mabuchi, Chihiro Akazawa. Molecular Interaction between Oligodendrocytes and Axons through Teneurins for CNS Myelination. XIV European Meeting on Glial Cells in Health and Disease 2019.07.11
3. Chinami Onchi, Momo Ooishi, Chikako Hayashi, Yukina Hosoda, Nobuharu Suzuki. Biological Activity of Laminin E3 Fragments on Oligodendrocyte Precursor Cells. The 42nd Annual Meeting of the Molecular Biology Society of Japan 2019.12.03
4. Chikako Hayashi, Riko Takahashi, Yukina Hosoda, Chinami Onchi, Nobuharu Suzuki. Teneurin-4 Controls the Development of Type I/Type II Oligodendrocytes and Myelination of Small Diameter Axons. The 42nd Annual Meeting of the Molecular Biology Society of Japan 2019.12.04
5. Yukina Hosoda, Yuki Munakata, Chikako Hayashi, Chinami Onchi, Nobuharu Suzuki. The molecular interaction of Teneurin-4 with actin binding protein CNP in oligodendrocytes. The 42nd Annual Meeting of the Molecular Biology Society of Japan 2019.12.04

[Others]

1. 2019 Inamori Research Grants, 2019.04
Elucidation of the molecular mechanism of neuronal activity-dependent myelination in the central nervous system
2. The research grant for medicine by Takeda Science Foundation in 2019, 2019.06
The mechanism of CNS myelination through axon diameters and oligodendrocyte subtypes

Department of Molecular Pathology

Professor: Motoji Sawabe

Assistant Professor: Yurie Soejima

Graduate student (Doctoral Program): Tamami Denda, Ayana Horiguchi, Nobuyuki Nakamura, Kana Miyata, Yuichi Koyama, Mizuho Sato, Yoshifumi Morita, Mayumi Kinoshita, Akiya Tatsumi, Minami Kikuchi

Graduate student (Master's Program): Miho Takeuchi, Satsuki Yuba, HATTHAKONE THAVISOUK, Nao Miyamoto, KO PO JUI, SAKHA SUJATA

Graduate Research student: OUNDAVONG SUNTI

Clerical assistant: Hitomi Sasaki

(1) Outline

Pathology is the basic science of medicine that involved both the basic and clinical stages to elucidate the essence of diseases.

Pathological techniques play a role in conducting higher quality diagnoses by various examinations and methods such as histology, cytology, immunohistochemistry, electron microscopy, and genetic analysis. We explore the essence of the diseases in both aspects of pathology and pathological techniques.

(2) Research

In our department, we research the following programs in order to investigate and elucidate the etiology and pathophysiology, and further to explore and develop the theoretics and methods of examination that can contribute to the diagnosis.

1. Immunohistochemical analysis of human and mouse cardiac conduction system
2. Proteomic analysis of human cardiac aging
3. Proteome analysis and immunohistochemical study of arterial and cardiac aging
4. Molecular epidemiologic and clinicopathological study of Lipoprotein(a)
5. Molecular pathological study of hepatobiliary tumors
6. Histological and cytological analysis for early diagnosis of biliary tract cancer

(3) Education

In the undergraduate course, students learn the etiology and pathophysiology of basic disease in Pathological Technology, lecture and practice (Medical Technology), and Pathology (Nursing science).

In graduate school, we provide education and conduct the research with the aim of exploring, developing, and systematizing the theoretics and methods of molecular pathological techniques with a higher level of pathological expertise and a broad international perspective.

(4) Lectures & Courses

In order to cultivate medical professionals with interdisciplinary and international perspectives, precious humanity and high ethical values, the ability of self-problem raising and solution, life-long-thinking, the following education are providing.

1) Undergraduate education

- ・ In the second grade of Medical Technology and Nursing science, students learn common changes in disease, the essence of pathogenesis, and their origins systematically in the general theory of Pathology/Pathological technology.
- ・ In the second grade of Medical Technology, practical training of pathological examination is organized to contribute to the diagnosis of diseases and elucidation the pathogenesis, such as various special staining methods, immunohistochemistry, cytology, and frozen section, in addition to visual inspection of organs, basic preparation of specimens and observation.
- ・ In the second grade of Nursing science, we have pathological anatomical observation as a part of the Practice of Medical Sciences.
- ・ In the fourth grade of Medical Technology, we provide the education of the basics of research, such as how to proceed with the study and how to write the research paper as the Undergraduate Research, and pathological examination practice is carried out at the Department of Pathology in TMDU hospital as Clinical Practice.

2) Graduate education

- ・ In the Master' s Program, we discuss essentials of diseases, with the investigation and understanding the origin, pathophysiology, and pathological characteristics (macroscopical, histological, cytological and molecular pathological) of the disease. Furthermore, students learn the theory and method of pathological techniques (immunohistochemistry, electron microscopy, image analysis, etc.), which useful for elucidation pathophysiology and diagnosis. In addition, students will acquire the skills of quality management and problem-solving in the laboratory. We participate in various research meetings and academic societies and learn about the current status and prospects of international and interdisciplinary research in the pathology/pathological techniques field. Through this course, students will complete their research as a Master' s thesis and acquire basic research ability.
- ・ In the Doctoral Program, we provide higher education, research instruction and medical English learning to acquire the independent research skills that internationally applicable.

(5) Clinical Services & Other Works

- ・ In the Pathology department of the Medical hospital, Sawabe participates in the pathological diagnosis of autopsy cases, Soejima participates in the cytological diagnosis.
- ・ At the Ministry of Health, Labor and Welfare, medical technology international development promotion project 2019 "Human Resource and System Developments for Cervical Cancer Screening in Cambodia", Sawabe and Soejima participated as an instructor of pathologists and medical technologists in the request of the National Center for Global Health and Medicine, Japan.

(6) Publications

[Original Articles]

1. Soulideth Vilayvong, Kiyomi Hando, Masaki Sekine, Thitsamay Luangxay, Phetsamone Arounlangsy, Pheangvilay Xaysomphet, Phetlammone Xayaphet, Hatthakone Thavisouk, Yurie Soejima, Masanobu Kitagawa, Motoji Sawabe. Useful Application of Immunostaining to Malignant Pleural Effusion among Lao People in Vientiane Capital, Lao PDR Asian Pac. J. Cancer Prev. 2019.01; 20(1); 243-248
2. 梅澤 敬, 落合 和彦, 山田 恭介, 落合 和徳, 岡本 愛光, 九十九 葉子, 坂本 穆彦, 沢辺 元司. 子宮頸がん健診における split-sample による液状化細胞診法と従来法の子宮頸部扁平上皮内病変検出率と検体不適正率に関する研究 日本での経験 (Comparative study of squamous intraepithelial lesion detection and unsatisfactory rates

- between liquid-based cytology and conventional smears from a split sample in cervical cancer screening: A Japanese experience) 医学検査. 2019.01; 68(1); 19-25
3. Luangxay T, Virachith S, Hando K, Vilayvong S, Xaysomphet P, Arounlangsy P, Phongsavan K, Mieno MN, Honma N, Kitagawa M, Sawabe M. Subtypes of Breast Cancer in Lao P.D.R.: A Study in a Limited-Resource Setting Asian Pacific journal of cancer prevention : APJCP. 2019.02; 20(2); 589-594
 4. Matsuda Y, Tanaka M, Sawabe M, Mori S, Muramatsu M, Mieno MN, Ishiwata T, Arai T. The stem cell-specific intermediate filament nestin missense variation p.A1199P is associated with pancreatic cancer. Oncology letters. 2019.05; 17(5); 4647-4654
 5. Tanaka Nobuho, Tashiro Toshiyuki, Katsuragawa Yozo, Sawabe Motoji, Furukawa Hiroshi, Fukui Naoshi. Expression of minor cartilage collagens and small leucine rich proteoglycans may be relatively reduced in osteoarthritic cartilage BMC MUSCULOSKELETAL DISORDERS. 2019.05; 20(1); 232
 6. Nomura Y, Tanaka T, Kobayashi H, Kimura Y, Soejima Y, Sawabe M. A 3-Dimensional Model of the Human Round Window Membrane. The Annals of otology, rhinology, and laryngology. 2019.06; 128(6_suppl); 103S-110S
 7. Matsuda Y, Nonaka K, Seki A, Kakizaki M, Takakuma S, Hamamatsu A, Wang T, Nakano Y, Takata T, Takahashi-Fujigasaki J, Murayama S, Sawabe M, Arai T. Disseminated varicella zoster virus infection and acute hepatitis: Autopsy-proven cases from a single institute. Pathology international. 2019.06; 69(6); 378-380
 8. Matsuda Yoko, Nonaka Keisuke, Seki Atsuko, Kakizaki Mototsune, Takakuma Shoichiro, Hamamatsu Akihiko, Wang Tan, Nakano Yuta, Takata Tadayuki, Takahashi-Fujigasaki Junko, Murayama Shigeo, Sawabe Motoji, Arai Tomio. Disseminated varicella zoster virus infection and acute hepatitis: Autopsy-proven cases from a single institute(和訳中) Pathology International. 2019.06; 69(6); 378-380
 9. Morita Y, Kurano M, Sakai E, Nishikawa M, Sawabe M, Aoki J, Yatomi Y. Evaluation of Lysophospholipid Measurement in Cerebrospinal Fluid Samples using Liquid Chromatography-Tandem Mass Spectrometry. Lipids. 2019.08; 54(8); 487-500
 10. An J, Naruse TK, Hinohara K, Soejima Y, Sawabe M, Nakagawa Y, Kuwahara K, Kimura A. MRTF-A regulates proliferation and survival properties of pro-atherogenic macrophages. Journal of molecular and cellular cardiology. 2019.08; 133; 26-35
 11. Tsumoto H, Iwamoto M, Yamaguchi Y, Ko P, Soejima Y, Yoshida S, Miura Y, Toda T, Arai T, Hamamatsu A, Endo T, Sawabe M. Age-associated proteomic alterations in human aortic media. Geriatrics & gerontology international. 2019.08;
 12. Nobuyuki Nakamura, Takeshi Fujii, Yurie Soejima, Motoji Sawabe. Optimization of trypsin treatment condition utilizing immunohistochemistry for chromogenic in situ hybridization. Pathol. Int.. 2019.09;
 13. Sugino Mire, Naitou Takeshi, Sawabe Motoji, Kanbara Masayuki, Sawabe Taishi, Mizohata Satoko, Aryal Gopi, Dahal Minakshi, Jha Ranjana, Shrestha Bimash, Sha Ashish, Biraj Singh, Bhattarai Prashanta, Sareesha Shrestha, Paudyal Binay. Developing school health record system for government school students in Nepalese villages(和訳中) 国際保健医療. 2019.09; 34(3); 168
 14. Kana Miyata-Morita, Shigeki Morita, Noriyuki Matsutani, Fukuo Kondo, Yurie Soejima, Motoji Sawabe. Frequent appearance of club cell (Clara cell)-like cells as a histological marker for ALK-positive lung adenocarcinoma. Pathol. Int. 2019.10;
 15. Morita Yoshifumi, Kurano Makoto, Sakai Eri, Nishikawa Takako, Nishikawa Masako, Sawabe Motoji, Aoki Junken, Yatomi Yutaka. Analysis of urinary sphingolipids using liquid chromatography-tandem mass spectrometry in diabetic nephropathy JOURNAL OF DIABETES INVESTIGATION. 2019.10;
 16. Wang T, Matsuda Y, Nonaka K, Kakizaki M, Ishiwata T, Kanazawa N, Uegaki S, Muramatsu M, Sawabe M, Mori S, Tanaka M, Kitagawa M, Arai T. Clinicopathological characteristics of gastric cancer with carbohydrate antigen 19-9 expression occurring in elderly individuals: An autopsy study. Pathology international. 2019.12;
 17. Miura Y, Hayakawa A, Kikuchi S, Tsumoto H, Umezawa K, Chiba Y, Soejima Y, Sawabe M, Fukui K, Akimoto Y, Endo T. Fumarate accumulation involved in renal diabetic fibrosis in Goto-Kakizaki rats. Archives of biochemistry and biophysics. 2019.12; 678; 108167

18. Akaba Hiroki, Fujita Noriko, Stauch Gerhard, Matsumoto Yasuyo, Wakasa Tomoko, Kawahara Kunimitsu, Sawabe Motoji, Kawai Toshiaki. How can we strengthen pathology services in Cambodia?(和訳中) Global Health & Medicine. 2019.12; 1(2); 110-113

[Books etc]

1. Junichi Koyatsu, Sadayuki Hiroi, Yurie Soejima, Sakae Hata, Osamu Nunobiki, Daisuke Sano, Hitoshi Abe, Hironori Katayama, Kyoko Komatsu. “The 5 Ms “ Practical Guide to Histologic, Cytologic, and Pathologic Preparation — Materials, Methods, Machines, Maintenance, and Management. 2019.08

[Conference Activities & Talks]

1. Kei Kono, Keiichi Kinowaki, Yurie Soejima, Junichiro Sato, Atsuko Hosoi, Yoshifumi Ubara, Masaji Hashimoto, Takeshi Fujii, Fukuo Kondo, Toshio Fukusato. Multiple focal nodular hyperplasia in polycystic liver disease associated with ADPKD:A case report. The 108th Annual Meeting of The Japanese Society of Pathology 2019.05.09
2. 廣井禎之, 小松京子, 沢辺元司, 副島友莉恵, 片山博徳, 布引治, 河合俊明, 若狭朋子. 子宮頸がん検診のための病理技術者育成と体制整備事業(カンボジア)における病理標本の質向上 2018. 第 108 回日本病理学会総会 2019.05.09 東京
3. Miho Takeuchi, Yurie Soejima, Nao Miyamoto, Takumi Akashi, Motoji Sawabe, Toshio Fukusato. Expression analysis of beta6 integrin and TGF- β 1, alpha-SMA in intrahepatic cholangiocarcinoma. The 108th Annual Meeting of The Japanese Society of Pathology 2019.05.09
4. 副島友莉恵, 高槻祐菜, 中嶋裕, 今田安津子, 明石巧, 小林正典, 田邊稔, 沢辺元司, 福里利夫. 胆道上皮内腫瘍における $\alpha 6 \beta 4$, $\alpha v \beta 6$ インテグリンの発現. 第 108 回日本病理学会総会 2019.05.09 東京
5. Proteomic Analysis of Human Myocardium in Heart Failure with Preserved Ejection Fraction. 2019.07.24
6. Huy Chan Kong, Matsumoto Yasuyo, Sovanara Hang, Rayounette Krouch, Akaba Hiroki, Ohara Kaori, Soejima Yurie, Katayama Hironori, Hiroi Sadayuki, Wakasa Tomoko, Komatsu Kyoko, Fujita Noriko, Kawai Toshiaki. Preparation of the establishment of National Maternal and Child Health Center (NM-CHC) pathology department. 第 58 回日本臨床細胞学会秋期大会 2019.11.16 岡山
7. Pich Pintuna, Yasuyo Matsumoto, Kaori Ohara, Tomoko Wakasa, Yurie Soejima, Hironori Katayama, Sadayuki Hiroi, Kyoko Komatsu, Noriko Fujita, Toshiaki Kawai. Our Training course for Cambodian technologists in Japan. 第 58 回日本臨床細胞学会秋期大会 2019.11.16 岡山
8. 安健博, 成瀬妙子, 日野原邦彦, 副島友莉恵, 沢辺元司, 中川靖章, 桑原宏一郎, 久場敬司, 木村彰方. MRTF-A はマクロファージ機能を制御して動脈硬化形成に関わる. 第 29 回日本循環薬理学会 第 55 回高血圧関連疾患モデル学会 合同学会 2019.11.29 香川

Department of Respiratory and Nervous System Science

Professor: Yuki Sumi, MD, PHD.

Assistant Professor: Miho Akaza, MD, PHD.

Part-time: Keiko Hara, MD, PHD. Katsuya Ota, MD, PHD.

Doctoral: Yuri Ichikawa, MT, Msc.

Master's: Fumika Koike MT. Takao Miyoshi MT. Yuri Yoshimura MT.

Students: Saori Kaminaka. Nozomi Sano. Miri Takahashi. Yuki Takemoto

(1) Outline

We research and educate on the respiratory and nerves systems. Our interests are looking at the living body as an integrated system from the molecular and cellular level to the organs and looking at the relationship between clinical medicine and physiological tests.

Until last year, research and education on respiratory, cardiovascular, and nerves were conducted by the name of "Biofunctional Informatics". At the time of reorganization of Tokyo Medical and Dental University, cardiovascular division separated, and we moved from "Graduate School of Health Care Sciences" to "Graduate School of Medical and Dental Sciences" and was renamed to "Respiratory and Nervous System Science".

(2) Research

The research is conducted independently in each field by specialists in the respiratory and nervous system.

In the respiratory field, we are studying the clinical significance of new lung function tests, mechanisms and endotype classification of bronchial asthma and COPD, gene therapy for lung diseases, and diagnostic imaging using AI.

In the central nervous system area, we are researching on electroencephalogram (EEG) and epilepsy, and in the peripheral nervous system area, we are developing a new imaging methods.

(3) Education

In education, we provide education in general clinical medicine and acquire theory and skills through lectures and practical training in physiological function tests (lung function, EEG, peripheral nerve tests, various sonography, etc.). Undergraduate and graduate research educations are conducted in each specialized field.

1) Undergraduate student education

In the 1st year, a lecture on "Respiratory and Nervous System Science" is given on Advanced Laboratory Sciences. Second-year students have Physiological Laboratory Science, Lecture(I). Here students learn the basics of EEG, lung function tests, and sonographies. Physiological Laboratory Science, Lecture(II) and Physiological Laboratory Science, Laboratory(II) will be conducted jointly with the cardiovascular field in the 3rd years (2nd and 3rd years in the new curriculum). The contents include neurophysiological examination, respiratory examination, circulatory examination, ultrasonic examination, image analysis, thermography, sense of equilibrium function examination, fundus examination, and other basic examinations such as blood sampling practice, sample collection, etc. We also provide education on clinical techniques in general, including taking vital signs and procedures for critical care. In the 4th graders, students undergo Undergraduate research given on the research methods and minds, focusing on the research theme assigned to each person. In the clinical training, practical training of respiratory tests including blood gas measurement, EEG, evoked potential test,

and abdominal ultrasonography will be given during two weeks.

2) Graduate education

In the Master's course, we are in charge of Medical Technology I, Medical Technology II, Seminar of Respiratory and Nervous System Science, Practice of Respiratory and Nervous System Science, and Respiratory and Nervous System Analysis Research for Thesis. Medical Technology I deepens the understanding of the scientific knowledge that is the basis of clinical tests currently being conducted in the medical field from various levels of genes, molecules, cells, tissues, and individuals, and further toward the future. The purpose is to reinforce the foundation for studying research topics. The purpose of Medical Technology II is to deepen the understanding of clinical tests currently being conducted in the medical field and to develop the ability to consider future research issues. In each lecture of Respiratory and Nervous Systems Science, we educate new knowledge and techniques, clarify areas that have already been elucidated and areas that do not, and acquire scientific research attitudes to clarify areas that are still unknown.

In the Doctoral course, we are in charge of Clinical Reasoning and Respiratory and Nervous System Science. In the Clinical Reasoning, we aim to cultivate the clinical laboratory technologists who can discuss with physicians of inferring disease conditions from laboratory data. In the Respiratory and Nervous System Science, we aim to teach the theory and techniques to inspect the living body as an integrated system. In particular, students learn the cutting edge medical knowledge in the respiratory or nervous system, the methodology to analyze the relationship between the biological information obtained by the examination and the pathogenesis, and the theory and techniques to developed novel examination methods.

(4) Lectures & Courses

What is important in education is to motivate learning. In particular, in the lower grades of undergraduate students, many students do not understand how basic learning is useful, and are not motivated to study despite being important. For this reason, we have increased practical training, conducted early exposure to understand how it is needed in the clinical setting. We wish students to be eager to learn and to acquire competency as if the water is soaking into dry sand.

In particular, as the physiological function testing is a clinical front line that is conducted in direct contact with patients, we educate from the standpoint of clinical medicine. The goal is that students learn theories and techniques of clinical physiological examinations in nerves, respiration, cardiovascular, digestive organs, and diagnostic imaging, and be able to apply them to researches. Physiological function testing involves not only device operation, safety measures, recording of biological phenomena, data organization / analysis techniques and knowledge, but also testing directly in contact with humans, so medical knowledge about diseases, medical ethics and communication skills are also required. It is also important to cultivate the ability to quickly recognize and take appropriate measures for test results that require emergency treatment of patients. In addition to these, we are also educating students on how to respond to sudden changes in patients during testing.

(5) Clinical Services & Other Works

Dr. Sumi is a Respiratory specialist and Respiratory instructor, and Allergy specialist certified by the academic society. He treats patients at respiratory medicine department in the hospital. He also takes care of the study groups of doctors and takes part in as discussant. He gave lecture at Evening seminar for medical interns, at CC (Clinical Clerkship) in respiratory medicine for undergraduate 5th and 6th grade medical students, at PCC (Preparation for Clinical Clerkship) in respiratory internal medicine for 4th year undergraduate medical students, at Respiratory Internal medicine for 3rd year undergraduate medical students, at Respiratory physiology for 2nd year undergraduate medical students, and at MIC (Medical Introductory Course) for 1st year undergraduate medical students.

The neurologist, Dr. Akaza, is familiar with peripheral neuropathy in addition to neurological diseases in general, and plays a central role in performing peripheral nerve tests and evaluating results in medical hospitals.

Dr. Hara is the psychiatrist, Mental health designated physician, specialist / instructor of the Japan Epilepsy Society, certified by the Japanese Society of Clinical Neurophysiology (EEG), and Delegate of the Japanese Society of Clinical Neurophysiology, Councilor of the Japan Pharmacology-EEG Society, Board secretary of the Japan Epilepsy Society. She examines many patients with epilepsy in the outpatient department including second opinions. In cooperation with the Department of Neurosurgery, she attends weekly EEG conferences, monthly EEG and epilepsy lectures, and analyzes high frequency EEG (HFO). She also performs intraoperative electroencephalogram measurements in many brain surgeries.

(6) Clinical Performances

Dr. Akaza is a specialist in peripheral nerve function testing and performs most tests for neurological patients. She is conducting clinical research on peripheral neuropathy in diabetic patients.

Dr. Hara treats many patients with epilepsy including second opinions. She specializes in the treatment of pregnant women with epilepsy. In cooperation with obstetrics and gynecology doctors, patients with epilepsy are referred to her consultant before pregnancy since 2013.

(7) Publications

[Original Articles]

1. Yoshimura Yuri, Hara Keiko, Akaza Miho, Ohta Kaseya, Sumi Yuki, Inaji Motoki, Yanagisawa Eriko, Maehara Taketoshi. Effects of antiepileptic monotherapy on hematological and biochemical parameters(和訳中) *Epilepsy & Seizure*. 2019; 11(1); 1-13
2. Jinta T., Fruie W., Otani Y., Tani C., Takemoto Y., Waku M., Miyoshi T., Koike F., Kubota T., Miyazaki Y., Akaza M., Sumi Y.. Evaluating the Effectiveness of a Commercial Portable Air Purifier in Asthma *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE*. 2019; 199;
3. Yuri Yoshimura, Keiko Hara, Miho Akaza, Kaseya Ohta, Yuki Sumi, Motoki Inaji, Eriko Yanagisawa, Taketoshi Maehara. Effects of antiepileptic monotherapy on hematological and biochemical parameters *Epilepsy and Seizure*. 2019.01; 11(1); 1-13
4. Furuie Wakaba, Nagai Saya, Kudo Toshifumi, Inoue Yoshinori, Akaza Miho, Sasano Tetsuo, Sumi Yuki. Predictive preoperative factors of long-term survival rate after open surgery for abdominal aortic aneurysm *Journal of Medical and Dental Sciences*. 2019.03; 66(1); 13-22
5. Waku Marika, Furuie Wakaba, Otani Yoshio, Takemoto Yuki, Koike Fumika, Miyoshi Takao, Tani Chihiro, Miyazaki Yasunari, Inase Naohiko, Akaza Miho, Kubota Tetsuo, Sumi Yuki. 喘息患者の寝室内の空気の質と空気清浄機の使用効果 (Indoor air quality in the bedrooms of patients with asthma and the effect of using air purifiers) *日本呼吸器学会誌*. 2019.03; 8(増刊); 365
6. Takao Miyoshi, MSc, Ikumi Sasaki, MT, Fumika Koike, MSc, Saki Oyama, MT, Wakaba Furuie, MT, Miho Akaza, MD, PhD, Tetsuo Sasano, MD, PhD, Meiyo Tamaoka, MD, PhD, Yasunari Miyazaki, MD, PhD, Naohiko Inase, MD, PhD and Yuki Sumi, MD, PhD. Efficacy and Tolerability of the Nasal Airway Stent in the Treatment of Snoring *Clinical Medical Reviews and Case Reports*. 2019.04; 6(3); 1-7
7. Takao Miyoshi, Ikumi Sasaki, Fumika Koike, Miho Akaza, Tetsuo Sasano, Meiyo Tamaoka, Yasunari Miyazaki, Naohiko Inase and Yuki Sumi. Phenotype classification of Chronic Obstructive Pulmonary Disease in Tokyo *Diseases and Disorders*. 2019.04; 2; 1-7-7-7
8. Waku Marika, Furuie Wakaba, Otani Yoshio, Koike Fumika, Miyoshi Takao, Takemoto Yuki, Takahashi Miri, Akaza Miho, Sasano Tetsuo, Sumi Yuki. Indoor air quality in the bedrooms of patients with asthma and the effect of using air purifiers *アレルギー*. 2019.05; 68(4-5); 443
9. Iino Hiroko, Okano Tomoko, Daimon Masao, Sasaki Kazuno, Chigira Mayumi, Nakao Tomoko, Mizuno Yoshiko, Yamazaki Tsutomu, Kurano Makoto, Yatomi Yutaka, Sumi Yuki, Sasano Tetsuo, Miyata Tetsuro. 動脈硬化症の評価における頸動脈ストレイン値の有用性 (Usefulness of Carotid Arterial Strain Values for Evaluating the Arteriosclerosis) *Journal of Atherosclerosis and Thrombosis*. 2019.05; 26(5); 476-487
10. Iijima Y, Tateishi T, Tsuchiya K, Sumi Y, Akashi T, Miyazaki Y. A Case of Pneumoconiosis Caused by Inhalation of Metallic Titanium Grindings. *Internal medicine (Tokyo, Japan)*. 2019.10;
11. Kaminaka S., Akaza M., Kawabata S., Watanabe T., Miyano Y., Iida S., Sasaki T., Adachi Y., Sekihara K., Kanouchi T., Sumi Y., Okawa A., Yokota T.. Diagnosis of C8 radiculopathy by magnetospinogram *JOURNAL OF THE NEUROLOGICAL SCIENCES*. 2019.10; 405;
12. Akaza Miho, Kawabata Shigenori, Watanabe Taishi, Hasegawa Yuki, Iida Shintaro, Sasaki Toru, Adachi Yoshiaki, Sekihara Kensuke, Kanouchi Tadashi, Sumi Yuki, Okawa Atsushi, Yokota Takanori. Diagnosis of C8 radiculopathy by magnetospinogram(和訳中) *臨床神経学*. 2019.11; 59(Suppl.); S406

[Conference Activities & Talks]

1. Marika Waku, Wakaba Furuie, Yoshio Otani, Yuki Takemoto, Fumika Koike, Takao Miyoshi, Chihiro Tani, Yasunari Miyazaki, Naohiko Inase, Miho Akaza, Tetsuo Kubota, Yuki Sumi. Indoor air quality in the bedrooms of patients with asthma and the effect of using air purifiers.. The 59th Annual Meeting of the Japanese Respiratory Society 2019.04.12 Tokyo, Japan
2. T. Jinta, W. Fruie2, Y. Otani, C. Tani, Y. Takemoto, M. Waku, T. Miyoshi, F. Koike, T. Kubota, Y. Miyazaki, M. Akaza, Y. Sumi. Evaluating the Effectiveness of a Commercial Portable Air Purifier in Asthma. ATS INTERNATIONAL CONFERENCE 2019.05.19 dallas, tx
3. Marika Waku, Wakaba Furuie, Yoshio Otani, Yuki Takemoto, Fumika Koike, Takao Miyoshi, Chihiro Tani, Yasunari Miyazaki, Naohiko Inase, Miho Akaza, Tetsuo Kubota, Yuki Sumi. Indoor air quality in the bedrooms of patients with asthma and the effect of using air purifiers. The 68th Annual Meeting of Japanese Society of Allergology 2019.06.14 Tokyo, Japan
4. 上中 沙鈴、赤座 実穂、笹野 哲郎、窪田 哲朗、角 勇樹、市川 由理. 腹部エコー技術習得のための新たな active learning の試み. 第 14 回日本臨床検査学教育学会学術大会 2019.08.22 熊本保健科学大学 50 周年記念館・1 号館・3 号館

Department of Cardiovascular Physiology

Associate Professor
Tetsuo Sasano
PhD course student
D3 Hiroko Iino
D2 Kayoko Takada
D1 Hiroaki Komuro
Master course student
M2 Anna Suzuki, Naomi Takahashi
M1 Kanae Sasaki, Risako Chiba, Ryota Mieda, Fuyuko Watanabe
Collaborator
Satomi Hamada
Technical assistant
Yuuka Nakagama

(1) Outline

Our department performs basic research focusing on the cardiovascular disease and clinical research regarding physiological assessment of cardiovascular system. Our another mission is to cultivate academic medical technologists who can design basic and clinical studies from clinical questions.

