ANNUAL PUBLICATIONS

2021



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

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Oral Pathology

Professor Tohru Ikeda

Junior Associate Professor Kei Sakamoto

Assistant Professor Kou Kayamori

Technical Staff Miwako Hamagaki

Graduate Students TEERAWONG CHANYANUCH Akiyo Sanpei NGUYEN PHAN THE HUY Fukawa Hironori HERDIANTOPUTRI RANNY RAHANINGRUM

(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. Shibata E, Morita KI, Kayamori K, Tange S, Shibata H, Harazono Y, Michi Y, Ikeda T, Harada H, Imoto I, Yoda T. Detection of novel fusion genes by next-generation sequencing-based targeted RNA sequencing analysis in adenoid cystic carcinoma of head and neck. Oral surgery, oral medicine, oral pathology and oral radiology. 2021.10; 132(4); 426-433
- 2. Yoshitake H, Kayamori K, Wake S, Sugiyama K, Yoda T. Biomarker expression related to chondromatosis in the temporomandibular joint. Cranio : the journal of craniomandibular & sleep practice. 2021.07; 39(4); 362-366
- 3. Kaida A, Yamamoto S, Parrales A, Young ED, Ranjan A, Alalem MA, Morita KI, Oikawa Y, Harada H, Ikeda T, Thomas SM, Diaz FJ, Iwakuma T. DNAJA1 promotes cancer metastasis through interaction with mutant p53. Oncogene. 2021.06;
- 4. Oikawa Yu, Tanaka Kae, Ohsako Toshimitsu, Kugimoto Takuma, Kuroshima Takeshi, Hirai Hideaki, Tomioka Hirofumi, Shimamoto Hiroaki, Michi Yasuyuki, Sakamoto Kei, Ikeda Tohru, Harada Hiroyuki. Comparison of Clinicopathological Characteristics Between the Anterior and Posterior Type of Squamous Cell Carcinoma of the Floor of the Mouth: The Anterior Type Is a Risk Factor for Multiple Primary Cancer FRONTIERS IN ONCOLOGY. 2021.06; 11; 682428
- 5. Takayuki Suga, Trang Thi Huyen Tu, Miho Takenoshita, Lou Mikuzuki, Yojiro Umezaki, Hiroaki Shimamoto, Yasuyuki Michi, Chaoli Hong, Yoshihiro Abiko, Tohru Ikeda, Narikazu Uzawa, Hiroyuki Harada, Akira Toyofuku. Case Report: Hidden Oral Squamous Cell Carcinoma in Oral Somatic Symptom Disorder. Front Psychiatry. 2021.04; 12; 651871
- 6. Cuong Minh Tran, Takeshi Kuroshima, Yu Oikawa, Yasuyuki Michi, Kou Kayamori, Hiroyuki Harada. Clinicopathological and immunohistochemical characteristics of pigmented oral squamous cell carcinoma. Oncol Lett. 2021.04; 21(4); 339
- Hiroaki Shimono, Hideaki Hirai, Yu Oikawa, Yumi Mochizuki, Takeshi Kuroshima, Hirofumi Tomioka, Kou Kayamori, Tohru Ikeda, Hiroyuki Harada. Metastatic tumors in the oral region: a retrospective chart review of clinical characteristics and prognosis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2021.04;
- Yuki Fukawa, Kei Sakamoto, Takuma Kugimoto, Yasuyuki Michi, Hiroyuki Harada, Masahide Yamamoto, Masanobu Kitagawa, Tohru Ikeda, Kouhei Yamamoto. Nodular lymphocyte-predominant Hodgkin lymphoma involving the hard palate. Pathol Int. 2021.03; 71(3); 213-215
- 9. Kaname Sakamoto, Kaori Endo, Kei Sakamoto, Kou Kayamori, Shogo Ehata, Jiro Ichikawa, Takashi Ando, Ryosuke Nakamura, Yujiro Kimura, Kunio Yoshizawa, Keisuke Masuyama, Tomoyuki Kawataki, Kunio Miyake, Hiroki Ishii, Tomonori Kawasaki, Keiji Miyazawa, Masao Saitoh. EHF suppresses cancer progression by inhibiting ETS1-mediated ZEB expression. Oncogenesis. 2021.03; 10(3); 26
- Fukawa Yuki, Sakamoto Kei, Kugimoto Takuma, Michi Yasuyuki, Harada Hiroyuki, Yamamoto Masahide, Kitagawa Masanobu, Ikeda Tohru, Yamamoto Kouhei. Nodular lymphocyte-predominant Hodgkin lymphoma involving the hard palate(和訳中) Pathology International. 2021.03; 71(3); 213-215
- 11. 布川 裕規, 坂本 啓, 釘本 琢磨, 道 泰之, 原田 浩之, 山本 正英, 北川 昌伸, 池田 通, 山本 浩平. 硬口蓋に発生した nodular lymphocyte-predominant Hodgkin lymphoma の一例 (A case of nodular lymphocyte-predominant Hodgkin lymphoma involving the hard palate) 日本病理学会会誌. 2021.03; 110(1); 274
- 12. グエン・ファン・テーフィ,坂本 啓,池田 通. 舌疾患での異形成を分類する際に、口腔病理学者を補助する ためのディープラーニングの利用 (Deep-learning application for supporting oral pathologists in dysplasia grading of tongue lesions) 日本病理学会会誌. 2021.03; 110(1); 264
- 13. Baba Shunichi, Akashi Takumi, Kayamori Kou, Ohuchi Tomoyuki, Ogawa Ikuko, Kubota Nobuhisa, Nakano Keisuke, Nagatsuka Hitoshi, Hasegawa Hiromasa, Matsuzaka Kenichi, Tomii Shohei, Uchida Keisuke, Katsuta Noriko, Sekiya Takahiro, Ando Noboru, Miura Keiko, Ishibashi Hironori, Ariizumi Yousuke, Asakage Takahiro, Michi Yasuyuki, Harada Hiroyuki, Sakamoto Kei, Eishi Yoshinobu, Okubo Kenichi, Ikeda Tohru. Homeobox transcription factor engrailed homeobox 1 is a possible diagnostic marker for adenoid cystic carcinoma and polymorphous adenocarcinoma(和訳中) Pathology International. 2021.02; 71(2); 113-123

- Kayamori K, Tsuchiya M, Michi Y, Kuribayashi A, Mikami T, Sakamoto K, Yoda T, Ikeda T. Primordial odontogenic tumor occurred in the maxilla with unique calcifications and its crucial points for differential diagnosis. Pathol Int. 2021.01; 71(1); 80-87
- 15. Kayamori Kou, Tsuchiya Maiko, Michi Yasuyuki, Kuribayashi Ami, Mikami Toshinari, Sakamoto Kei, Yoda Tetsuya, Ikeda Tohru. Primordial odontogenic tumor occurred in the maxilla with unique calcifications and its crucial points for differential diagnosis(和訳中) Pathology International. 2021.01; 71(1); 80-87
- 16. Chanyanuch Teerawong, Kei Sakamoto, Yuki Fukawa, Maiko Tsuchiya, Kou Kayamori, Takumi Akashi, Miwako Hamagaki, Hirofumi Tomioka, Takeshi Kuroshima, Kei-ichi Morita, Hiroyuki Harada, Tohru Ikeda. Immunohistochemical Positivity for p16 Unrelated to Human Papillomavirus (HPV) Infection in Lingual Squamous Cell Carcinomas The Journal of the Stomatological Society, Japan. 2021;
- 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

- 1. 土谷麻衣子、栢森 高、坂本 啓、池田 通. 口腔扁平上皮癌由来エクソソームによる新規の破骨細胞誘導 経路とカンナビジオールによる阻害効果. 第 110 回日本病理学会総会 2021.04.23
- グエン・ファン・テーフィ,坂本 啓,池田 通. 舌疾患での異形成を分類する際に、口腔病理学者を補助する ためのディープラーニングの利用 (Deep-learning application for supporting oral pathologists in dysplasia grading of tongue lesions). 日本病理学会会誌 2021.03.01
- Ami Kuribayashi, Sakurako Kawashima, Junichiro Sakamoto, Kou Kayamori, Hiroshi Tomisato, Tohru Kurabayashi. MR Imaging of Methotrexate-related Lymphoproliferative Disease with chief complaint of oral symptoms. 2021.05.22

Bacterial Pathogenesis, Infection and Host Response

Professor SUZUKI Toshihiko Associate Professor ASHIDA Hiroshi Assistant Professor SUZUKI Shiho Research fellow of JSPS OKANO Tokuju Graduate Student ABASS Adiza (Department of Molecular Virology) Graduate Student BOONYALEKA Kotchakorn Graduate Student HSU Chen Wei Graduate Student EFA Bernard Bahaah AKwasi Graduate Student IWASAWA Marie Graduate Student **TAKAHASHI** Yuto 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. Abass A, Okano T, Boonyaleka K, Kinoshita-Daitoku R, Yamaoka S, Ashida H, Suzuki T. Effect of low oxygen concentration on activation of inflammation by Helicobacter pylori Biochem Biophys Res Commun. 2021.06; 560; 179-185
- 2. Kinoshita-Daitoku R, Kiga K, Miyakoshi M, Otsubo R, Ogura Y, Sanada T, Bo Z, Phuoc TV, Okano T, Iida T, Yokomori R, Kuroda E, Hirukawa S, Tanaka M, Sood A, Subsomwong P, Ashida H, Binh TT, Nguyen LT, Van KV, Ho DQD, Nakai K, Suzuki T, Yamaoka Y, Hayashi T, Mimuro H. A bacterial small RNA regulates the adaptation of Helicobacter pylori to the host environment Nat Commun. 2021.04; 12(1); 2085
- 3. Okano Tokuju, Suzuki Toshihiko. Inflammasome activation inducer produced by Aggregatibacter actinomycetemcomitans causes arthritis(和訳中) 口腔病学会雑誌. 2021.03; 88(1); 70-71
- 4. Prah Isaac, Ayibieke Alafate, Nguyen Thi Thu Huong, Iguchi Atsushi, Mahazu Samiratu, Sato Wakana, Hayashi Takaya, Yamaoka Shoji, Suzuki Toshihiko, Iwanaga Shiroh, Ablordey Anthony, Saito Ryoichi. Virulence Profiles of Diarrheagenic Escherichia coli Isolated from the Western Region of Ghana(和訳中) Japanese Journal of Infectious Diseases. 2021.03; 74(2); 115-121
- 5. Kurashima Y, Kigoshi T, Murasaki S, Arai F, Shimada K, Seki N, Kim YG, Hase K, Ohno H, Kawano K, Ashida H, Suzuki T, Morimoto M, Saito Y, Sasou A, Goda Y, Yuki Y, Inagaki Y, Iijima H, Suda W, Hattori M, Kiyono H. Pancreatic glycoprotein 2 is a first line of defense for mucosal protection in intestinal inflammation. Nature communications. 2021.02; 12(1); 1067
- Abass Adiza, 鈴木 敏彦. ピロリ菌によって誘導されるインフラマソーム活性化における低酸素環境下での影響 (The effect of hypoxia on Helicobacter pylori induced inflammasome activation) 日本細菌学雑誌. 2021.02; 76(1); 107
- 7. 岡野 徳壽, 鈴木 敏彦. 低酸素環境と疾患 (がん、感染症)の分子論 低酸素環境下において TRIF-HIF-1 α経路は P.gingivalis によるインフラマソーム活性化亢進を制御している (TRIF-HIF-1 α signaling under hypoxia drives enhancement of inflammasome activation by P. gingivalis) 日本細菌学雑誌. 2021.02; 76(1); 57
- Isaac Prah, Alafate Ayibieke, Samiratu Mahazu, Chihiro Tani Sassa, Takaya Hayashi, Shoji Yamaoka, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Emergence of oxacillinase-181 carbapenemase-producing diarrheagenic Escherichia coli in Ghana. Emerg Microbes Infect. 2021.12; 10(1); 865-873

[Misc]

1. Ashida H, Suzuki T, Sasakawa C. Shigella infection and host cell death: A double-edged sword for the host and pathogen survival Current Opinion in Microbiology. 2021.02; 59; 1-7

- 1. Okano Tokuju, Suzuki Toshihiko. Aggregatibacter actinomycetemcomitans が産生するインフラマソー ム活性化誘導因子は関節炎の原因となる (Inflammasome activation inducer produced by Aggregatibacter actinomycetemcomitans causes arthritis). 口腔病学会雑誌 2021.03.01
- 2. Okano Tokuju, Suzuki Toshihiko. Aggregatibacter actinomycetemcomitans が産生するインフラマソー ム活性化誘導因子は関節炎の原因となる (Inflammasome activation inducer produced by Aggregatibacter actinomycetemcomitans causes arthritis). 口腔病学会雑誌 2021.03.01
- 3. Adiza Abass, Toshihiko Suzuki. The effect of hypoxia on Helicobacter pylori induced inflammasome activation. 第 76 回日本細菌学会総会 2021.02

Molecular Immunology

Professor Miyuki Azuma AssociateProfessor Shigenori Nagai AssistantProfessor Chenyang Zhang Specially Appointed Assistant Professor Eri Ikeda (Jul. ~)

Adjunct instructor

Hiroshi Kiyono Emi Nishii

Graduate Students(Doctor)

Xiang Ao (Pulp Biology and Endodontics)(\sim Mar.) Keeratika Wongtim (\sim Sep.) Amrita Widyagarini Subagyo Droonpan Pissacha Farzana Sultana(Apr. \sim) (Master) Yuto Nagatomo(Apr. \sim) Honoka Aoshima(Apr. \sim)

(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. Tanaka D, Ikeda Y, Ikeda E, Yokose M, Ganss B, Iwata T. Effect of Amelotin on Bone Growth in the Murine Calvarial Defect Model. Annals of Biomedical Engineering. 2021.12; 49(12); 3676-3684
- 2. Ikeda Y, Kawada A, Tanaka D, Ikeda E, Kobayashi H, Iwata T. A comparative questionnaire study of patient complaint levels between magnetostrictive ultrasonic scaler (Cavitron(R)) and piezoelectric ultrasonic scalers International Journal of Dental Hygiene. 2021.08; 19(3); 273-278
- Wongtim K, Ikeda E, Ohno T, Nagai S, Okuhara S, Kure K, Azuma M. Overexpression of PD-L1 in gingival basal keratinocytes reduces periodontal inflammation in a ligature-induced periodontitis model. Journal of Periodontology. 2021.06;
- 4. Takehara T, Wakamatsu E, Machiyama H, Nishi W, Emoto K, Azuma M, Soejima K, Fukunaga K, Yokosuka T. PD-L2 suppresses T cell signaling via coinhibitory microcluster formation and SHP2 phosphatase recruitment. Communications biology. 2021.05; 4(1); 581
- 5. Ao X, Yang Y, Okiji T, Azuma M, Nagai S. Polymorphonuclear Myeloid-derived cells that contribute to the immune paralysis are generated in the early phase of sepsis via PD-1/PD-L1 pathway. Infection and Immunity. 2021.05; 89(6); e00771-20
- 6. Ben J E Raveney, Wakiro Sato, Daiki Takewaki, Chenyang Zhang, Tomomi Kanazawa, Youwei Lin, Tomoko Okamoto, Manabu Araki, Yukio Kimura, Noriko Sato, Terunori Sano, Yuko Saito, Shinji Oki, Takashi Yamamura. Involvement of cytotoxic Eomes-expressing CD4 ⁺T cells in secondary progressive multiple sclerosis Proc Natl Acad Sci U S A. 2021.03; 118(11);
- Kawasaki M, Ikeda Y, Ikeda E, Takahashi M, Tanaka D, Nakajima Y, Arakawa S, Izumi Y, Miyake S. Oral infectious bacteria in dental plaque and saliva as risk factors in patients with esophageal cancer. Cancer. 2021.02; 127(4); 512-519
- Ishihama H, Ishii K, Nagai S, Kakinuma H, Sasaki A, Yoshioka K, Kuramoto T, Shiono Y, Funao H, Isogai N, Tsuji T, Okada Y, Koyasu S, Toyama Y, Nakamura M, Aizawa M, Matsumoto M. An antibacterial coated polymer prevents biofilm formation and implant-associated infection. Scientific Reports. 2021.02; 11(1); 3602
- 9. Nagata M, Toyonaga K, Ishikawa E, Haji S, Okahashi N, Takahashi M, Izumi Y, Imamura A, Takato K, Ishida H, Nagai S, Illarionov P, Stocker BL, Timmer MSM, Smith DGM, Williams SJ, Bamba T, Miyamoto T, Arita M, Appelmelk BJ, Yamasaki S. Helicobacter pylori metabolites exacerbate gastritis through C-type lectin receptors. Journal of Experimental Medicine. 2021.01; 218(1); e20200815

- 1. W Namangkalakul, S Nagai, K Nakahama, M Takechi, S Iseki. Fibroblast growth factor 18 Activity on Calvarial Bone Regeneration. The 2021 IADR/AADR/CADR General Session & Exhibition 2021.07.21 U.S.A. (Web)
- 2. L Huixin, S Yasuda, S Aoyama, C Zhang, Y Kawano, M Azuma, N Kawamata . CD80 can be the marker of chronic myeloid leukemia stem cells and regulated by BCR-ABL signaling. AACR Annual Meeting 2021 2021.04.10 U.S.A (Web)

Advanced Biomaterials

Professor UO Motohiro Assistant Professor WADA Takahiro Graduate Student Wang Liwei Graduate Student OKAJIMA Natsuki Graduate Student TSUKADA Saho 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]

- Hatano K, Inokoshi M, Tamura M, Uo M, Shimizubata M, Tonprasong W, Wada T, Takahashi R, Imai K, Minakuchi S. Novel antimicrobial denture adhesive containing S-PRG filler. Dent Mater J. 2021.12; 40(6); 1365-1372
- 2. Hiroshi Churei, Ruman Uddin Chowdhury, Yuriko Yoshida, Gen Tanabe, Shintaro Fukasawa, Takahiro Shirako, Takahiro Wada, Motohiro Uo, Hidekazu Takahashi, Toshiaki Ueno. Use of the fiberglass reinforcement method in thermoplastic mouthguard materials to improve flexural properties for enhancement of functionality. Dent Mater J. 2021.12; 40(6); 1338-1344
- 3. Tonprasong W, Inokoshi M, Tamura M, Uo M, Wada T, Takahashi R, Hatano K, Shimizubata M, Minakuchi S. Tissue Conditioner Incorporating a Nano-Sized Surface Pre-Reacted Glass-Ionomer (S-PRG) Filler. Materials (Basel). 2021.11; 14(21); 6648

- 4. Mark Kondo, Kohei Soga, Kazuhiro Suga, Naoki Mikami, Wei-Jen Lai, Sunmin Kim, Ikuo Yonemitsu, Zuisei Kanno, Motohiro Uo, Hiroshi Takemura. Quantitative Evaluation by Orthodontic Moment Measurement Device: Comparative study of the two types of wire during orthodontic treatment 2021 6th International Conference on Intelligent Informatics and Biomedical Sciences (ICIIBMS). 2021.11; 6; 239-242
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- 6. T. Wada, D. Kido, B. Hu, K. Dong, Y. Wakisaka, Q. Yuan, Md Harun Al Rashid, Y. Takeichi, S. Takakusagi, K. Asakura. Pt/Au(111) prepared by Surface limited redox replacement method using X-ray absorption near edge structure spectroscopy with log-spiral bent crystal Laue analyzers Photon Factory Activity Report 2020. 2021.07; 38;
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Oral Radiation Oncology

Professor	Masahiko MIURA
Assistant Professor	Atsushi KAIDA
	Hisao HOMMA (\sim March)
SA Assistant Professor	Hitomi NOJIMA
Graduate Students	Hiroaki SHIMONO (~March)
	Esther NG FENG YING
	Kohki TOHYAMA
Adjunct Instructor	Yusuke Onozato (\sim March)

(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.

Research (2)

- 1) Visualization of tumor radioresponse by moleculr 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.

Clinical Services & Other Works (5)

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. Yoshimura Ryo-ichi, Toda Kazuma, Watanabe Hiroshi, Kaida Atsushi, Harada Hiroyuki, Asakage Takahiro, Miura Masahiko. Efficacy and Safety of Induction Chemotherapy and/or External Beam Radiotherapy Followed by Brachytherapy in Patients With Tongue Cancer ANTICANCER RESEARCH. 2021.12; 41(12); 6259-6266
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- 1. Atsushi Kaida, Masahiko Miura. Effects of radiation-induced cell cycle kinetics on cell fate. 34th Annual Meeting of JASTRO 2021.11.12 Web
- 2. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. 2021.04.18

Oral and Maxillofacial Surgery

Professor: Hiroyuki HARADA Associate Professor: Yasuyuki MICHI Junior Associate Professor: Fumihiko TSUSHIMA, Hirofumi TOMIOKA Assistant Professor: Hiroaki SHIMAMOTO, Hideaki HIRAI, Takeshi KUROSHIMA, Takuma KUGIMOTO Specially Appointed Assistant Professor: Toshimitsu OHSAKO, Yu OIKAWA Naoto NISHII, Rikuka SHIMIZU Graduate Student: Yoshimitu SATO, Misako TANAKA, Takuya KOMIYAMA, Shunya HAYASHI, Yuta IKAMI, Junko TAKEI, Phung TRAN XUAN, Rika NOJI, Shiori TOKIZAKI, Haruka IBI

(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 4,000 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 and oral mucosal disease which need high degree of specialty and long term follow up. We also prepare some groups for inpatients with an emphasis on specialties, to provide the recent and advanced treatment.

(2) Publications

[Original Articles]

1. Yoshimura Ryo-ichi, Toda Kazuma, Watanabe Hiroshi, Kaida Atsushi, Harada Hiroyuki, Asakage Takahiro, Miura Masahiko. Efficacy and Safety of Induction Chemotherapy and/or External Beam Radiotherapy Followed by Brachytherapy in Patients With Tongue Cancer ANTICANCER RESEARCH. 2021.12; 41(12); 6259-6266

- 2. Tsushima F, Sakurai J, Shimizu R, Harada H. A case report of oral lichenoid lesions related to cross-reactivity between nickel and palladium. Contact Derm. 2021.12; 85(6); 700-701
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- Tohyama K, Kano Y, Noji R, Aoyagi Y, Matsudera S, Ohno K, Ariizumi Y, Michi Y, Tomioka H, Shimamoto H, Asakage T, Harada H, Yoshimura R, Miyake S, Miura M, and Ikeda S. The clinical utility of comprehensive genomic profiling for Recurrent / Metastatic Head and Neck Cancer Head and Neck Cancer. 2021.12; 47(4); 359-365
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- 1. Yoshihide Ota, Tadahide Noguchi, Masahiko Miura et al.. General rules for clinical and pathological studies on oral cancer (2nd edition): a synopsis. Int J Clin Oncol. 2021.04; 26(4); 623-635
- 1. Misako T, Hiroshi K. Histone modification 2021.04; 36; 27-30

[Conference Activities & Talks]

- 1. Pissacha Daroonpan, 加島義久, 濱垣美和子, 西井直人, 津島文彦, 原田浩之, 池田 通, 東みゆき. マルチプ レックス免疫組織染色による舌扁平上皮癌の免疫プロファイリング解析. 第 66 回口腔外科学会総会 · 学術大 会 2021.11.12 千葉市
- Shimamoto H, Oikawa Y, Ohsako T, Kugimoto T, Kuroshima T, Hirai H, Tomioka H, Michi Y, Harada H. Analysis of cervical lymph node metastasis at levels IV and V of oral squamous cell carcinoma. 第58 回日本癌治療学会学術集会 2021.10.22 横浜市
- 3. 高田嘉宝, 黒嶋雄志, 島本裕彰, 大迫利光, 栢森 高, 池田 通, 原田浩之. 頬リンパ節転移をきたした下顎歯 肉扁平上皮癌の一例. 第 52 回日本口腔外科学会近畿支部学術集会 2021.07.03 WEB 開催
- 4. Tran MC, Marukawa E, Oshibe N, Uo M, Yoda T, Harada H.. Effects on bone regeneration of different centrifugation conditions and coagulation systems during platelet concentrate and fibrin network formation. 14th Asian Congress on Oral & Maxillofacial Surgery 2021.06.04
- 5. Tran Cuong Minh, 黒嶋雄志, 及川 悠, 道 泰之, 栢森 高, 原田浩之. Clinicopathological and immunohistochemical characteristics of pigmented oral squamous cell carcinoma.. 第 75 回日本口腔科 学会学術集会 2021.05.12 豊中市
- 6. Yuji Kabasawa, Kanade Ito, Shiori Tokura, Itsuki Takazawa,Rio Kimura, Tohko Nakanishi, Kikue Akiyama, Yuki Onuma, Toshiko Adachi, Ruri Komiya, Hiroyuki Harada, Hitomi Nojima, Masahiko Miura, Ryoichi Yoshimura. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. The 1st Annual Meeting of the International Society of Oral Care 2021.04.18 東京
- 7. Kano Y, Noji R, Yamashita Y, Kudo R, Onishi I, Tanimoto K, Miya F, Nakagawa T, Ishikawa T, Uetake H, Kinugasa Y, Tanabe M, Asakage T, Harada H, Okamoto R, Miyake S, and Ikeda S. Detection of RAS mutation in solid cancers using NGS-based genome profiling tests. 第18回日本臨床腫瘍学会学術集会 2021.02.18 WEB 開催
- 8. Kano Y, Noji R, Yamashita Y, Kudo R, Tasaki A, Ohno K, Ariizumi Y, Hirai H, Tomioka H, Shimamoto H, Michi Y, Miura M, Yoshimura R, Asakage T, Harada H, Okamoto R, Miyake S, Ikeda S. using NGS-based genome profiling tests. 第 18 回日本臨床腫瘍学会学術集会 2021.02.18 WEB 開催
- 9. Kudo R, Kano Y, Noji R, Yamashita Y, Ishikawa T, Kudo A, Oshima N, Ariizumi Y, Nakagawa T, Mitsumura T, Onishi I, Kimura K, Miya F, Yokobori J, Ohki M, Takamine E, Yoshida M, Tanabe M, Miyake S, Ikeda S. Clinical utility of comprehensive genome profiling using FoundationOne CDx. 第18回日本臨床腫瘍学会学術集会 2021.02.18 WEB 開催

[Awards & Honors]

1. 14th Asian Congress on Oral & Maxillofacial Surgery (ACOMS) Oral Paper Competition runner up, Asian Congress on Oral & Maxillofacial Surgery (ACOMS), 2021.06

Oral and Maxillofacial Radiology

Professor: Tohru KURABAYASHI Associate Professor: Hiroshi WATANABE Junior Associate Professor: Naoto OHBAYASHI Assistant Professor: Shin NAKAMURA, Ami KURIBAYASHI, Junichiro SAKAMOTO Hospital Staff: Yoshikazu NOMURA, Sakurako KAWASHIMA Graduate Student: Miharu TAGUCHI, Natnicha WAMASING

(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]

- Watanabe H, Kurabayashi T. Letters to the Editor. Effects of differences in pixel size on image characteristics of digital intraoral radiographic systems: A physical and visual evaluation. Dentomaxillofacial Radiology. 2021.12; 50; 20210093
- Yoshimura R, Toda K, Watanabe H, Kaida A, Harada H, Asakage T, Miura M. Efficacy and Safety of Induction Chemotherapy and/or External Beam Radiotherapy Followed by Brachytherapy in Patients With Tongue Cancer Anticancer Research. 2021.12; 41(12); 6259-6266