(2) Research

We perform basic research and clinical physiological research. The first topic of basic research is to elucidate the pathophysiological mechanisms focusing on the intercellular communication in cardiovascular diseases. The second topic is to clarify the functional contribution of genes identified by genome-wide association study in the field of cardiac diseases. The third topic is to develop a novel therapeutic strategy using novel gene transfer method and new biomaterials.

Regarding the clinical physiological research, we develop the novel frequency analysis of surface electrocardiogram (ECG), and application of artificial intelligence on the analysis of ECG. In addition, we are inventing the noninvasive monitoring of blood pressure using novel biosensors. Our another purpose is to establish biomarkers to assess cardiovascular diseases, focusing on the extracellular nucleotides and vesicles.

(3) Education

Our mission on the education is to acquire the technique of physiological examinations on the cardiovascular field like electrocardiogram, ultrasound echocardiogram, vascular ultrasonography, pulse wave velocity measurement, vascular endothelial function, and venous function assessment.

(4) Lectures & Courses

We aim to cultivate an academic technologist who can design the basic and clinical researches based on the clinical questions.

(5) Clinical Services & Other Works

Our clinical service includes outpatient clinic in medical hospital, and the supervision of ECG assessment in dental hospital. Dr. Sasano also works as several committee chairs in Japanese Heart Rhythm Society.

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

1. Kawaguchi N, Okishige K, Yamauchi Y, Kurabayashi M, Nakamura T, Keida T, Sasano T, Hirao K, Valderrábano M. Clinical impact of ethanol infusion into the vein of Marshall on the mitral isthmus area evaluated by atrial electrograms recorded inside the coronary sinus. *Heart rhythm*. 2019.01;
2. Komuro Hiroaki, Sasano Tetsuo, Horiuchi Naohiro, Yamashita Kimihiro, Nagai Akiko. The effect of glucose modification of hydroxyapatite nanoparticles on gene delivery *JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A*. 2019.01; 107(1); 61-66
3. Shigeta Takatoshi, Okishige Kaoru, Aoyagi Hideshi, Nishimura Takuro, Nakamura Rena A., Ito Naruhiko, Tsuchiya Yusuke, Asano Mitsutoshi, Shimura Tsukasa, Suzuki Hidetoshi, Kurabayashi Manabu, Fukami Yuichi, Sakita Shinya, Keida Takehiko, Sasano Tetsuo, Hirao Kenzo, Yamauchi Yasuteru. Clinical investigation of esophageal injury from cryoballoon ablation of persistent atrial fibrillation *PACE-PACING AND CLINICAL ELECTROPHYSIOLOGY*. 2019.02; 42(2); 230-237
4. Nishimura T, Yamauchi Y, Aoyagi H, Tsuchiya Y, Shigeta T, Nakamura R, Yamashita M, Asano M, Nakamura T, Suzuki H, Shimura T, Kurabayashi M, Keida T, Sasano T, Hirao K, Okishige K. The clinical impact of the left atrial posterior wall lesion formation by the cryoballoon application for persistent atrial fibrillation: Feasibility and clinical implications. *Journal of cardiovascular electrophysiology*. 2019.02;
5. Suzuki Y, Miyajima M, Ohta K, Yoshida N, Watanabe T, Fujiwara M, Okumura M, Nakamura M, Sasano T, Kawara T, Matsuura M, Matsushima E. Changes in cardiac autonomic nervous system activity during a course of electroconvulsive therapy. *Neuropsychopharmacology reports*. 2019.03; 39(1); 2-9
6. Suzuki Yoko, Miyajima Miho, Ohta Katsuya, Yoshida Noriko, Watanabe Takafumi, Fujiwara Mayo, Okumura Masaki, Nakamura Mitsuru, Sasano Tetsuo, Kawara Tokuhiro, Matsuura Masato, Matsushima Eisuke. Changes in cardiac autonomic nervous system activity during a course of electroconvulsive therapy(和訳中) *Neuropsychopharmacology Reports*. 2019.03; 39(1); 2-9
7. Okishige K, Shigeta T, Nishimura T, Nakamura RA, Hirao T, Yoshida H, Yamauchi Y, Sasano T, Hirao K. Cryofreezing catheter ablation of adenosine triphosphate sensitive atrial tachycardia. *Journal of cardiovascular electrophysiology*. 2019.04; 30(4); 528-537
8. Nakamura R, Okishige K, Shigeta T, Nishimura T, Kurabayashi M, Yamauchi Y, Sasano T, Hirao K. Clinical comparative study regarding interrupted and uninterrupted dabigatran therapy during perioperative periods of cryoballoon ablation for paroxysmal atrial fibrillation. *Journal of cardiology*. 2019.04;

Analytical Laboratory Chemistry

Professor:

- 2019.1-3 : Minoru Tozuka
- 2019.4-12 : Ryunosuke Ohkawa

Assistant Professor:

- 2019.1-3 : Ryunosuke Ohkawa
- 2019.10-12 : Takahiro Kameda

Graduate Students:

(Master students)

- 2019.1-3 : Konomi Igarashi, Mai Sasaoka, Yuki Fujii
- 2019.4-12 : Mayu Nambu, Yuka Yamagata

(Doctoral Students)

- 2019-1-12 : Yuna Horiuchi, Shao Jui Lai
- 2019-1-12 : Yuko Mishima, Tamaki Kobayasi

(Under Graduate Students)

- 2019.1-3 : Mutumi Gotanda, Yuri Sonoda
- 2019.4-12 : Ayuko Hara, Yume Mutuda

(1) Outline

The central mission of the Analytical Laboratory Chemistry is to educate and research through “Clinical Chemistry” in Clinical Laboratory Science. Our topic is “Development of a new biomarker to predict a risk for cardiovascular disease”. To achieve our goal, skill and ability to create new reliable method are required. Development of students who can give back to a society through active outreach like publishing a paper and presenting at a congress is most important. We also aim to develop a Biomedical Laboratory Scientist who not only plays a pivotal role in medical front but also be active in education or research institutes. For that reason, creation of a laboratory where students can throw themselves into their research with enjoyment is essential.

(2) Research

We analyze lipoproteins and its components; cholesterol, triglyceride, apolipoproteins and their metabolites. Through these studies, we are aiming toward developing a new biomarker to predict a risk for cardiovascular disease in an early stage. In detail, we are focusing on cholesterol efflux capacity (reverse cholesterol transport, RCT), antioxidant ability and anti-inflammatory effect for high-density lipoprotein and its main apolipoprotein, apolipoprotein A-I. Our hypothesis is that evaluation of these capacities would be available to make a specific diagnosis for coronary artery disease (CAD).

Many risk factors for CAD have been reported and testing these factors have been contributing to reduce the risk in some patients with CAD. However, despite many people are trying to keep their health to reduce their risk for heart disease, the actual number of heart event have not been decreased. We believe that investigating the mechanism of progression of atherosclerosis by analyzing RCT, antioxidant ability and anti-inflammatory

effect in HDL would lead to find useful biomarker and establish new assay for diagnosis for cardiovascular disease.

Research Focus

- Development of a new biomarker to estimate residual risk for cardiovascular disease
- Study on the functions of chemically modified HDL and apolipoprotein A-I
- Study on the functions and clinical significance of apolipoprotein E containing HDL

(3) Lectures & Courses

Undergraduate education: Main topic is Analytical Laboratory Chemistry which includes Urinalysis & Body Fluid Tests and Clinical Chemistry. In addition, Associate Professor Masayuki Hara from General Isotope Research Division helps to educate radioisotope. We aim to educate student to become a leader of biomedical laboratory scientist in hospital or company. Our final goal is that student develop their creativities to think, solve a problem and improve by themselves.

Graduate education: Analytical skill is essential for research. There is no research achievement without analytical skill. Our first purpose is to understand an importance of reliable analytical skill and obtain the skill. Next, by using these skills, we aim to find new biomarker and develop a novel assay for the biomarker. Though these research process, students can obtain the analytical skill and cultivate capacity as researcher to make a research plan and choose the optimal way to proceed by themselves. Moreover, students can develop their outreach skill through presenting their research achievements at a congress and publishing their papers.

(4) Publications

[Original Articles]

1. Yuna Horiuchi, Ryunosuke Ohkawa, Shao-Jui Lai, Azusa Yamazaki, Hayato Ikoma, Kouji Yano, Takahiro Kameda, Minoru Tozuka. Characterization of the cholesterol efflux of apolipoprotein E-containing high-density lipoprotein in THP-1 cells. *Biol. Chem.*. 2019.01; 400(2); 209-218
2. Megumi Sato, Ryunosuke Ohkawa, Hann Low, Madoka Nishimori, Shigeo Okubo, Akira Yoshimoto, Kouji Yano, Takahiro Kameda, Yutaka Yatomi, Minoru Tozuka. Serum amyloid A does not affect high-density lipoprotein cholesterol measurement by a homogeneous assay. *Clin. Biochem.*. 2019.01; 63; 97-101
3. Yuna Horiuchi, Ryunosuke Ohkawa, Shao-Jui Lai, Shitsuko Shimano, Michio Hagihara, Shuji Tohda, Takahiro Kameda, Minoru Tozuka. Usefulness of apolipoprotein B-depleted serum in cholesterol efflux capacity assays using immobilized liposome-bound gel beads. *Biosci. Rep.*. 2019.03;
4. Shao-Jui Lai, Ryunosuke Ohkawa, Yuna Horiuchi, Tetsuo Kubota, Minoru Tozuka. Red blood cells participate in reverse cholesterol transport by mediating cholesterol efflux of high-density lipoprotein and apolipoprotein A-I from THP-1 macrophages. *Biol. Chem.*. 2019.06;
5. Nigora Mukhamedova, Anh Hoang, Dragana Dragoljevic, Larisa Dubrovsky, Tatiana Pushkarsky, Hann Low, Michael Ditiatkovski, Ying Fu, Ryunosuke Ohkawa, Peter J Meikle, Anelia Horvath, Beda Brichacek, Yury I Miller, Andrew Murphy, Michael Bukrinsky, Dmitri Sviridov. Exosomes containing HIV protein Nef reorganize lipid rafts potentiating inflammatory response in bystander cells. *PLoS Pathog.*. 2019.07; 15(7); e1007907

[Conference Activities & Talks]

1. Horiuchi Y., Ohkawa R., Lai SJ., Shimano S., Hagihara M., Tohda S., and Tozuka M. Availability of apoB-depleted serum in clinical assay for cholesterol efflux capacity using immobilized liposome-bound gel beads. 3rd IFCC-EFLM European Congress of Clinical Chemistry and Laboratory Medicine 2019.05.19 Barcelona
2. Fujii Y., Ohkawa R., Lai SJ., Horiuchi Y., Shimano S., Ohno K., Ichimura N., Hagihara M., Tozuka M., Tohda S. Analysis of Serum Amyloid A Containing HDL Formation in HepG2. 2019 KAMT congress & International conference 2019.08.31 Pyeongchang

3. Yamazaki A., Ohkawa R., Horiuchi Y., Lai S.J., Shimano S., Itoi A., Ichimura N., Hagihara M., Tozuka M., Tohda S. Analysis of Apolipoprotein C-II and C-III Transfers between High-density Lipoprotein and Very Low-density Lipoprotein. 2019 KAMT congress & International conference 2019.08.31 Pyeongchang

Department of Laboratory Molecular Genetics of Hematology

Associate professor :
Miwako NISHIO

Adjunct Lecturer :
Takatoshi KOYAMA, Ken-ichi IMADOME, Yoichi NAKAYAMA

Graduate Student :
Shiho HASHIMOTO, Shisei GO, Megumi TATEISHI

(1) Outline

For undergraduate education, we are in charge of Clinical Laboratory Hematology, Hematology, Clinical Practice, Clinical clerkship (School of Medicine), Clinical Hematology (Track of Nursing Science). We provide lectures on hematopoiesis, mechanisms of coagulation and fibrinolysis, pathology and clinical features of main hematological disorders as well as fundamental laboratory practices.

For graduate education, we focus on clarifying molecular mechanisms of development of hematological disorders. We apply the results to develop new diagnostic procedures and treatment strategies. Our current research subject is EB virus-positive T- and NK-cell neoplasms.

(2) Research

Our research goals:

1. Clarifying pathogenesis of hematopoietic malignancies and innovation of a new treatment strategies
2. Clarifying mechanisms of EB virus-positive T- and NK-cell neoplasms and developing new treatment strategies
3. Creating new methods for diagnosing hematopoietic tumors

We collaborate on several researches with doctors of Deps. Hematology, Pediatrics, Neurology, Molecular Virology, Center for Stem Cell and Regenerative Medicine, Ophthalmology, Dermatology, Department of Comprehensive Pathology, and Diagnostic Radiology on-campus in TMDU. We are also doing research with members of National Center for Child Health and Development, Osaka Women's and Children's Hospital, Biochemistry department at Justus-Liebig Universität (Gießen. We collaborate with several companies as well.

(3) Education

1. Undergraduate Education

We are in charge of Clinical Laboratory Hematology, Clinical Hematology, clinical clerkship (School of Medicine), Clinical Hematology (Track of Nursing Science). We provide lectures on hematopoiesis, hematological disorders, mechanism of coagulation and fibrinolysis, hematopoietic malignancies as well as fundamental laboratory

practices.

Students are also involved in Undergraduate Research, which objective is to learn basis of research including how to plan and carry out research activities, how to write theses, and how to give an academic presentation. They also experience as trainees for Clinical Practice for hematological examination in cooperation with Clinical Laboratory at Medical Hospital. These lectures and practices are conducted in collaboration with the members of Departments of Hematology and Pediatrics.

2. Graduate Education

For graduate education, we focus on clarifying molecular mechanisms of development of hematological neoplasms. We apply the results to develop new diagnostic procedures and treatment strategies for these disorders. Our current research subject is EB virus-positive T- and NK-cell neoplasms. We instruct students to summarize what they investigated and complete English manuscripts for publication.

Detailed educational contents are shown below:

- 1) Investigating and understanding pathogenesis and pathology of hematopoietic disorders, especially neoplasms
- 2) Acquiring skills for cellular, molecular and genetic examination that play significant roles for diagnosing and clarifying cause and state of diseases. These molecular techniques are useful not only for clinical situation, but also for elucidating mechanisms of developing diseases
- 3) Acquiring current information for diagnosis and treatment of hematological diseases
- 4) Publishing papers on hematological laboratory testing and clinical hematology on main international academic journals and present them at international conferences

(4) Lectures & Courses

Cultivating interdisciplinary- and internationally-minded medical staffs with rich humanity, a strong sense of ethics, and ability to suggest and solve unmet medical issues

(5) Clinical Services & Other Works

Research:

Our research group is also a principal investigator of Japan Agency for Medical Research and Development (AMED) study group ‘the Investigator-initiated clinical research of a JAK1/2 inhibitor ruxolitinib for chronic active Epstein-Barr virus infection’ .

We are supporting patients with chronic active Epstein-Barr virus infection (CAEBV) through CAEBV patient’s association (SHAKE).

<http://caebv.com/>

(6) Clinical Performances

We are the only group that specialize EBV-positive T- or NK-cell neoplasms especially chronic active EBV infection. We accept referral patients with CAEBV from all over Japan and abroad. We analyze the blood sample in CAEBV patients.

(7) Publications

[Original Articles]

1. Hiroyuki Takahashi, Hiroshi Takase, Ayako Arai, Manabu Mochizuki, Kyoko Ohno-Matsui. Bilateral granulomatous panuveitis in two patients with T-cell type of chronic active Epstein-Barr virus infection. *BMC Ophthalmol.* 2019.03; 19(1); 83
2. Masako Oka, Norihiko Kobayashi, Kazunori Matsumura, Miwako Nishio, Kumiko Saeki. Exogenous Cytokine-Free Differentiation of Human Pluripotent Stem Cells into Classical Brown Adipocytes. *Cells.* 2019.04; 8(4);

[Misc]

1. Arai A.. Chronic active Epstein–Barr virus infection: a bi-faceted disease with inflammatory and neoplastic elements *Immunological Medicine.* 2019.01;
2. Arai A.. Advances in the Study of Chronic Active Epstein-Barr Virus Infection: Clinical Features Under the 2016 WHO Classification and Mechanisms of Development *Frontiers Pediatrics.* 2019.02;

Department of Immunopathology

Professor: Tetsuo Kubota

Associate Professor: Yuko Kato, Ayaka Ohashi

Doctor Course Graduate Students: Naoko Hisasue, Kumi Inoue, Siriphone Virachith

Master Course Graduate Students: Yoshino Watanabe, Ayane Ono

Under Graduate Research Students: Kotone Tatsuno, Yui Satomura

(1) Outline

We have made a progress in research on the roles of autoantibodies in pathogenesis of connective tissue diseases. Foreign student Siriphone Virachith who had been financially supported by the Japanese government published a novel mechanism of pro-thrombotic state in antiphospholipid syndrome caused by anti-phospholipid antibodies, and achieved PhD. On the other hand, Kumi Inoue published her results about the pathogenic role of anti-DNA antibodies in systemic lupus erythematosus. Yuko Kato has been studying in USA since March 2019, and published a paper, which was performed before leaving, on the mechanism of pulmonary arterial hypertension caused by autoantibodies against enolase 1. She also published another paper in 2019. It revealed a novel mechanism in cell migration via a signal transduction molecule “Epac1” . This paper has got the award of 2019th Hiroshi and Aya Irisawa Memorial Award for Excellent Papers on Research in Circulation in The Journal of Physiological Sciences. In addition, a master course student Ayane Ono studied abroad at Chulalongkorn University in Thailand, and analyzed the expression of immune checkpoint molecules on the blood lymphocytes of HIV-infected patients.

(2) Research

1. Role of autoantibodies in pathogenesis of systemic autoimmune diseases.
2. Pathogenesis of autoinflammatory diseases.
3. Production of novel antibodies useful for immunological experiments or clinical diagnosis.

(3) Education

[Undergraduate Course] Clinical Immunology Lecture, Clinical Immunology Laboratory, Undergraduate Research, Clinical Practice, General Medical Technology, Clinical Medicine

[Master Course] Introductory Experiments for Medical Technologist Internship, Medical Technologist Internship I, Medical Technologist Internship II, Medical Technology II, Seminar of Medical Laboratory Science, Practice of Medical Laboratory Science, Research for Thesis

[Doctor Course] Introductory Experiments for Medical Technologist Advanced Internship, Medical Technologist Advanced Internship I, Medical Technologist Advanced Internship II, Medical Technology II, Clinical Reasoning, Immunopathology Practice, Immunopathology Laboratory

(4) Lectures & Courses

[Undergraduate]

In order to cultivate human resources capable of studying and developing novel methods of clinical laboratory tests, besides what we have already known, we teach how to think from a scientific point of view. To cultivate application skills, therefore, the classes spend a lot of time for teaching basic immunology introducing how the findings were revealed.

[Graduate]

To cultivate professionals, we administer the internship program in TMDU hospital. In addition, we show students actual clinical data and discuss how we should interpret them. As for research, we encourage not only the doctor course students, but also the master course students to publish the results.

(5) Clinical Services & Other Works

In TMDU hospital, Kubota works for the Department of Rheumatology.

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

1. Kato Y, Yokoyama U, Fujita T, Umemura M, Kubota T, Ishikawa Y. Epac1 deficiency inhibits basic fibroblast growth factor-mediated vascular smooth muscle cell migration. *Journal of Physiological Sciences*. 2019; 69(2); 175-184
2. Virachith S, Saito M, Watanabe Y, Inoue K, Hoshi O, Kubota T. Anti-beta2-glycoprotein I antibody with DNA binding activity enters monocytes via cell surface DNA and induces tissue factor expression *Clinical and Experimental Immunology*. 2019; 195(2); 167-178
3. Inoue K, Ishizawa M, Kubota T. Monoclonal anti-dsDNA antibody 2C10 escorts DNA to intracellular DNA sensors in normal mononuclear cells and stimulates secretion of multiple cytokines implicated in lupus pathogenesis *Clin Exp Immunol*. 2019;
4. Kato Y, Kasama T, Soejima M, Kubota T. Anti-enolase 1 antibodies from a patient with systemic lupus erythematosus accompanied by pulmonary arterial hypertension promote migration of pulmonary artery smooth muscle cells *Immunology Letters*. 2019;
5. Shao-Jui Lai, Ryunosuke Ohkawa, Yuna Horiuchi, Tetsuo Kubota, Minoru Tozuka. Red blood cells participate in reverse cholesterol transport by mediating cholesterol efflux of high-density lipoprotein and apolipoprotein A-I from THP-1 macrophages. *Biol. Chem.*. 2019.06;

[Conference Activities & Talks]

1. Ayaka Ohashi. The expression and the secretion of ribonuclease inhibitors by tumor and vascular endothelial cells. The 81st Annual Meeting of the Japanese Society of Hematology 2019.10.11

Department of Molecular Microbiology

Associate Professor : Ryoichi SAITO

Graduate Student (doctor's course): Miyuki MIZOGUCHI, Alafate AYIBIEKE, Yuko KAMICHI

Graduate Student (master's course): Ayaka OTA, Yukino USUI, Wakana SATO, Akari SAMEJIMA, Eimi HASEGAWA

(1) Outline

Our department is engaged in both lecture and practical course for medical microbiology. These include education on prevention, diagnosis and treatment of infectious diseases for both undergraduate and graduate students. Regarding our research, we are interested in investigating molecular mechanisms of antibiotic resistance and virulence gene regulation in bacteria.

(2) Research

Research Interests:

1. Molecular mechanism of antibiotic resistance in bacteria
2. Mechanism of sporulation, spore germination and toxin production in *Clostridioides difficile* and *Clostridium perfringens*

(3) Education

Our course provides the conceptual basis for understanding pathogenic microorganisms including host response in infectious diseases, antimicrobial resistance, and epidemiologic surveillance. It also provides opportunities for undergraduate and graduate students to gain basic techniques, such as identification of microorganisms and antimicrobial susceptibility testing which are performed in the clinical laboratory at medical facilities.