- 3. Ozaki Y, Watanabe H, Kurabayashi T. Effective dose estimation in cone-beam computed tomography for dental use by Monte Carlo simulation optimizing calculation numbers using a step and shoot method Dentomaxillofacial Radiology. 2021.10; 50(7); 20210084
- 4. Kazuya Watanabe, Motoko Watanabe, Chihiro Takao, Chaoli Hong, Zhenyan Liu, Takayuki Suga, Trang Thi Huyen Tu, Junichiro Sakamoto, Yojiro Umezaki, Tatsuya Yoshikawa, Miho Takenoshita, Akihito Uezato, Haruhiko Motomura, Tohru Kurabayashi, Yoshihiro Abiko, Akira Toyofuku. Clinical Characteristics of Predominantly Unilateral Oral Cenesthopathy With and Without Neurovascular Contact. Front Neurol. 2021.10; 12; 744561
- Mochizuki Y, Marukawa E, Harada H, Kinoshita N, Nakatani R, Oikawa Y, Hirai H, Tomioka H, Yoda T, Nakamura S, Kurabayashi T. Postoperative morphological changes over time of vascularized scapular bone used for mandibular reconstruction: A retrospective cohort study Journal of Plastic, Reconstructive & Aesthetic Surgery . 2021.09; 74(9); 1984-1990
- Takayuki Suga, Trang T H Tu, Junichiro Sakamoto, Akira Toyofuku. A case of vestibular schwannoma with oral burning sensation: surgical complication or burning mouth syndrome? Biopsychosoc Med. 2021.08; 15(1); 13
- Harazono Y, Kayamori K, Sakamoto J, Akaike Y, Kurasawa Y, Tsushima F, Sasaki Y, Harada H, Yoda T. Retrospective analysis of schwannoma in the oral and maxillofacial region: clinicopathological characteristics and specific pathology of ancient change. The British journal of oral & maxillofacial surgery. 2021.07;
- Taguchi M, Wamasing P, Watanabe H, Sakamoto J, Kurabayashi T. Applying the paralleling technique in periapical radiographs for Japanese patients by analyzing CT images. Oral Radiology. 2021.04; 37(2); 311-320
- Ohbayashi N, Wamasing P, Tonami K, Kurabayashi T. Incidence of hypercementosis in mandibular third molars determined using cone beam computed tomography. Journal of Oral Science. 2021.03; 63(2); 179-183
- Asai S, Nakamura S, Kuribayashi A, Sakamoto J, Yoshino N, Kurabayashi T. Effective combination of 3 imaging modalities in differentiating between malignant and benign palatal lesions Oral surgery Oral Medicine Oral pathology Oral Radiology. 2021.02; 131(2); 256-264
- 11. Kayamori K, Tsuchiya M, Michi Y, Kuribayashi A, Mikami T, Sakamoto K, Yoda T, Ikeda T. Primordial odontogenic tumor occurred in the maxilla with unique calcifications and its crucial points for differential diagnosis. Pathol Int. 2021.01; 71(1); 80-87
- 12. Adel S, Wada T, Kawashima N, Abdou A, Watanabe H, Kurabayashi T, Okiji T, Uo M. Preparation and properties of tristrontium aluminate as an alternative component of mineral trioxide aggregate (MTA) cement Dental Materials Journal. 2021.01; 40(1); 184-190
- 13. Yamada I, Yoshino N, Yokokawa M, Oikawa Y, Harada H, Hikishima K, Kurabayashi T, Saida Y, Tateishi U, Ohata Y . Diffusion tensor imaging of oral carcinoma: clinical evaluation and comparison with histopathological findings. Magn Reson Imaging. 2021; 77; 99-108
- 14. Hla-Myint T, Tsuji M, Suzuki S, Obayashi N, Kurabayashi T, Moriyama K. Establishment of a novel method for qualitative and quantitative evaluation of deglutitive tongue movement by integration of ultrasound video imaging and lateral cephalogram. Orthodontic Waves. 2021; 80(1); 23-31
- 15. Ozawa E, Honda E, Tomizato H, Kurabayashi T, Nunthayanon K, Ohmori H, Shimazaki K, Ono T. Preliminary study of articulatory characteristics in open bite subjects revealed by 3T MRI movies. APOS Trends in Orthodontics. 2021; 11(1); 14-22
- 16. Harada H, Tomioka H, Hirai H, Kuroshima T, Oikawa Y, Nojima H, Sakamoto J, Kurabayashi T, Kayamori K, Ikeda T.. MRI before biopsy correlates with depth of invasion corrected for shrinkage rate of the histopathological specimen in tongue carcinoma. Sci Rep.. 2021; 11(1); 20992
- 17. Aragaki T, Nakamura S, Sakamoto K, Suzuki M, Yoda T, Kurabayashi T.. MRI findings of a dermoid cyst in the floor of the mouth with "sac of marbles" sign: an immunohistopathological study. J Oral Maxillofac Surg Med Pathol.. 2021;

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- Taguchi A, Tanaka R, Kakimoto N, Morimoto Y, Arai Y, Hayashi T, KurabayashiT, Katsumata A, Asaumi J. Clinical guidelines for the application of panoramic radiographs in screening for osteoporosis. Oral Radiol. 2021; 37(2); 189-208
- Kurabayashi T, Ohbayashi N, Sakamoto J, Nakamura S. Usefulness of MR imaging for odontogenic tumors. Odontology. 2021; 109(1); 1-10

- 1. Watanabe H, Ozaki Y, Kurabayashi T. Effective dose estimation in cone-beam computed tomography for dental use (CBCT) by Monte Carlo simulation employing a step and shoot method. The 23rd International Congress of Oral and Maxillofacial Radiology 2021.04.28 Web
- 2. Taguchi M, Sakamoto J, Watanabe H, Kurabayashi T.. Application of texture analysis to odontogenic lesions. The 23rd International Congress of DentoMaxilloFacial Radiology 2021.04.28 Web
- 3. Kurabayashi T. MRI characteristics of odontogenic tumors and cysts. Invited Session: The 23rd International Congress of DentoMaxillofacial Radiology 2021.04.30 Web
- Ami Kuribayashi, Sakurako Kawashima, Junichiro Sakamoto, Kou Kayamori, Hiroshi Tomisato, Tohru Kurabayashi. MR Imaging of Methotrexate-related Lymphoproliferative Disease with chief complaint of oral symptoms. 2021.05.22
- 2. Naoto Ohbayashi, Shin Nakamura, Junichirou Sakamoto, Kei Sakamoto, Tohru Kurabayashi. A case report: Epithelial-myoepithelial carcinoma at palate. 231th Kantoh-chihoukai, Japanese Society of Oral and Maxillofacial Radiology 2021.01.30 Web

Department of Dental Anesthesiology and Orofacial Pain Management

Professor Shigeru MAEDA

Associate Professor Ryo WAKITA, Akira NISHIYAMA

Junior Associate Professor Tomoka MATSUMURA

Assistant Professors Yukiko Baba, Takuya FUNAYAMA, Yoko YAMAZAKI

Specially Appointed Assistant Professor Hiroyuki ISHIYAMA, Hiroko IMURA, Chihiro SUZUKI

Hospital Staffs Yushi ABE, Nanako IKEDA, Yukiko ICHIHASHI, Hiroko KIMURA, Chihiro KUTSUMIZU, Haruna KONO, Maya SAKAMOTO, Syoko TOBE, Miho HANAOKA, Keisuke MIYAZONO, Yoshihiro YAMAGUCHI

Graduate Students Keiko ABE, Ryoko KURISU, HILMANDA, KAY THWE YE MIN SOE, Shoko TOBE, Saki,OKABE, Ken TAKAHASHI, Keisuke MIYAZONO, Kotomi UCHINUMA, Nozomi UTSUMI, Li Xinyue, Fares Raafat, ANGKULMAHASUK SUVICHAYA

Research Students Hidemasa KUSUNOKI, Fumiko HATA, Satoshi YAMADA, Erika YAMAHARA

(1) **Outline**

Our department is responsible for both dental anesthesiology and orofacial pain control. In addition, orofacial pain control consists of orofaical pain clinic and TMD clinic (former TMJ clinic). In the field of dental anesthesiology, the aim is to provide safe and painless dental treatment. The education includes lectures and practical training on local anesthesia, general anesthesia, sedation, and monitoring. In addition, basic and clinical research is conducted to achieve the above objectives. The number of cases of general anesthesia and sedation is about 1,000 and 2,000, respectively, per year, which is the largest number of anesthesia management among public universities in Japan. In the field of oral and maxillofacial anesthesiology, the orofacial pain clinic and TMJ outpatient clinic are staffed by dedicated specialists.

(2) Research

- 1) Development of a non-invasive drug delivery system
- 2) Development of a new local anesthesia method for dentistry
- 3) Elucidation of the etiology of neuropathic pain in the maxillofacial region and its treatment
- 4) Clinical research on psychosedation and systemic management in dentistry

5) Elucidation of the pathogenesis of temporomandibular joint disorder and the relationship between social, psychological and dental factors

(3) Education

The purpose of our department is to provide knowledge and basic skills in local anesthesia for daily dental practice, sedation and general anesthesia for specialized anesthesia management, systemic management of patients with complications, and maxillofacial pain treatment. Lectures are given on dental anesthesia (general anesthesia, local anesthesia, sedation, cardiopulmonary resuscitation), orofacial pain clinic, temporomandibular disorders (TMD), and bruxism. In the section on general anesthesia, students learn the physiology of respiration and circulation, and the pharmacological effects and mechanisms of inhaled anesthetics, intravenous anesthetics, and muscle relaxants. In the section on sedation, students learn about the differences between general anesthesia and sedation. As a first aid training, students learn not only basic life support but also advanced life support using a cardiopulmonary resuscitation training system. In ofofacial pain clinic, students are instructed on the basis of physiology and pharmacology as a field of neuroscience. In TMD and bruxism, we teach not only anatomy and dentistry of temporomandibular joint and masticatory muscles, but also social and psychological factors that may be involved in TMD and bruxism.

(4) Lectures & Courses

The specialty of dental anesthesia is to provide safe and painless dental care. For this purpose, information about the patient's health status is collected and evaluated, which is an important prerequisite for dental care, regardless of the administration of anesthetics. The importance of such patient assessment is emphasized to undergraduate students. In addition, the meaning of anesthesia management by dentists is discussed with the students. In graduate school, the main objective is to accumulate clinical experience and learn basic and clinical research methods and concepts while aiming for certification and specialist training. After graduation, students are expected to obtain research funding and become involved in clinical practice, research, and education as potential supervisors.

(5) Clinical Services & Other Works

In the operating room, about 1,000 cases of general anesthesia are performed annually for oral surgery. These include lengthy surgeries like as reconstruction with free flap, and 2 jaw osteotomies. In the outpatient dental anesthesia clinic, we perform more than 2,000 sedation procedures per year to treat patients, who is difficult to receive in general dentistry, as well as long procedures such as implant-related procedures. In addition, we respond promptly to emergencies that occur in our hospital on average several times a month, and if necessary, we collaborate with the ER of the medical school hospital. The Department of Orofacial Pain Clinic and the Department of Temporomandibular Joint Treatment are two of the few specialized outpatient clinics in Japan, and we accept referrals from inside and outside the hospital. In the Orofacial Pain Clinic, we mainly treat neuropathic pain and trigeminal neuralgia, and provide multidisciplinary treatment with medication, nerve blocks, oriental medicine and physical therapy. In the outpatient clinic for temporomandibular joint, after definitive diagnosis by imaging, we provide treatment based on lifestyle and self-management approaches.

(6) Clinical Performances

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

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

(7) **Publications**

[Original Articles]

- 1. Nakashima Soichiro, Koeda Michihiko, Ikeda Yumiko, Hama Tomoko, Funayama Takuya, Akiyama Tomomi, Arakawa Ryosuke, Tateno Amane, Suzuki Hidenori, Okubo Yoshiro. Effects of anodal transcranial direct current stimulation on implicit motor learning and language-related brain function: An fMRI study Psychiatry and Clinical Neurosciences. 2021.06; 75(5-6); 200-207
- Hidaka R, Furuya J, Nishiyama A, Suzuki H, Aoyagi M, Matsubara C, Yoshizumi Y, Yoshimi K, Nakane A, Tohara H, Sato Y, Minakuchi S. Structural Equation Modeling of Tongue Function and Tongue Hygiene in Acute Stroke Patients. International journal of environmental research and public health. 2021.04; 18(9); 4567
- 3. Higuchi H, Takaya-Ishida K, Miyake S, Fujimoto M, Nishioka Y, Maeda S, Miyawaki T. Comparison of Oxygen Saturation Between Nasal High-Flow Oxygen and Conventional Nasal Cannula in Obese Patients Undergoing Dental Procedures With Deep Sedation: A Randomized Crossover Trial. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2021.04;
- 4. Hiroyuki Ishiyama, Masayuki Hideshima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki. Evaluation of Respiratory Resistance as a Predictor for Oral Appliance Treatment Response in Obstructive Sleep Apnea: A Pilot Study. Journal of Clinical Medicine. 2021.03; 10(6); 1255-1268
- 5. Nakashima S, Koeda M, Ikeda Y, Hama T, Funayama T, Akiyama T, Arakawa R, Tateno A, Suzuki H, Okubo Y. Effects of anodal transcranial direct current stimulation on implicit motor learning and language-related brain function: An fMRI study. Psychiatry and clinical neurosciences. 2021.02;
- 6. Fujimoto M, Higuchi H, Honda-Wakasugi Y, Miyake S, Nishioka Y, Yabuki-Kawase A, Maeda S, Miyawaki T. Dexmedetomidine inhibits LPS-induced inflammatory responses through peroxisome proliferator-activated receptor gamma (PPAR γ) activation following binding to $\alpha < \text{sub} > 2 < /\text{sub} >$ adrenoceptors. European journal of pharmacology. 2021.02; 892; 173733
- 7. Wakita Ryo, Ito Takaya, Fukayama Haruhisa. Small doses of adrenaline contained in the local anaesthetic may result in prolonged increased cardiac function even after the vital signs return to normal Advances in Oral Maxillofacial Surgery. 2021; 3; 100-104

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1. MAEDA Shigeru. Characteristics of Intravenous Anesthesia Used for Dental Treatment The Journal of the Stomatological Society. 2021.11; 88(2/3); 89-95

- 1. Tomoka Matsumura, Shigeru Maeda. Lidocaine suppresses cell proliferation and induces apoptosis of myofibroblasts. Neuroscience 2021 2021.11.08 on-line
- 2. Hilmanda, Ryo Wakita, Chihiro Suzuki, Shigeru Maeda. Factors Associated with Variation in Pulse Transit Time using Pulse Oximetry. The 49th Annual Meeting of the Japanese Dental Society of Anesthesiology 2021.10 on line
- 3. Kay Thwe Ye Min Soe, Akira Nishiyama. Effect of different Upper Oral Appliance designs on sleep-associated-respiratory status. 2021 ADR/AADR/CADR General Session & Exhibition 2021.07.24 (online)