(4) Publications

[Original Articles]

1. Kageyama Yamada, Ryoichi Saito, Saori Muto, Masakazu Sasaki, Hinako Murakami, Kotaro Aoki, Yoshikazu Ishii, Kazuhiro Tateda. Long-term observation of antimicrobial susceptibility and molecular characterization of *Campylobacter jejuni* isolated in a Japanese general hospital 2000-2017. *J Glob Antimicrob Resist.* 2019.02; 18; 59-63
2. Yohei Washio, Shun-ichiro Sakamoto, Ryoichi Saito, Takahito Nei, Masayo Morishima, Akihiro Shinozaki, Ayaka Tashiro, Ryoji Sugimoto. Infective endocarditis caused by *Cardiobacterium valvarum*. *Access Microbiology.* 2019.06;
3. Yoko Nukui, Alafate Ayibieke, Makoto Taniguchi, Yoshibumi Aiso, Yuka Shibuya, Kazunari Sonobe, Jun Nakajima, Saki Kanehira, Yoshiro Hadano, Shuji Tohda, Ryuji Koike, Ryoichi Saito. Whole-genome analysis of EC129, an NDM-5-, CTX-M-14-, OXA-10- and MCR-1-co-producing *Escherichia coli* ST167 strain isolated from Japan. *J Glob Antimicrob Resist.* 2019.09; 18; 148-150
4. Ryoichi Saito, Yukino Usui, Alafate Ayibieke, Jun Nakajima, Isaac Prah, Kazunari Sonobe, Yoshibumi Aiso, Shiori Ito, Yasuhiro Itsui, Yoshiro Hadano, Yoko Nukui, Ryuji Koike, Shuji Tohda. Hypervirulent

- clade 2, ribotype 019/sequence type 67 *Clostridioides difficile* strain from Japan. *Gut Pathog.* 2019.11; 11; 54
5. Francesco Comandatore, Davide Sasser, Sion C Bayliss, Erika Scaltriti, Stefano Gaiarsa, Xiaoli Cao, Ana C Gales, Ryoichi Saito, Stefano Pongolini, Sylvain Brisse, Edward J Feil, Claudio Bandi. Gene Composition as a Potential Barrier to Large Recombinations in the Bacterial Pathogen *Klebsiella pneumoniae*. *Genome Biol Evol.* 2019.11; 11(11); 3240-3251
 6. Nukui Y, Chino T, Tani C, Sonobe K, Aiso Y, Tohda S, Koike R, Saito R. Molecular epidemiologic and clinical analysis of *Helicobacter cinaedi* bacteremia in Japan. *Helicobacter.* 2019.11; e12675
 7. Saori MUTO, Kageto YAMADA, Yoshiko TAMAMORI, Hiroyuki NISHIYAMA, Ryoichi SAITO. Comparison of butyrate test, selective media, and hockey puck test as a simple identification method for *Moraxella catarrhalis* The Journal of the Japanese Society for Clinical Microbiology. 2019.12; 30(1); 13-17
 8. Yuta Okada, Yuka Yagihara, Yoshitaka Wakabayashi, Gene Igawa, Ryoichi Saito, Yoshimi Higurashi, Mahoko Ikeda, Keita Tatsuno, Shu Okugawa, Kyoji Moriya. Epidemiology and virulence-associated genes of *Clostridioides difficile* isolates and factors associated with toxin EIA results at a University Hospital in Japan. *Access Microbiology.* 2019.12;

[Misc]

1. Ryoichi Saito. Molecular Typing of Bacterial Pathogens for Infection Control and Prevention in Clinical Practice *Rinsho-Byori.* 2019.11; 67(11); 1174-1178

[Conference Activities & Talks]

1. Saori Muto, Kageto Yamada, Hiroyuki Nishiyama, Ryoichi Saito. Performance for identification of *Moraxella catarrhalis*. The 30th Annual Meeting of Japanese Society for Clinical Microbiology 2019.02.01 Tokyo, Japan
2. Ayaka Ota, Takeshi Ohtsuka, Eimi Hasegawa, Ayako Kasai, Kageto Yamada, Yoshihiro Yamaguchi, Wachino Jun-ichi, Koji Kimura, Yoshichika Arakawa, Ryoichi Saito. Molecular mechanism of resistance to β -lactam/ β -lactamase inhibitor combinations in *Moraxella catarrhalis*. The 30th Annual Meeting of Japanese Society for Clinical Microbiology 2019.02.01 Tokyo, Japan
3. Yukino Usui, Yuko Kamiichi, Nozomi Uchida, Shu Okugawa, Kazunari Sonobe, Shuji Tohda, Ryoichi Saito. Impact of deoxycholic acid for growth, sporulation and toxin production in *Clostridioides difficile*. The 30th Annual Meeting of Japanese Society for Clinical Microbiology 2019.02.01 Tokyo, Japan
4. Wakana Sato, Alafate Ayibieke, Ayumi Kobayashi, Chihiro Tani, Ryoichi Saito. Antimicrobial susceptibility among Enterobacteriaceae isolated in Ghana. The 30th Annual Meeting of Japanese Society for Clinical Microbiology 2019.02.01 Tokyo, Japan
5. Alafate Ayibieke, Wakana Sato, Samiratu Mahazu, Mitsuko Ohhashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Emergence of an NDM-1-producing *Escherichia coli* from Ghana. The 30th Annual Meeting of Japanese Society for Clinical Microbiology 2019.02.01
6. Yukino Usui, Yuko Kamiichi, Shu Okugawa, Shuji Tohda, Ryoichi Saito. Role of deoxycholic acid for physiology in *Clostridioides difficile*. The 49th Annual Meeting of Japanese association for anaerobic infection 2019.03.02 Tokyo, Japan
7. Yoko Nukui, Yoshiro Hadano, Ryoichi Saito, Tetushi Aiso, Shuji Toda, Ryuji Koike. Case report caused by EC129, an NDM-5-, CTX-M-14-, OXA-10-, and mcr-1-co-producing *Escherichia coli* ST167 strain isolated from Japan. The 93rd Annual Meeting of the Japanese association for infectious diseases 2019.04.04 Aichi, Japan
8. Ryoichi Saito. Investigation of storage and transport system in *Neisseria meningitidis*. The 68th JAMT Congress 2019 2019.05.18 Yamaguchi, Japan

9. Alafate Ayibieke, Ayumi Kobayashi, Samiratu Mahazu, Wakana Sato, Isaac Prah, John Addow-Thompson, Shiroh Iwanaga, Anthony Ablordy, Ryoichi Saito. Antibiotic resistance among Gram-negative glucose non-fermenting bacilli from Ghana. The 23rd IFCC-EFLM European Congress of Clinical Chemistry and Laboratory Medicine 2019.05.19 Barcelona, Spain
10. Wakana Sato, Samiratu Mahazu, Isaac Prah, John Addow-Thompson, Alafate Ayibieke, Shiroh Iwanaga, Anthony Ablordy, Ryoichi Saito. Antimicrobial susceptibility and extended-spectrum β -lactamase profiles of *Escherichia coli* and *Klebsiella* spp. isolated from Ghana. The 23rd IFCC-EFLM European Congress of Clinical Chemistry and Laboratory Medicine 2019.05.19 Barcelona, Spain
11. Yukino Usui, Yuko Kamiichi, Shu Okugawa, Ryoichi Saito. Impact of deoxycholate on the growth, toxin production, and spore formation of *Clostridioides difficile*. The 23rd IFCC-EFLM European Congress of Clinical Chemistry and Laboratory Medicine 2019.05.19 Barcelona, Spain
12. Shigeki MISAWA, Mitsuaki NAGASAWA, Hideji YANAGISAWA, Atsushi YUKI, Ryoichi SAITO, Vansith KET, Hironori KATAYAMA, Yoshifumi MIYAZIMA. The Project for Quality Improvement of Clinical Laboratory Testing in Kingdom of Cambodia Standardization and Development of a Clinical Microbiology Testing System. The 6th Congress of the Asia Association of Medical Laboratory Scientists (AAMLS 2019) 2019.05.29 Pattaya, Thailand
13. Y. Nukui, Y. Maki, Y. Hadano, Y. Aiso, J. Nakajima, K. Sonobe, R. Saito, S. Tohda, R. Koike. Molecular Epidemiological Analysis of Multidrug-Resistant *Pseudomonas aeruginosa* that Caused an Outbreak in an Intensive Care Unit in Japan. ASM Microbe 2019 2019.06.20 San Francisco, CA, USA
14. Yuta Okada, Yuka Yagihara, Yoshitaka Wakabayashi, Gene Igawa, Ryoichi Saito, Yoshimi Higurashi, Mahoko Ikeda, Keita Tatsuno, Shu Okugawa, Kyoji Moriya. Clinical features, molecular epidemiology, and virulence-associated genes of *Clostridioides difficile* isolates in patients at a University Hospital in Japan. ASM Microbe 2019 2019.06.20 San Francisco, CA, USA
15. Ryoichi Saito. Molecular Typing of Bacterial Pathogens for Infection Control and Prevention in Clinical Practice. The 75th Annual Meeting of Japanese Society of Laboratory Medicine 2019.06.22 Tokyo, Japan
16. Iwasawa Marie, Wakana Sato, Alafate Ayibieke, Isaac Prah, Samiratu Mahazu, Shiro Iwanaga, Anthony Ablordey, Ryoichi Saito. Molecular epidemiological research among fluoroquinolone-resistant and ESBL-producing *Escherichia coli* isolated in Ghana. The 14th Annual Meeting of Japanese Association of Medical Technology Education 2019.08.22 Kumamoto, Japan
17. Ryoichi Saito, Alafate Ayibieke, Ayumi Kobayashi, Samiratu Mahazu, Wakana Sato, Isaac Prah, John Addow-Thompson, Shiroh Iwanaga, Anthony Ablordy. Antibiotic resistance among Gram-negative glucose non-fermenting bacilli from Ghana. Asian-African Research Forum on Emerging and Reemerging Infections 2019 2019.09.05 Sapporo, Japan
18. Ryoichi Saito. Role of lysophospholipid and diacylphospholipid in *Escherichia coli*. The 67th Annual Meeting of Japanese Society of Laboratory Medicine 2019.10.24 Okayama, Japan

Department of Liver Disease Control

Professor : Yasuhiro ASAHINA
Associate Professor : Sei KAKINUMA

Graduate Student
(collaboration with Department of Gastroenterology and Hepatology in TMDU)
Emi INOUE-SHINOMIYA, Tomoyuki TSUNODA, Masato MIYOSHI, Ayako SATO,
Jun TUCHIYA, Taro SHIMIZU, Eiko TAKEICHI

(1) Outline

Patients died of chronic liver diseases, including liver cancer, are about 40,000 persons per a year in Japan. Liver transplantation remains the only effective treatment available to patients with end-stage liver diseases. Because of a serious shortage of donors for allogeneic liver transplantation, an alternative therapy is needed. Prevention of hepatocarcinogenesis and hepatic fibrosis is also necessary for patients with chronic hepatitis, and the development of effective treatment for progressive liver diseases has been quite essential. We believe that the central role of clinical departments in the graduate school of TMDU is to establish basis for the innovative medical treatment in the next generation. To achieve our mission, both basic research lead by clinical concepts and development of novel therapeutics established upon basic research are required.

Our section is a donation-funded department collaborating with the Department of Gastroenterology and Hepatology in TMDU. Most of basic research projects, education for students, and clinical contributions including multicenter studies are collaboration with the Department of Gastroenterology and Hepatology in TMDU. The goal of our education is to promote students to become a well-developed hepatologist, and also a leading expert in the field of Hepatology and Gastroenterology.

(2) Research

Our principle is to achieve a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice.

We focus on the basic studies of molecular mechanism regulating development, pathophysiology, progression, and therapeutic resistance of hepatocellular carcinoma (HCC). We also focus on the development of novel disease models using human induced pluripotent stem cells, the research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis, the study for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells, analysis of mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and factors for therapeutic resistance against antiviral agents.

Research projects

- Research for mechanism regulating development, pathophysiology, progression, and therapeutic resistance of HCC, based on molecular biology and genome informatics
- Development of novel disease models using human induced pluripotent stem cells to elucidate the pathophysiology of liver diseases
- Research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis
- Research for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells

- Analyses of molecular mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and clinical factors for therapeutic resistance against antiviral agents.

(3) Education

Primary goal for education in our section is to train highly educated and experienced clinician-researchers in the field of hepatology. Our goal for education of graduate students is to produce clinical researchers thinking from a wide perspective and to bring up leaders of the next generation in hepatology.

(4) Lectures & Courses

Our lectures and courses are collaboration with the Department of Gastroenterology and Hepatology in School of Medicine, TMDU. We also educate clinical residents in Medical Hospital of TMDU and graduate students of the Department of Gastroenterology and Hepatology, in TMDU in collaboration with such department.

(5) Clinical Services & Other Works

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. In the clinical section, we pursue development and application of highly advanced technologies, including novel procedures, for sophisticated diagnosis and treatment of diseases of liver, biliary duct, and pancreas. We also operate a lot of multicenter study collaborating with the Department of Gastroenterology and Hepatology in TMDU. We participate in 8 research projects for treatment and eradication of hepatitis virus funded by Japan Agency for Medical Research and Development (AMED). From April 2019, our clinical research program, “Development of innovative disease models using hepatic organoids derived from human induced pluripotent stem cells and construction of new treatments to suppress carcinogenesis in liver” , was started as Programs for Basic and Clinical Research on Hepatitis in Division of infectious disease research, AMED. This program is primarily operated by our department in cooperation with several departments in TMDU and other institute. We are trying to develop novel therapeutic strategies to treat progressive liver diseases. We published a lot of studies in peer-reviewed international journals and presented the recent works in a lot of international and domestic conferences as described below.

(6) Clinical Performances

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. We have recently established the outpatient department specialized for chronic hepatitis, cirrhosis, and HCC. We have operated a lot of multicenter study about efficacy of treatment against viral hepatitis, named as “Ochyanomizu Liver Conference”. More than 2000 patients with viral hepatitis were enrolled in such studies. We have clarified the clinical factors predicting accurately the therapeutic prognosis and risk for development of HCC. We are developing the screening programs for the early detection of HCC in patients with chronic hepatitis after eradication of viruses utilizing non-invasive elastography, novel serum markers, and dynamic contrast-enhanced ultrasonography. For the treatment of HCC, three-dimensional location and structure of tumors and vessels are evaluated by multilateral approaches using dynamic contrast-enhanced ultrasonography, Gd-EOB-DTPA enhanced MRI, and real-time virtual ultrasonography (RVS). We have reported the utility and safety of such therapeutic approaches. We are providing patients the appropriate therapeutic option based on collective multimodal therapeutic strategy in collaboration with departments of surgery and radiology.

(7) Publications

[Original Articles]

1. Seishin Azuma, Yasuhiro Asahina, Sei Kakinuma, Keiko Azuma, Masato Miyoshi, Emi Inoue, Tomoyuki Tsunoda, Ayako Sato, Shun Kaneko, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri

- Nitta, Yasuhiro Itsui, Makoto Tomita, Mina Nakagawa, Mamoru Watanabe. Diabetic Retinopathy as a Risk Factor Associated with the Development of Hepatocellular Carcinoma in Nonalcoholic Fatty Liver Disease. *Dig Dis.* 2019; 37(3); 247-254
2. Masato Miyoshi, Sei Kakinuma, Akihide Kamiya, Tomoyuki Tsunoda, Jun Tsuchiya, Ayako Sato, Shun Kaneko, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. LIM homeobox 2 promotes interaction between human iPS-derived hepatic progenitors and iPS-derived hepatic stellate-like cells. *Sci Rep.* 2019.02; 9(1); 2072
 3. Sayuri Nitta, Yasuhiro Asahina, Takanobu Kato, Jun Tsuchiya, Emi Inoue-Shinomiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Hayato Hikita, Tetsuo Takehara, Mamoru Watanabe. Impact of novel NS5A resistance-associated substitutions of hepatitis C virus detected in treatment-experienced patients. *Sci Rep.* 2019.04; 9(1); 5722
 4. Emi Inoue-Shinomiya, Miyako Murakawa, Yasuhiro Asahina, Mina Nakagawa, Jun Tsuchiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Sayuri Nitta, Fukiko Kawai-Kitahata, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Kazumoto Murata, Masashi Mizokami, Mamoru Watanabe. Association of serum interferon- λ 3 levels with hepatocarcinogenesis in chronic hepatitis C patients treated with direct-acting antiviral agents *Hepatol Res.* 2019.05; 49(5); 500-511
 5. Akira Doi, Hayato Hikita, Yugo Kai, Yuki Tahata, Yoshinobu Saito, Tasuku Nakabori, Ryoko Yamada, Takahiro Kodama, Ryotaro Sakamori, Asako Murayama, Sayuri Nitta, Yasuhiro Asahina, Hiroshi Suemizu, Tomohide Tatsumi, Takanobu Kato, Tetsuo Takehara. Combinations of two drugs among NS3/4A inhibitors, NS5B inhibitors and non-selective antiviral agents are effective for hepatitis C virus with NS5A-P32 deletion in humanized-liver mice. *J Gastroenterol.* 2019.05; 54(5); 449-458
 6. Tomoyuki Tsunoda, Sei Kakinuma, Masato Miyoshi, Akihide Kamiya, Shun Kaneko, Ayako Sato, Jun Tsuchiya, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Tsuyoshi Sogo, Haruki Komatsu, Ryutaro Mukouchi, Ayano Inui, Tomoo Fujisawa, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Loss of fibrocystin promotes interleukin-8-dependent proliferation and CTGF production of biliary epithelium. *J Hepatol.* 2019.07; 71(1); 143-152
 7. Wan Wang, Kaoru Tsuchiya, Masayuki Kurosaki, Yutaka Yasui, Kento Inada, Sakura Kirino, Koji Yamashita, Shuhei Sekiguchi, Yuka Hayakawa, Leona Osawa, Mao Okada, Mayu Higuchi, Kenta Takaura, Chiaki Maeyashiki, Shun Kaneko, Nobuharu Tamaki, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Yasuhiro Asahina, Nobuyuki Enomoto, Namiki Izumi. Sorafenib-Regorafenib sequential therapy in Japanese patients with unresectable hepatocellular carcinoma-relative dose intensity and post-regorafenib therapies in real world practice. *Cancers (Basel).* 2019.10; 11(10); E1517
 8. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Emi Inoue-Shinomiya, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Minoru Tanabe, Emiko Sugawara, Akira Takemoto, Hidenori Ojima, Michie Sakamoto, Masaru Muraoka, Shinichi Takano, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive genetic analysis of cholangiolocellular carcinoma with a coexistent hepatocellular carcinoma-like area and metachronous hepatocellular carcinoma. *Hepatol Res.* 2019.12; 49(12); 1466-1474
 9. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient.[Epub ahead of print] *Hepatol Res.* 2019.12;
 10. Ayako Sato, Sei Kakinuma, Masato Miyoshi, Akihide Kamiya, Tomoyuki Tsunoda, Shun Kaneko, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Naohiko Koshikawa, Motoharu Seiki, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Vasoactive intestinal peptide derived from liver mesenchymal cells mediates tight junction assembly in mouse intrahepatic bile ducts. *Hepatol Commun.* 2019.12; 4(2); 235-254

[Misc]

1. Sei Kakinuma, Akihide Kamiya. A rodent model for cell transplantation of hepatic progenitor cells. *Methods Mol Biol.* 2019; 1905; 211-219
2. Sei Kakinuma, Mamoru Watanabe. Analysis of the mechanism underlying liver diseases using human induced pluripotent stem cells. *Immunol Med.* 2019.06; 42(2); 71-78
3. Sei Kakinuma. Research of hepatic fibrosis using human induced pluripotent stem cells. *Gastroenterology & Hepatology.* 2019.12; 6(6); 548-554

[Conference Activities & Talks]

1. Miyako Murakawa, Yasuhiro Asahina, Emi Inoue, Mina Nakagawa, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Fukiko Kawai-Kitahata, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. The association of serum IFN-lambda 3 levels with liver fibrosis and hepatocarcinogenesis in chronic hepatitis C patients treated with direct-acting antiviral agents. *EASL, The International Liver Congress 2019* 2019.04.13 Vienna (Austria)
2. Mina Nakagawa, Yasuhiro Asahina, Jun Tsuchiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Emi Inoue, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Makoto Tomita, Mamoru Watanabe. Impact of HCV clearance on HCC development and patient survival: Propensity score-matched analysis of an ongoing database of 2173 CHC patients. *EASL, The International Liver Congress 2019* 2019.04.13 Vienna (Austria)
3. Yasuhiro Asahina. Prevention and Risk for Liver Cancer after Anti-Viral Therapy in Patients with HBV/HCV. *JSH International Liver Conference* 2019.10.02 Osaka (Japan)
4. Yasuhiro Asahina, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma. Comprehensive analysis of cancer gene mutations and viral integration in hepatocellular carcinoma arising from non-fibrotic liver. *AASLD The Liver Meeting 2019* 2019.11.10 Boston (USA)

Department of Advanced Therapeutics for GI Diseases

Professor : Tetsuya NAKAMURA

Associate Professor : Takashi NAGAISHI

Assistant Professor : Michio ONIZAWA, Yasuhiro NEMOTO

Graduate Student : Naoya TSUGAWA, Daiki YAMADA, Takehito ASAKAWA, Ai MASUMOTO, Yuria TAKEI, Shohei TANAKA, Ryo MORIKAWA

(1) Outline

The goal of our department is to develop novel therapeutic strategies for inflammatory bowel diseases (IBD) in humans. With multiple layers of support of corporations who wish to contribute to our mission, we have been focusing on IBD research from the clinical and basic science perspectives, providing an exceptional education program for graduate students at TMDU.

(2) Research

Our research activities focus on the key areas listed below. We have a particular emphasis on translational (bench to clinic) research on IBD.

- Research on the intestinal epithelium to develop regenerative medicine approaches for IBD
- The study of mucosal immunology to develop novel approaches for the diagnosis and treatment of IBD

(3) Education

We share our expertise and teaching program in graduate course education with the Department of Gastroenterology and Hepatology at TMDU. We are also involved in many programs designed for undergraduates.

(4) Lectures & Courses

Our goal is to create future leaders who are able to reach the highest level of quality in IBD research through the training of fellows and graduate/undergraduate students.

(5) Clinical Services & Other Works

We focus on developing highly advanced technologies, including novel procedures, for diagnosis and treatment of IBD in collaboration with the Department of Gastroenterology and Hepatology at TMDU. In addition, we have been playing a major role in nation-wide survey and multi-center studies on IBD, which is funded by the Japanese Ministry of Health, Labor and Welfare.

(6) Clinical Performances

- Development of new treatment protocol for IBD patients with stem cell therapy or immunomodulators.
- Development of minimally-invasive diagnostic modalities for inflammatory bowel diseases (i.e. MRE).

- Diagnosis and treatment of small intestinal lesions of inflammatory bowel diseases by double-balloon enteroscopy.

(7) Publications

[Original Articles]

1. Ryu Nishimura, Tomoaki Shirasaki, Kiichiro Tsuchiya, Yoshihide Miyake, Yusuke Watanabe, Shuji Hibiya, Sho Watanabe, Tetsuya Nakamura, Mamoru Watanabe. Establishment of a system to evaluate the therapeutic effect and the dynamics of an investigational drug on ulcerative colitis using human colonic organoids. *J Gastroenterol.* 2019.01; 54(7); 608-620
2. Nagaishi T, Yamada D, Suzuki K, Fukuyo R, Saito E, Fukuda M, Watabe T, Tsugawa N, Takeuchi K, Yamamoto K, Arai A, Ohtsuka K, Watanabe M. Indolent T cell lymphoproliferative disorder with villous atrophy in small intestine diagnosed by single-balloon enteroscopy. *Clinical journal of gastroenterology.* 2019.04;
3. Sho Watanabe, Kiichiro Tsuchiya, Ryu Nishimura, Tomoaki Shirasaki, Nobuhiro Katsukura, Shuji Hibiya, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Mutation by CRISPR System Enhances the Malignant Potential of Colon Cancer. *Mol Cancer Res.* 2019.07; 17(7); 1459-1467

[Conference Activities & Talks]

1. Suzuki K, Shimizu H, Kawai M, Takahashi J, Anzai S, Kawamoto A, Nagata S, Hiraguri Y, Yui S, Tsuchiya K, Nakamura T, Ohtsuka K, Okamoto R, Watanabe M. UC-related and segment-specific properties of patient-derived colonic organoids. ECCO2019 2019.03.07 Copenhagen (Denmark)
2. Kawamoto A, Nagata S, Anzai S, Takahashi J, Kawai M, Hama M, Nogawa D, Yamamoto K, Kuno R, Suzuki K, Shimizu H, Hiraguri Y, Yui S, Oshima S, Tsuchiya K, Nakamura T, Ohtsuka K, Kitagawa M, Okamoto R, Watanabe M. Synergy of Notch signalling and TNF- α in the inflamed intestinal epithelia of IBD patients leads to up-regulation of UBD, a ubiquitin-like protein. ECCO2019 2019.03.08 Copenhagen (Denmark)
3. Shuji Hibiya, Kiichiro Tsuchiya, Ryu Nishimura, Tomoaki Shirasaki, Sho Watanabe, Nobuhiro Katsukura, Tetsuya Nakamura, Mamoru Watanabe. Establishment of an in vitro system to evaluate the therapeutic effect of the investigational drug on ulcerative colitis using human colonic organoids.. ECCO2019 2019.03.08 Copenhagen (Denmark)
4. Takashi Nagaishi, Yudai Kojima, Daiki Yamada, Taro Watabe, Naoya Tsugawa, Nisha Jose, Michio Onizawa, Mamoru Watanabe.. APL expression is downregulated in an animal model of chronic colitis.. ECCO2019 2019.03.08 Copenhagen (Denmark)
5. Tsuchiya K, Watanabe S, Shirasaki T, Nishimura R, Katsukura N, Hibiya S, Okamoto R, Nakamura T, Watanabe M. TP53 mutation in human colonic organoids acquires resistance to in vitro long-term inflammation.. ECCO2019 2019.03.09 Copenhagen (Denmark)
6. Eiko Saito, Kohei Suzuki, Shuji Hibiya, Maiko Motobayashi, Kento Takenaka, Nobukatsu Horita, Hiromichi Shimizu, Michio Onizawa, Toshimitsu Fujii, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. The clinical efficacy of ustekinumab (UST) in patients with Crohn's disease (CD). AOCC2019 2019.06.15 Taipei (Taiwan)
7. Shuji Hibiya, Kiichiro Tsuchiya, Ryu Nishimura, Tomoaki Shirasaki, Sho Watanabe, Nobuhiro Katsukura, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Long-term inflammation model using human colonic organoids. AOCC2019 2019.06.15 Taipei (Taiwan)
8. Daiki Yamada, Takashi Nagaishi, Yudai Kojima, Taro Watabe, Naoya Tsugawa, Nisha Jose, Akinori Hosoya, Masahiro Suzuki, Michio Onizawa, Mamoru Watanabe. APL downregulation in an animal model of chronic colitis. AOCC2019 2019.06.15 Taipei (Taiwan)
9. Takashi Nagaishi, Yudai Kojima, Taro Watabe, Naoya Tsugawa, Daiki Yamada, Nisha Jose, Akinori Hosoya, Masahiro Suzuki, Michio Onizawa, Mamoru Watanabe. Analysis of APL expression in an animal model of chronic colitis. FOCIS2019 2019.06.20 Boston (USA)

10. Daiki Yamada, Takashi Nagaishi, Taro Watabe, Naoya Tsugawa, Yudai Kojima, Takahiro Adachi, Mamoru Watanabe. Analysis of Ileocecal Immune Response in an Animal Model of Colitis. ICMI2019 2019.07.17 Brisbane (Australia)
11. Naoya Tsugawa, Takashi Nagaishi, Daiki Yamada, Toshimitsu Fujii, Yudai Kojima, Arisa Tokai, Taro Watabe, Shuang Wang, Michio Onizawa, Takahiro Adachi, Mamoru Watanabe. BCR signaling in the activated B cells may be regulated by the long isoform of Ceacam1. The 48th Annual Meeting of the Japanese Society for Immunology 2019.12.11 Hamamatsu (Japan)
12. Takahiro Adachi, Taro Watabe, Takashi Nagaishi, Mamoru Watanabe, Hajime Karasuyama, Soichiro Yoshikawa. IgA-deficiency causes spontaneous enteritis.. The 48th Annual Meeting of the Japanese Society for Immunology 2019.12.13 Hamamatsu (Japan)

Department of Women's Health

Professor Masakazu Terauchi MD PhD; Assistant Professor Asuka Hirose MD PhD (concurrent)

(1) Outline

Japanese women boast world's #1 longevity, although the final stage of their lives is not necessarily of good health-related quality. To stay physically and psychologically sound in later life, women need to optimize their health starting from their midlife, especially through good diet and exercise. Tokyo Medical and Dental University (TMDU) Department of Obstetrics and Gynecology have promoted midlife women's health with our renowned Systemic Health and Nutrition Education Program (SHNEP) since 1995, which inspired Kikkoman Corporation to generously support to establish a new department in TMDU focusing on "Health Maintenance of Women through Food and Nutrition" in 2012. Dr. Masakazu Terauchi, Associate Professor and Chair of TMDU Department of Women's Health, is intensively studying with his colleagues about the changes in women's bodies and minds induced by aging, and the effects of bioactive food ingredients on them.

(2) Research

Department of Women's Health has dealt with a variety of topics listed below since its inception in 2012, mainly focusing our research on the effects of bioactive food ingredients on women's physical and psychological health.

- Effects of grape seed extract on middle-aged women's health-related quality of life
- Effects of hormone therapy and keishibukuryogan on blood pressure in perimenopausal and postmenopausal women
- Effects of nonbenzodiazepine, melatonin receptor agonist, and Kampo medication on sleep disturbances in perimenopausal and postmenopausal women
- Effects of selective serotonin reuptake inhibitors on subjective and objective sleep parameters in middle-aged women with depression
- Effects of oral contraceptive pills on sleep disturbances in young women with primary dysmenorrhea
- Effects of tomato juice on cardiovascular risk markers in middle-aged women
- Effects of soy isoflavone aglicone on middle-aged women's health-related quality of life
- Menopausal hormone therapy: route of administration and platelet-derived microparticles
- Effects of soy lecithin on middle-aged women's tiredness
- Effects of soy milk on middle-aged women's sleep
- Long-term effectiveness of eszopiclone on chronic insomnia disorder in middle-aged women
- Oxidative stress and postmenopausal osteoporosis: prevention of fragility fractures with healthy dietary habits
- Effects of grape seed proanthocyanidin extract on the endothelial function in patients with stage 1 hypertension

(3) Education

Cooperating with the Department of Obstetrics and Gynecology, we have shared responsibility in the education of Obstetrics and Gynecology, as well as in the training of medical students on clinical clerkship.

(4) Clinical Services & Other Works

Cooperating with the Department of Obstetrics and Gynecology, we have provided a comprehensive diagnosis, treatment, and disease management solution for women suffering from:

- menopausal symptoms
- premature ovarian insufficiency
- postmenopausal osteoporosis
- dyslipidemia
- hypertension
- pelvic organ prolapse
- lower urinary tract syndrome
- depression
- anxiety disorder
- insomnia
- dysmenorrhea
- premenstrual syndrome etc.

(5) Publications

[Original Articles]

1. Ryuji Kawaguchi, Koji Matsumoto, Shigeo Akira, Ken Ishitani, Kazuhiro Iwasaku, Yutaka Ueda, Ryugo Okagaki, Hiroya Okano, Toshimichi Oki, Kaori Koga, Michiko Kido, Takumi Kurabayashi, Yasushi Kuribayashi, Yuichi Sato, Kaori Shiina, Yasushi Takai, Satoshi Tanimura, Osamu Chaki, Masakazu Terauchi, Yukiharu Todo, Yasuyuki Noguchi, Sayaka Nose-Ogura, Tsukasa Baba, Akira Hirasawa, Takuma Fujii, Tsuneo Fujii, Tetsuo Maruyama, Etsuko Miyagi, Kaoru Yanagida, Osamu Yoshino, Mitsutoshi Iwashita, Tsugio Maeda, Takashi Minegishi, Hiroshi Kobayashi. Guidelines for office gynecology in Japan: Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG) 2017 edition J. Obstet. Gynaecol. Res.. 2019.04; 45(4); 766-786
2. Tamami Odai, Masakazu Terauchi, Daisaku Okamoto, Asuka Hirose, Naoyuki Miyasaka. Unsalted tomato juice intake improves blood pressure and serum low - density lipoprotein cholesterol level in local Japanese residents at risk of cardiovascular disease Food Sciency & Nutrition. 2019.05;
3. Tamami Odai, Masakazu Terauchi, Asuka Hirose, Kiyoko Kato, Naoyuki Miyasaka. Bone mineral density in premenopausal women is associated with the dietary Intake of alpha-tocopherol: a cross-sectional study Nutrients. 2019.10; 11; 2474
4. Tamami Odai, Masakazu Terauchi, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Severity of hot flushes is inversely associated with dietary intake of vitamin B6 and oily fish Climacteric. 2019.11; 22(6); 617-621
5. Tamami Odai, Masakazu Terauchi, Kiyoko Kato, Asuka Hirose, Naoyuki Miyasaka. Effects of grape seed proanthocyanidin extract on vascular endothelial function in participants with prehypertension: a randomized, double-blind, placebo-controlled study Nutrients. 2019.11; 11; 2844

[Misc]

1. Masakazu Terauchi. The effect of estradiol on muscle breakdown may be different between women in early and late postmenopause Menopause Live. 2019.07; (7/22);

[Conference Activities & Talks]

1. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Chilliness in Japanese middle-aged women is associated with low intake of n-3 fatty acids: a cross-sectional study. 12th European Congress on Menopause and Andropause 2019.05.15 Berlin
2. Masakazu Terauchi. The Asia-Pacific Perspective: Real-World Practice and Management of the Menopause in Japan. 7th Scientific Meeting of the Asia Pacific Menopause Federation 2019.05.29 Manila, Philippines

3. Masakazu Terauchi. Is the combined transdermal estradiol and micronized progesterone the better and safer MHT?. 7th Scientific Meeting of the Asia Pacific Menopause Federation 2019.05.29 Manila, Philippines
4. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Chilliness in Japanese middle-aged women is associated with anxiety and low intake of n-3 fatty acids: a cross-sectional study. 19th International Society of Psychosomatic Obstetrics and Gynecology Congress 2019.10.12 Den Haag

Department of Nutrition and Metabolism in Cardiovascular Disease

Makiko Egawa
Mizuko Osaka

(1) Outline

This course was established as a donated research division attached to the Department of Life Sciences and Medical Ethics.

The main themes are investigating the mechanism of arteriosclerosis development, which are one of the main causes of lifestyle-related diseases such as cardiovascular diseases and diabetes. This course also has been interested in the treatment and prevention of atherosclerosis and its relationship toward pregnancy in women.

Our education is being developed with the aim of training excellent researchers and highly specialized professionals with specialized knowledge and abilities capable of playing an active role in the international community.

(2) Publications

[Original Articles]

1. Egawa M, Imai K, Taketani Y, Morio T, Miyasaka N.. Two Prenatal Cases of Hyper-IgE Syndrome. J. Clin. Immunol.. 2019.01;
2. Hirose Asuka, Terauchi Masakazu, Odai Tamami, Yomogita Hiroshi, Tsurane Kotoi, Egawa Makiko, Miyasaka Naoyuki. 産後うつは出産後数日以内の抗酸化活性と関連している (Postpartum depression is associated with antioxidative activity within few days after delivery) 日本産科婦人科学会雑誌. 2019.02; 71(臨増); S-263
3. Dewan Syed Masudur Rahman, Shiraishi Orie, Deushi Michiyo, Tani Mariko, Osaka Mizuko, Yoshida Masayuki. C5a による好中球 β 2 インテグリン活性化は PKC δ の膜移行に関与する (C5a-induced β 2 integrin activation in neutrophils involves membrane translocation of PKC δ) 日本動脈硬化学会総会プログラム・抄録集. 2019.07; 51 回; 2-P
4. Hirose Asuka, Terauchi Masakazu, Odai Tamami, Yomogita Hiroshi, Tsurane Kotoi, Egawa Makiko, Miyasaka Naoyuki. Postpartum depression is associated with antioxidative activity within few days after delivery(和訳中) The Journal of Obstetrics and Gynaecology Research. 2019.08; 45(8); 1749-1750
5. Makiko Egawa, Hirokazu Kanegane, Kohsuke Imai, Tomohiro Morio, Naoyuki Miyasaka. Intravenous immunoglobulin (IVIG) efficiency in women with common variable immunodeficiency (CVID) decreases significantly during pregnancy. J. Matern. Fetal. Neonatal. Med.. 2019.09; 32(18); 3092-3096
6. Nishi H., Inoue R., Osaka M., Inoue T., Yoshida M., Nangaku M.. Neutrophil interferon-induced, double-stranded RNA-activated protein kinase (EIF2AK2) mediates vascular adhesion and transmigration in non-viral inflammatory disease EUROPEAN JOURNAL OF IMMUNOLOGY. 2019.10; 49; 582

[Conference Activities & Talks]

1. Syed Masudur Rahman Dewan, Mizuko Osaka, Masayuki Yoshida. C5a induces PKC δ dependent β 2 integrin activation in neutrophil-like differentiated HL-60.. 第四回 J-ISCP 年次学術集会 国際心血管薬物療学会日本部会 2019.06.08

2. Mizuko Osaka. Mechanism of vascular inflammation in LDLR null mice by PAD4-induced citrullination.
The 51st Annual Scientific Meeting of the Japan Atherosclerosis Society 2019.07.16

Department of Lifetime Clinical Immunology

MORI Masaaki
SUGIHARA Takahiko
YAMAZAKI Susumu
NARUTO Takuya
MATSUMOTO Takumi

(1) Outline

(Overview)

In response to the rapid rise of social interest, the importance of medical care throughout lifelong, including the development of transitional medical care, has been reviewed. In addition, since 2015, the incurable disease policy in Ministry of Health, Labor and Welfare has been enriched as a national policy. However, the university courses in Japan have not successfully departed from the traditional framework of internal medicine and pediatrics so far; and these two departments have developed separately. Especially in intractable immune diseases, because the cause has not yet been fully elucidated; the commonalities and differences between children, adults, and the elderly in these diseases have not at all been sorted out, and studies of these diseases have independently been developed by age groups with little being merged across groups. The universal and uniform diagnostic methods and/or treatment for a lifetime have not yet been available in the current situation.

Therefore, it is now required to establish a system to study of and treat immune intractable diseases such as rheumatic diseases seamlessly from children to the elderly. Following such circumstances, in 2016, our university established a donation course in cooperation with a course in which specialists in immunological intractable diseases play an important role (Rheumatology and Pediatrics), and Masaaki Mori who had been conducting Pediatric rheumatology at Yokohama City University joined as a member. Pediatrics staff and Rheumatology staff shared a room, and very started the course as a "mixed team". This course, with the cooperation of Department of Rheumatology and Pediatrics, promotes the integration of research, education, and clinical system for life-long immunological intractable diseases which have not been achieved by existing courses, and aims to develop a new course that leads the reform and enhancement of medical care and learning for all intractable diseases.

(2) Research

(Research activities)

1) Establishment of a research system in cooperation with Pediatrics and Rheumatology

This course clarifies the differences and similarities of rheumatic diseases between children and adults, and develops and embodies a universal approach to "countermeasures for intractable diseases throughout life-full courses". Especially in the transitional phase from pediatric to adult, there may be many transition-specific problems such as changes in the department/physician in charge from pediatrics to internal medicine, and changes in the required amount of medication due to changes in drug metabolism and physique.

In addition, we will propose treatment strategies that consider the needs and issues of those who wish to have children and are restricted from treatment with immunosuppressive drugs, and the elderly who are concerned about complications and compliance.

2) Clinical epidemiological study aiming to construct a database in the transition from childhood to adulthood

This course will lead the construction of a nationwide database of pediatric rheumatic diseases that has not been organized in Japan so far. The cohort studies in Japan have independently investigated children and adults in the recognition as "specified pediatric chronic diseases" and "designated intractable diseases" by the Ministry of Health, Labor and Welfare.

This course will construct a database of patients from childhood to adulthood in cooperation with the international community to clarify the current situation of the treatment of patients with childhood rheumatism and collagen diseases in Japan. Then, basic data to unify the description of registered items will be presented for immune intractable diseases that cross both the childhood chronic specific disease system and the designated intractable disease system.

Specifically, we will complete CoNinJa, a database focusing on JIA patients, based on NinJa which is a database that focuses on adult patients with rheumatoid arthritis. We will collect data in the future and clarify the actual situation of JIA medical treatment.

3) Genomic and immunological marker studies related to differences and similarities between children and adults

In this course, we will utilize the disease bioresource center of our university, which has the latest technology such as whole exome sequencing, next-generation sequence analysis and immunomarker research to make an effort to clarify all the intractable diseases of children and adults (rheumatic and collagen diseases, vascular inflammatory diseases, primary immunodeficiency syndrome, and autoinflammatory syndrome), and comprehensively explore the childhood-onset, transition from childhood to adulthood, adult onset, and elderly.

4) Development and expansion of new treatments through doctor-initiated clinical trials, etc.

Clinical tests (clinical trials) for drug approval have rapidly been globalizing, and an increasing number of people have been participating in international joint trials. In addition, the review period has been significantly reduced following the establishment of a drug approval review system, and improvements in medical drug lag are expected.

In this course, we will actively promote clinical tests and trials of new drugs in the transitional phase, which are considered difficult to be implemented in the transition period between children and adults. As a result, it is expected that the therapeutic goals of rheumatic/collagen diseases for children through adults will be advanced, and that the treatment options will be complicated and diverse; hence, the direction of establishing the tailor-made treatments for children to the elderly are explored, considering the actual use of these drugs.

5) Implementation of clinical studies for adults to the elderly and preparation of clinical guidelines.

The following studies were conducted in cooperation with the rheumatology. Rheumatoid arthritis: analysis of cohort study of the elderly-onset rheumatoid arthritis, analysis of NinJa of elderly patient data, systematic review of elderly rheumatoid arthritis and preparation of clinical guidelines for rheumatoid arthritis, continuation of a multi-center prospective cohort study of rheumatoid arthritis, and implementation of a new prospective cohort study of middle age to the elderly. Vasculitis syndrome: Implementation of a cohort study of large and small vasculitis, data analysis, preparation of clinical guidelines for vasculitis, establishment of the remission criteria and treatment strategies for large vessel vasculitis, and starting a cohort study using an intractable disease platform. Adult-onset Still's disease, systemic juvenile idiopathic arthritis: Implementation of a Tokyo Medical and Dental University cohort study for children and adults, preparation of a prospective cohort study using intractable disease platform.

(3) Education

(Educational activities)

Fostering a "hybrid physician" who can provide consistent medical care from children to adults

The clinical system so far has been separated for children and adults. From the perspective of patients, many feel confused and anxious about the change of the department in charge and the attending physician once they reach a certain age when they grow up despite the same disease. The adult physicians also often struggle with how those patients have progressed the diseases, what problems or worries of patients have had other than medical concerns while growing up, and whether those patients in carry-over case can be treated in the same manner as adults. For this purpose, this course plays a central role in providing an educational system for fostering "hybrid physicians" who are specialists in rheumatism treatment, are well familiar with treatment for both children and adults, and transcend the boundaries between children and adults.

(4) Lectures & Courses

(Education policy)

In this course, with the cooperation of Department of Rheumatology and Pediatrics, we will promote the integration of research, education, and clinical systems for intractable immune diseases throughout the life of patients, and further aim to be a pioneer of renovation and enhancement of medical treatment and academics for intractable diseases. And this course is intending to foster pediatricians and adult physicians who can solve various problems for patients in the transition from childhood to adulthood and from adulthood to the elderly.

(5) Clinical Services & Other Works

(Clinical and off-campus activities)

Clinical activities

Pediatrics and rheumatology cooperated to provide treatment for collagen and rheumatic diseases from children to the elderly.

Off-campus activities

Professor Masaaki Mori plays a role as the research representative in the followings.

1. Health and Labor Sciences Research Fund Grant/Refractory Disease Policy Research Project (Immune and Allergic Disease Policy Research Project (Immune and Allergic Disease Policy Research Field))(Ministry of health, labor and welfare 2017 2019)

"Analysis of national survey data of patients with pediatric rheumatism in childhood and a transitional phase to adulthood, and standardization of standard treatment by establishing a nationwide "seamless" clinical network based on their differences and similarities"

2. Health and Labor Sciences Research Fund Grants/Refractory Disease Policy Research Project (Refractory Disease Policy Research Project)

(2017-2019, Ministry of Health, Labor and Welfare) "Research on autoimmune diseases" [Research representative: XXX]

3. Research Grant for NPO Japan Kawasaki Disease Research Center (2017/2018, Japan Kawasaki Disease Research Center) "Elucidation of Kawasaki disease by clustering based on clinical information and new biomarkers"

Associate Professor XXXX works as a research coordinator for the followings:

Research designated by the Ministry of Health, Labor and Welfare, research to support for patients with rheumatoid arthritis according to life stages

Health Labor Administration Promotion Research Project Subsidy, Immune/Allergic Disease Policy Research Project, Clinical epidemiological study in regard to standardization of rheumatoid arthritis medical care in Japan

Health and Labor Sciences Research Grants, Intractable Disease Policy Research Project, Investigation and research on intractable vasculitis

#AMED multi-layer study for CQ solution of intractable vasculitis treatment

Health and Labor Sciences Research Grants, Intractable Disease Policy Research Project, Investigation and research on autoimmune diseases

The results of the research indicated above were reported at academic conferences and workshops in Japan and overseas.

(6) Clinical Performances

(Clinical features)

The Lifelong Intractable Immunological Diseases Lecture, "is a unique university course that cannot be found

elsewhere in the world, which aims to integrate research, education, and treatment systems for "immune intractable diseases", such as collagen and rheumatic diseases, for a lifetime from children to adults and the elderly". This course in our University has assessed various problems for patients with intractable diseases in the transitional phase from pediatric to adult or adult to elderly, which have not been solved by conventional medical system of Pediatrics and Internal medicine.

(7) Publications

[Original Articles]

1. Asano, T. and Sato, S. and Furuya, M. Y. and Takahashi, H. and Shichishima-Nakamura, A. and Ohkawara, H. and Fujiwara, T. and Gunji, N. and Hashimoto, C. and Momma, T. and Saito, M. and Nakano, H. and Watanabe, G. and Temmoku, J. and Fujita, Y. and Matsuoka, N. and Kobayashi, H. and Watanabe, H. and Mouri, M. and Mashiya, F. and Sakuma, H. and Ohira, H. and Mori, M. and Ikezoe, T. and Migita, K.. Intestinal Behcet disease associated with myelodysplastic syndrome accompanying trisomy 8 successfully treated with abdominal surgery followed by hematopoietic stem cell transplantation: A case report *Medicine (Baltimore)*. 2019; 98(46); e17979
2. Hara, R. and Umebayashi, H. and Takei, S. and Okamoto, N. and Iwata, N. and Yamasaki, Y. and Nakagishi, Y. and Kizawa, T. and Kobayashi, I. and Imagawa, T. and Kinjo, N. and Amano, N. and Takahashi, Y. and Mori, M. and Itoh, Y. and Yokota, S.. Intravenous abatacept in Japanese patients with polyarticular-course juvenile idiopathic arthritis: results from a phase III open-label study *Pediatr Rheumatol Online J*. 2019; 17(1); 17
3. Maeda, Y. and Takasawa, K. and Ishii, T. and Nagashima, A. and Mouri, M. and Kunieda, J. and Morisaki, H. and Ito, T. and Mori, M. and Kashimada, K. and Doi, S. and Morio, T.. A Nonsense SMAD3 Mutation in a Girl with Familial Thoracic Aortic Aneurysm and Dissection without Joint Abnormality *Cardiology*. 2019; 144(1-2); 53-59
4. Mori, M.. In order to identify immunocompromised patients, what should general pediatricians do first? *Pediatr Int*. 2019; 61(1); 4
5. Nakaseko, H. and Iwata, N. and Yasuoka, R. and Kohagura, T. and Abe, N. and Kawabe, S. and Mori, M.. Pharmacokinetics of mycophenolate mofetil in juvenile patients with autoimmune diseases *Mod Rheumatol*. 2019; 29(6); 1002-1006
6. Okamoto, N. and Yokota, S. and Takei, S. and Okura, Y. and Kubota, T. and Shimizu, M. and Nozawa, T. and Iwata, N. and Umebayashi, H. and Kinjo, N. and Kunishima, T. and Yasumura, J. and Mori, M.. Clinical practice guidance for juvenile idiopathic arthritis (JIA) 2018 *Mod Rheumatol*. 2019; 29(1); 41-59
7. Sakurai, N. and Hino-Shishikura, A. and Nozawa, T. and Kamide, H. and Ohara, A. and Nishimura, K. and Kikuchi, M. and Hara, R. and Mori, M. and Ito, S.. Clinical significance of subcutaneous fat and fascial involvement in juvenile dermatomyositis *Mod Rheumatol*. 2019; 29(5); 808-813
8. Terashita, S. and Tanaka, T. and Taneichi, H. and Adachi, Y. and Mori, M.. Mycophenolate mofetil and prednisolone for cerebral sinus venous thrombosis with Behcet's disease *Pediatr Int*. 2019; 61(9); 920-922
9. Yasumura, J. and Yashiro, M. and Okamoto, N. and Shabana, K. and Umebayashi, H. and Iwata, N. and Okura, Y. and Kubota, T. and Shimizu, M. and Tomiita, M. and Nakagishi, Y. and Nishimura, K. and Hara, R. and Mizuta, M. and Yasumi, T. and Yamaide, F. and Wakiguchi, H. and Kobayashi, M. and Mori, M.. Clinical features and characteristics of uveitis associated with juvenile idiopathic arthritis in Japan: first report of the pediatric rheumatology association of Japan (PRAJ) *Pediatr Rheumatol Online J*. 2019; 17(1); 15
10. 井上, 健斗 and 森, 雅亮. 【小児における抗菌薬適正使用-最新の考え方からのアプローチ】小児における抗菌薬の選び方・使い方 感染と抗菌薬. 2019; 22(2); 138-144
11. 岡田, 賢司 and 水野, 美穂子 and 森内, 浩幸 and 楠田, 聡 and 森岡, 一朗 and 森, 雅亮 and 岡本, 圭祐 and 岡田, 邦之 and 吉原, 重美 and 山岸, 敬幸 and 横山, 詩子 and 久保田, 知洋 and 工藤, 寿子 and 高木, 正稔 and 伊藤, 秀一 and 金森, 豊 and 笹原, 洋二 and 日本小児科学会予防接種・感染症対策委員会「日本におけるパブリックマブの使用に関するガイドライン」改訂検討ワーキンググループ and 日本小児科学会 and 日本

新生児成育医学会 and 日本小児感染症学会 and 日本小児呼吸器学会 and 日本小児循環器学会 and 日本小児リウマチ学会 and 日本小児血液・がん学会 and 日本小児腎臓病学会 and 日本小児外科学会 and 日本免疫不全・自己炎症学会. 日本におけるバリビズマブの使用に関するコンセンサスガイドライン 日本小児科学会雑誌. 2019; 123(5); 807-813

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13. 森, 雅亮. 炎症性疾患に対する生物学的製剤の応用性 小児科. 2019; 60(8); 1173-1181
14. 森, 雅亮. 【血液浄化療法 2019】小児の血液浄化 川崎病 腎と透析. 2019; 87(3); 492-497
15. 森, 雅亮. 【小児リウマチ性疾患の診療～これまでのエビデンスに基づく最近の知見～】小児リウマチ性疾患の移行期医療 Pharma Medica. 2019; 37(7); 69-73
16. 森, 雅亮. 【全身性疾患と腎 update】(第1章) 膠原病、血管炎、自己免疫疾患 IgA 血管炎・リウマチ専門医の視点より 腎と透析. 2019; 86(増刊); 106-108
17. 森, 雅亮. 【膠原病診療 update-診断・治療の最新知見-】小児の膠原病 日本臨床. 2019; 77(3); 408-413
18. 毛利, 万里子 and 森, 雅亮. 【小児科医に必要な免疫の知識】免疫関連分子を標的とした生物学的製剤 update 小児内科. 2019; 51(8); 1205-1208
19. Mari Kubota-Tanaka, Tomoo Osumi, Shouko Miura, Hiroshi Tsujimoto, Toshihiko Imamura, Akira Nishimura, Kentaro Oki, Kozue Nakamura, Satoshi Miyamoto, Kento Inoue, Maiko Inoue, Takahiro Kamiya, Masakatsu Yanagimachi, Tsubasa Okano, Noriko Mitsuki, Takeshi Isoda, Kohsuke Imai, Hirokazu Kanegane, Tomohiro Morio, Shinji Kounami, Mikiya Endo, Motohiro Kato, Masatoshi Takagi. B-lymphoblastic lymphoma with the TCF3-PBX1 fusion gene. Haematologica. 2019.01; 104(1); 35-37
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21. Natsumi Namba, Aya Kawasaki, Ken-Ei Sada, Fumio Hirano, Shigeto Kobayashi, Hidehiro Yamada, Hiroshi Furukawa, Kota Shimada, Atsushi Hashimoto, Toshihiro Matsui, Kenji Nagasaka, Takahiko Sugihara, Aika Suzuki, Kunihiro Yamagata, Takayuki Sumida, Shigeto Tohma, Sakae Homma, Shoichi Ozaki, Hiroshi Hashimoto, Hirofumi Makino, Yoshihiro Arimura, Masayoshi Harigai, Naoyuki Tsuchiya, . Association of *MUC5B* promoter polymorphism with interstitial lung disease in myeloperoxidase-antineutrophil cytoplasmic antibody-associated vasculitis. Annals of the Rheumatic Diseases. 2019.02;
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23. Takahiro Kamiya, See Voon Seow, Desmond Wong, Murray Robinson, Dario Campana. Blocking expression of inhibitory receptor NKG2A overcomes tumor resistance to NK cells. J. Clin. Invest.. 2019.03; 130;
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[Conference Activities & Talks]

1. Hematopoietic cell transplantation with reduced intensity conditioning regimen using fludarabine/busulfan and fludarabine/melphalan for primary immunodeficiency diseases . 2019.02.02
2. Nishimura Akira, Aoki Yuki, Ishiwata Yasuyoshi, Inoue Maiko, Ichimura Takuya, Ueyama Junichi, Matsumoto Kazuaki, Inoue Kento, Hiroki Haruka, Ono Shintaro, Okano Tsubasa, Tanaka Mari, Miyamoto Satoshi, Ashiarai Miho, Miyawaki Reiji, Yamagishi Chika, Tezuka Mari, Okawa Teppei, Hoshino Akihiro, Endo Akifumi, Yasuhara Masato, Kamiya Takahiro, Mitsuiki Noriko, Ono Toshiaki, Yanagimachi Masakatsu, Isoda Takeshi, Tomizawa Daisuke, Nagasawa Masayuki, Kajiwara Michiko, Takagi Masatoshi, Mizutani Shuki, Kanegane Hirokazu, Imai Kohsuke, Morio Tomohiro. Hematopoietic cell transplantation with reduced intensity conditioning regimen using fludarabine/busulfan and fludarabine/melphalan for primary immunodeficiency diseases . The 45th Annual Meeting of the European Society for Blood and Marrow Transplantation 2019.03.25 Frankfurt
3. Mori M.. Development of a novel diagnostic method for atypical and treatment-refractory Kawasaki disease using newly identified proteins as biomarkers related to Kawasaki disease. . 2019 EULAR Meeting. 2019.06 Madrid, Spain.
4. 森 雅亮. 皮疹から考える小児膠原病（ランチョンセミナー）. 第43回日本小児皮膚科学会学術大会. 2019.07
5. Mori M.. plasma exchange therapy for cases refractory to IVIG treatment in Kawasaki disease in Japan. Applications and effectiveness of apheresis therapy for severe conditions in children (Symposium).. 12th World Congress of International Society for Apheresis. 2019.11
6. Genetic test for the suspected patients of inborn errors of immunity. 2019.11.07
7. Satoshi Miyamoto, Takuya Naruto, Tomohiro Morio, Kevin Y Urayama, Atsushi Manabe, Masatoshi Takagi. Association of Germline Variants of TCF3 and PAX5 with Pediatric Acute Lymphoblastic Leukemia Development. 61st American Society of Hematology (ASH) Annual Meeting and Exposition 2019.12.07 Orlando

Department of Collaborative Medicine for Gastroenterology and Hepatology (CMGH)

Associate Professor : Seishin Azuma
Assistant Professor : Kento Takenaka

(1) Outline

Our department was established for the aim to support the medical care at Tokyo Medical and Dental University (TMDU), and to foster experts in the field of gastroenterology and hepatology who engaged a community medicine such as Ibaraki prefecture. In collaboration with the Department of Gastroenterology and Hepatology in TMDU, we will strengthen an information sharing system and an education training support system that build up with Tsuchiura Kyodo General Hospital and other related facilities. We hope to develop the community medicine through the communication and personal exchanges between such hospitals and us.

(2) Research

- Clinical research on liver diseases related to lifestyle-related diseases
- Establishment of optimized therapy in hepatobiliary diseases
- Development of evaluation and treatment of small bowel lesions in Crohn's disease.
- Development of support technology for diagnosis of digestive and liver diseases by artificial intelligence (AI).

(3) Education

Primary goal for education in our department is to train highly educated and experienced clinicians in the field of gastroenterology and hepatology. Therefore, our goal for education of graduate students is to produce clinicians thinking from a wide perspective and to bring up leaders of the next generation in the field of gastroenterology and hepatology.

(4) Lectures & Courses

Our lectures and courses for medical students are collaboration with the Department of Gastroenterology and Hepatology in School of Medicine, TMDU. We also educate clinical residents in Medical Hospital of TMDU and graduate students of the Department of Gastroenterology and Hepatology, TMDU in collaboration with such department.

(5) Clinical Services & Other Works

In collaboration with the Department of Gastroenterology and Hepatology, we mainly provide outpatient and inpatient care of gastrointestinal and hepatobiliary diseases. In addition, we are managing a lot of multicenter studies including Tsuchiura Kyodo General Hospital. We are conducting industry-academic collaborative research in the field of AI research using the comprehensive collaboration program of TMDU.

(6) Clinical Performances

In collaboration with the Department of Gastroenterology and Hepatology, TMDU, we provide a medical care of liver and inflammatory bowel diseases. We have recently established special outpatient clinics for chronic hepatitis, liver cirrhosis, hepatocellular carcinoma and inflammatory bowel diseases.

We are operating a lot of multicenter studies. One of the multicenter studies evaluates the efficacy of treatment against viral hepatitis, named as “Ochanomizu Liver Conference”, in which more than 2,000 patients have been enrolled. We approach to improve the safety and reliance of treatment for hepatocellular carcinoma, the patients are treated using multilateral approaches by dynamic contrast-enhanced ultrasonography, Gd-EOB-DTPA enhanced MRI, and real-time virtual ultrasonography (RVS). We have reported the utility and safety of such therapeutic approaches. We have also performed balloon-assisted enteroscopy for the small intestine. The patients' number were top-class in the world.