- 4. Maeda S, Miyake S, Fujimoto M, Nishioka Y, Higuchi H, Miyawaki T. Delta Opioid receptor ligand suppresses increase in IL-6 in cultured microglia . 2021.07.22
- 5. Kay Thwe Ye Min Soe, Akira Nishiyama. Effect of palatal width and vertical dimension of the upper oral appliance on respiratory status during sleep. The 75th Annual Meeting of Japanese Stomatological Society 2021.05.13 (online)
- 6. Kay Ye Min Soe, Akira Nishiyama, Hiroyuki Ishiyama. Effect of different Upper Oral Appliance Designs on Sleep-associated Respiratory Status. 99th General Session & Exhibition of the IADR 2021.07.22 Online
- 1. Yushi Abe, Tomoka Matsumura, Shigeru Maeda. General anesthesia for a child with CPVT in the outpatient dental department. The annual meeting of Japanese society of pediatric anesthesiology 2021.10.17 Sendai
- 2. Yukiko Ichihashi, Chihiro Kutsumizu, Ryo Wakita, Shigeru Maeda. Difficult Intubation due to Laryngeal Edema after Heavy Ion radiotherapy: a case report. Japanese Society of Dental Anesthesiology 49th Annual Conference 2021.10
- 3. Hiroko Kimura, Yoko Yamazaki, Masato Kawashima. A case of effective treatment using a mitriptyline for persistent dental pain after pulp extirpation. The 50th Annual Meeting of the Japanese Society for the Study of Chronic Pain 2021.03.19
- 4. Yushi Abe, Tomoka Matsumura, Shigeru Maeda. A retrospective study of perioperative factors related to the prognosis of free skin flaps in oral surgery reconstruction.. Japanese Society of Dental Anesthesiology 49th Annual Conference 2021 on line

Pediatric Dentistry / Special Needs Dentistry

Professor Tsutomu Iwamoto

Junior Associate Professor Satoko Kakino

Assistant Professor Yasuka Kusumoto, Tomoki Uehara (-Mar), Kanae Wada, Atsushi Oishi(Apr-), Asuna Sugimoto (Mar-)

Project assistant professor Atsushi Oishi (-Mar), Taiji Hoshiai

Hospital staff Yuko Seki (-Mar), Shigeki Nagahiro, Haruka Naito, Kaori Konuma, Kaori Kohi, Karen Inoue (Apr-), Emi Kanai (Apr-), Kie Aida, Anna Kumakura(-Mar), Kana Hayashi

Graduate Student Manami Takenoshita (-Sep), Aiko Hoshiai, Cho Li, Yujeong Shin, Yusuke Iwabuchi, Kokoro Iwata (Mar-), Rika Kodama (-Dec),

Research Student Emi Kanai (-Mar), Kaori Konuma, Haruka Naito, Karen Inoue (-Mar), Daishi Saito, Yumiko Nakashima, Yoshihito Yamakawa, Gen Takahashi (Apr-), Yuga Toyomura (Apr-), Kanade Yamaki (Apr-)

Special Research Student Rika Kurogoshi

Clinical Professor: Michiyo Miyashin (-Mar)

Adjunct Lecturer Ryu Matsubara, Natsumi Tsuchihashi, Takeshi Okamura, Shoji Takahashi, Asuri jayawarudeina, Yuko Matumura, Makiko Takashi, Taki Sekiya, Kennichi Miura, Jo Inada, Yosuke Kinoshita, Seiji Sakurai, Osamu Shinozuka, Tomo Suzuki, Goro Sekiguchi (-Mar), Yohei Takeuchi, Shohei Tamura, Moriyuki Nakamura

(1) Publications

[Original Articles]

1. Kokoro Iwata, Keita Kawarabayashi, Keigo Yoshizaki, Tian Tian, Kan Saito, Asuna Sugimoto, Rika Kurogoushi, Aya Yamada, Akihito Yamamoto, Yasuei Kudo, Naozumi Ishimaru, Satoshi Fukumoto, Tsutomu Iwamoto. von Willebrand factor D and EGF domains regulate ameloblast differentiation and

enamel formation Journal of Cellular Physiology. 2021.12;

- Iwabuchi Y, Nakamura T, Kusumoto Y, Nakao R, Iwamoto T, Shinozuka O, Senpuku H. Effects of pH on the Properties of Membrane Vesicles Including Glucosyltransferase in Streptococcus mutans. Microorganisms. 2021.11; 9(11);
- 3. Sekiya T, Sugimoto K, Kubota A, Tsuchihashi N, Oishi A, Yoshida N. Assessment of psychological changes in young children during dental treatment: Analysis of the autonomic nervous activity and electroencephalogram. International journal of paediatric dentistry. 2021.09;
- 4. Yamada A, Yoshizaki K, Ishikawa M, Saito K, Chiba Y, Fukumoto E, Hino R, Hoshikawa S, Chiba M, Nakamura T, Iwamoto T, Fukumoto S. Connexin 43-Mediated Gap Junction Communication Regulates Ameloblast Differentiation via ERK1/2 Phosphorylation. Frontiers in physiology. 2021.09; 12; 748574
- 5. Rika Kurogoushi, Tomokazu Hasegawa, Yuki Akazawa, Kokoro Iwata, Asuna Sugimoto, Kimiko Yamaguchi-ueda, Aya Miyazaki, Anrizandy Narwidina, Keita Kawarabayashi, Takamasa Kitamura, Hiroshi Nakagawa, Tomonori Iwasaki, Tsutomu Iwamoto. Fibroblast growth factor 2 suppresses the expression of C-C motif chemokine 11 through the c-Jun N-terminal kinase pathway in human dental pulp-derived mesenchymal stem cells Experimental and Therapeutic Medicine. 2021.09; 22(6); 1356
- 6. Yuko Seki, Tomoki Uehara, Miki Uehara, Haruko Fujita, Satoko Kakino, Michiyo Miyashin. Intentional replantation to the endodontic-periodontal disease associated with misplacement of a rubber band-like foreign body: A case report Pediatric Dental Journal. 2021.08; 32(2); 191-196
- 7. Tamura Yukihiko, Fuangtharnthip Pornpoj, Uehara Tomoki, Iwamoto Tsutomu, Waki Yoshihiro. Metallothionein expression in zinc-treated cartilage precursor ATDC5 cells Biomedical Research on Trace Elements. 2021.06; 32(1); 23-29
- 8. Atsushi Oishi,Yohei Hama,Emi Kanai,Michiyo Miyashin. Color-changeable chewing gum to motivate chewing training with complete dentures for a male patient with hypohidrotic ectodermal dysplasia and oligodontia Pediatric Dental Journal. 2021.04; 31(1); 123-127
- Hideo Yonezawa, Mizuho Motegi, Atsushi Oishi, Fuhito Hojo, Seiya Higashi, Eriko Nozaki, Kentaro Oka, Motomichi Takahashi, Takako Osaki, Shigeru Kamiya. Lantibiotics Produced by Oral Inhabitants as a Trigger for Dysbiosis of Human Intestinal Microbiota International Journal of Molecular Sciences. 2021.04; 22(7); 3343
- Takenoshita M, Takechi M (Co-first), Vu TH, Furutera T, Akagawa C, Namangkalakul W, Aoto K Kume T, Miyashin M, Iwamoto T, Iseki S. Cell lineage- and expression-based inference of the roles of forkhead box transcription factor Foxc2 in craniofacial development. Developmental Dynamics. 2021.03;
- 1. Hirokazu ITO, Chinami IGARASHI, Satstuki Wakae-Morita, Kaori KOHI, Masashi SUGISAKI, Kaoru KOBAYASHI. 3DCT imaging results for masticatiry muscle tendon-aponeurosis hyperplasia 2021.12; 33(3); 81-88
- 2. Reliability of quantitative analysis of the glenoid fossa with magnetic resonance imaging 2021.04;

- 1. Yusuke Iwabuchi, Tomoyo Nakamura, Yasuka Kusumoto, Ryoma Nakao, Tsutomu Iwamoto, Osamu Shinozuka, Hidenobu Senpuku. Effect of initial pH conditions on the membrane vesicles produced by Streptococcus mutans. EMBO The Company of Biologists Workshop -Bacterial membrane vesicles: Biogenesis, functions and medical applications- 2021.11.24 Ibaraki, Japan
- 2. Iwata Kokoro, Kawarabayashi Keita, Yoshizaki Keigo, Sugimoto Asuna, Fukumoto Satoshi, Iwamoto Tsutomu. Identification and characterization of von Willebrand factor D and EGF domains as a novel extracellular matrix protein in teeth. The 69th Annual Meeting of Japanese Association of Dental Research (JADR) 2021.10.24 Kyushu University
- 3. Itaru Suzuki, Yusuke Iwabuchi, Hidenobu Senpuku. Effect of extracellular DNA for biofilm formation of Actinomyces by membrane vesicle of Streptococcus mutans. 2021 The 63rd Annual Meeting of Japanese Association for Oral Biology All Rights Reserved. 2021.10.09

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- 2. Wear evaluation of 3D printing resin material opposing deciduous teeth : fabrication of esthetic full crown restoration and removable space maintainer. 2021.06.06

Orthodontic Science

Professor	Takashi ONO				
Associate Professor					
Junior Associate Profes	ssor Yoshiro MATSUMOTO, Jun HOSOMICHI				
Assistant Professor	Ippei WATARI, Ikuo YONEMITSU, Yuji ISHIDA, Takayoshi ISHIDA				
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				S	Saranya SERIRUKCHUTARUNGSEE, Yixin LOU
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Arisa KUBO (Apr-), Rika KUWABARA (Apr-), Midori WADA (Apr-),					
1	Manaka MORO(Apr-)				
Graduate School Resea	rch Students Vuta NAKAI (-Mar), Masamu INOUE (-Mar)				
n N H	vloe SATO, Kasumi HATANO, Keiko FUKINO (-Mar), Makiko OKUZAWA (-Mar) vlasako KAWADA, Shuko ARAI, Aiko ISHIZAKI, Misa TAKAHASHI Kazuki SAWAYA, Chiyo SHIMIZU, Naoaki MIKAMI				
I	rumi NAKANO, Saori WATAYA, Doyoon KIM (-Mar), Jia QI (-Mar) fori SUGITA (Apr-), Yukari MIZOGUCHI (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]

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- 12. Fujita K, Minamiyama S, Usumi-Fujita R, Omura S, Takasu H, Yamashita Y, Honda K, Imai H, Iwai T, Hirota M, Ono T, Mitsudo K. Temporomandibular joint stability after two types of maxillary impaction surgery in patients with skeletal class II open bite due to condylar deformations: a preliminary study Orthodontic Waves. 2021.03; 80(1); 47-54
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[Social Contribution]

1. EECD, 2020.04.01 - Now

Cariology and Operative Dentistry

Professor: Junji Tagami (\sim March), Yasushi Simada (September \sim) Associate Professor: Masavuki Otsuki Junior Associate Professor: Masatoshi Nakajima (\sim March), Noriko Hiraish Assistant Professor: Takako Yoshikawa, Go Inoue, Keiichi Hosaka(\sim March), Rena Takahashi, Takaaki Sato, Hospital Staff: Ayako Nakamoto, Nami Takashino, Tomoko Tabata(\sim March), Hisaichi Nakagawa (\sim December), Kazuhide Yonekura (\sim March) Specially Appointed Assistant Professor: NHM Khairul Matin, Takashi Hatayama, Tomoko Tabata (April \sim), Kazuhide Yonekura (April \sim August) Specially Appointed Researcher: AHMED MOHAMED ABDELRAHMAN ABDOU Staff Assistant: Shiori Ogi(~ March), Takako Nakagawa(~ March), Rieko Sugiyama Graduate Student: RUMMANI GHASSAN MAHMOOD S (~ September), Yukiko Tanno, (\sim March), ALMASABI WALEED ABDULQADER M, Ueda Nanako (\sim March), Saki Uchiyama (\sim March), Misa Kashiwa (\sim March), Shun Kobayashi (\sim March), Toyoaki Kobayashi (\sim March), Miyuki Shimizu (\sim March), Motoi Takahashi (\sim March), Mayu Hasegawa (\sim March), Yuta Baba (~ March), Kim Seunggun (~ March), ERICK LUZ MADRIGAL (~ March), MARTINA GEORGIEVA (\sim March), LEILA NASIRY KHANLAR (\sim May), VICHEVA Pa Pa Kay Khine (\sim Sptember), Min Khant Ko Ko (\sim Sptember), Antonin TICHY (\sim Sptember), Kyoko Ishikawa, Meiken Hayashi, Yosuke Minato, Ryuta Andou, Yutaro Oda, Yusuke Koshimitsu, Ayaka Sato, Yorichika Shioya, Chin Akane, Mayuri Nshimaki, Shiori Yamamoto, NOORULDEEN ALI SAEED, MURTUZA AYED ALI, WAHYUNI SUCI DWIANDHANY, Satoshi Akiya, Yuko Ogawa, Kiyoka Furusawa, Yutaro Motoyama, Ako Yamashita, QI Feng, Kittisak SANON, TAGHREED ABDULRAHMAN ALREFAIE, MULTUZA AYED ALI, Soe Kay Thwe Than Naing, Soe Kay Thwe Than Naing, YANG Yi, WEI Diantong, Mika Simojima, Hiroki Ishihara, Koudai Akabane, Kouta Kibe, CHEN XUEFEI, Panchanit UBOLSA-ARD, Tadamu Gondo (April \sim), Shunsuke Takano (April \sim), Tsuji Yukiko (April \sim), Iwabuchi Hirotoshi (April \sim), Kei Ushijima (April \sim), Mahiro Iizuka (April \sim), ZENG Chen (April \sim), ZHAO Mengtian (April \sim), Abu Hasan Mohammad KHALED (October \sim), Shamima JAHAN (November \sim) Research Student: Shinji Ogura, Mineo Kijima, ZENG SIQI, San San May Phyo Aung (\sim March), DU Zijuan (April \sim)

(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]