(7) Publications

[Original Articles]

1. Seishin Azuma, Yasuhiro Asahina, Sei Kakinuma, Keiko Azuma, Masato Miyoshi, Emi Inoue, Tomoyuki Tsunoda, Ayako Sato, Shun Kaneko, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Makoto Tomita, Mina Nakagawa, Mamoru Watanabe. Diabetic Retinopathy as a Risk Factor Associated with the Development of Hepatocellular Carcinoma in Nonalcoholic Fatty Liver Disease. *Dig Dis.* 2019; 37(3); 247-254
2. Yoshio Kitazume, Tomoyuki Fujioka, Kento Takenaka, Jun Oyama, Kazuo Ohtsuka, Toshimitsu Fujii, Ukihide Tateisi. Crohn Disease: A 5-Point MR Enterocolonography Classification Using Enteroscopic Findings. *AJR Am J Roentgenol.* 2019.01; 212(1); 67-76
3. Masato Miyoshi, Sei Kakinuma, Akihide Kamiya, Tomoyuki Tsunoda, Jun Tsuchiya, Ayako Sato, Shun Kaneko, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. LIM homeobox 2 promotes interaction between human iPS-derived hepatic progenitors and iPS-derived hepatic stellate-like cells. *Sci Rep.* 2019.02; 9(1); 2072
4. Kaho Yamasaki, Kento Takenaka, Kazuo Ohtsuka. Laterally Spreading Tumor-like Early Cancer in Ileum. *Intern Med.* 2019.03; 58(6); 885-886
5. Sayuri Nitta, Yasuhiro Asahina, Takanobu Kato, Jun Tsuchiya, Emi Inoue-Shinomiyama, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Hayato Hikita, Tetsuo Takehara, Mamoru Watanabe. Impact of novel NS5A resistance-associated substitutions of hepatitis C virus detected in treatment-experienced patients. *Sci Rep.* 2019.04; 9(1); 5722
6. Tomoyuki Tsunoda, Sei Kakinuma, Masato Miyoshi, Akihide Kamiya, Shun Kaneko, Ayako Sato, Jun Tsuchiya, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Tsuyoshi Sogo, Haruki Komatsu, Ryutaro Mukouchi, Ayano Inui, Tomoo Fujisawa, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Loss of fibrocystin promotes interleukin-8-dependent proliferation and CTGF production of biliary epithelium. *J Hepatol.* 2019.07; 71(1); 143-152
7. Kento Takenaka, Toshimitsu Fujii, Kohei Suzuki, Hiromichi Shimizu, Maiko Motobayashi, Shuji Hibiya, Eiko Saito, Masakazu Nagahori, Mamoru Watanabe, Kazuo Ohtsuka. Small Bowel Healing Detected by Endoscopy in Patients With Crohn's Disease After Treatment With Antibodies Against Tumor Necrosis Factor.[Epub ahead of print] *Clin Gastroenterol Hepatol.* 2019.08;
8. Shintaro Akiyama, Katsuyoshi Matsuoka, Kyoko Fukuda, Shunsuke Hamada, Mikiko Shimizu, Kosaku Nanki, Shinta Mizuno, Hiroki Kiyohara, Mari Arai, Shinya Sugimoto, Yasushi Iwao, Haruhiko Ogata, Tadakazu Hisamatsu, Makoto Naganuma, Maiko Motobayashi, Kohei Suzuki, Kento Takenaka, Toshimitsu Fujii, Eiko Saito, Masakazu Nagahori, Kazuo Ohtsuka, Mayumi Mochizuki, Mamoru Watanabe, Masayuki Hashiguchi, Takanori Kanai. Long-term effect of NUDT15 R139C on hematologic indices in inflammatory bowel disease patients treated with thiopurine. *J Gastroenterol Hepatol.* 2019.10; 34(10); 1751-1757

9. Kento Takenaka, Maiko Kimura, Kazuo Ohtsuka. Colonic strictures mimicking Crohn's disease.[Epub ahead of print] *Gut*. 2019.11;
10. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Emi Inoue-Shinomiya, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Minoru Tanabe, Emiko Sugawara, Akira Takemoto, Hidenori Ojima, Michie Sakamoto, Masaru Muraoka, Shinichi Takano, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive genetic analysis of cholangiolocellular carcinoma with a coexistent hepatocellular carcinoma-like area and metachronous hepatocellular carcinoma. *Hepatol Res*. 2019.12; 49(12); 1466-1474

[Conference Activities & Talks]

1. Miyako Murakawa, Yasuhiro Asahina, Emi Inoue, Mina Nakagawa, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Fukiko Kawai-Kitahata, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. The association of serum IFN-lambda 3 levels with liver fibrosis and hepatocarcinogenesis in chronic hepatitis C patients treated with direct-acting antiviral agents. EASL, The International Liver Congress 2019 2019.04.13 Vienna (Austria)
2. Mina Nakagawa, Yasuhiro Asahina, Jun Tsuchiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Emi Inoue, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Makoto Tomita, Mamoru Watanabe. Impact of HCV clearance on HCC development and patient survival: Propensity score-matched analysis of an ongoing database of 2173 CHC patients. EASL, The International Liver Congress 2019 2019.04.13 Vienna (Austria)
3. Eiko Saito, Kohei Suzuki, Shuuji Hibiya, Maiko Motobayashi, Kento Takenaka, Nobukatsu Horita, Hiromichi Shimizu, Michio Onizawa, Toshimitsu Fujii, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. The clinical efficacy of ustekinumab (UST) in patients with Crohn's disease (CD). AOCC2019 2019.06.15 Taipei (Taiwan)
4. Kento Takenaka, Kazuo Ohtsuka, Toshimitsu Fujii, Kohei Suzuki, Hiromichi Shimizu, Maiko Motobayashi, Shuuji Hibiya, Eiko Saito, Masakazu Nagahori, Mamoru Watanabe. Small bowel endoscopic healing of Crohn's disease treated with anti-TNF antibodies. AOCC2019 2019.06.15 Taipei (Taiwan)
5. Yasuhiro Asahina, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma. Comprehensive analysis of cancer gene mutations and viral integration in hepatocellular carcinoma arising from non-fibrotic liver. AASLD The Liver Meeting 2019 2019.11.10 Boston (USA)

Department of Child Health and Development

Professor: Hirokazu KANEGANE

Project Assistant Professor: Kei TAKASAWA(∼ March 2019), Motoi YAMASHITA, Tsubasa OKANO

(1) Outline

In addition to acute diseases of medicine and child health care, “growth and medical care” include transition to the chronic phase, long-term medical treatment of patients with intractable diseases, medicine encompassing healthy growth of children. As a philosophy of “growth and medical care”, we establish a developmental and medical system closely related to regional medical care in the suburbs of the metropolitan area, and to foster human resources of pediatricians responsible for next-generation medical care.

(2) Research

We conduct survey research and education based on the organic collaboration between Tokyo Medical and Dental University and Kashiwa City Kashiwa Hospital.

The current main projects are the following.

- 1.Establishment of pediatric medical system in Kashiwa city.
- 2.Study of primary immunodeficiency (PID) predisposing to Epstein-Barr virus infection
- 3.Study of primary antibody deficiency

(3) Education

We conduct a broader range of more specialized clinical education for acquiring pediatric specialists at the University Hospital.

(4) Lectures & Courses

We mainly train young pediatric researchers and specialists. We make them to be familiar with chronic diseases and intractable diseases of childhood and to be responsible for next generation medical care.

(5) Clinical Services & Other Works

We treat children with PID, hematological malignancies, hematological disorders, and malignant solid tumors in the University Hospital.

At Kashiwa City Kashiwa Hospital, we provide pediatric medicine mainly for acute diseases, cooperating with

medical facilities in the suburbs, and establish a reliable medical system for children in the local residents.

(6) Clinical Performances

We provide diagnosis, treatment of pathological analysis of primary immunodeficiency (PID) and hematological malignancies, and perform hematopoietic cell transplantation for refractory diseases. Especially, we treat the largest number of patients with PID in Japan.

(7) Publications

[Original Articles]

1. [Department of Child Health and Development : KANEGANE Hirokazu] Yuki Yatsushiro, Takuro Nishikawa, Aki Saito, Yozo Nakazawa, Ken-Ichi Imadome, Shunsuke Nakagawa, Yuichi Kodama, Yasuhiro Okamoto, Hirokazu Kanegane, Yoshifumi Kawano. Epstein-Barr Virus (EBV)-induced B-cell Lymphoproliferative Disorder Mimicking the Recurrence of EBV-associated Hemophagocytic Lymphohistiocytosis. *J. Pediatr. Hematol. Oncol.* 2019.01; 41(1); e44-e46
2. [Pediatrics : KASHIMADA Kenichi] Kei Takasawa, Atsumi Tsuji-Hosokawa, Shigeru Takishima, Yasunori Wada, Keisuke Nagasaki, Sumito Dateki, Chikahiko Numakura, Atsushi Hijikata, Tsuyoshi Shirai, Kenichi Kashimada, Tomohiro Morio. Clinical characteristics of adolescent cases with Type A insulin resistance syndrome caused by heterozygous mutations in the β -subunit of the insulin receptor (INSR) gene. *J Diabetes.* 2019.01; 11(1); 46-54
3. [Pediatrics and Developmental Biology : MORIO Tomohiro] Keiichi Iwanami, Tsubasa Okano, Osamu Ohara, Tomohiro Morio. Recurrent Acute Abdomen as the Main Manifestation of Hereditary Angioedema. *Intern Med.* 2019.01; 58(2); 213-216
4. [Pediatrics and Developmental Biology : MORIO Tomohiro] Mari Kubota-Tanaka, Tomoo Osumi, Shouko Miura, Hiroshi Tsujimoto, Toshihiko Imamura, Akira Nishimura, Kentaro Oki, Kozue Nakamura, Satoshi Miyamoto, Kento Inoue, Maiko Inoue, Takahiro Kamiya, Masakatsu Yanagimachi, Tsubasa Okano, Noriko Mitsuiki, Takeshi Isoda, Kohsuke Imai, Hirokazu Kanegane, Tomohiro Morio, Shinji Kounami, Mikiya Endo, Motohiro Kato, Masatoshi Takagi. B-lymphoblastic lymphoma with the TCF3-PBX1 fusion gene. *Haematologica.* 2019.01; 104(1); 35-37
5. [Department of Child Health and Development : KANEGANE Hirokazu] Sahoko Ono, Junko Matsuda, Etsuko Watanabe, Hiroto Akaike, Hideto Teranishi, Ippei Miyata, Takanobu Otomo, Yoshito Sadahira, Tatsuki Mizuochi, Hironori Kusano, Masayoshi Kage, Hiroo Ueno, Kenichi Yoshida, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Seishi Ogawa, Yasuhide Hayashi, Hirokazu Kanegane, Kazunobu Ouchi. Novel neuroblastoma amplified sequence (NBAS) mutations in a Japanese boy with fever-triggered recurrent acute liver failure. *Hum Genome Var.* 2019.01; 6; 2
6. [Department of Child Health and Development : KANEGANE Hirokazu] Hirokazu Kanegane. Inflammatory bowel diseases and primary immunodeficiency diseases. *Immunol Med.* 2019.01; 41(4); 154-161
7. [Department of Child Health and Development : KANEGANE Hirokazu] Ryu Yanagisawa, Yozo Nakazawa, Kazuyuki Matsuda, Takahiro Yasumi, Hirokazu Kanegane, Shouichi Ohga, Akira Morimoto, Yoshiko Hashii, Masue Imaizumi, Yasuhiro Okamoto, Akiko M Saito, Keizo Horibe, Eiichi Ishii, . Outcomes in children with hemophagocytic lymphohistiocytosis treated using HLH-2004 protocol in Japan. *Int. J. Hematol.* 2019.02; 109(2); 206-213
8. [Pediatrics and Developmental Biology : TAKAGI Masatoshi] Kay Tanita, Akihiro Hoshino, Ken-Ichi Imadome, Takahiro Kamiya, Kento Inoue, Tsubasa Okano, Tzu-Wen Yeh, Masakatsu Yanagimachi, Akira Shiraishi, Masataka Ishimura, Tilmann Schober, Meino Rohlf, Masatoshi Takagi, Kohsuke Imai, Hidetoshi Takada, Shouichi Ohga, Christoph Klein, Tomohiro Morio, Hirokazu Kanegane. Epstein-Barr Virus-Associated $\gamma \delta$ T-Cell Lymphoproliferative Disorder Associated With Hypomorphic IL2RG Mutation. *Front Pediatr.* 2019.02; 7; 15

9. [Comprehensive Pathology : YAMAMOTO Kouhei] Nagatsuma Misako, Takasawa Kei, Yamauchi Takeru, Nakagawa Ryuichi, Mizuno Tomoko, Tanaka Eriko, Yamamoto Kouhei, Uemura Noriko, Kashimada Kenichi, Morio Tomohiro. 脂肪腫症、腎血管性高血圧および糖尿病を呈する Schimmelpenning 症候群患者における接合後の KRAS 変異 (A postzygotic KRAS mutation in a patient with Schimmelpenning syndrome presenting with lipomatosis, renovascular hypertension, and diabetes mellitus) *Journal of Human Genetics*. 2019.02; 64(2); 177-181
10. [Pediatrics : KASHIMADA Kenichi] Yuichi Miyakawa, Kei Takasawa, Yohei Matsubara, Kenji Ihara, Yoshiaki Ohtsu, Hotaka Kamasaki, Kazuteru Kitsuda, Hironori Kobayashi, Mari Satoh, Sinichiro Sano, Sumito Dateki, Hiroshi Mochizuki, Ichiro Yokota, Yukihiro Hasegawa, Kenichi Kashimada. Language delay and developmental catch-up would be a clinical feature of pseudohypoparathyroidism type 1A during childhood. *Endocr. J.* 2019.03; 66(3); 215-221
11. [Department of Child Health and Development : KANEGANE Hirokazu] Zeinab A El-Sayed, Irina Abramova, Juan Carlos Aldave, Waleed Al-Herz, Liliana Bezrodnik, Rachida Boukari, Ahmed Aziz Bousfiha, Caterina Cancrini, Antonio Condino-Neto, Ghassan Dbaiibo, Beata Derfalvi, Figen Dogu, J David M Edgar, Brian Eley, Rasha Hasan El-Owaidy, Sara Elva Espinosa-Padilla, Nermeen Galal, Filomeen Haerynck, Rima Hanna-Wakim, Elham Hossny, Aydan Ikinciogullari, Ebtihal Kamal, Hirokazu Kanegane, Nadia Kechout, Yu Lung Lau, Tomohiro Morio, Viviana Moschese, Joao Farela Neves, Monia Ouederni, Roberto Paganelli, Kenneth Paris, Claudio Pignata, Alessandro Plebani, Farah Naz Qamar, Sonia Qureshi, Nita Radhakrishnan, Nima Rezaei, Nelson Rosario, John Routes, Berta Sanchez, Anna Sediva, Mikko Rj Seppanen, Edith Gonzalez Serrano, Anna Shcherbina, Surjit Singh, Sangeetha Siniah, Guiseppe Spadaro, Mimi Tang, Ana Maria Vinet, Alla Volokha, Kathleen E Sullivan. X-linked agammaglobulinemia (XLA):Phenotype, diagnosis, and therapeutic challenges around the world. *World Allergy Organ J.* 2019.03; 12(3); 100018
12. [Pediatrics and Developmental Biology : MORIO Tomohiro] Eri Kumaki, Keisuke Tanaka, Kohsuke Imai, Yuki Aoki-Nogami, Akira Ishiguro, Satoshi Okada, Hirokazu Kanegane, Fumihiko Ishikawa, Tomohiro Morio. Atypical SIFD with novel TRNT1 mutations: a case study on the pathogenesis of B-cell deficiency. *Int J Hematol.* 2019.04; 109(4); 382-389
13. [Department of Child Health and Development : KANEGANE Hirokazu] Ryu Yanagaisawa, Kazuyuki Matsuda, Shouichi Ohga, Hirokazu Kanegane, Akira Morimoto, Yasuhiro Okamoto, Akira Ohara, Keitaro Fukushima, Manabu Sotomatsu, Keiko Nomura, Akiko M Saito, Keizo Horibe, Eiichi Ishii, Yozo Nakazawa. Factors predicting the recurrence of Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis in children after treatment using the HLH-2004 protocol. *Int. J. Hematol.* 2019.05; 109(5); 612-617
14. [Department of Child Health and Development : KANEGANE Hirokazu] Motoi Yamashita, Ryosuke Wakatsuki, Tamaki Kato, Tsubasa Okano, Shingo Yamanishi, Nobuko Mayumi, Mayuri Tanaka, Yumi Ogura, Hirokazu Kanegane, Shigeaki Nonoyama, Kohsuke Imai, Tomohiro Morio. A synonymous splice site mutation in IL2RG gene causes late-onset combined immunodeficiency. *Int. J. Hematol.* 2019.05; 109(5); 603-611
15. [Department of Pediatrics, Perinatal and Maternal Medicine : IMAI Kohsuke] Hoshino A, Kanegane H, Nishi M, Tsuge I, Tokuda K, Kobayashi I, Imai K, Morio T, Takagi M. Identification of autoantibodies using human proteome microarrays in patients with IPEX syndrome. *Clin. Immunol.* 2019.06; 203; 9-13
16. [Pediatrics and Developmental Biology : MORIO Tomohiro] Takashi Okumura, Yumi Horie, Chen-Yi Lai, Huan-Ting Lin, Hirofumi Shoda, Bunki Natsumoto, Keishi Fujio, Eri Kumaki, Tsubasa Okano, Shintaro Ono, Kay Tanita, Tomohiro Morio, Hirokazu Kanegane, Hisanori Hasegawa, Fumitaka Mizoguchi, Kimito Kawahata, Hitoshi Kohsaka, Hiroshi Moritake, Hiroyuki Nunoi, Hironori Waki, Shin-Ichi Tamaru, Takayoshi Sasako, Toshimasa Yamauchi, Takashi Kadowaki, Hiroyuki Tanaka, Sachiko Kitanaka, Ken Nishimura, Manami Ohtaka, Mahito Nakanishi, Makoto Otsu. Robust and highly efficient hiPSC generation from patient non-mobilized peripheral blood-derived CD34+ cells using the auto-erasable Sendai virus vector. *Stem Cell Res Ther.* 2019.06; 10(1); 185
17. [Department of Pediatrics, Perinatal and Maternal Medicine : IMAI Kohsuke] Ibusuki A, Nishikawa T, Hiraki T, Okano T, Imai K, Kanegane H, Ohnishi H, Kato Z, Fujii K, Tanimoto A, Kawano Y, Kanekura T.. Prominent dermal Langerhans cells in an Omenn syndrome patient with a novel mutation in the IL2RG gene. *J. Dermatol.* 2019.08;

18. [Department of Pediatrics, Perinatal and Maternal Medicine : IMAI Kohsuke] Makiko Egawa, Hirokazu Kanegane, Kohsuke Imai, Tomohiro Morio, Naoyuki Miyasaka. Intravenous immunoglobulin (IVIG) efficiency in women with common variable immunodeficiency (CVID) decreases significantly during pregnancy. *J. Matern. Fetal. Neonatal. Med.*. 2019.09; 32(18); 3092-3096
19. [Pediatrics and Developmental Biology : TAKAGI Masatoshi] Sutani A, Miyakawa Y, Tsuji-Hosokawa A, Nomura R, Nakagawa R, Nakajima K, Maru M, Aoki Y, Takasawa K, Takagi M, Imai K, Kashimada K, Morio T. Gonadal failure among female patients after hematopoietic stem cell transplantation for non-malignant diseases. *Clinical pediatric endocrinology : case reports and clinical investigations : official journal of the Japanese Society for Pediatric Endocrinology*. 2019.10; 28(4); 105-112
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21. [Pediatrics and Developmental Biology : MORIO Tomohiro] Takeru Yamauchi, Kei Takasawa, Takahiro Kamiya, Shizuka Kirino, Maki Gau, Kento Inoue, Akihiro Hoshino, Kenichi Kashimada, Hirokazu Kanegane, Tomohiro Morio. Hematopoietic stem cell transplantation recovers insulin deficiency in type 1 diabetes mellitus associated with IPEX syndrome. *Pediatr Diabetes*. 2019.11; 20(7); 1035-1040
22. [Pediatrics and Developmental Biology : TAKASAWA Kei] Hosokawa Y, Higuchi S, Kawakita R, Hata I, Urakami T, Isojima T, Takasawa K, Matsubara Y, Mizuno H, Maruo Y, Matsui K, Aizu K, Jinno K, Araki S, Fujisawa Y, Osugi K, Tono C, Takeshima Y, Yorifuji T.. Pregnancy outcome of Japanese patients with glucokinase-maturity-onset diabetes of the young. *Journal of Diabetes Investigation*. 2019.11; 10(6); 1586-1589
23. [Department of Child Health and Development : KANEGANE Hirokazu] Tao Xu, Qin Zhao, Wenyan Li, Xuemei Chen, Xiuhong Xue, Zhi Chen, Xiao Du, Xiaoming Bai, Qian Zhao, Lina Zhou, Xuemei Tang, Xi Yang, Hirokazu Kanegane, Xiaodong Zhao. X-linked lymphoproliferative syndrome in mainland China: review of clinical, genetic, and immunological characteristic. *Eur. J. Pediatr.*. 2019.11;
24. [Department of Child Health and Development : KANEGANE Hirokazu] Kazufumi Kunimura, Daiji Sakata, Xin Tun, Takehito Uruno, Miho Ushijima, Tomoya Katakai, Akira Shiraishi, Ryosuke Aihara, Yasuhisa Kamikaseda, Keisuke Matsubara, Hirokazu Kanegane, Shinichiro Sawa, Gérard Eberl, Shouichi Ohga, Yasunobu Yoshikai, Yoshinori Fukui. S100A4 Protein Is Essential for the Development of Mature Microfold Cells in Peyer's Patches. *Cell Rep*. 2019.11; 29(9); 2823-2834.e7
25. [Department of Child Health and Development : KANEGANE Hirokazu] Takuro Nishikawa, Ken Okamura, Mizuki Moriyama, Kenji Watanabe, Atsuko Ibusuki, Seiji Sameshima, Izumi Masamoto, Ieharu Yamazaki, Kay Tanita, Takuro Kanekura, Hirokazu Kanegane, Tamio Suzuki, Yoshifumi Kawano. Novel AP3B1 compound heterozygous mutations in a Japanese patient with Hermansky-Pudlak syndrome type 2. *J. Dermatol*. 2019.12; 19(7); 529
26. [Department of Child Health and Development : KANEGANE Hirokazu] Hamidah Alias, Abdul Halim Abdul Rashid, Sie Chong Doris Lau, C-Khai Loh, Jamari Sapuan, Sharaf Ibrahim, Reena R Md Zin, Yock Ping Chow, Hirokazu Kanegane, Mariko Eguchi. Early Surgery Is Feasible for a Very Large Congenital Infantile Fibrosarcoma Associated With Life Threatening Coagulopathy: A Case Report and Literature Review. *Front Pediatr*. 2019.12; 7; 529

[Misc]

1. [Department of Child Health and Development : KANEGANE Hirokazu] Ryu Yanagisawa, Kazuyuki Matsuda, Shouichi Ohga, Hirokazu Kanegane, Akira Morimoto, Yasuhiro Okamoto, Akira Ohara, Keitaro Fukushima, Manabu Sotomatsu, Keiko Nomura, Akiko M Saito, Keizo Horibe, Eiichi Ishii, Yozo Nakazawa. Correction to: Factors predicting the recurrence of Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis in children after treatment using the HLH-2004 protocol. *Int. J. Hematol*. 2019.05; 109(5); 629

[Conference Activities & Talks]

1. [Pediatrics and Developmental Biology : TAKAGI Masatoshi] Hematopoietic cell transplantation with reduced intensity conditioning regimen using fludarabine/busulfan and fludarabine/melphalan for primary immunodeficiency diseases . 2019.02.02
2. [Department of Child Health and Development : KANEGANE Hirokazu] Yeh TW, Okano T, Okamoto K, Yamashita M, Takashima T, Mitsuiki N, Okada S, Kanegane H, Imai . APRIL deficiency as a cause of common variable immunodeficiency. 第2回日本免疫不全・自己炎症学会総会・学術集会 2019.02.02 東京
3. [Department of Child Health and Development : KANEGANE Hirokazu] Tanita K, Cardinez C, Miraghanzadeh B, Hoshino A, Okada S, Asano T, Tsumura M, Ohnishi H, Kato Z, Morio T, Vinuesa CG, Kanegane H, Cook MC. Gain-of-function IKBKB mutation causes human combined immune deficiency. 第2回日本免疫不全・自己炎症学会総会・学術集会 2019.02.02 東京
4. [Department of Child Health and Development : KANEGANE Hirokazu] Yamada Y, Cho K, Age-matsu K, Kanegane H, Miyake N, Ueki M, Akimoto T, Kobayashi N, Ikemoto S, Tanino M, Fujita A, Hayasaka I, Miyamoto S, Tanaka-Kubota M, Nakata K, Shiina M, Ogata K, Minakami H, Matsumoto N, Ariga T. Heterozygous mutations in OAS1 cause infantile-onset pulmonary alveolar proteinosis with hypogammaglobulinemia. 第2回日本免疫不全・自己炎症学会総会・学術集会 2019.02.02 東京
5. [Rheumatology : KIMURA Naoki] An adult case of cytotoxic T-lymphocyte antigen 4 (CTLA-4) insufficiency treated successfully with abatacept. 2019.02.03
6. [Pediatrics and Developmental Biology : MORIO Tomohiro] An experience of allogeneic stem cell transplantation for NFKB1 deficiency. 2019.02.03
7. [Pediatrics and Developmental Biology : MORIO Tomohiro] Combined immunodeficiency of ICF syndrome. 2019.02.03
8. [Pediatrics and Developmental Biology : MORIO Tomohiro] Three families with X-linked agammaglobulinemia caused by transcriptional. 2019.02.03
9. [Pediatrics and Developmental Biology : TAKAGI Masatoshi] Nishimura Akira, Aoki Yuki, Ishiwata Yasuyoshi, Inoue Maiko, Ichimura Takuya, Ueyama Junichi, Matsumoto Kazuaki, Inoue Kento, Hiroki Haruka, Ono Shintaro, Okano Tsubasa, Tanaka Mari, Miyamoto Satoshi, Ashiarai Miho, Miyawaki Reiji, Yamagishi Chika, Tezuka Mari, Okawa Teppei, Hoshino Akihiro, Endo Akifumi, Yasuhara Masato, Kamiya Takahiro, Mitsuiki Noriko, Ono Toshiaki, Yanagimachi Masakatsu, Isoda Takeshi, Tomizawa Daisuke, Nagasawa Masayuki, Kajiwarra Michiko, Takagi Masatoshi, Mizutani Shuki, Kanegane Hirokazu, Imai Kohsuke, Morio Tomohiro. Hematopoietic cell transplantation with reduced intensity conditioning regimen using fludarabine/busulfan and fludarabine/melphalan for primary immunodeficiency diseases . The 45th Annual Meeting of the European Society for Blood and Marrow Transplantation 2019.03.25 Frankfurt
10. [Department of Child Health and Development : KANEGANE Hirokazu] Kanegane H. Revisit X-linked agammaglobulinemia. 2019 Samsung Medical Center Primary Immunodeficiency Symposium. 2019.07.06 Seoul
11. [Pediatrics and Developmental Biology : MORIO Tomohiro] Okano T, Imai K, Naruto T, Okada S, Okamoto K, Yamashita M, Yeh T. W, Takagi M, Kanegane H, Morio T. Diagnostic Approach by Whole Exome Sequencing for 141 Patients of Inborn Errors of Immunity. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.19 Brussels
12. [Pediatrics and Developmental Biology : MORIO Tomohiro] Cardinez C, Miraghanzadeh B, Tanita K, da Silva E, Hoshino A, Okada S, Chand R, Asano T, Tsumura M, Yoshida K, Ohnishi H, Kato Z, Yamazaki M, Okuno Y, Miyano S, Kojima S, Ogawa S, Andrews TD, Field MA, Burgio G, Morio T, Vinuesa CG, Kanegane H, Cook M. Gain-of-Function IKBKB Mutation Causes Human Combined Immune Deficiency. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.19 Brussels
13. [Pediatrics and Developmental Biology : MORIO Tomohiro] Hoshino A, Okano T, Matsumoto K, Nishimura A, Shintaku H, Tokoro S, Okamoto H, Wada T, Mitsuiki N, Kajiwarra M, Takagi M, Imai K, Kanegane H, Morio T. Plasmacytoma-Like Post-Transplant Lymphoproliferative Disorder with Multiple Autoantibodies in a XIAP Deficient Patient. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.20 Brussels

14. [Pediatrics and Developmental Biology : MORIO Tomohiro] Nishimura A, Naruto T, Hoshino A, Amano K, Iwamoto S, Hirayama M, Grigg A, Bosco J J, Migita M, Takagi M, Ohara O, Morio T, van Zelm MC, Kanegane H. Genomics Analysis of Leukemia Predisposition in X-Linked Agammaglobulinemia. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019) 2019.09.20 Brussels
15. [Department of Child Health and Development : KANEGANE Hirokazu] Honda Y, Yasumi T, Miyamoto T, Nishitani M, Nihira H, Shiba T, Shibata H, Tanaka T, Kanda K, Izawa K, Kanegane H, Heike T, Takita J, Nishikomori R.. A CTLA-4 Haploinsufficiency Case with Multiple Brain and Pulmonary Lesions - Dilemmas in Management. 19th Biennial Meeting of the European Society of Immunodeficiencies (ESID2019). 2019.09.20 Brussels
16. [Pediatrics and Developmental Biology : TAKAGI Masatoshi] Genetic test for the suspected patients of inborn errors of immunity. 2019.11.07
17. [Department of Child Health and Development : KANEGANE Hirokazu] Efficacy of Azacitidine for MDS due to germline GATA2 haploinsufficiency. 2019.11.14
18. [Department of Child Health and Development : KANEGANE Hirokazu] BRAFV600E-POSITIVE PRECURSORS AS MOLECULAR MARKERS OF BONE MARROW INVOLVEMENT IN PEDIATRIC LANGERHANS CELL HISTIOCYTOSIS. 2019.11.14
19. [Department of Child Health and Development : KANEGANE Hirokazu] Clonal evolution of leukemia with MLL-AF9 from myeloid to T-lineage. 2019.11.14
20. [Department of Child Health and Development : KANEGANE Hirokazu] Treatment of platelet transfusion refractoriness in patients with Wiskott-Aldrich syndrome. 2019.11.14
21. [Department of Child Health and Development : KANEGANE Hirokazu] A case of type 1 hyper-IgE syndrome with leukemoid reaction in an infant. 2019.11.14
22. [Department of Child Health and Development : KANEGANE Hirokazu] A case with relapsed acute lymphoblastic leukemia treated with blinatumomab under the active GVHD after unrelated bone marrow transplantation. 2019.11.15
23. [Department of Child Health and Development : KANEGANE Hirokazu] Intrinsically Vancomycin resistant enterococcal (*Enterococcus gallinarum*) meningitis occurred early after hematopoietic stem cell transplantation for activated PI3K delta syndrome type2. 2019.11.16
24. [Department of Child Health and Development : KANEGANE Hirokazu] Successful case of donor lymphocyte infusion for refractory T cell acute lymphoblastic leukemia which lead to one year of remission. 2019.11.16
25. [Department of Child Health and Development : KANEGANE Hirokazu] Pay attention to selective Immunoglobulin G2 deficiency - a case of Invasive pneumococcal infection after allogenic hematopoietic stem cell transplantation. 2019.11.16
26. [Department of Child Health and Development : KANEGANE Hirokazu] Usefulness of respiratory infection early diagnosis with multiplex PCR method for immunocompromised patients. 2019.11.16

Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA
Junior Associate Professor Keiko KONDO
Specially Appointed Assistant Professor Masayuki TOI
Graduate Student Nami ISHIZAKA
Resident Shinta SUZUKI

(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 ultrafine bubble water (OUFBW) :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. Anongwee Leewananthatwet, Shinichi Arakawa, Tokuju Okano, Ryo Daitoku Kinoshita, Hiroshi Ashida, Yuichi Izumi, Toshihiko Suzuki. Ozone ultrafine bubble water induces the cellular signaling involved in oxidative stress responses in human periodontal ligament fibroblasts Science and Technology of Advanced Materials . 2019.05; 20(1); 589-598
2. Kazuki Watanabe, Yujin Ohsugi, Shogo Maekawa, Naoki Sasaki, Takahiko Shiba, Sayaka Katagiri, Shinichi Arakawa. Ozone Ultrafine Bubble Water improves wound healing via modification of inflammation 口腔病学会雑誌. 2019.07; 86(2);
3. 渡辺 数基, 大杉 勇人, 前川 祥吾, 佐々木 直樹, 芝 多佳彦, 片桐 さやか, 荒川 真一. 創傷治癒モデルマウスにおける炎症因子を介したオゾンウルトラファインバブル水の効果 (Ozone Ultrafine Bubble Water Improves Wound Healing via Modification of Inflammation) 口腔病学会雑誌. 2019.07; 86(2); 25-35
4. Watanabe K, Ohsugi Y, Maekawa S, Sasaki N, Shiba T, Katagiri S, Arakawa S. Ozone Ultrafine Bubble Water improves wound healing via modification of inflammation Journal of the Stomatological Society. 2019.07; 86(2); 25-34

[Misc]

1. Shinichi Arakawa. Ozone antiseptic shows potential for treating severe gum infections Asia Research News 2015.

[Conference Activities & Talks]

1. The Validation of Introduction of Dental Hygiene Students' Practical Training on Medical Visiting Care. 2019.12.07
2. Kanade Ito, Shinichi Arakawa, Keiko Kondo, Yuji Kabasawa. The Validation of Introduction of Dental Hygiene Students' Practical Training on Medical Visiting Care. 2019.12.08

Oral Care for Systemic Health Support

Professor Yuhji Kabasawa
Assistant Professor Kanade Ito

(1) Outline

(1) Education

We teach the knowledge and skills necessary for oral health activities through classes in charge. Specifically, we will teach about the relationship between oral health and general health such as perioperative oral function management and periodontal disease and diabetes. In addition to teaching health assessment of the oral and maxillofacial area, we will acquire basic knowledge and skills through vital signs measurement practice, emergency life-saving activity practice, which is one of general health evaluation indicators.

Furthermore, we lecture on the pathology, pathology, diagnosis and treatment related to mandibular oral cavity disease, and teach necessary knowledge on oral health education, prevention of oral diseases of people with basic diseases in the medical field.

(2) Research

We will conduct research to support maintenance and promotion of health by oral health. Especially contribute to people's health and well-being through research on perioperative oral cavity function management, research on oral care of people with underlying diseases, research on regeneration of jawbone with FGF-2, etc.

We also working about the Research on social inequalities in oral health.

(3) Clinical

In order to maintain and promote general health through oral health, we cooperate with each outpatient at the dentistry hospital and do dental prophylactic treatment of the patient and oral health education at oral care outpatient. In addition to oral care for inpatients at dental and medical hospital while working in cooperation with nurses, nutritionists, pharmacists and others, they practice oral care according to the condition of patients as a member of team medicine.

(2) Research

1. Oral health care of patients with oral cancer, cleft lip and palate and other oral diseases
2. Research for safety in supplements in oral functions
3. Research on social inequalities in oral health.
4. Basic research for bone regeneration using FGF-2.

(3) Education

Team medical practice, clinical practice, clinical practice, oral surgery and dental anesthesiology, clinical medicine, graduation research, health care services, biomaterials science, oral disease prevention basics and practical training, clinical oral health practice, Dental practice support theory,etc

(4) Lectures & Courses

The purpose is to develop dental hygienist who can contribute to oral and general health. Train student who can contribute to the health and welfare of people based on the knowledge and skills for oral health activities,

understanding oral medicine and social environmental factors that affect health.

(5) Clinical Services & Other Works

Oral care department, in cooperation with each outpatient in the dental school attached hospital, in order to maintain and improve the general health through oral health, do patients' dental preventive measures and oral health education in oral care outpatient. In addition, we do oral care for hospitalized patients in the dentistry department and medical hospital affiliated hospitals, we receive consultation about patient oral care from ward nurses, and instruct oral care methods according to patient condition.

In oral surgery unit, we are engaged in diagnosis, treatment, oral health guidance etc of various oral disease patients.

(6) Clinical Performances

Based on knowledge of oral medicine through oral care department, we are conducting perioperative oral function management with more specialized expertise.

(7) Publications

[Conference Activities & Talks]

1. Kanade Ito, Aya Isumi, Satomi Doi, Manami Ochi, Takeo Fujiwara. The association between eating vegetables at start of meal and dental caries among Japanese children. 12th European Public Health Conference 2019.11.20 Marseille, France
2. Kanade Ito, Shinichi Arakawa, Keiko Kondo, Yuji Kabasawa. The Validation of Introduction of Dental Hygiene Students' Practical Training on Medical Visiting Care. 2019.12.08

Preventive Oral Health Care Sciences

Professor Kayoko SHINADA
Assistant Professor Naoko ADACHI(April- leave)
Kanaoka TODA(April-)
Part-time lecturer Atsushi OHYAMA,
Hiromi OTSUKA.
Kenichi TANAKA
Technical assistant Xu Zheng Yang
Graduate Students Master Course
Sakura Hayashi,
Liu Zhenyan.
Miu YASUI(April-),
HSU CHEN WEI(April-),
Graduate Students(research) WANG (April-),WANG RAN(April-)

(1) Outline

In order to cultivate students' abilities to prevent and detect oral diseases at an early stage, which are important to maintain and improve the nation's health, we help students acquire deep academic knowledge and high standard skills in preventive oral health care such as skills to check over the condition of oral cavities. Additionally, we help students develop skills to provide oral health counseling and oral health promotion, and nurture human resources who can actively contribute the development of oral health promotion.

(2) Research

- 1) Preventive Oral Health Care Sciences
 - ① Incident factors and preventive methods on dental caries
 - ② Incident factors and preventive methods on periodontal disease
 - ③ Incident factors and preventive methods on oral malodor
 - ④ Incident factors and preventive methods on other oral diseases
- 2) Development of education system for the patients to prevent oral diseases and for dental hygiene students.
- 3) Development of new assessment programs in technical education for dental hygienist students.

(3) Clinical Services & Other Works

In our Oral Health Care Clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases, for the patients to maintain their oral health for the entire lifetime.

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

1. Toda Kanako, Mizutani Koji, Minami Isao, Ye Ming, Arakawa Takahiro, Mitsubayashi Kohji, Ogawa Yoshihiro, Araki Kouji, Shinada Kayoko. Effects of oral health instructions on glycemic control and oral health status of periodontitis patients with type 2 diabetes mellitus: A preliminary observation JOURNAL OF DENTAL SCIENCES. 2019.06; 14(2); 171-177

[Conference Activities & Talks]

1. Seki N, Moross J, Osato A, Sunaga M, Shinada K, Morio I, Kinoshita A. Development of clinical simulation teaching materials in English for dental hygienist education -the second report-. 38th Annual Meeting of the Japanese Dental Education Association 2019.07.19 Fukuoka
2. Naoko Adachi, Yasuki Kobayashi. The Association between Decayed Teeth and Periodontitis, and Metabolic Syndrome: One-year Follow-up Study. International Symposium on Dental Hygiene 2019.08.15 Brisbane, Australia
3. Naomi Yoshida, Kumiko Sugimoto, Ayako Kubota, Naoko Adachi, Hitomi Suzuki, Sato Yamanaka, Yoshikazu Okawa, Hiroyuki Sakamaki, Hiromi Otsuka, Yukie Yoshida and Manabu Yanagita. Association between oral health status and self-reported complaints in adolescence. CED-IADR/NOF Oral Health Research Congress 2019.09.20 Melia Castilla Hotel & Convention Center, Madrid, Spain
4. Xu Zheng Yang, Kanako Toda, Kayoko Shinada. A study on Japanese residing condition overseas. 2019.12.06 Tokyo
5. Liu Zhenyan, Kanako Toda, Kayoko Shinada. A Survey on Oral Health Status and Oral Health Habits of Foreign Students . The 84th Congress of the Stomatological Society, Japan 2019.12.06 Tokyo

Oral Health Sciences for Community Welfare

Professor Junichi FURUYA
Junior Associate Professor Rena NAKAYAMA
Graduate Student Akane BENIYA
Graduate Student Ayano AKATSUKA
Graduate Student Nei KOSHITANI
Graduate Student Saki MIYAJIMA
Graduate Research Student Junji TOKUNAGA
Graduate Student (Gerodontology and Oral rehabilitation) Chiaki MATSUBARA
Graduate Student (Gerodontology and Oral rehabilitation) Michiyo OBANA

(1) Outline

The role of Department of Oral Health Sciences for Community Welfare is to develop education, practice, research for turning out dental profession who can play an important role as profession of oral function and eating in medical care and welfare of super-aging society. All of our research and education is based on daily medical and dental care so that we can produce medical and dental professions who can work globally and locally.

The department is particularly focusing on improving oral health such as mastication, swallowing, dentures and oral hygiene through dysphagia rehabilitation, diet modification support, multi-disciplinary team approach so that the department contributes to prevent and improve aspiration pneumonia, malnutrition, and quality of life. Recently, we're also focusing on oral function of stroke patients and community cooperation, oral function of dementia and MCI patients and dental care, and dentures and swallowing in team approach.

All educational and research activities are based on clinical practice and experiences so that knowledge and skills of oral function will be acquired. Concretely, oral functional rehabilitation and oral hygiene care are performed as oral health management for hospitalized and institutionalized patients, and out patient in clinic. In addition, we supply multi-disciplinary team approach as a member of NST (Nutrition Support Team), PCT (Palliative Care Team), Oral hygiene care team in medical hospital of TMDU, and Visiting Dysphagia Rehabilitation Team.

(2) Research

1. Oral function, mastication, swallowing and dentures for dysphagia rehabilitation of older people
2. Oral health management for multidisciplinary team approach (NST and palliative care team) in medical care and community welfare
3. Frailty, malnutrition and oral frailty of older people
4. Oral function of patients with stroke and dementia
5. Home care dentistry and team approach for enjoyment of oral intake in community welfare

(3) Education

Gerodontology
Welfare for older people
Nursing-care for older people
Prosthodontics

Home visiting dentistry
Community dental care
Social work
etc

(4) Publications

[Original Articles]

1. Taniguchi H, Matsuo K, Nakagawa K, Furuya J, Kanazawa M, Minakuchi S.. Decline in tongue pressure during perioperative period in cancer patients without oral feeding. *Clinical Nutrition ESPEN*. 2019.02; 29; 183-188
2. Chantaramanee A, Tohara H, Nakagawa K, Hara K, Nakane A, Yamaguchi K, Yoshimi K, Junichi F, Minakuchi S. Association between echo intensity of the tongue and its thickness and function in elderly subjects. *Journal of oral rehabilitation*. 2019.03;
3. Nomura T, Murakami T, Shimoyama Y, Kobayashi T, Furuya J, Sasaki M, Kondo H. Effects of denture adhesives on growth and morphological transformation of *Candida albicans*. *Journal of prosthodontic research*. 2019.05;
4. Obana M, Furuya J, Matsubara C, Haruka T, Inaji M, Miki K, Numasawa Y, Minakuchi S, Maehara T. Effect of a collaborative transdisciplinary team approach on oral health status in acute stroke patients. *Journal of oral rehabilitation*. 2019.07;
5. Kurosawa Y, Hara K, Tohara H, Namiki C, Chantaramanee A, Nakane A, Nakagawa K, Yamaguchi K, Yoshimi K, Furuya J, Minakuchi S. Calf Circumference Is a Useful Index for Assessing Dysphagia among Community Dwelling Elderly Recipients of Long-Term Care. *The Tohoku journal of experimental medicine*. 2019.07; 248(3); 201-208
6. Kurosawa Yukiko, Hara Koji, Tohara Haruka, Namiki Chizuru, Chantaramanee Ariya, Nakane Ayako, Nakagawa Kazuharu, Yamaguchi Kohei, Yoshimi Kanako, Furuya Junichi, Minakuchi Shunsuke. Calf Circumference Is a Useful Index for Assessing Dysphagia among Community Dwelling Elderly Recipients of Long-Term Care(和訳中) *The Tohoku Journal of Experimental Medicine*. 2019.07; 248(3); 201-208
7. Yuriko Kurosawa¹, Koji Hara, Haruka Tohara, Chizuru Namiki, Ayako Nakane, Kazuharu Nakagawa, Kohei Yamaguchi, Kanako Yoshimi, Junichi Furuya, Shunsuke Minakuchi. Calf Circumference Is a Useful Index for Assessing Dysphagia among Community Dwelling Elderly Recipients of Long-Term Care. *Tohoku Journal of Experimental Medicine*. 2019.07; 248(3); 201-208
8. Hara K, Tohara H, Chizuru N, Yamaguchi K, Chantaramanee A, Kobayashi K, Saito T, Nakagawa K, Okumura T, Yoshimi K, Nakane A, Furuya J, Minakuchi S. Relationship between displacement of the masseter muscle during biting and masseter muscle quality and bite force in healthy elderly persons. *Journal of oral rehabilitation*. 2019.11;
9. Rena Hidaka, Junichi Furuya, Hiroyuki Suzuki, Chiaki Matsubara, Michiyo Obana, Junji Tokunaga, Keiko Endo. Survey on the oral health status of community-dwelling older people with visual impairment. *Spec Care Dentist*. 2019.12;

[Conference Activities & Talks]

1. Junichi Furuya. Geriatric dentistry in Japan. 2019.03.13 Ann Arbor
2. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matubara, Yuko Kagifuku, Haruka Tohara, Shunsuke Minakuchi. Investigation of oral health status and function in Mild Cognitive Impairment (MCI) patients -An interim report of cross sectional study-. The 1st TAGD-JSG Gerodontology Summit 2019.03.23 Taipei
3. Junichi Furuya. Geriatric dentistry focusing on oral hypofunction and dysphagia rehabilitation. The 1st TAGD-JSG Gerodontology Summit 2019.03.23 Taipei

4. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Yuko Kagihuku, Haruka Tohara, Shunsuke Minakuchi. Investigation of oral function in patients with Mild Cognitive Impairment (MCI) by medical and dental cooperation. The 30th Annual Meeting of the Japanese Society of Gerodontology 2019.06.08 Sendai
5. Junichi Furuya. Functional occlusal scheme for complete dentures.. 南方医科大学附属口腔医院 2019.09.20 Guangdong
6. Yamaguchi K Hara K Nakagawa K Chantaramanee A Namiki C Yoshimi K Nakane A Furuya J Tohara H. AGING AND TOOTH LOSS RELATED CHANGES OF MASSETER MUSCLE CHARACTERISTICS - ULTRASONOGRAPHIC STUDY ON YOUNG AND OLD SUBJECTS -. 9th ESSD annual meeting 2019.09.21 Vienna
7. FURUYA J. Geriatric Dentistry in Japan. Korean Society of Dental Hygiene 2019 symposium 2019.11.02 Cheonan, Korea.

Oral Health Care Education

Professor Naomi Yoshida
Junior Associate Professor Yuki Ohara
Assistant Professor Hitomi Suzuki
Part-time Lecturer Kumiko Sugimoto

(1) Research

- 1) Research on oral health behavior
- 2) Research on oral health management
- 3) Research on flailty and oral flailty
- 4) Research and development of education methods in dental hygienists education

(2) Education

Oral health care education is special field of study which deals with establishment of theoretid 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 the their oral and general health in the entire lifetime.

(4) Publications

[Original Articles]

1. Keiichiro Sagawa, Hiroyasu Furuya, Yuki Ohara, Mitsuyoshi Yoshida, Hirohiko Hirano, Katsuya Iijima, Takeshi Kikutani. Tongue function is important for masticatory performance in the healthy elderly: a cross-sectional survey of community-dwelling elderly. J Prosthodont Res. 2019.01; 63(1); 31-34
2. Haruka Nakata, Koichiro Matsuo, Hitomi Suzuki, Akihiro Yoshihara. Perioperative changes in knowledge and attitude toward oral health by oral health education. Oral Dis. 2019.05; 25(4); 1214-1220
3. Suzuki H, Matsuo K, Okamoto M, Nakata H, Sakamoto H, Fujita M. Preoperative periodontal treatment and its effects on postoperative infection in cardiac valve surgery. Clinical and experimental dental research. 2019.10; 5(5); 485-490
4. Suzuki H, Matsuo K, Okamoto M, Nakata H, Sakamoto H, Fujita M. Perioperative changes in oral bacteria number in patients undergoing cardiac valve surgery. Journal of oral science. 2019.11; 61(4); 526-528

[Conference Activities & Talks]

1. N Yoshida, K Sugimoto, H Hobo, A Kubota, A Yamanaka, N Adachi, Y Ohkawa, M Yanagida, H Sakamaki, K Araki. Oral health status and oral health behavior of newly enrolled university students in Japan. ISDH 2019 2019.08.15 Brisbane, Austraria
2. Naomi Yoshida, Kumiko Sugimoto, Ayako Kubota, Hiromi Otsuka, Yoshikazu Okawa, Sato Yamanaka, Hiroyuki Sakamaki, Yukie Yoshida, Manabu Yanagida. Oral health status and oral health behavior of newly enrolled university students in Japan. International Symposium on Dental Hygiene 2019 2019.08.15 Brisbane, Australia
3. Naomi Yoshida, Noriko Takei. Establishing a System for Dental Hygienists During Disaster Relief Activities. International symposium on dental hygiene 2019.08.16 Brisbane, Australia
4. Naomi Yoshida, Kumiko Sugimoto, Ayako Kubota, Naoko Adachi, Hitomi Suzuki, et al. Association between oral health status and self-reported complaints in adolescence. CED-IADR/NOF Oral Health Research Congress 2019.09
5. Naomi Yoshida, Kumiko Sugimoto, Ayako Kubota, Naoko Adachi, Hitomi Suzuki, Sato Yamanaka, Yoshikazu Okawa, Hiroyuki Sakamaki, Hiromi Otsuka, Yukie Yoshida, Manabu Yanagita. Association between oral health status and self-reported complaints in adolescence . 2019 CED-IADR/NOF Oral Health Research Congress 2019.09.19 Madrid, Spain
6. Naomi Yoshida, Kumiko Sugimoto, Ayako Kubota, Naoko Adachi, Hitomi Suzuki, Sato Yamanaka, Yoshikazu Okawa, Hiroyuki Sakamaki, Hiromi Otsuka, Yukie Yoshida and Manabu Yanagita. Association between oral health status and self-reported complaints in adolescence. CED-IADR/NOF Oral Health Reseach Congress 2019.09.20 Melia Castilla Hotel & Convention Center, Madrid, Spain
7. 鈴木瞳、吉田直美、杉本久美子、久保田絢子、則武加奈子、梅森幸、荒木孝二. 歯学部新入生における口腔内状況と口腔保健行動の調査. 第 84 回口腔病学会学術大会 2019.12.06 東京
8. 鈴木 瞳, 吉田直美, 杉本久美子, 久保田絢子, 則武加奈子, 梅森 幸, 荒木孝二. 歯学部新入生における口腔内状況と口腔保健行動の調査. 第 84 回口腔病学会学術大会 2019.12.06 東京

Basic Sciences of Oral Health Care

Junior Associate Professor Yujiro Sakamoto

(1) Outline

Graduate School of Medical and Dental Sciences has been reorganized in April 2012, and the section of Basic Sciences of Oral Health Care was established in Medical and Dental Science and Technology master' s program course.

(2) Research

- 1) Basic medical and dental studies for oral health care
- 2) Basic study on clinical application of oral health care
- 3) Gross anatomical study of head and neck region

(3) Education

Purpose of Education

Basic sciences of oral health care is a branch of morphological sciences, developmental biology, pathology and the neurosciences to understand the structure and function of human body and its pathological conditions. Students are taught in more detail about the normal tooth anatomy and occlusal function as well as the anatomy of the head and neck with specific attention to the skull, muscles, nerves, and arteries associated with the mouth and teeth. In addition, students are also taught the oral pathology and dental pharmacology and pharmaceuticals.

Subjects and contents.

- Structure and function of human body I and II: anatomy, histology, physiology, embryology, oral anatomy, oral histology, oral physiology.
- Mechanism of disease and promotion of recovery process: pathology, oral pathology, microbiology, immunology, pharmacology.
- Dental pharmacology and pharmaceuticals.
- Graduation thesis:

Other education.

- Human anatomy (in School of Medicine, Faculty of Medicine).
- Head and neck basic medical sciences (in School of Medicine, Faculty of Medicine and School of Dentistry, Faculty of Dentistry).
- Structure and function of human body (in Course for Oral Health Engineering, School of Oral Health Care Sciences, Faculty of Dentistry).
- Oral health generic care sciences (in Health Sciences and Biomedical Engineering, Graduate School of Medical and Dental Sciences).

(4) Publications

[Original Articles]

1. Sakamoto Y. Morphological features of the glossopharyngeal nerve in the peripharyngeal space, the oropharynx and the tongue. *Anatomical Record*. 2019.04; 302(4); 630-638
2. Sakamoto Y. Morphological Features of the Branching Pattern of the Hypoglossal Nerve. *Anatomical Record*. 2019.04; 302(4); 558-567

[Conference Activities & Talks]

1. Sakamoto Y. Spatial relations of the lingual, facial, and occipital arteries with the submandibular triangle. The 36th Annual Meeting of the American Association of Clinical Anatomists. 2019.06.13 Tulsa, USA.
2. Sakamoto Y. Positional relations of the hypoglossal and superior laryngeal nerves with the superior thyroid, lingual, facial and occipital arteries. International Congress of Anatomia Clinica, a Joint Meeting of the 15th European Association of Clinical Anatomists and the 11th International Symposium of Clinical and Applied Sciences. 2019.06.24 Madrid, Spain.

Basic Oral Health Engineering

Professor Kazuhiro Aoki
Associate Professor Meiko Oki
Assistant Professor Shingo Kamijo

(1) Outline

Basic Oral Health Engineering is a department assigned to basic science field of oral health in three master course departments which were reorganized from the departments of Oral Health Engineering Course in 2015. The department is originated in Basic Oral Health Sciences.

The department of Basic Oral Health Engineering aims to create a scientific foundation for the clinical applications based on interdisciplinary research between engineering and biology and/or interface studies between basic and clinical sciences. We believe that these research activities, which are focused on the region of the oral cavity, can contribute to attaining healthy and happy living conditions. We have the responsibility to train our students to be medical personnel who are eager to contribute to people's happiness through a broad range of educational courses from basic level courses to professional level courses, which integrate areas of study such as the structure and function of the human body, stomatognathic region, pharmacology and the research process.

(2) Research

Research Subjects

- 1) The development of non-invasive methods of bone mass augmentation (Interdisciplinary research)
- 2) Research related to the connection between oral bacteria and systemic diseases
- 3) The development of surface coating materials for the prevention of plaque growth (International collaboration)
- 4) The fabrication of facial prostheses using a three-dimensional rapid manufacturing method
- 5) Clinical studies of treatments for patients with maxillofacial defects
- 6) The development of materials for facial prostheses
- 7) The education of dental technicians using computer simulation training

(3) Lectures & Courses

Basic Oral Health Engineering is a department of oral health engineering which deals with the basic oral health sciences to perform evidence-based oral health care and prosthetic treatments to support people to promote oral health and improve quality of life. Main objective of Basic Oral Health Engineering in the undergraduate course is to provide students opportunity to study the structure and function of the human body, pharmacology, fabrication of dental and maxillofacial prostheses, dental CAD/CAM technology and research process.