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- 10. Keiichi Hosaka, Shisei Kubo, Antonin Tichy, Masaomi Ikeda, Koichi Shinkai, Toshio Maseki, Akitomo Rikuta, Hiromi Sasazaki, Kaori Satoh, Morioki Fujitani, Masao Hanabusa, Takatsugu Yamamoto, Kazushi Yoshikawa, Makoto Morigami, Shigeru Uno, Junpei Sugizaki, Hirofumi Yatani, Toru Nikaido. Clinical effectiveness of direct resin composite restorations bonded using one-step or two-step self-etch adhesive systems: A three-year multicenter study. Dent Mater J. 2021.09; 40(5); 1151-1159
- 11. Nanako Ueda, Tomohiro Takagaki, Toru Nikaido, Rena Takahashi, Masaomi Ikeda, Junji Tagami. The effect of different ceramic surface treatments on the repair bond strength of resin composite to lithium disilicate ceramic. Dental Materials Journal. 2021.09; 40(5); 1073-1079
- 12. Saki Uchiyama, Rena Takahashi, Takaaki Sato, Shin Rozan, Masaomi Ikeda, Masanao Inokoshi, Toru Nikaido, Junji Tagami. Effect of a temporary sealing material on the bond strength of CAD/CAM inlay restorations with resin-coating technique. Dental Materials Journal. 2021.09; 40(5); 1122-1128
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- 33. Hasegawa M, Tichy A, Hosaka K, Kuno Y, Ikeda M, Nozaki K, Chiba A, Nakajima M, Tagami J. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents. Dental Materials Journal. 2021.03; 40(4); 877-884
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- 3. TAKAHASHI Rena, ENOMOTO Megumi, ODA Yutaro, UCHIYAMA Saki, ROZAN Shin, KANAMORI Yuna, AKEHASHI Sae, TAGAMI Atsuko, TAKAHASHI Akifumi, NORITAKE Kanako, SATO Takaaki, TAGAMI Junji. Effects of Clinical Experience and Adhesive Systems on the Dentin Bonding Strength and Dentin Bonding Reliability The Japanese Journal of Conservative Dentistry. 2021.06; 64(3); 220-226

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- 2. Nassar M, Nassar R, Maki H, Al-Yagoob A, Hachim AY, Senok A, Williams D, Hiraishi N. Phytic Acid: Properties and Potential Applications in Dentistry Frontiers in Materials. 2021; (8); 638909
- 1. Mikako Hayashi, Yuichi Kitasako, Rena Takahashi, Toru Nikaido. A key aspect of pulp protection using modern adhesive technology The Journal of Japan Endodontic Association . 2021.05; 42(2); 77-82
- 2. Yasushi Shimada. The Application of Optical Coherence Tomography(OCT) in Conservative Dentistry 2021.02; 64(1); 36-38
- 3. Ushida Keisuke, Noriko Hiraishi, Junji Tagami. Establishment of Preventive Measures in Dental Practice against COVID-19 during its Outbreak: A Report from Wuhan, China 2021.02; 64(1); 6-16

- 1. Sanon Kittisak, Hatayama Takashi, Hosaka Keiichi, Shimada Yasushi, Nakajima Masatoshi. . SrCl2/HOCl Smear Layer Deproteinization Improves Dentin Bonding Durability of 1-SEAs. International Academy for Adhesive Dentistry 2021.11.19 Web
- 2. Diantong Wei, Ayako Nakamoto, Akira Nakane, Masayuki Otsuki, Noriko Hiraishi, Yasushi Shimada, Junji Tagami. Effect of Er:YAG laser irradiation with additional low energy on resin-dentin bonding and morphology of bonded interface. The 33rd Annual meeting of Japanese Society for Laser Dentistry 2021.11
- 3. Sanon Kittisak, Hatayama Takashi, Hosaka Keiichi, Shimada Yasushi, Nakajima Masatoshi. . Effect of Zinc Chloride on HOCl-Smear Layer Deproteinization. Academy of Dental Materials 2021.10.07 Web
- 4. Sanon Kittisak, Hatayama Takashi, Hosaka Keiichi, Shimada Yasushi, Nakajima Masatoshi. Effect of strontium chloride-containing HOCl-smear layer deproteinization on dentin bond strength of 1-SEAs. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.01 Web
- 5. Shimada Y, Sumi Y, Tagami J, Yoshiyama M. 3D Imaging of OCT for Diagnosis of Dentin Caries. 2021 IADR/AADR/CADR General Session (Virtual Experience) 2021.07.23
- 6. Sanon Kittisak, Hatayama Takashi, Tagami Junji, Hosaka Keiichi, Nakajima Masatoshi.. Bonding Durability of 1-SEAs to HOCl-Smear Layer Deproteinized Dentin. 99th General Session of International Association of Dental Research 2021.07.21 Web
- 7. Noriko Hiraishi, Fumikai Hayashi, Junji Tagami. 19F and 31P solid state NMR study on fluoridate apatite in human dental calculus. The 98th, the IADR/AADR/CADR General Session & Exhibition 2021.07
- 8. Sanon Kittisak, Hatayama Takashi, Tagami Junji, Hosaka Keiichi, Nakajima Masatoshi. Effect of HOCI-application and wash-out time on dentin bond strength of one-step self-etch adhesives. The 154th Meeting of the Japanese Society of Conservative Dentistry 2021.05.01 Web
- 9. T. Yoshikawa, A. Sadr. Polymerization Behavior of Composites at Top/Bottom of Cavity using Different-Lights. Academy of Dental Materials 2021.10.07 Web
- 1. Go Inoue, Chen Xuefei, Yasushi Shimada. The effect of POs-Ca in toothpaste on decalcified enamel. 86th The Stomatological Society Congress 2021.12.04 Tokyo
- 2. Yuna KANAMORI, Rena TAKAHASHI, Masaomi IKEDA, Shingo KAMIJO, Shin ROZAN, Kanako NORITAKE, Ken-ichi TONAMI, Hiroshi NITTA, Toru NIKAIDO, Yasushi SHIMADA, Junji TAGAMI. The effect of resin coating technique on internal fit of CAD/CAM composite resin crowns. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Web
- 3. Yamamoto M, Inokoshi M, Shimizubata M, Nozaki K, Takahashi R, Yoshihara K, Minakuchi S. Shear bond strength to root dentin of 4-META/MMA-TBB resin containing antibacterial agents. The 77th General Session of the Japanese Society for Dental Materials and Devices 2021.04.10
- 4. Takako Yoshikawa, Makoto Arakawa. Optimal light curing method for light-cured resin composite restorations. The 21st meeting of Japan Association of Dental Traumatolgy 2021.09.18

[Social Contribution]

- 1. Editorial board (Takako Yoshikawa), Asian Pacific Journal of Dentistry, 2016.01.01 Now
- 2. Sensors Guest Editor (Yasushi Shimada), 2020.09 Now
- 3. Materials Guest Editor (Yasushi Shimada), 2021.01 Now

Pulp Biology and Endodontics

Professor: Takashi OKIJI

Associate Professor: Nobuyuki KAWASHIMA (December \sim), Mitsuhiro Sunakawa (\sim March)

Junior Associate Professor: Nobuyuki KAWASHIMA (
 \sim November), Satoshi WATANABE (December
 $\sim)$

Assistant Professor: Arata EBIHARA, Satoshi WATANABE (\sim November), Kento TAZAWA (Leave for research), Kentaro HASHIMOTO, Yoshiko IINO, Keisuke SUNADA-NARA

Specially Appointed Assistant Professor Sonoko NODA (April $\sim)$

Hospital Staff: Sonoko NODA (~ March), Mayuko FUJII, Keiichiro MAKI, Syunsuke KIMURA, Akira KOUNO, Yasuhiro HOSHIHARA, Shinya YAMAUCHI, Nanami NIKAIDO, Hiroko SOEDA, Taro NAKATSUKASA (~ September) Hiroki MURANO (April ~ September)

Graduate Student: Yasuhiro HOSHIHARA (~ March), Shinya YAMAUCHI (~ March), Taro NAKATSUKASA(~ March), Hiroki MURANO(~ September), Yadanar Su Phyo (~ March), Ao Xiang (~ September), Aung Nyein Pyae Sone (~ September), Htoo Shwe Sin Thein (~ September), Sherif Adel Abdelfattah, Zar Chi Thein Zaw (~ September), Yamato OKADA, Shion ORIKASA, Dumrogvute KUNLANUN, Myint Thu, Kieu Quoc Thoai, Hayate UNNO, Satoshi Oomori, Hiroki OKUDA, Jiayi LIU, Aseel Alchawoosh, Han Peifeng, Moe Sandar Kyaw, Yuka KASUGA, Souta MOCHIDUKI, Nyein Chan Ko, Ryota ITO (April ~), Keiko HIRANO (April ~), Yu Ziniu (April ~), Wang Shihan (April ~), Alghamdi Faisal Turki A, Khaing Nyein Pwint (October ~), Ren Chunmei (October ~), Kazuhisa SATAKE(April ~)

Research Student: Sousuke IZAWA, Yu Ziniu (\sim March), Wang Shihan (\sim March), Yadanar Su Phyo (April \sim), Takuya KAWAMURA (April \sim), Risako YAMAMOTO (April \sim), Phu Yadanar Aung Myint (October \sim) Chen Yanyan (October \sim), Bai Xiyuan (October \sim)

(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

- · Establishment of an experimental model of rat dental pulp tissue engineering using mesenchymal stem cells
- · Immunohistochemical and gene expression analysis of stem-cell-associated markers in rat dental pulp
- · Effects BCL9 signaling on osteo-/odontoblastic differentiation of dental pulp stem cells

2. Root canal irrigation

 \cdot Evaluation of efficacy- and safety-related properties of laser-activated root canal irrigation

3. Evaluation of newly developed endodontic sealers and pulp capping materials

- \cdot Cytotocompatibility of an experimental sealer containing surface reaction type pre-reacted glassionomer (S-PRG) to osteoblastic cells
- · Evaluation of tristrontium aluminate and distrontium cerate as endodontic materials

4. Nickel-titanium rotary root canal instrumentation

- \cdot Comparison of torque, screw-in force and shaping ability of glide path instruments in continuous rotation and optimum glide path motion.
- \cdot Influence of rotational speed on torque/force generation and shaping ability during root canal instrumentation of extracted teeth with continuous rotation and optimum torque reverse motion.
- \cdot Clinical application of endodontic motors
- \cdot Evaluation of the shaping ability of different NiTi rotary instruments used by undergraduate dental students in curved canals.
- \cdot Characteristics of highly flexible endodontics rotary files
- 5. Evaluation of root canal anatomy in a Japanese population using cone-beam computed tomography (CBCT)

(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;

- \cdot Vital pulp therapy,
- \cdot Nonsurgical root can al therapy,
- \cdot Root can al 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 magni fied view . Also , we seek to provide evidence -based endodontic treatment based on our laboratory and clinical research.

(6) Publications

[Original Articles]

- Sunada-Nara K, Kawashima N, Okiji T. Micro-endodontic management of a fused mandibular molar with rare anatomical features: a case report. The International Journal of Microdentistry. 2021.12(2); 70-76
- 2. Aung NPS, Watanabe S, Okiji T. Er:YAG laser-activated irrigation in comparison with different irrigation systems for cleaning the apical root canal area beyond ledge.Photobiomodulation,Photomedicine,and Laser Surgery. 2021.12; 39(12); 759-765
- 3. Thein HSS, Hashimoto K, Kawashima N, Noda S, Okiji T. Evaluation of the anti-inflammatory effects of surface -reaction -type pre-reacted glass-ionomer filler containing root canal sealer in lipopolysaccharide stimulated RAW264.7 macrophages. Dental Materials Journal. 2021.10
- 4.Moe Sandar Kyaw, Ebihara A, Kasuga Y, Maki K, Kimura S, Pyae Hein Htun, Nakatsukasa T, Okiji T. Influence of rotational speed on torque /force generation and shaping ability during root canal instrumentation of extracted teeth with continuous rotation and optimum torque reverse motion. International Endodontic Journal. 2021.09; 54(9); 1614-1622
- 5. Zaw ZCT, Kawashima N, Kaneko T, Okii T. Angiogenesis during coronal pulp regeneration using rat dental pulp cells : neovascularization in rat molars *in vivo* and proangiogenic dental pulp cell-endothelial cell interactions *in vitro*. Journal of Dental Sciences. 2021.07; in press
- 6. Phyo Y, Hashimoto K, Kawashima N, Kuramoto M, Okiji T. Evaluation of the cytocompatibility of methacrylate resin-based root canal sealers with osteoblast-like cells. Dental Materials Journal. 2021.07; 40 (4); 942-948
- 7.Kimura S, Ebihara A, Okiji T. Characteristics of highly flexible endodontics rotary files. The Journal of the Japanese Society for Dental Materials and Devices. 2021.05; 40(2); 121-124
- 8.Maki K, Ebihara A, Omori S, Unno H, Nakatsukasa T, Kimura S, Okiji T. Evaluation of the shaping ability of different NiTi rotary instruments used by undergraduate dental students in curved canals. The Journal of Japan Endodontic Assiciation. 2021.05; 42(3); 91-97
- 9. Maki K, Ebihara A, Okiji T. Clinical application of endodontic motors. The Journal of the Japanese Society for Dental Materials and Devices. 2021.05; 40 (2); 117-120
- 10. Nakatsukasa T, Ebihara A, Kimura S, Maki K, Nishijo M, Tokita D, Okiji T. Comparative evaluation of mechanical properties and shaping performance of heat-treated nickel titanium rotary instruments used in the single-length technique. Dental Materials Journal. 2021.05; 40(3); 743-749
- 11. Murano H, Kaneko T, Zaw SYM, Sone PP, Zaw ZCT, Okada Y, Sunakawa M, Katsube K-I, Okiji T. Pulp inflammation induces Kv1.1 K⁺channel down-regulation in rat thalamus. Oral Diseases. 2021.04
- 12. Ao X, Yang Y, Okiji T, Azuma M, Nagai S. Polymorphonuclear myeloid-derived cells that contribute to the immune paralysis are generated in the early phase of sepsis via PD-1/PD-L1 pathway. Infection and Immunity. 2021.05; 89(6) e00771-20