(4) Clinical Services & Other Works

Clinical activities

- Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects
- Making dental and maxillofacial prostheses

(5) Publications

[Original Articles]

1. Sone E, Noshiro D, Ikebuchi Y, Nakagawa M, Khan M, Tamura Y, Ikeda M, Oki M, Murali R, Fujimori T, Yoda T, Honma M, Suzuki H, Ando T, Aoki K. The induction of RANKL molecule clustering could stimulate early osteoblast differentiation. *Biochemical and biophysical research communications*. 2019.02; 509(2); 435-440
2. Suzuki A, Hoshiai T, Nakata H, Otomaru T, Oki M, Taniguchi H, Kasugai S, Kuroda S. Modal analysis of two different types of fixed implant-supported prostheses embedded in edentulous maxillae. *Journal of Prosthodont Res*. 2019.07; 63(3); 327-333
3. Tsuchida Y, Takahashi H, Watanabe H, Oki M, Shiozawa M, Kurabayashi T, Suzuki T. Effects of number of metal restorations and mandibular position during computed tomography imaging on accuracy of maxillofacial models *J Prosthodont Res*. 2019.04; 63(2); 239-244
4. Touyama K, Khan M, Aoki K, Matsuda M, Hiura F, Takakura N, Matsubara T, Harada Y, Hirohashi Y, Tamura Y, Gao J, Mori K, Kokabu S, Yasuda H, Fujita Y, Watanabe K, Takahashi Y, Maki K, Jimi E. Bif-1/Endophilin B1/SH3GLB1 regulates bone homeostasis. *Journal of cellular biochemistry*. 2019.06;
5. Amano Hitoshi, Iwaki Futoshi, Oki Meiko, Aoki Kazuhiro, Ohba Shinsuke. An osteogenic helioxanthin derivative suppresses the formation of bone-resorbing osteoclasts *REGENERATIVE THERAPY*. 2019.12; 11; 290-296

[Conference Activities & Talks]

1. Preksa Keo, Yoshiro Matsumoto, Shigeki Nagahiro, Kazuhrio Aoki, Takashi Ono. Time-course study of bones induced by the co-injection of RANKL-binding peptide and BMP-2 and the effects of subsequent screw placement in murine maxilla. The 61st Annual Meeting of Japanese Association for Oral Biology 2019.10.01 Tokyo, Japan
2. Phyu Sin TUN, Hiroshi CHUREI, Gen TANABE, Thet Khaing AUNG, Shingo KAMIJO, Meiko OKI, Hidekazu TAKAHASHI, Kazuhiro HIKITA, Toshiaki UENO. Shock-absorbing capability of rubber-like and rigid 3D printing materials compared to commercial mouthguard materials . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
3. Nakamura S, Matin K, Aoki K. Histological observations of organs after intravenous injection of *Streptococcus mutans*. the 41st Annual meeting of Nippon Academy of Dental Technology 2019.11.02 Kanazawa, Ishikawa, Japan
4. Yuna Hirohashi, Yuri Shimizu, Masud Khan, Yukihiro Tamura, Kazuhiro Aoki. A new RANKL-binding peptide for the development of the bone anabolic reagent. the 2nd Meeting of International Oral Health Engineering Consortium 2019.11.18 Taipei, Taiwan
5. Yosuke Sasaki, Masud Khan, Kazuhiro Aoki. Development of a suitable for bone formation using the BMP-2 and osteogenic peptide OP3-4 combination therapy. 2019.11.18 Taipei, Taiwan
6. Kazuhiro Aoki. The effects of RANKL-binding peptides on osteoblast differentiation. The 42nd Annual Meeting of the Molecular Biology Society of Japan 2019.12.04 Kitakyusyu, Fukuoka, Japan
7. Kazuhiro Aoki. The peptide drug delivery for bone regeneration. Cutting Edge of Bone and Mineral Research in 2019 2019.12.05 Kyusyu University, Fukuoka, Japan

[Awards & Honors]

1. The 2nd and 3rd prizes of the student competition at the 2nd Meeting of International Oral Health Engineering Consortium (Yosuke Sasaki, Yuna Hirohashi), The 2nd International Oral Health Engineering Consortium (Taipei), 2019.11

Oral Biomaterials Development Engineering

Professor Hidekazu TAKAHASHI
Junior Associate Professor Tohru YASUE (until March)
Assistant Professor Naohiko IWASAKI
Assistant Professor Yumi TSUCHIDA (from April)

Graduate student (Master course) Yusuke YAMAMOTO (until March)
Graduate student (Doctor course) Patcharanun CHAIAMORNSUP (Advanced Biomaterials)
Research student Ha Rou Bing (from December)

(1) Outline

Basic knowledge of dental materials and devices for oral health engineering are provided for student. Basic exercise for dental materials and prosthetic training are also provided. Development and evaluation of new dental materials are performed.

(2) Research

1. Evaluation of various factors on mechanical properties of teeth substance.
2. Evaluation of fatigue properties of dentin and dental materials using miniature testing pieces
3. Measurement of characteristics of dental ceramic materials and establishment of new testing methods for dental ceramics
4. Measurement of precise deformation using non-contact methods
5. Development of new composite resin with similar machinability of dentin
6. Study on dental root fracture mechanism
7. Application of various types of fiberglass for dentistry
8. Evaluation of composite resin mechanical properties and improvement their bonding efficiency to various materials.
9. Evaluation of impact force absorption of mouthguard and face protect materials

(3) Education

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.

(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. Wamasing P, Watanabe H, Tsuchida Y, Ohbayashi N, Suzuki T, Kurabayashi T. The development of new image receptor-holding instruments with appropriate horizontal X-ray beam angulation for periapical radiographs Dentomaxillofacial Radiology. 2019.01; 48; 20180354
2. Tsuchida Y, Takahashi H, Watanabe H, Oki M, Shiozawa M, Kurabayashi T, Suzuki T. Effects of number of metal restorations and mandibular position during computed tomography imaging on accuracy of maxillofacial models J Prosthodont Res. 2019.04; 63(2); 239-244
3. Hidekazu Takahashi, Naohiko Iwasaki. The fiberpost as fiber reinforced polymer materials-From the view of dental materials sciences 2019.05; 38(2); 78-82
4. Yamazaki T, Murakami N, Suzuki S, Handa K, Yatabe M, Takahashi H, Wakabayashi N. Influence of block-out on retentive force of thermoplastic resin clasps: an in vitro experimental and finite element analysis. Journal of prosthodontic research. 2019.07; 63(3); 303-308
5. Kanehira M, Ishihata H, Araki Y, Takahashi H, Sasaki K, Finger WJ. Effect of artificial saliva on permeability of dentin treated with phosphate containing desensitizer measured by digital flow meter. Dental Materials Journal. 2019.08; 38(6); 963-969
6. Alsandi Q, Ikeda M, Nikaido T, Tsuchida Y, Sadr A, Yui N, Suzuki T, Tagami J. Evaluation of mechanical properties of new elastomer material applicable for dental 3D printer. J Mech Behav Biomed Mater. 2019.08; 100; 103390
7. Jialin Hao, Murakami Natsuko, Yamazaki Toshiki, Iwasaki Naohiko, Yatabe Masaru, Takahashi Hidekazu, Wakabayashi Noriyuki. 義歯用被削性ポリエステル製の摩耗耐性 (Fatigue resistance of machinable polyester for dentures) 日本歯科理工学会誌. 2019.09; 38(Special Issue74); 62
8. Yasue T, Iwasaki N, Shiozawa M, Tsuchida Y, Suzuki T, Takahashi H. Effect of fiberglass orientation on flexural properties of fiberglass-reinforced composite resin block for CAD/CAM. Dental materials journal. 2019.10; 38(5); 738-742
9. Kittikundecha N, Kajima Y, Takaichi A, Wai Cho HH, Htat HL, Doi H, Takahashi H, Hanawa T, Wakabayashi N. Fatigue properties of removable partial denture clasps fabricated by selective laser melting followed by heat treatment. Journal of the mechanical behavior of biomedical materials. 2019.10; 98; 79-89
10. Chaiamornsup P, Iwasaki N, Yasue T, Uo M, Takahashi H. Effects of build conditions and angle acuteness on edge reproducibility of casting patterns fabricated using digital light projection. Dental materials journal. 2019.10;
11. Yasue Tohru, Iwasaki Naohiko, Shiozawa Maho, Tsuchida Yumi, Suzuki Tetsuya, Takahashi Hidekazu. Effect of fiberglass orientation on flexural properties of fiberglass-reinforced composite resin block for CAD/CAM(和訳中) Dental Materials Journal. 2019.10; 38(5); 738-742
12. Hada T, Suzuki T, Minakuchi S, Takahashi H. Reduction in maxillary complete denture deformation using framework material made by computer-aided design and manufacturing systems. J Mech Behav Biomed Mater. 2019.11; 103; 103514

[Conference Activities & Talks]

1. Uchikura K, Murakami N, Handa K, Takahashi H, Wakabayashi N. Influence of the fit of the rest on fracture resistance of tooth-colored CAD-CAM materials with the rest seat. The 128 Annual Meeting of Japan Prosthodontic Society 2019.05.10 Sapporo
2. Takaichi A, Kittikundecha N, Kajima Y, Takahashi H, Hanawa T, Wakabayashi N. Enhanced Fatigue Strength of SLMed Co-Cr-Mo clasp by Post-heat Treatment Clasp . 97th General Session & Exhibition of the IADR 2019.06.22 Vancouver
3. Hidekazu TAKAHASHI, Kazuyuki HANDA, Yashuhiro HOTTA, Naohiko IWASAKI, Patcharanun CHAIAMORNSUP, Yumi TSUCHIDA . Dimensional stability of dental model fabricated with vat photopolymerization . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
4. Kazuhiro HIKITA, Takeo MAIDA, Yumiko ENAMI, Masahiro IJIMA, Tun Sin PHYU, Hiroshi CHUREI, Toshiaki UENO, Hidekazu TAKAHASHI. Manufacturing of sports mouthguard by digital technology . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
5. Phyu Sin TUN, Hiroshi CHUREI, Gen TANABE, Thet Khaing AUNG, Shingo KAMIJO, Meiko OKI, Hidekazu TAKAHASHI, Kazuhiro HIKITA, Toshiaki UENO. Shock-absorbing capability of rubber-like and rigid 3D printing materials compared to commercial mouthguard materials . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
6. Uchikura K, Murakami N, Yamazaki T, Nagata K, Ona M, Iwasaki N, Takahashi H, Wakabayashi N. Fracture behavior of tooth-colored CAD/CAM materials with the rest seat - Influence of misfit-. The 74th General Session of the Japanese Society for Dental Materials and Devices 2019.10.05 Nagasaki University Bunkyo Campus
7. Hao Jialin, Murakami Natsuko, Yamazaki Toshiki, Iwasaki Naohiko, Yatabe Masaru, Takahashi Hidekazu, Wakabayashi Noriyuki. Fatigue resistance of machinable polyester for dentures. 第 74 回日本歯科理工学会学術講演会 2019.10.06 長崎大学文京キャンパス
8. Chaiamornsup P, Arksornnukitt M, Takahashi H. Build Angle Influences Adaptability of DLP Bridge Casting Patter. the 4th Asia Pacific Regional Congress of the International Association for Dental Research 2019.11.29 Brisbane Convention Center, Australia
9. Kogure M, Miyazaaki H, Tobita S, Takahashi H.. Effectiveness of AR-based Practical Training Support Approach using smartphone. the 4th Asia Pacific Regional Congress of the International Association for Dental Research 2019.11.30 Brisbane Convention Center, Australia

[Awards & Honors]

1. Brilliant Poster Awar, International Academy for Digital Dental Medicine, 2019.10

Oral Prosthetic Engineering

Professor Tetsuya SUZUKI

Junior Associate Professor Masaomi IKEDA

Assistant Professor Maho SHIOZAWA

(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 learn 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) Advanced technology which utilized a CAD/CAM system.
- 2) 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, 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, Globalization for Oral Health Engineering, Gerodontology, Laws for Dental Technologists, CAD/CAM System Technology, CAD/CAM System Technology Practice, Special Lectures for Advanced Technology, Management and Regulation for Dental Technologists, Oral Appliances, Aesthetic Dentistry Practice, Orthodontic Dentistry, Comprehensive Oral Rehabilitation Engineering Practice, Graduation Research

(4) Publications

[Original Articles]

1. Sato T, Takagaki T, Baba Y, Vicheva M, Matsui N, Hiraishi N, Ikeda M, Nikaido T, Tagami J. Effects of Different Tooth Conditioners on the Bonding of Universal Self-etching Adhesive to Dentin. J Adhes Dent. 2019; 21(1); 77-85

2. Ayako Nakamoto, Takaaki Sato, Naoko Matsui, Masaomi Ikeda, Toru Nikaido, Michael F Burrow, Junji Tagami. Effect of fluoride mouthrinse and fluoride concentration on bonding of a one-step self-etch adhesive to bovine root dentin. *J Oral Sci.* 2019; 61(1); 125-132
3. Kitasako Y, Sadr A, Shimada Y, Ikeda M, Sumi Y, Tagami J. Remineralization capacity of carious and non-carious white spot lesions: clinical evaluation using ICDAS and SS-OCT *Clin Oral Investig.* 2019; 23(2); 863-872
4. Wamasing P, Watanabe H, Tsuchida Y, Ohbayashi N, Suzuki T, Kurabayashi T. The development of new image receptor-holding instruments with appropriate horizontal X-ray beam angulation for periapical radiographs *Dentomaxillofacial Radiology.* 2019.01; 48; 20180354
5. Nagano M, Ogata Y, Ikeda M, Tsukada K, Tokunaga K, Iida S. Peristomal Moisture-Associated Skin Damage and Independence in Pouching System Changes in Persons With New Fecal Ostomies. *Journal of Wound, Ostomy and Continence Nursing.* 2019.01;
6. Sone E, Noshiro D, Ikebuchi Y, Nakagawa M, Khan M, Tamura Y, Ikeda M, Oki M, Murali R, Fujimori T, Yoda T, Honma M, Suzuki H, Ando T, Aoki K. The induction of RANKL molecule clustering could stimulate early osteoblast differentiation. *Biochemical and biophysical research communications.* 2019.02; 509(2); 435-440
7. Shinagawa J, Inoue G, Nikaido T, Ikeda M, Burrow MF, Tagami J. Early bond strengths of 4-META/MMA-TBB resin cements to CAD/CAM resin composite *Dent Mater J.* 2019.02; 38(1); 28-32
8. Lyann SK, Takagaki T, Nikaido T, Wada T, Uo M, Ikeda M, Sadr A, Tagami J. Efficacy of Various Surface Treatments on the Bonding Performance of Saliva-contaminated Lithium-Disilicate Ceramics *J Adhes Dent.* 2019.02; 21(1); 51-58
9. Dhaifallah Alqarni, Masatoshi Nakajima, Keiichi Hosaka, Kurumi Ide, Daiki Nagano, Takehiro Wada, Masaomi Ikeda, Teerapong Mamane, Ornnicha Thanatvarakorn, Taweesak Prasansuttiporn, Richard Foxton, Junji Tagami. The repair bond strength to resin matrix in cured resin composites after water aging. *Dent Mater J.* 2019.03; 38(2); 233-240
10. Tsuchida Y, Takahashi H, Watanabe H, Oki M, Shiozawa M, Kurabayashi T, Suzuki T. Effects of number of metal restorations and mandibular position during computed tomography imaging on accuracy of maxillofacial models *J Prosthodont Res.* 2019.04; 63(2); 239-244
11. Alqarni D, Nakajima M, Hosaka K, Ide K, Nagano D, Wada T, Ikeda M, Mamane T, Thanatvarakorn O, Prasansuttiporn T, Foxton R, Tagami J. The repair bond strength to resin matrix in cured resin composites after water aging(和訳中) *Dent Mater J.* 2019.04; 38(2); 233-240
12. G Ohwada, S Minakuchi, Y Sato, H Kondo, T Nomura, A Tsuboi, G Hong, Y Itoh, Y Kawai, S Kimoto, A Gunji, A Suzuki, T Suzuki, K Kimoto, N Hoshi, M Saita, Y Yoneyama, Y Sato, M Morokuma, J Okazaki, T Maeda, K Nakai, T Ichikawa, K Nagao, K Fujimoto, H Murata, T Kurogi, K Yoshida, M Nishimura, Y Nishi, M Murakami, T Hosoi, T Hamada. Subjective Evaluation of Denture Adhesives: A Multicenter Randomized Controlled Trial. *JDR Clinical & Translational Research.* 2019.04; 2380084419837607
13. Aung SSMP, Takagaki T, Lyann SK, Ikeda M, Inokoshi M, Sadr A, Nikaido T, Tagami J. Effects of alumina-blasting pressure on the bonding to super/ultra-translucent zirconia. *Dent Mater.* 2019.05; 35(5); 730-739
14. Ali A, Takagaki T, Naruse Y, Abdou A, Nikaido T, Ikeda M, Tagami J. The effect of elapsed time following alumina blasting on adhesion of CAD/CAM resin block to dentin(和訳中) *Dent Mater J.* 2019.06; 38(3); 354-360
15. Ochiai Y, Inoue G, Nikaido T, Ikeda M, Tagami J. Evaluation of experimental calcium-containing primer in adhesive system on micro-tensile bond strength and acid resistance. *Dental materials journal.* 2019.07; 38(4); 565-572
16. San San May Phyo Aung, Tomohiro Takagaki, Aye Ko Ko, Somayah Halabi, Takaaki Sato, Masaomi Ikeda, Toru Nikaido, Michael F Burrow, Junji Tagami. Adhesion durability of dual-cure resin cements and acid-base resistant zone formation on human dentin. *Dent Mater.* 2019.07; 35(7); 945-952

17. Hosaka K, Tichy A, Ikeda M, Nakagawa K, Sadr A, Tagami J, Takahashi M, Sato K, Nishitani Y, Klein-Junior CA, Pashley DH, Nakajima M. Ultra-high-speed videography of resin-dentin interface failure dynamics under tensile load *Dent Mater.* 2019.07; 35(7); E153-E161
18. Ide K, Nakajima M, Hayashi J, Hosaka K, Ikeda M, Shimada Y, Foxton RM, Sumi Y, Tagami J. Effect of light-curing time on light-cure/post-cure volumetric polymerization shrinkage and regional ultimate tensile strength at different depths of bulk-fill resin composites *Dent Mater J.* 2019.07; 38(4); 621-629
19. Alsandi Q, Ikeda M, Nikaido T, Tsuchida Y, Sadr A, Yui N, Suzuki T, Tagami J. Evaluation of mechanical properties of new elastomer material applicable for dental 3D printer. *J Mech Behav Biomed Mater.* 2019.08; 100; 103390
20. Nishi Y, Nomura T, Murakami M, Kawai Y, Nishimura M, Kondo H, Ito Y, Tsuboi A, Hong G, Kimoto S, Gunji A, Suzuki A, Ohwada G, Minakuchi S, Sato Y, Suzuki T, Kimoto K, Hoshi N, Saita M, Yoneyama Y, Sato Y, Morokuma M, Okazaki J, Maeda T, Nakai K, Ichikawa T, Nagao K, Fujimoto K, Murata H, Kurogi T, Yoshida K, Hosoi T, Hamada T. Effect of denture adhesives on oral moisture: A multicenter randomized controlled trial. *J Prosthodont Res.* 2019.09;
21. Yasue T, Iwasaki N, Shiozawa M, Tsuchida Y, Suzuki T, Takahashi H. Effect of fiberglass orientation on flexural properties of fiberglass-reinforced composite resin block for CAD/CAM. *Dental materials journal.* 2019.10; 38(5); 738-742
22. Hada T, Suzuki T, Minakuchi S, Takahashi H. Reduction in maxillary complete denture deformation using framework material made by computer-aided design and manufacturing systems. *J Mech Behav Biomed Mater.* 2019.11; 103; 103514
23. Antonin Tichy, Keiichi Hosaka, Pavel Bradna, Masaomi Ikeda, Ahmed Abdou, Masatoshi Nakajima, Junji Tagami. Subsequent application of bonding agents to a one-step self-etch adhesive - Its effect with/without previous light-curing. *Dent Mater.* 2019.12; 35(12); e299-e309
24. Kuno Y, Hosaka K, Nakajima M, Ikeda M, Klein Junior CA, Foxton RM, Tagami J. Incorporation of a hydrophilic amide monomer into a one-step self-etch adhesive to increase dentin bond strength: Effect of application time(和訳中) *Dent Mater J.* 2019.12; 38(6); 892-899

[Conference Activities & Talks]

1. Vicheva M, Sato T, Takagaki T, Baba Y, Ikeda M, Nikaido T, Tagami J. Effect of Repair Systems on Dentin Bonding Performance. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
2. Matsunaga S, Takagaki T, Matsui N, Ikeda M, Arisaka Y, Tamura A, Yui N, Nikaido T, Tagami J. Development of "Reversible-adhesion" Resin Cement With a UV-cleavable PRX Cross-linker. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
3. Aung SS MP, Takagaki T, Ko Ko A, Halabi S, Sato T, Ikeda M, Nikaido T, Tagami J. Assessment of Dentin-resin Cement Interface after Acid-base Challenge. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
4. Muta S, Ikeda M, Nikaido T, Sayed M, Sadr A, Suzuki T, Tagami J. Dimensional Accuracy of Crown Fabricated on FDM-3D Printer PVA Model. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
5. Zin AS, Takagaki T, Ikeda M, Hayashi J, Sadr A, Nikaido T, Tagami J. Gap Formation of Flowable Composites with Different LCUs Using SS-OCT. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
6. Luz ME, Hosaka K, Nakajima M, Ikeda M, Abdou A, Tichy A, Tagami J. Influence of Tooth-storage in Chloramine-T Solution on Bovine Dentin TBS. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
7. Ko Ko MK, Takagaki T, Uo M, Ikeda M, Nikaido T, Tagami J. Influence of Cleansing Agent on Bond Durability of Saliva-contaminated Zirconia Ceramics.. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada

8. Lyann SK, Takagaki T, Ikeda M, Nikaido T, Hayashi J, Sadr A, Tagami J. Effect of Adhesive-Resin-Cements on Sealing Performance of Lithium-Disilicate Glass-Ceramic to Dentin. 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada
9. Kobayashi T, Horike A, Takagaki T, Ikeda M, Ozer F, Blatz M, Tagami J. Bond Strength of Self-adhesive Resin Cements to Y-TZP after Etching . 97th General Session & Exhibition of the IADR 2019.06.20 Vancouver, Canada

Clinical Laboratory

General Manager
-Professor : Shuji Tohda

Associate Manager
-Junior Associate Professor : Tadashi Kanouchi

Assistant Professor : Miyako Murakawa
Assistant Professor : Ayako Nogami
Assistant Professor : Hideki Arima
Medical Staff : Shintaro Iida

(1) Outline

The Clinical Laboratory is a central clinical department that conducts laboratory tests in order to obtain information about the diagnosis, treatment, and prevention of diseases. Physiological tests such as electrocardiogram, echocardiography, pulmonary function tests, and electroencephalogram are also performed at our facility.

(2) 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) Genotypic analysis of bacteria for monitoring those transmission in the hospital,
- 4) Development of electrophysiological diagnostic tests for peripheral neuropathies,
- 5) Clinical and electrophysiological study for amyotrophic lateral sclerosis,
- 6) Quality control of nerve conduction study,
- 7) Molecular mechanisms of treatment for hepatitis C.
- 8) Novel methods to analyze cardiac function using echocardiography.

(3) Education

We lecture on clinical laboratory medicine and give 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 give a labo tour and practice to master course graduate students, too. We gave a general training for clinical laboratory medicine to nine junior residents of university hospital in 2019. We also held hands-on seminars of Gram staining, urinary sediment, cardiac and abdominal ultrasonography for the residents.

(4) Clinical Services & Other Works

Clinical laboratory bears an important responsibility for advanced and high quality medical care. Our clinical laboratory is based on the principle of providing the speedy and high quality tests. The highest level of advanced tests, such as qualitative and quantitative analysis of various viral DNA by the PCR method, are also introduced here. 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 June 2018. It means that the clinical laboratory is an international standard on quality and that our hospital is allowed to conduct the international clinical trials. We give a lecture on laboratory tests at meetings of laboratory medicine-related societies.

(5) Clinical Performances

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

(6) Publications

[Original Articles]

1. Seishin Azuma, Yasuhiro Asahina, Sei Kakinuma, Keiko Azuma, Masato Miyoshi, Emi Inoue, Tomoyuki Tsunoda, Ayako Sato, Shun Kaneko, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Makoto Tomita, Mina Nakagawa, Mamoru Watanabe. Diabetic Retinopathy as a Risk Factor Associated with the Development of Hepatocellular Carcinoma in Nonalcoholic Fatty Liver Disease. *Dig Dis.* 2019; 37(3); 247-254
2. Kawaguchi-Ihara Noriko, Zhao Yan, Nakamura Suzune, Suzuki Keiko, Zhang Yi, Tohda Shuji, Murohashi Ikuo. Chloroquine Inhibits Self-Renewal of Blast Progenitors Synergistically With Phytochemicals or Non-steroidal Anti-inflammatory Drugs in Hematological Malignant Cell Lines *ANTICANCER RESEARCH.* 2019.01; 39(1); 87-98
3. Ayako Nogami, Keigo Okada, Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Osamu Miura. Inhibition of the STAT5/Pim Kinase Axis Enhances Cytotoxic Effects of Proteasome Inhibitors on FLT3-ITD-Positive AML Cells by Cooperatively Inhibiting the mTORC1/4EBP1/S6K/Mcl-1 Pathway. *Transl Oncol.* 2019.02; 12(2); 336-349
4. Masato Miyoshi, Sei Kakinuma, Akihide Kamiya, Tomoyuki Tsunoda, Jun Tsuchiya, Ayako Sato, Shun Kaneko, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. LIM homeobox 2 promotes interaction between human iPS-derived hepatic progenitors and iPS-derived hepatic stellate-like cells. *Sci Rep.* 2019.02; 9(1); 2072
5. Yuna Horiuchi, Ryunosuke Ohkawa, Shao-Jui Lai, Shitsuko Shimano, Michio Hagihara, Shuji Tohda, Takahiro Kameda, Minoru Tozuka. Usefulness of apolipoprotein B-depleted serum in cholesterol efflux capacity assays using immobilized liposome-bound gel beads. *Biosci. Rep.* 2019.03;
6. Hamada S, Hasegawa Y, Oono A, Suzuki A, Takahashi N, Nishimura T, Koyama T, Hagihara M, Tohda S, Furukawa T, Hirao K, Sasano T. Author Correction: Differential Assessment of Factor Xa Activity and Global Blood Coagulability Utilizing Novel Dielectric Coagulometry. *Scientific reports.* 2019.03; 9(1); 4957
7. Hiroki Akiyama, Yoshihiro Umezawa, Shinya Ishida, Keigo Okada, Ayako Nogami, Osamu Miura. Inhibition of USP9X induces apoptosis in FLT3-ITD-positive AML cells cooperatively by inhibiting the mutant kinase through aggresomal translocation and inducing oxidative stress. *Cancer Lett.* 2019.04; 453; 84-94

8. Sayuri Nitta, Yasuhiro Asahina, Takanobu Kato, Jun Tsuchiya, Emi Inoue-Shinomiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Hayato Hikita, Tetsuo Takehara, Mamoru Watanabe. Impact of novel NS5A resistance-associated substitutions of hepatitis C virus detected in treatment-experienced patients. *Sci Rep.* 2019.04; 9(1); 5722
9. Tomoyuki Tsunoda, Sei Kakinuma, Masato Miyoshi, Akihide Kamiya, Shun Kaneko, Ayako Sato, Jun Tsuchiya, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Tsuyoshi Sogo, Haruki Komatsu, Ryutaro Mukouchi, Ayano Inui, Tomoo Fujisawa, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Loss of fibrocystin promotes interleukin-8-dependent proliferation and CTGF production of biliary epithelium. *J Hepatol.* 2019.07; 71(1); 143-152
10. Mai Itoh, Yuki Okuhashi, Yusuke Takahashi, Yuri Sonoda, Salwa Mohammad, Tatsuya Saito, Erika Shiraori, Shuji Tohda. Hypoxia Up-regulates HIF Expression While Suppressing Cell Growth and NOTCH Activity in Leukaemia Cells. *Anticancer Research.* 2019.08; 39(8); 4165-4170
11. Yoko Nukui, Alafate Ayibieke, Makoto Taniguchi, Yoshibumi Aiso, Yuka Shibuya, Kazunari Sonobe, Jun Nakajima, Saki Kanehira, Yoshiro Hadano, Shuji Tohda, Ryuji Koike, Ryoichi Saito. Whole-genome analysis of EC129, an NDM-5-, CTX-M-14-, OXA-10- and MCR-1-co-producing *Escherichia coli* ST167 strain isolated from Japan. *J Glob Antimicrob Resist.* 2019.09; 18; 148-150
12. Ryoichi Saito, Yukino Usui, Alafate Ayibieke, Jun Nakajima, Isaac Prah, Kazunari Sonobe, Yoshibumi Aiso, Shiori Ito, Yasuhiro Itsui, Yoshiro Hadano, Yoko Nukui, Ryuji Koike, Shuji Tohda. Hypervirulent clade 2, ribotype 019/sequence type 67 *Clostridioides difficile* strain from Japan. *Gut Pathog.* 2019.11; 11; 54
13. Daisuke Watanabe, Ayako Nogami, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Osamu Miura. FLT3-ITD Activates RSK1 to Enhance Proliferation and Survival of AML Cells by Activating mTORC1 and eIF4B Cooperatively with PIM or PI3K and by Inhibiting Bad and BIM. *Cancers (Basel).* 2019.11; 11(12);
14. Nukui Y, Chino T, Tani C, Sonobe K, Aiso Y, Tohda S, Koike R, Saito R. Molecular epidemiologic and clinical analysis of *Helicobacter cinaedi* bacteremia in Japan. *Helicobacter.* 2019.11; e12675
15. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Shun Kaneko, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Emi Inoue-Shinomiya, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Minoru Tanabe, Emiko Sugawara, Akira Takemoto, Hidenori Ojima, Michie Sakamoto, Masaru Muraoka, Shinichi Takano, Shinya Maekawa, Nobuyuki Enomoto, Mamoru Watanabe. Comprehensive genetic analysis of cholangiolocellular carcinoma with a coexistent hepatocellular carcinoma-like area and metachronous hepatocellular carcinoma. *Hepatol Res.* 2019.12; 49(12); 1466-1474

[Conference Activities & Talks]

1. Miyako Murakawa, Yasuhiro Asahina, Emi Inoue, Mina Nakagawa, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Tomoyuki Tsunoda, Fukiko Kawai-Kitahata, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe. The association of serum IFN-lambda 3 levels with liver fibrosis and hepatocarcinogenesis in chronic hepatitis C patients treated with direct-acting antiviral agents. *EASL, The International Liver Congress 2019* 2019.04.13 Vienna (Austria)
2. Mina Nakagawa, Yasuhiro Asahina, Jun Tsuchiya, Ayako Sato, Tomoyuki Tsunoda, Masato Miyoshi, Emi Inoue, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Makoto Tomita, Mamoru Watanabe. Impact of HCV clearance on HCC development and patient survival: Propensity score-matched analysis of an ongoing database of 2173 CHC patients. *EASL, The International Liver Congress 2019* 2019.04.13 Vienna (Austria)
3. Horiuchi Y., Ohkawa R., Lai SJ., Shimano S., Hagihara M., Tohda S., and Tozuka M. Availability of apoB-depleted serum in clinical assay for cholesterol efflux capacity using immobilized liposome-bound gel beads. *3rd IFCC-EFLM European Congress of Clinical Chemistry and Laboratory Medicine* 2019.05.19 Barcelona

4. Yagi Y, Iida S, Kanouchi T, Kusunoki S, Sobue G, Kaji R, Kuwabara S, Yokota T, Glovenin-I CIDP Study Group. Maintenance treatment with IVIg for CIDP can prevent disease progression. 60th Annual Meeting of the Japanese Society of Neurology 2019.05.22 Osaka
5. Tatsuya Saito, Mai Itoh, Shuji Tohda. Metformin inhibits the growth of myeloid leukemia cells partly due to suppression of tyro3 expression. 24th Congress of European Hematology Association 2019.06.14 Amsterdam
6. Fujii Y., Ohkawa R., Lai SJ., Horiuchi Y., Shimano S., Ohno K., Ichimura N., Hagihara M., Tozuka M., Tohda S. Analysis of Serum Amyloid A Containing HDL Formation in HepG2. 2019 KAMT congress & International conference 2019.08.31 Pyeongchang
7. Yamazaki A., Ohkawa R., Horiuchi Y., Lai SJ., Shimano S., Itoi A., Ichimura N., Hagihara M., Tozuka M., Tohda S. Analysis of Apolipoprotein C-II and C-III Transfers between High-density Lipoprotein and Very Low-density Lipoprotein. 2019 KAMT congress & International conference 2019.08.31 Pyeongchang
8. Chihiro Tani, Kazunari Sonobe, Ayuka Kobayashi, Jun Nakajima, Rieko Takahashi, Saki Kanehira, Sonoka Yuasa, Tomoko Motohashi, Michio Hagihara, Takashi Yaguchi, Shuji Tohda. The impact of the morphological difference of fungal colonies among several potato dextrose agars on the identification. The 30th World Congress of World Association of Societies of Pathology and Laboratory Medicine 2019.09.20
9. Yasuhiro Asahina, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma. Comprehensive analysis of cancer gene mutations and viral integration in hepatocellular carcinoma arising from non-fibrotic liver. AASLD The Liver Meeting 2019 2019.11.10 Boston (USA)
10. Ayako Nogami, Watanabe Daisuke, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Toshikage Nagao, Shuji Tohda and Osamu Miura. FLT3-ITD Enhances Proliferation and Survival of AML Cells through Activation of RSK1 to Upregulate the mTORC1/eIF4F Pathway Cooperatively with PIM or PI3K and to Inhibit Bad and Bim. 60th ASH Annual Meeting and Exposition 2019.12.01 FL, Orange County Convention Center

Hyperbaric Medical Center

Senior Director and Associate Professor; Kazuyoshi YAGISHITA
Assistant Professor ; Toshiyuki OHHARA
Specially Appointed Assistant Professor ; Mikio SHIODA, Naoki YAMAMOTO
Adjunct Lecturer; Yasushi KOJIMA, Masaharu SHIBAYAMA (~ 2019.3) , Yumi NIIZEKI
Researcher; Masaki HORIE, Toshihiro KONDOH, Naohiro MITSUMOTO
Akira KAMEI
Staff Assistant; Kiyomi ITOH

(1) Outline

Hyperbaric oxygen therapy (HBO), which can dissolve oxygen in serum in population to atomic pressure and transport oxygen to ischemic tissue, is an established therapy for treatment of several conditions, including decompression illness, carbon monoxide poisoning, acute anterior disturbance, and peripheral ischemic disease. The mechanism of HBO can be described as hyperoxygenation in ischemic soft tissues, reduction of edema, stimulation of fibroblast proliferation and differentiation, increased collagen formation and cross-linking, angiogenesis, and improved preservation of energy metabolism.

This curious treatment has clinically many kinds of efficacy, however, the mechanism of the effect has not been fully understood, and many researchers in the world still attempt to reveal the mechanism of the effect of HBO. This HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

(2) Research

Research Subjects

- 1) Soft tissue injuries related with sports activities
- 2) HBO for conditioning in sports activities
- 3) Diving medicine
- 4) Hyperbaric oxygen therapy

(3) Education

HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

(4) Clinical Services & Other Works

In 2019, 548 times hyperbaric oxygen therapy (HBO) in 5,747 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. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Kazuyoshi Yagishita. Correlations between vertical ground reaction force, sagittal joint angles, and the muscle co-contraction index during single-leg jump-landing Asian journal of sports medicine. 2019.07; 10(3);
2. Junya Aizawa, Shunsuke Ohji, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Kazuyoshi Yagishita. Relationship between asymmetrical jump-landing impact and quadriceps strength after unilateral anterior cruciate ligament reconstruction Physical Medicine and Rehabilitation Research. 2019.07; 4; 1-6
3. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Kazuyoshi Yagishita, Toshitaka Yoshii, Atsushi Okawa. Supine versus lateral position for accurate positioning of acetabular cup in total hip arthroplasty using the modified Watson-Jones approach: A randomized single-blind controlled trial. Orthop Traumatol Surg Res. 2019.09; 105(5); 915-922
4. Kazuyoshi Yagishita, Mitsuhiro Enomoto, Yuji Takazawa, Jun Fukuda, Hideyuki Koga. Effects of hyperbaric oxygen therapy on recovery acceleration in Japanese professional or semi-professional rugby players with grade 2 medial collateral ligament injury of the knee: A comparative non-randomized study. Undersea Hyperb Med. 2019.09; 46(5); 647-654

[Books etc]

1. T. Ohmi, J. Aizawa, T. Yamada, A. Okawa, K Yagishita. ORTHOPEDIC SURGERY. 2019.04 (ISBN : 978-4-524-27775-9)

[Conference Activities & Talks]

1. Naoki Yamamoto, Tomoko Sakai, Dai Ukegawa, Chisato Hoshino, Jinno Tetsuya, Atsushi Okawa. Earlier mobility with T-cane after total knee arthroplasty influences long-term mobility . 13th International Spcoety of Physical and Rehabilitation medicine World Congress 2019 2019.06.09 Kobe, Japan
2. Ohara Toshiyuki, Yagishita Kazuyoshi, Shioda Mikio, Yamamoto Naoki. Examination of sham treatment for clinical research of hyperbaric oxygen therapy. 19th The Japanese Society of Hyperbaric and Undersea Medicine, Kanto Association 2019.06.22
3. Y Kojima. Toward a Decompression Sickness Registry in Japan.. 52th Undersea & Hyperbaric Medical Society Annual Scientific Meeting 2019.06.26 Puerto Rico
4. Naoki Yamamoto, Takuya Oyaizu, Masaki Horie, Mitsuhiro Enomoto, Masato Yuasa, Ryohei Takada, Kazuyoshi Yagishita. Hyperbalic Oxygen treatment promotes muscle regeneration via angiogenesis by triggering increased RNS in acute skeletal muscle injury . 52th Undersea & Hyperbaric Medical Society Annual scientific meeting 2019 2019.06.27 Kobe, Japan
5. Naoki Yamamoto, Takuya Oyaizu, Masaki Horie, Mitsuhiro Enomoto, Masato Yuasa, Ryohei Takada, Kazuyoshi Yagishita. Hyperbaric oxygen therapy promotes muscle regeneration via angiogenesis by reactive nitrogen species in muscle contusion injury of rat.. The 4th conference of Asia-pasific Undersea and Hyperbaric Medical Society 2019.10.25 nakatsu, Oita Japan
6. Ohara Toshiyuki, Yagishita Kazuyoshi, Shioda Mikio, Yamamoto Naoki. Effect of hyperbaric oxygen therapy on fatigue fractures of lower limbs. The 30th Annual Meeting of the Japanese Society of Clinical Sports Medicine. 2019.11.17

[Awards & Honors]

1. Undersea & Hyperbaric Medical Society 2019 Annual Scientific meeting - President's award: Best Resident/Trainee Oral Presentation (Naoki Yamamoto), Undersea & Hyperbaric Medical Society, 2019.06

Sports Medicine Center

Director and Associate Professor; Kazuyoshi YAGISHITA
 Head Physical Therapist ; Jyunya AIZAWA
 Assistant Professor ; Toshiyuki OHHARA
 Specially Appointed Assistant Professor ; Mikio SHIOTA
 Physical Therapist ; Kenji HIROHATA, Takehiro OHMI,
 Shunsuke OHJI
 Adjunct Lecturer ; Tomohiko TATEISHI
 Staff Assistant; Kiyomi ITOH

(1) Publications

[Original Articles]

1. Takashi Hoshino, Tomohiko Tateishi, Tsuyoshi Nagase, Arata Yuki, Teruhiko Nakagawa, Masamitsu Tsuchiya. Jones Fractures in Sumo Wrestlers: Three Case Reports. *Case Rep Orthop.* 2019; 2019; 9051327
2. Yuto Sugimine, Kentaro Sakaeda, Kazuta Yamashita, Hiroaki Manabe, Kosuke Sugiura, Fumio Hayashi, Yoshihiro Ishihama, Yoichiro Takata, Toshinori Sakai, Toru Maeda, Tomohiko Tateishi, Koichi Sairyo. Surgical Treatment of Lumbar Herniated Nucleus Pulposus Combined with Residual Bony Fragment of Apophyseal Ring Fracture in High-Level Athletes ■:■ A Report of Two Cases. *J. Med. Invest..* 2019; 66(3.4); 358-361
3. Mai Katakura, Masafumi Horie, Toshifumi Watanabe, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Kenta Katagiri, Hiroko Ueki, Stefano Zaffagnini, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Effect of meniscus repair on pivot-shift during anterior cruciate ligament reconstruction: Objective evaluation using triaxial accelerometer. *Knee.* 2019.01; 26(1); 124-131
4. Koji Nakamaru, Junya Aizawa, Keizo Kawarada, Yukari Uemura, Takayuki Koyama, Osamu Nitta. Immediate effects of thoracic spine self-mobilization in patients with mechanical neck pain: A randomized controlled trial. *J Bodyw Mov Ther.* 2019.04; 23(2); 417-424
5. Satoh Y, Yamada T, Shimamura R, Ohmi T. Comparison of foot kinetics and kinematics during gait initiation between young and elderly participants. *Journal of physical therapy science.* 2019.07; 31(7); 498-503
6. Ueki Hiroko, Katagiri Hiroki, Otabe Koji, Nakagawa Yusuke, Ohara Toshiyuki, Shioda Mikio, Kohno Yuji, Hoshino Takashi, Sekiya Ichiro, Koga Hideyuki. Contribution of Additional Anterolateral Structure Augmentation to Controlling Pivot Shift in Anterior Cruciate Ligament Reconstruction AMERICAN JOURNAL OF SPORTS MEDICINE. 2019.07; 47(9); 2093-2101
7. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Kazuyoshi Yagishita. Correlations between vertical ground reaction force, sagittal joint angles, and the muscle co-contraction index during single-leg jump-landing *Asian journal of sports medicine.* 2019.07; 10(3);
8. Junya Aizawa, Shunsuke Ohji, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Kazuyoshi Yagishita. Relationship between asymmetrical jump-landing impact and quadriceps strength after unilateral anterior cruciate ligament reconstruction *Physical Medicine and Rehabilitation Research.* 2019.07; 4; 1-6

9. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Kazuyoshi Yagishita, Toshitaka Yoshii, Atsushi Okawa. Supine versus lateral position for accurate positioning of acetabular cup in total hip arthroplasty using the modified Watson-Jones approach: A randomized single-blind controlled trial. *Orthop Traumatol Surg Res.* 2019.09; 105(5); 915-922
10. Kazuyoshi Yagishita, Mitsuhiro Enomoto, Yuji Takazawa, Jun Fukuda, Hideyuki Koga. Effects of hyperbaric oxygen therapy on recovery acceleration in Japanese professional or semi-professional rugby players with grade 2 medial collateral ligament injury of the knee: A comparative non-randomized study. *Undersea Hyperb Med.* 2019.09; 46(5); 647-654
11. Katakura M, Nakamura K, Watanabe T, Horie M, Nakamura T, Katagiri H, Otabe K, Nakagawa Y, Ohara T, Sekiya I, Muneta T, Koga H. Risk factors for residual anterolateral rotational instability after double bundle anterior cruciate ligament reconstruction: Evaluation by quantitative assessment of the pivot shift phenomenon using triaxial accelerometer. *The Knee.* 2019.10;
12. Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Ichiro Sekiya, Hideyuki Koga. The effect of a longitudinal tear of the medial meniscus on medial meniscal extrusion in anterior cruciate ligament injury patients. *Knee.* 2019.12; 26(6); 1292-1298

[Books etc]

1. T. Ohmi, J. Aizawa, T. Yamada, A. Okawa, K Yagishita. *ORTHOPEDIC SURGERY.* 2019.04 (ISBN : 978-4-524-27775-9)

[Conference Activities & Talks]

1. The Gait Analysis of the Patients after Bi-Cruciate Retaining TKA. 2019.02.16
2. The Gait Analysis of the Rotating Hinge knee in Revision TKA. 2019.02.16
3. Junpei Kato, Takumi Yamada, Yoshinao Satoh, Takhiro Omi, . Influence of Insoles on Healthy Young Women's Foot Motion and Knee Adduction Moment During Walking. 13 th World Congress of the International Society of Physical and Rehabilitation Medicine 2019.06.09 Kobe, Japan
4. Ohara Toshiyuki, Yagishita Kazuyoshi, Shioda Mikio, Yamamoto Naoki. Examination of sham treatment for clinical research of hyperbaric oxygen therapy. 19th The Japanese Society of Hyperbaric and Undersea Medicine, Kanto Association 2019.06.22
5. Ohara Toshiyuki, Yagishita Kazuyoshi, Shioda Mikio, Yamamoto Naoki. Effect of hyperbaric oxygen therapy on fatigue fractures of lower limbs. The 30th Annual Meeting of the Japanese Society of Clinical Sports Medicine. 2019.11.17

Clinical Center for Sports Medicine and Sports Dentistry

Clinical Center of Sports Medicine
Center Chief and Junior Associate Professor ; Kazuyoshi YAGISHITA
Assistant Professor ; Toshoyuki OHHARA
Specially Appointed Assistant Professor ; Mikio SHIODA
Physical therapy operator chief ; Junya AIZAWA
Physiotherapist; Kenji HIROHATA, Takehiro OHMI, Shunsuke OHJI
Staff Assistant; Kiyomi ITOH

Sports Medicine/Dentistry
Associate Professor; Toshiaki UENO
Assistant Professor; Hiroshi CHUREI
Specially Appointed Assistant Professor ; Kairi HAYASHI

(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 2019 to December 2019)

Section of out-patient clinic: 3,928

Section of athletic rehabilitation: 3,713

○ Sports Medicine/Dentistry, Sports dentistry clinic

Sports dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered dental diseases and traumatic injuries. Custom-fitted protective gears such as mouthguard and face-guard against sports-related dental and maxillofacial trauma are also handled for participants in contact sports such as a boxing, American football, rugby football, hockey, lacrosse, and martial art.

(4) Publications

[Original Articles]

1. Tomomasa Nakamura, Hideyuki Koga, Koji Otabe, Masafumi Horie, Toshifumi Watanabe, Kazuyoshi Yagishita, Ichiro Sekiya, Takeshi Muneta. Comparison of three approaches for femoral tunnel during double-bundle anterior cruciate ligament reconstruction: A case controlled study. *J Orthop Sci.* 2019.01; 24(1); 147-152
2. Mai Katakura, Masafumi Horie, Toshifumi Watanabe, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Kenta Katagiri, Hiroko Ueki, Stefano Zaffagnini, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Effect of meniscus repair on pivot-shift during anterior cruciate ligament reconstruction: Objective evaluation using triaxial accelerometer. *Knee.* 2019.01; 26(1); 124-131
3. Kimura Y, Yamada M, Ishiyama D, Nishio N, Kunieda Y, Koyama S, Sato A, Otobe Y, Ohji S, Suzuki M, Ogawa H, Ito D, Ichikawa T, Hamanaka K, Tanaka N, Muroh Y. Impact of unilateral spatial neglect with or without other cognitive impairments on independent gait recovery in stroke survivors. *Journal of rehabilitation medicine.* 2019.01; 51(1); 26-31
4. Yamada M, Kimura Y, Ishiyama D, Nishio N, Otobe Y, Tanaka T, Ohji S, Koyama S, Sato A, Suzuki M, Ogawa H, Ichikawa T, Ito D, Arai H. Synergistic effect of bodyweight resistance exercise and protein supplementation on skeletal muscle in sarcopenic or dynapenic older adults. *Geriatrics & gerontology international.* 2019.03;
5. Ohji S, Kimura Y, Otobe Y, Nishio N, Ito D, Taguchi R, Ogawa H, Yamada M. Measurement of self-propulsion distance of wheelchair using cycle computer excluding assistance distance by touch switch: A pilot study. *The journal of spinal cord medicine.* 2019.04; 1-5
6. Kimura Y, Yamada M, Ohji S, Ishiyama D, Nishio N, Otobe Y, Koyama S, Suzuki M, Ichikawa T, Ito D, Maehori N, Nagae H. Presence of sarcopenic obesity and evaluation of the associated muscle quality in Japanese older men with prostate cancer undergoing androgen deprivation therapy. *Journal of geriatric oncology.* 2019.04;
7. Koji Nakamaru, Junya Aizawa, Keizo Kawarada, Yukari Uemura, Takayuki Koyama, Osamu Nitta. Immediate effects of thoracic spine self-mobilization in patients with mechanical neck pain: A randomized controlled trial. *J Bodyw Mov Ther.* 2019.04; 23(2); 417-424

8. Satoh Y, Yamada T, Shimamura R, Ohmi T. Comparison of foot kinetics and kinematics during gait initiation between young and elderly participants. *Journal of physical therapy science*. 2019.07; 31(7); 498-503
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10. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Kazuyoshi Yagishita. Correlations between vertical ground reaction force, sagittal joint angles, and the muscle co-contraction index during single-leg jump-landing *Asian journal of sports medicine*. 2019.07; 10(3);
11. Junya Aizawa, Shunsuke Ohji, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Kazuyoshi Yagishita. Relationship between asymmetrical jump-landing impact and quadriceps strength after unilateral anterior cruciate ligament reconstruction *Physical Medicine and Rehabilitation Research*. 2019.07; 4; 1-6
12. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Kazuyoshi Yagishita, Toshitaka Yoshii, Atsushi Okawa. Supine versus lateral position for accurate positioning of acetabular cup in total hip arthroplasty using the modified Watson-Jones approach: A randomized single-blind controlled trial. *Orthop Traumatol Surg Res*. 2019.09; 105(5); 915-922
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14. Yusuke Nakagawa, Toshifumi Watanabe, Yusuke Amano, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Benefit of subcutaneous patient controlled analgesia after total knee arthroplasty. *Asia Pac J Sports Med Arthrosc Rehabil Technol*. 2019.10; 18; 18-22
15. Katakura M, Nakamura K, Watanabe T, Horie M, Nakamura T, Katagiri H, Otabe K, Nakagawa Y, Ohara T, Sekiya I, Muneta T, Koga H. Risk factors for residual anterolateral rotational instability after double bundle anterior cruciate ligament reconstruction: Evaluation by quantitative assessment of the pivot shift phenomenon using triaxial accelerometer. *The Knee*. 2019.10;
16. Tomomasa Nakamura, Monica A Linde, Brandon D Marshall, Hideyuki Koga, Takeshi Muneta, Patrick Smolinski, Freddie H Fu. Arthroscopic centralization restores residual knee laxity in ACL-reconstructed knee with a lateral meniscus defect. *Knee Surg Sports Traumatol Arthrosc*. 2019.11; 27(11); 3699-3704
17. Mai Katakura, Hideyuki Koga, Tomomasa Nakamura, Daisuke Araki, Kanto Nagai, Kyohei Nishida, Ryosuke Kuroda, Takeshi Muneta. Biomechanical Effects of Additional Anterolateral Structure Reconstruction With Different Femoral Attachment Sites on Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*. 2019.12; 47(14); 3373-3380
18. Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Ichiro Sekiya, Hideyuki Koga. The effect of a longitudinal tear of the medial meniscus on medial meniscal extrusion in anterior cruciate ligament injury patients. *Knee*. 2019.12; 26(6); 1292-1298
19. Daisuke Araki, Takehiko Matsushita, Yuichi Hoshino, Kanto Nagai, Kyohei Nishida, Hideyuki Koga, Tomomasa Nakamura, Mai Katakura, Takeshi Muneta, Ryosuke Kuroda. The Anterolateral Structure of the Knee Does Not Affect Anterior and Dynamic Rotatory Stability in Anterior Cruciate Ligament Injury: Quantitative Evaluation With the Electromagnetic Measurement System. *Am J Sports Med*. 2019.12; 47(14); 3381-3388

[Books etc]

1. T. Ohmi, J. Aizawa, T. Yamada, A. Okawa, K Yagishita. ORTHOPEDIC SURGERY. 2019.04 (ISBN : 978-4-524-27775-9)

[Conference Activities & Talks]

1. The Gait Analysis of the Patients after Bi-Cruciate Retaining TKA. 2019.02.16
2. The Gait Analysis of the Rotating Hinge knee in Revision TKA. 2019.02.16
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6. Ueno T. Sports dentistry and mouthguard. GAMEX 2019-Gyeonggi International Dental Academic Meeting 2019.08.31 Seoul, Korea
7. Kazuhiro HIKITA, Takeo MAIDA, Yumiko ENAMI, Masahiro IJIMA, Tun Sin PHYU, Hiroshi CHUREI, Toshiaki UENO, Hidekazu TAKAHASHI. Manufacturing of sports mouthguard by digital technology . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
8. Phyu Sin TUN, Hiroshi CHUREI, Gen TANABE, Thet Khaing AUNG, Shingo KAMIJO, Meiko OKI, Hidekazu TAKAHASHI, Kazuhiro HIKITA, Toshiaki UENO. Shock-absorbing capability of rubber-like and rigid 3D printing materials compared to commercial mouthguard materials . 5th International Academy for Digital Dental Medicine 2019.10.04 Nara Kasugano International Forum IRAKA
9. Naoki Yamamoto, Takuya Oyaizu, Masaki Horie, Mitsuhiro Enomoto, Masato Yuasa, Ryohei Takada, Kazuyoshi Yagishita. Hyperbaric oxygen therapy promotes muscle regeneration via angiogenesis by reactive nitrogen species in muscle contusion injury of rat.. The 4th conference of Asia-pacific Undersea and Hyperbaric Medical Society 2019.10.25 nakatsu, Oita Japan
10. Ohara Toshiyuki, Yagishita Kazuyoshi, Shioda Mikio, Yamamoto Naoki. Effect of hyperbaric oxygen therapy on fatigue fractures of lower limbs. The 30th Annual Meeting of the Japanese Society of Clinical Sports Medicine. 2019.11.17
11. Togawa K, Aung TK, Takahashi Y, Suzaka M, Tanabe G, Hayashi K, Churei H, Ueno T. Application of custom-designed faceguard to prevent eye injury for professional futsal player: a case report. World Congress on Dentistry and Oral Health 2019 2019.11.21 Kuala Lumpur, Malaysia
12. Hayashi K, Chowdhury RU, Chowdhury NU, Togawa K, Toyoshima Y, Churei H, Ueno T. Survey on thickness changes and deformations of custom-made mouthguards after 2 years of use by Bangladesh field hockey players. World Congress on Dentistry and Oral Health 2019 2019.11.21 Kuala Lumpur, Malaysia

[Awards & Honors]

1. Best Poster Award (Hayashi K), World Congress on Dentistry and Oral Health 2019, 2019.11

Sports Dentistry

(1) Publications

[Conference Activities & Talks]

1. Material and methods for improving the efficacy of the mouthguards. 2019.09.29
2. Kairi Hayashi, Chowdhury Rnman Uddin, Chowdhury Nafees Uddin, Kaito Togawa, Yukako Toyoshima, Hiroshi Churei, Toshiaki Ueno. Survey on thickness change and deformation of custom-made mouthguards after 2 years of use by Bangladesh Field Hockey players.. 2nd World congress on dentistry and oral health. 2019.11.21 Kuala Lumpur