- 13. Hoshihara Y, Watanabe S, Kouno A, Yao K, Okiji T. Effect of tip insertion depth and irradiation parameters on the efficacy of cleaning calcium hydroxide from simulated lateral canals using Er:YAG laser- or ultrasonicactivated irrigation. Journal of Dental Sciences. 2021.02; 16(2); 654-660
- 14. Tanaka T, Kawano S, Ebihara A, Sato N, Tanaka H, Nishitani Y, Hirose K, Matsuzaki E, Nakata K, Kitamura C. A survey on instruments, materials and medicines of endodontic treatment in Japanese dental schools: questionnaire findings in 2019. The Journal of Japan Endodontic Association . 2021.01; 42(1); 31-40
- 15. Htun PH, Ebihara A, Maki K, Kimura S, Nishijo M, Kyaw MS, Okiji T. Comparison of torque, screw-in force and shaping ability of glide path instruments in continuous rotation and optimum glide path motion. Journal of Endodontics. 2021.01; 47(1); 94-99
- 16 .Yamauchi S, Watanabe S, Okiji T. Effects of heating on the physical properties of premixed calcium silicate-based root canal sealers. Journal of Oral Science. 2021.01; 63(1); 65-69
- 17. Adel S, Wada T, Kawashima N, Abdou A, Watanabe H, Kurabayashi T, Okiji T, Uo M. Preparation and properties of tristrontium aluminate as an alternative component of mineral trioxide aggregate (MTA) cement. Dental Materials Journal. 2021.01; 40(1); 184-190

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- 1. Okiji T. Current trends in the development of MTA cements. The Journal of the Japanese Society for Dental Materials and Devices. 2021.05; 40(2); 109-112
- 2. Thu M, Ebihara A, Adel S, Okiji T. Analysis of torque and force induced by rotary nickel-titanium instruments during root canal preparation: A systematic review. Applied Sciences. 2021.04; 11(7); 3079
- 3. Yahata A, Handa K, Thomas A, Ito S, Kawashima N, Noiri Y, Hayashi M, Okiji T, Saito M. Application of autologous concentrated growth factors (CGF) in endodontic microsurgery. Journal of the Japanese Association for Dental Science. 2021.03; 40(1); 43-48

- 1. Thein HSS, Hashimoto K, Noda S, Kawashima N, Okiji T. Surface-reaction-type prereacted glass-ionomer filler containing root canal sealer down-regulates the pro-inflammatory cytokines in lipopolysaccharide-stimulated macrophages. The 154th Meeting of the Japanese Society of Conservative Dentistry 2021.06.10 Virtual Meeting
- 2. Liu J, Watanabe S, Kouno A, Okiji T. Intracanal vaporized cavitation bubble kinetics in the apical area beyond the fractured instrument during Er:YAG laser-activated irrigation: Effect of pulse frequency and pulse energy. The 154th Meeting of the Japanese Society of Conservative Dentistry 2021.06.10 Virtual Meeting.
- 3. Kasuga Y, Kimura S, Maki K, Nakatsukasa T, Unno H, Oomori S, Ebihara A, Okiji T. Cyclic fatigue resistance and bending properties of heat treated NiTi rotary instruments. The 154th Meeting of the Japanese Society of Conservative Dentistry 2021.06.10 Virtual Meeting
- 4. Fujii M, Kawashima N, Nara K, Noda S, Hashimoto K, Okiji T. Hypoxia-induced microRNA-210 regulates inflammatory cytokine expression in lipopolysaccharide-stimulated dental-pulp cells. 2021 IADR/AADR/CADR General Session 2021.07.22 Virtual Meeting
- 5. Sunada-Nara K, Kawashima N, Fujii M, Noda S, Hashimoto K, Okiji T. MicroRNA -146b downregulates proinflammatory cytokine expression in LPS-stimulated human pulp cells. 2021 IADR/AADR/ CADR General Session 2021.07.22 Virtual Meeting
- 6. Kawashima N, Kuramoto M, Okiji T. Anti-inflammatory action of mineral trioxide aggregate; a new insight. Asian Pacific Endodontic Confederation 2021.09.10 Beirut, Lebanon
- 7. Okiji T. Diagnosis and treatment of traumatized teeth: Endodontic considerations. Clinical Workshop, Japan Association of Dental Traumatology 2021.09.12 Tokyo

- 8. Thu M, Ebihara A, Maki K, Nishijo M, Kimura S, Nakatsukasa T, Kyaw M, Okiji T. Effect of different axial speed patterns on fatigue resistance of rotary Nickel-titanium instruments .The 24th Scientific Meeting of the Japanese Assosiation for Dental Science 2021.09.23 Virtual Meeting
- 9. Okiji T. Calcium silicate endodontic materials : properties and clinical application. FDI World Dental Congress 2021.09.26 Virtual Meeting
- 10. Okiji T. Endodontic considerations of traumatized teeth. FDI World Dental Congress 2021.09.26 Virtual Meeting
- 11. Okiji T. Vital pulp therapy. Clinical Workshop, Japan Endodontic Association 2021.10.13 Virtual Meeting
- 12. Orikasa S, Kawashima N, Fujii M, Noda S, Hashimoto K, Tazawa K, Okiji T. BCL 9-mediated Wnt / β -catenin signaling activation is involved in hypoxia -induced osteo /odontoblastic differentiation of human dental pulp stem cells. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28
- 13. Han P, Sunada-Nara K, Kawashima N, Wang S, Kieu QT, Okiji T. Anti-inflammatory effects of microRNA 146 b on lipopolysaccharide-stimulated human dental pulp cells. The 155 th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Virtual Meeting
- 14. Soeda H, Watanabe S, Okiji T. Cone-beam computed tomography analysis of root canal configuration of maxillary and mandibular third molars . The 155 th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Virtual Meeting
- 15. Mochizuki S, Watanabe S, Liu J, Okiji T. Evaluation of the cleanliness of conservatively shaped root canals after irrigation with different systems. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Virtual Meeting
- 16. Okada Y, Kawashima N, Noda S, Murano H, Zaw ZCT, Han P, Hashimoto K, Okiji T. Vascular endothelial growth factor promotes migration and osteo/odontoblastic differentiation of SHEDs via ERK signaling. The International Scientific Meeting of 30th Anniversary of Korean Academy of Endodontics & the 19th JEA-KAE Joint Scientific Meeting 2021.10.29 Seoul, Korea.
- 17. Noritake K, Sunaga M, Ebihara A, Hideshima M, Tonami K, Umemori S, Kanamori Y, Kinoshita A, Nitta H. A Trial of Online Examination for Recruitment of Dental Residents at Dental Hospital, Tokyo Medical and Dental University. The 40th General and Scienti fic Meeting of the Japanese Dental Education Association 2021.11.20 Virtual Meeting
- 18. Kanamori Y, Noritake K, Kimura Y, Kido D, EbiharaA, Hideshima M, Tonami K, Umemori S, Nitta H. TMDU dental trainee residents' ability to evaluate abutment tooth preparation. The 40th General and Scientific Meeting of the Japanese Dental Education Association 2021.11.20 Virtual Meeting
- Okiji T. Innovations in endodontics induced by optical application technologies. The 33rd Annual Meeting of Japanese Society for Laser Dentistry 2021.11.29 Virtual meeting
- 20. Adel S, Hashimoto K, Kawashima N, Wada T, Uo M, Okiji T. Biocompatibility and pro-mineralization effect of tristrontium aluminate cement. The 86th Stomatological Society 2021.12.04

[Awards & Honors]

- 1. Sunada-Nara K. The Japanese Society of Conservative Dentistry encouragement award, The Japanese Society of Conservative Dentistry, 2021.06
- 2. Maki K. The Japanese Society of Conservative Dentistry poster award, The Japanese Society of Conservative Dentistry, 2021.06
- 3. Okada Y.The best poster, Korean Academy of Endodontics, 2021.11

Removable Partial Prosthodontics

Professor - Noriyuki Wakabayashi

Associate professor - Kenji Fueki(- August)

Senior Lecturer - Takeshi Ueno

Assistant professors - Eiko Kohno, Junnichiro Wada, Natsuko Murakami, Atsushi Takaichi, Yuka Inamochi

Specially Appointed Assistant Professors - Kensuke Takakusaki, Toshiki Yamazaki

Hospital staff

- Keigo Isoshima, Hisami Okawara, Taihei Kasai, Hirokazu Sato, Yasuo Nakajima, Tomiharu Nagayama, Yoko Hayashi

Graduate students

- AMR GAMAL, Yurika Ishioka, Keiichiro Uchikura, Hirofumi Uchida, Yuji Uchida, Miona Utsumi, Wang Zuo, Kim Eung Yeol, QU WENRUI, Wu huaze, Yoshio Kobayashi, Kohei Komine, Kazuki Sakamoto, SAN WIN THANT, Yuka Shichiri, Xu Huichuan, Tenhaku Tan, Thida Phyo, Zhao Qian, Taku Nemoto, Hao Jialin, Huichuan Xu, Hein Linn Htat, Hitomi Matsuno, Yang Shiyi, Hla Htoot Wai Cho, Li Bin, Lyu Huaxin, Tetsu Sato, Zou Shiqi, Chai Xinyi, Shintaro Suzuki, Ding Zhiyuan,Dong Jialin, Li Yajie, Yaping Li

(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. Tan T, Zhao Q, Kuwae H, Ueno T, Chen P, Tsutsumi Y, Mizuno J, Hanawa T, Wakabayashi N. Surface properties and biocompatibility of sandblasted and acid-etched titanium-zirconium binary alloys with various compositions. Dental materials journal. 2021.12;
- Ikeda T, Ueno T, Saruta J, Hirota M, Park W, Ogawa T. Ultraviolet Treatment of Titanium to Enhance Adhesion and Retention of Oral Mucosa Connective Tissue and Fibroblasts. International journal of molecular sciences. 2021.11; 22(22);
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- 9. Ishikawa Kyoko, Yamauti Monica, Tichy Antonin, Ikeda Masaomi, Ueno Takeshi, Wakabayashi Noriyuki, Thanatvarakorn Ornnicha, Prasansuttiporn Taweesak, Klein-Junior Celso Afonso, Takahashi Akifumi, Takagaki Tomohiro, Nakajima Masatoshi, Tagami Junji, Hosaka Keiichi. UV-Mediated Photofunctionalization of Indirect Restorative Materials Enhances Bonding to a Resin-Based Luting Agent BIOMED RESEARCH INTERNATIONAL. 2021.05; 2021; 9987860
- Kenji Fueki, Yuka Inamochi, Eiko Yoshida-Kohno, Yoko Hayashi, Noriyuki Wakabayashi. Responsiveness of methods to evaluate chewing ability after removable partial denture treatments. J Oral Rehabil. 2021.04; 48(4); 449-457
- 11. Tsutsumi-Arai Chiaki, Arai Yuki, Terada-Ito Chika, Imamura Takahiro, Tatehara Seiko, Ide Shinji, Wakabayashi Noriyuki, Satomura Kazuhito. Microbicidal effect of 405-nm blue LED light on Candida albicans and Streptococcus mutans dual-species biofilms on denture base resin LASERS IN MEDICAL SCIENCE. 2021.04;
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- 13. Okawara H, Arai Y, Matsuno H, Marcián P, Borák L, Aoki K, Wakabayashi N. Effect of load-induced local mechanical strain on peri-implant bone cell activity related to bone resorption and formation in mice: An analysis of histology and strain distributions. Journal of the mechanical behavior of biomedical materials. 2021.01; 116; 104370
- 14. Hao J, Murakami N, Yamazaki T, Iwasaki N, Yatabe M, Takahashi H, Wakabayashi N. Flexural and fatigue properties of polyester disk material for milled resin clasps Dental Materials Journal. 2021; 40(6); 1359-1364
- 15. Uchida H, Wada J, Watanabe C, Nagayama T, Mizutani K, Mikami R, Inukai S, Wakabayashi N.. Effect of night denture on tooth mobility in denture wearers with sleep bruxism: a pilot randomized controlled trial. Journal of Prosthodontic Research. 2021;
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- 2. Junichiro Wada, Noriyuki Wakabayashi. Current evidences and available treatment options to increase occlusal vertical dimension reliably and safely. Part 3 Should we level the occlusal plane along with occlusal vertical dimension increasing? The Quintessence. 2021.06; 40(6); 92-114
- 3. Junichiro Wada, Noriyuki Wakabayashi. Current evidences and available treatment options to increase occlusal vertical dimension reliably and safely. Part 3 Occlusal vertical dimension increasing based on tapping movement or maximal intercuspation The Quintessence. 2021.05; 40(5); 78-100
- 4. Junichiro Wada, Noriyuki Wakabayashi. Current evidences and available treatment options to increase occlusal vertical dimension reliably and safely. Part 2 Occlusal vertical dimension increasing based on centric relation The Quintessence. 2021.04; 40(4); 102-125
- 5. Junichiro Wada, Noriyuki Wakabayashi. Current evidences and available treatment options to increase occlusal vertical dimension reliably and safely. Part 1 Essential information to figure out how to increase occlusal vertical dimension The Quintessence. 2021.03; 40(3); 42-63

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- 1. MTJohn, M Omara, N Su, T List, S Sekulic, B Häggman-enrikson, CM Visscher K Bekesk, DR Reissmann, K Baba, O Schierz, N Theis-Mahon, K Fueki, T Stamm, L Bondemark, I Oghli, Avan Wijk, P Larsson. RECOMMENDATIONS FOR USE AND SCORING OF ORAL HEALTH IMPACT PROFILE VERSIONS Journal of Evidence Based Dental Practice. 2021.08; 101619
- 2. Oliver Schierz, Kazuyoshi Baba, Kenji Fueki. Functional oral health-related quality of life impact: A systematic review in populations with tooth loss. J Oral Rehabil. 2021.03; 48(3); 256-270
- 3. M T John, B Häggman-Henrikson, S Sekulic, T Stamm, I Oghli, O Schierz, T List, K Baba, K Bekes, A van Wijk, N Su, D R Reissmann, K Fueki, P Larsson, N Theis-Mahon, M Omara, L Bondemark, C M Visscher. Mapping Oral Disease Impact with a Common Metric (MOM) - Project Summary and Recommendations. J Oral Rehabil. 2021.03; 48(3); 305-307

- 1. BUI Ngoc Huyen Trang. CED-IADR/NOF Oral Health Research Congress in Brussels. CED-IADR/NOF Oral Health Research Congress in Brussels 2021.09.16
- 1. Matsumura M, Nozaki K, Yanaka W, Uchida E, Komine K, Matsumura M, Miura H, Fueki K. Development of the cutting resistance measurement method during high-speed milling in dental CAD/CAM system. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2021.12.05
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- 7. Yuka Inamochi. Progress of a systematic review on dementia and oral function : Review of intervention study. The 2nd Annual Meeting of Japan Research Society for Dementia and Oral Function 2021.08.08 online conference
- 8. Junichiro Wada. Let's balance utilization and protection of weakened abutment teeth via prostheses. 2021.06.19
- 9. Yuka Inamochi, Kenji Fueki, Eiko Yoshida-Kohno, Junichiro Wada, Natsuko Murakami, Atsushi Takaichi, Takeshi Ueno, Noriyuki Wakabayashi. Effectiveness of a digital full-remote active learning on knowledge acquisition in prosthodontic class. The 130th Annual Meeting of the Japan Prosthodontic Society 2021.06.19 online conference
- 10. Kenji Fueki. A systematic review of digital removable partial dentures. The 130th Annual Meeting of the Japan Prosthodontic Society 2021.06.19 online conference
- 11. Effect of post-heat treatments on metal-ceramic bond properties of Co-Cr-Mo-W alloy fabricated by selective laser melting. 2021.03.01
- 12. Atsushi Takaichi. Current state of denture framework manufacturing by selective laser melting. 2021.02.07

[Awards & Honors]

- 1. Best oral award, Japan Prosthodontic Society, 2021.06
- 2. Corporate award , The Japanese Society for Dental Materials and Devices, 2021.10

[Social Contribution]

- 1. Associate editor of Annals of Dentistry University of Malaya, 2019.04 Now
- 2. Associate editor of Journal of Prosthodontic Research, the Japan Prosthodontic Society, 2019.07 Now
- 3. Japan Prosthodontic Society publicity committee, Japan Prosthodontic Societ, 2021.09.01 Now

Advanced Prosthodontics

Professor - Noriyuki Wakabayashi

Associate professor - Takeshi Ueno (November-)

Assistant professors

- Eiko Kohno, Junnichiro Wada, Natsuko Murakami, Atsushi Takaichi, Yuka Inamochi

Specially Appointed Assistant Professors - Kensuke Takakusaki, Toshiki Yamazaki

Hospital staff

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(1) **Outline**

Department of Advanced Prosthodontics made a fresh start in November 2021, taking over from our predecessor, the Department of Removable Partial Prosthodontics. Historically, our Department has inherited the clinical and research backgrounds that the First Department of Prosthodontics and the Department of Masticatory Function Rehabilitation were proud of, and we specialized in removable partial prosthodontics. Now we are responsible for bridging the gap between basic sciences and clinical research on development of the prosthetic materials and technologies, as well as teaching and training dental professionals as our future human resources.

(2) Research

- 1. Treatment Planning, Treatment and Evaluation in Prosthodontics
- 2. Design Optimization of Prosthodontic Biomaterials
- 3. Biological Evaluation of Oral Tissues in Prosthodontic Patients
- 4. Educational Development in Prosthodontics

(3) Education

School of Dentistry Year 1 Introduction to Dentistry **Oral Health Sciences**

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

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School of Oral Health Care Sciences, School of Oral Health Care Sciences Year 2 Prosthodontics Years 3 and 4 Practice for Dental Hygiene Care

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(7) Publications

[Original Articles]

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- 2. Tan T, Zhao Q, Kuwae H, Ueno T, Chen P, Tsutsumi Y, Mizuno J, Hanawa T, Wakabayashi N. Surface properties and biocompatibility of sandblasted and acid-etched titanium-zirconium binary alloys with various compositions. Dental materials journal. 2021.12;
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- Yamamoto M, Inokoshi M, Tamura M, Shimizubata M, Nozaki K, Takahashi R, Yoshihara K, Minakuchi S. Development of 4-META/MMA-TBB resin with added benzalkonium chloride or cetylpyridinium chloride as antimicrobial restorative materials for root caries. J Mech Behav Biomed Mater. 2021.09; 124; 104838
- Wang Z, Kohno EY, Fueki K, Ueno T, Inamochi Y, Takada K, Wakabayashi N. Multilevel factor analysis of flipped classroom in dental education: A 3-year randomized controlled trial. PloS one. 2021.09; 16(9); e0257208
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- Nakai H, Inokoshi M, Nozaki K, Komatsu K, Kamijo S, Liu H, Shimizubata M, Minakuchi S, Van Meerbeek B, Vleugels J, Zhang F. Additively Manufactured Zirconia for Dental Applications. Materials (Basel). 2021.07; 14(13); 3694
- Yuka Inamochi, Kenji Fueki, Nobuo Usui, Masato Taira, Noriyuki Wakabayashi. Adaptive brain activity changes during tongue movement with palatal coverage from fMRI data. Scientific Reports. 2021.07; 11(1); 13907
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- Ahmed Abdou, Rena Takahashi, Amr Saad, Kosuke Nozaki, Toru Nikaido, Junji Tagami. Influence of resin-coating on bond strength of resin cements to dentin and CAD/CAM resin block in single-visit and multiple-visit treatment. Dental Materials Journal. 2021.05; 40(3); 674-682
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- YOSHIMATSU S., KOMADA W., NEMOTO R., OISHI S., TSUKAHARA R., OMORI S., NOZAKI K., MIURA H.. Effect of Glass Fiber Sleeve for Reinforcement of Flared Root. The 69th Annual Meeting of Japanese Association for Dental Research 2021.10.24
- Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Cho Too TD, Minakuchi S. Long-Term low-Temperature Degradation Behavior of High-Speed Sintered Zirconia. 2021 CED-IADR/NOF Oral Health Research congress 2021.09.16 hybrid (web, Brussels)
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- 4. BUI Ngoc Huyen Trang. CED-IADR/NOF Oral Health Research Congress in Brussels. CED-IADR/NOF Oral Health Research Congress in Brussels 2021.09.16
- 5. Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Cho Too TD, Minakuchi S. Translucency and crystallography of speed-sintered highly translucent dental zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
- 6. Nakai H, Inokoshi M, Nozaki K, Kamijo S, Shimizubata M, Liu H, Minakuchi S. Crystallography and flexural strength of additive manufactured zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
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- 4. Uchikura K, Murakami N, Yamazaki T, Lyu H, Nagata K, Iwasaki N, Takahashi H, Wakabayashi N. Fracture resistance of CAD/CAM restorative materials as removable partial denture's abutment. The 78th General Session of the Japanese Society for Dental Materials and Devices 2021.10.16 Web meeting
- 5. Yuka Inamochi, Kenji Fueki, Eiko Yoshida-Kohno, Junichiro Wada, Natsuko Murakami, Atsushi Takaichi, Takeshi Ueno, Noriyuki Wakabayashi. The effect of remote flipped classroom under COVID-19 pandemic. The 24th Scientific Meeting of the Japanese Association for Dental Science, Japan 2021.09.23 online conference
- 6. Yuka Inamochi, Kenji Fueki, Eiko Yoshida-Kohno, Junichiro Wada, Natsuko Murakami, Atsushi Takaichi, Takeshi Ueno, Noriyuki Wakabayashi. A new masticatory performance scale to integrate food biting, comminution, and mixing ability in removable partial denture wearers. The 24th Scientific Meeting of the Japanese Association for Dental Science, Japan 2021.09.23 online conference
- 7. Yuka Inamochi. Progress of a systematic review on dementia and oral function : Review of intervention study. The 2nd Annual Meeting of Japan Research Society for Dementia and Oral Function 2021.08.08 online conference
- 8. Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Minakuchi S. Flexural strength of speed-sintered highly translucent dental zirconia. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19
- 9. Junichiro Wada. Let's balance utilization and protection of weakened abutment teeth via prostheses. 2021.06.19
- 10. Yuka Inamochi, Kenji Fueki, Eiko Yoshida-Kohno, Junichiro Wada, Natsuko Murakami, Atsushi Takaichi, Takeshi Ueno, Noriyuki Wakabayashi. Effectiveness of a digital full-remote active learning on knowledge acquisition in prosthodontic class. The 130th Annual Meeting of the Japan Prosthodontic Society 2021.06.19 online conference
- 11. Randomized controlled clinical evaluation of ceramic crown restoration with press ceramics for premolar and molar teeth -short term follow-up study-. 2021.06.19
- 12. Yanaka W, Nozaki K, Matsumura M, Shin C, Saleh O, Takita M, Nemoto R, Matsumura M, Miura H. Optimized stage movement improves the marginal and internal fit of CAD/CAM crown. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19
- 13. Yayoi Oishi, Kosuke Nozaki, Chiharu Shin, Shinya Oishi, Reina Nemoto, Hiroyuki Miura. The internal fitness of crowns using lithium disilicate glass ceramics without heat treatment.. Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19

- 14. Yamamoto M, Inokoshi M, Shimizubata M, Nozaki K, Takahashi R, Yoshihara K, Minakuchi S. Shear bond strength to root dentin of 4-META/MMA-TBB resin containing antibacterial agents. The 77th General Session of the Japanese Society for Dental Materials and Devices 2021.04.10
- 15. Effect of post-heat treatments on metal-ceramic bond properties of Co-Cr-Mo-W alloy fabricated by selective laser melting. 2021.03.01
- 16. Atsushi Takaichi. Current state of denture framework manufacturing by selective laser melting. 2021.02.07

[Awards & Honors]

- 1. Best oral award, Japan Prosthodontic Society, 2021.06
- 2. Corporate award , The Japanese Society for Dental Materials and Devices, 2021.10

[Social Contribution]

1. Japan Prosthodontic Society - publicity committee, Japan Prosthodontic Societ, 2021.09.01 - Now

Oral Implantology and Regenerative Dental Medicine

Professor Shohei KASUGAI Associate Professor Makoto SHIOTA Senior Lecturer Noriko TACHIKAWA, Sinji KURODA Assistant Professor Hidemi NAKATA, Kazuhiro KON, Masahiro SHIMOGISHI Clinical Fellow Maiko YAMAMOTO, You-Kyoung KIM, Munemitsu MIYASAKA Seiji OHARA, Maki SHIBASAKI, Reo IKUMI

(1) Outline

Prosthodontic treatment with dental implants (dental implant treatment) is very effective. We are conducting researches and educations of clinical procedures, materials and tissue regeneration related to dental implant treatment. In addition, we are treating patients with dental implants in the university dental hospital.

(2) Research

We conducted the following studies: Development of bone substitute stimulating bone formation, development of implant surface stimulating bone formation and preventing infection, stimulation of bone formation with dissociated soft tissue, development of resorbable DBG membrane and effects of liposomal chlodronate on osteoblastic differentiation.

(3) Education

We gave lectures about basic knowledge necessary for implant treatment to dental students. Dental students also practiced treatment planning using computer soft wear and real patient data. In dental implant clinic, dental students also learned every step of dental implant treatment: Examinations, implant placement surgery and bone augmentation, prosthetic treatment and maintenance. We also gave lectures about advanced knowledge of dental implant treatment and regenerative medicine to post-graduate students.

(4) Lectures & Courses

Acquire basic knowledge and an attitude of thinking continuously.

(5) Clinical Services & Other Works

In dental implant clinic we treated patients, who missed teeth, with dental implants recovering aesthetics and functions. We further observed and followed these patients after the treatments (Maintenance Procedure).

(6) Clinical Performances

In dental implant clinic in TMDU, the number of clinical cases of dental implant treatments is the most in 29 dental schools in Japan. Difficult cases of dental implant treatments in other hospitals and clinics and problem

cases, which have been treated by other dentists, are increasing. We can handle most of these difficult and problem cases.

(7) Publications

[Original Articles]

- Masahiro Shimogishi, Takayasu Watanabe, Masaki Shibasaki, Takahiko Shiba, Keiji Komatsu, Takashi Nemoto, Kazuyuki Ishihara, Yoshio Nakano, Takanori Iwata, Shohei Kasugai, Ichiro Nakagawa. Patient-specific establishment of bacterial composition within the peri-implant microbiota during the earliest weeks after implant uncovering. J Periodontal Res. 2021.10; 56(5); 964-971
- Yoichiro Ogino, Yasunori Ayukawa, Noriko Tachikawa, Masahiro Shimogishi, Youji Miyamoto, Keiko Kudoh, Naoyuki Fukuda, Kunio Ishikawa, Kiyoshi Koyano. Staged Sinus Floor Elevation Using Novel Low-Crystalline Carbonate Apatite Granules: Prospective Results after 3-Year Functional Loading. Materials (Basel). 2021.10; 14(19); 5760
- 3. Takashi Nemoto, Takahiko Shiba, Keiji Komatsu, Takayasu Watanabe, Masahiro Shimogishi, Masaki Shibasaki, Tatsuro Koyanagi, Takahiko Nagai, Sayaka Katagiri, Yasuo Takeuchi, Takanori Iwata. Discrimination of Bacterial Community Structures among Healthy, Gingivitis, and Periodontitis Statuses through Integrated Metatranscriptomic and Network Analyses. mSystems. 2021.10; e0088621
- 4. Sabbagh Afnan, Nakata Hidemi, Abdou Ahmed, Kasugai Shohei, Kuroda Shinji. Fluctuation of salivary alpha-amylase activity levels and vital signs during dental implant surgery INTERNATIONAL JOURNAL OF IMPLANT DENTISTRY. 2021.06; 7(1); 58
- 5. Wang F, Nakata H, Sun X, Maung WM, Sato M, Kon K, Ozeki K, Ikumi R, Kasugai S, Kuroda S. A novel hydroxyapatite fiber material for the regeneration of critical-sized rabbit calvaria defects Dental materials journal. 2021.04;
- Kawakami S, Shiota M, Kon K, Shimogishi M, Iijima H, Shohei K. Autologous micrografts from the palatal mucosa for bone regeneration in calvarial defects in rats: a radiological and histological analysis. International Journal of Implant Dentistry. 2021.01; 7(6);
- 7. Taninokuchi H, Nakata H, Takahashi Y, Inoue K, Kasugai S, Kuroda S. Evaluation of a Cetylpyridinium Chloride, Dipotassium Glycyrrhizinate, and Tranexamic Acid-based-mouthwash after implant placement: a double-blind randomized clinical trial Oral Health and Preventive Dentistry. 2021.01; 19(1); 157-167
- YOKOTA Kaori, NAKATA Hidemi, MIURA Motoi, KASUGAI Shohei, KURODA Shinji. Effect of Osteoblast/Periosteal Cell-derived Exosomes on Periosteal Cells during Osteogenic Differentiation 口腔病 学会雑誌. 2021; 88(2·3);
- 9. Abdulrazzaq Ben Eessa, Hidemi Nakata, Wai Myo Maung, Shinji Kuroda. Effects of glucose reduction and recovery on mouse bone marrow cells in vitro Journal of Bio-Integration. 2021; 11(1);

- 1. Mika Tsuno, Hidemi Nakata, Atsushi Oka, Masahiro Shimogishi, Shinji Kuroda. Comparison of attachment location for mandibular implant overdenture by experimental modal analysis. EAO Digital Days 2021 2021.10.12
- 2. Atsushi Oka, Hidemi Nakata, Mika Tsuno, Kazuhiro Kon, Shinji Kuroda. Characteristics of fibroblasts in peri-implantitis tissue. EAO Digital Days 2021 2021.10.12
- 3. 柴崎 真樹, 下岸 将博, 渡辺 孝康, 丸川 恵理子. 遊離歯肉移植術により角化粘膜を付与したインプラント周囲の細菌叢構成の変化. 第 63 回 歯科基礎医学会学術大会 2021.10.06 オンライン開催
- 4. Abdulrazzaq Ben EESSA, Hidemi NAKATA, Wai Myo MAUNG, Shohei KASUGAI, Shinji KURODA. Effects of Diet-mimic Fasting in Mouse Bone Marrow Cells. バイオインテグレーション学会 第10回学術 大会・総会 2021.04.18
- 1. Masaki Shibasaki,Masahiro Shimogishi,Takayasu Watanabe,Eriko Mawaruka. Free gingival graft on peri-implant mucosa alters sub-mucosal b acterial composition. 2021.12.11

Regenerative and Reconstructive Dental Medicine

Professor Eriko MARUKAWA Associate Professor Noriko TACHIKAWA Senior Lecturer Sinji KURODA Assistant Professor Hidemi NAKATA, Kazuhiro KON, Masahiro SHIMOGISHI, Munemitsu MIYASAKA Clinical Fellow Masaki SHIBASAKI, Shintaro NAKAMURA, Sawako KAWAKAMI, Motoi MIURA, Akihiro TAKAHASHI, Yoshitaka OISHI

(1) Outline

Prosthodontic treatment with dental implants (dental implant treatment) is very effective. We are conducting researches and educations of clinical procedures, materials and tissue regeneration related to dental implant treatment. In addition, we are treating patients with dental implants in the university dental hospital.

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We conducted the following studies: Development of bone substitute stimulating bone formation, development of implant surface stimulating bone formation and preventing infection, stimulation of bone formation with dissociated soft tissue, development of resorbable DBG membrane and effects of liposomal chlodronate on osteoblastic differentiation.

(3) Education

We gave lectures about basic knowledge necessary for implant treatment to dental students. Dental students also practiced treatment planning using computer soft wear and real patient data. In dental implant clinic, dental students also learned every step of dental implant treatment: Examinations, implant placement surgery and bone augmentation, prosthetic treatment and maintenance. We also gave lectures about advanced knowledge of dental implant treatment and regenerative medicine to post-graduate students.

(4) Lectures & Courses

Acquire basic knowledge and an attitude of thinking continuously.

(5) Clinical Services & Other Works

In dental implant clinic we treated patients, who missed teeth, with dental implants recovering aesthetics and functions. We further observed and followed these patients after the treatments (Maintenance Procedure).

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In dental implant clinic in TMDU, the number of clinical cases of dental implant treatments is the most in 29 dental schools in Japan. Difficult cases of dental implant treatments in other hospitals and clinics and problem cases, which have been treated by other dentists, are increasing. We can handle most of these difficult and problem cases.

(7) Publications

[Original Articles]

- Masahiro Shimogishi, Takayasu Watanabe, Masaki Shibasaki, Takahiko Shiba, Keiji Komatsu, Takashi Nemoto, Kazuyuki Ishihara, Yoshio Nakano, Takanori Iwata, Shohei Kasugai, Ichiro Nakagawa. Patient-specific establishment of bacterial composition within the peri-implant microbiota during the earliest weeks after implant uncovering. J Periodontal Res. 2021.10; 56(5); 964-971
- Yoichiro Ogino, Yasunori Ayukawa, Noriko Tachikawa, Masahiro Shimogishi, Youji Miyamoto, Keiko Kudoh, Naoyuki Fukuda, Kunio Ishikawa, Kiyoshi Koyano. Staged Sinus Floor Elevation Using Novel Low-Crystalline Carbonate Apatite Granules: Prospective Results after 3-Year Functional Loading. Materials (Basel). 2021.10; 14(19); 5760
- 3. Takashi Nemoto, Takahiko Shiba, Keiji Komatsu, Takayasu Watanabe, Masahiro Shimogishi, Masaki Shibasaki, Tatsuro Koyanagi, Takahiko Nagai, Sayaka Katagiri, Yasuo Takeuchi, Takanori Iwata. Discrimination of Bacterial Community Structures among Healthy, Gingivitis, and Periodontitis Statuses through Integrated Metatranscriptomic and Network Analyses. mSystems. 2021.10; e0088621
- 4. Mochizuki Y, Marukawa E, Harada H, Kinoshita N, Nakatani R, Oikawa Y, Hirai H, Tomioka H, Yoda T, Nakamura S, Kurabayashi T. Postoperative morphological changes over time of vascularized scapular bone used for mandibular reconstruction: A retrospective cohort study. Journal of plastic, reconstructive & aesthetic surgery : JPRAS. 2021.09; 74(9); 1984-1990
- 5. Sabbagh Afnan, Nakata Hidemi, Abdou Ahmed, Kasugai Shohei, Kuroda Shinji. Fluctuation of salivary alpha-amylase activity levels and vital signs during dental implant surgery INTERNATIONAL JOURNAL OF IMPLANT DENTISTRY. 2021.06; 7(1); 58
- 6. Wang F, Nakata H, Sun X, Maung WM, Sato M, Kon K, Ozeki K, Ikumi R, Kasugai S, Kuroda S. A novel hydroxyapatite fiber material for the regeneration of critical-sized rabbit calvaria defects Dental materials journal. 2021.04;
- Kawakami S, Shiota M, Kon K, Shimogishi M, Iijima H, Shohei K. Autologous micrografts from the palatal mucosa for bone regeneration in calvarial defects in rats: a radiological and histological analysis. International Journal of Implant Dentistry. 2021.01; 7(6);
- 8. Taninokuchi H, Nakata H, Takahashi Y, Inoue K, Kasugai S, Kuroda S. Evaluation of a Cetylpyridinium Chloride, Dipotassium Glycyrrhizinate, and Tranexamic Acid-based-mouthwash after implant placement: a double-blind randomized clinical trial Oral Health and Preventive Dentistry. 2021.01; 19(1); 157-167
- YOKOTA Kaori, NAKATA Hidemi, MIURA Motoi, KASUGAI Shohei, KURODA Shinji. Effect of Osteoblast/Periosteal Cell-derived Exosomes on Periosteal Cells during Osteogenic Differentiation 口腔病 学会雑誌. 2021; 88(2·3);
- 10. Abdulrazzaq Ben Eessa, Hidemi Nakata, Wai Myo Maung, Shinji Kuroda. Effects of glucose reduction and recovery on mouse bone marrow cells in vitro Journal of Bio-Integration. 2021; 11(1);

- 1. Mika Tsuno, Hidemi Nakata, Atsushi Oka, Masahiro Shimogishi, Shinji Kuroda. Comparison of attachment location for mandibular implant overdenture by experimental modal analysis. EAO Digital Days 2021 2021.10.12
- 2. Atsushi Oka, Hidemi Nakata, Mika Tsuno, Kazuhiro Kon, Shinji Kuroda. Characteristics of fibroblasts in peri-implantitis tissue. EAO Digital Days 2021 2021.10.12
- 3. 柴崎 真樹, 下岸 将博, 渡辺 孝康, 丸川 恵理子. 遊離歯肉移植術により角化粘膜を付与したインプラント周囲の細菌叢構成の変化. 第 63 回 歯科基礎医学会学術大会 2021.10.06 オンライン開催
- 4. Abdulrazzaq Ben EESSA, Hidemi NAKATA, Wai Myo MAUNG, Shohei KASUGAI, Shinji KURODA. Effects of Diet-mimic Fasting in Mouse Bone Marrow Cells. バイオインテグレーション学会 第10回学術 大会・総会 2021.04.18
- 1. Masaki Shibasaki,Masahiro Shimogishi,Takayasu Watanabe,Eriko Mawaruka. Free gingival graft on peri-implant mucosa alters sub-mucosal b acterial composition. 2021.12.11

[Awards & Honors]

1. The 1st runner-up prize for the Oral Paper Competition, 14th Asian Congress on Oral & Maxillofacial Surgery, 2021.06

Masticatory Function and Health Science

Professor: Kenji FUEKI Associate professor: Wataru KOMADA Assistant professor: Kosuke NOZAKI, Chiharu Shin, Shiho OHTAKE, Satoshi OMORI, Reina NEMOTO, Yuka INAMOCHI Project assistant professor: Miho SATO, Mina TAKITA, Mayuko MASTUMURA Clinical staff: Erika SUKUMODA, Michiko NODA, Sinya OISHI, Yasuyuki KOWAKA, Ruri TSUKAHARA, Tomoyuki MIHARA, Wataru YANAKA, Shu YOSHIMATSU

(1) Outline

This department researches the association between oral function with prosthetic treatments and health, and provides dental care and education on prosthodontics, sports dentistry, and TMD.

(2) Research

Research on the association between oral function and health, AI and data science, dental education, dental materials, dental allergy, sports dentistry, and TMD

(3) Education

Basic and clinical education on prosthodontics (fixed prosthodontics and removable partial denture), sports dentistry, and TMD

(4) Lectures & Courses

Evidence-based clinical education

(5) Clinical Services & Other Works

Dental care at prosthetic clinic, advanced dental clinic, dental allergy clinic, sports dentistry clinic, and TMD clinic

(6) Clinical Performances

Prosthetic treatments using digital technology, examination of allergies to dental materials, specialized treatment to sports injury using mouse guard and face guard, diagnosis and treatment of TMD

(7) **Publications**

[Original Articles]

- 1. Cho Too TD, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Liu H, Minakuchi S. Influence of sintering conditions on translucency, biaxial flexural strength, microstructure, and low-temperature degradation of highly translucent dental zirconia. Dent Mater J. 2021.12; 40(6); 1320-1328
- Yoko Hayashi, Kenji Fueki, Eiko Yoshida-Kohno, Yuka Inamochi, Noriyuki Wakabayashi. Responsiveness of methods to evaluate objective masticatory function in removable partial denture treatments. J Prosthodont Res. 2021.10; 65(4); 495-501
- 3. Yamamoto M, Inokoshi M, Tamura M, Shimizubata M, Nozaki K, Takahashi R, Yoshihara K, Minakuchi S. Development of 4-META/MMA-TBB resin with added benzalkonium chloride or cetylpyridinium chloride as antimicrobial restorative materials for root caries. J Mech Behav Biomed Mater. 2021.09; 124; 104838
- 4. Wang Z, Kohno EY, Fueki K, Ueno T, Inamochi Y, Takada K, Wakabayashi N. Multilevel factor analysis of flipped classroom in dental education: A 3-year randomized controlled trial. PloS one. 2021.09; 16(9); e0257208
- 5. Mizutani K, Mikami R, Tsukui A, Nagai S, Pavlic V, Komada W, Iwata T, Aoki A. Novel flapless esthetic procedure for the elimination of extended gingival metal tattoos adjacent to prosthetic teeth: Er:YAG laser micro-keyhole surgery. Journal of prosthodontic research. 2021.09; 66(2); 346-352
- Inamochi Y, Fueki K, Yoshida-Kohno E, Hayashi Y, Wakabayashi N. . A new masticatory performance scale to integrate food biting, comminution, and mixing ability in removable partial denture wearers J Oral Rehabil. 2021.07; 48(7); 809-816
- 7. Nakai H, Inokoshi M, Nozaki K, Komatsu K, Kamijo S, Liu H, Shimizubata M, Minakuchi S, Van Meerbeek B, Vleugels J, Zhang F. Additively Manufactured Zirconia for Dental Applications. Materials (Basel). 2021.07; 14(13); 3694
- Yuka Inamochi, Kenji Fueki, Nobuo Usui, Masato Taira, Noriyuki Wakabayashi. Adaptive brain activity changes during tongue movement with palatal coverage from fMRI data. Scientific Reports. 2021.07; 11(1); 13907
- Kunihiko Mizusawa, Chiharu Shin, Daizo Okada, Reiko Ogura, Wataru Komada, Omnia Saleh, Ling Huang, Hiroyuki Miura. The investigation of the stress distribution in abutment teeth for connected crowns. J Dent Sci. 2021.07; 16(3); 929-936
- Ahmed Abdou, Rena Takahashi, Amr Saad, Kosuke Nozaki, Toru Nikaido, Junji Tagami. Influence of resin-coating on bond strength of resin cements to dentin and CAD/CAM resin block in single-visit and multiple-visit treatment. Dental Materials Journal. 2021.05; 40(3); 674-682
- Kenji Fueki, Yuka Inamochi, Eiko Yoshida-Kohno, Yoko Hayashi, Noriyuki Wakabayashi. Responsiveness of methods to evaluate chewing ability after removable partial denture treatments. J Oral Rehabil. 2021.04; 48(4); 449-457
- 12. Inokoshi M, Shimizubata M, Nozaki K, Takagaki T, Yoshihara K, Minakuchi S, Vleugels J, Van Meerbeek B, Zhang F. Impact of sandblasting on the flexural strength of highly translucent zirconia. J Mech Behav Biomed Mater. 2021.03; 115; 104268
- 13. Hasegawa M, Tichy A, Hosaka K, Kuno Y, Ikeda M, Nozaki K, Chiba A, Nakajima M, Tagami J. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents. Dental Materials Journal. 2021.03; 40(4); 877-884
- 14. Noda M, Omori S, Nemoto R, Sukumoda E, Takita M, Foxton R, Nozaki K, Miura H. Strain analysis of anterior resin-bonded fixed dental prostheses with different thicknesses of high translucent zirconia. Journal of dental sciences. 2021.03; 16(2); 628-635
- 15. Inokoshi M, Nozaki K, Takagaki T, Okazaki Y, Yoshihara K, Minakuchi S, Van Meerbeek B. Initial curing characteristics of composite cements under ceramic restorations. J Prosthodont Res. 2021.02; 65(1); 39-45

- Kenji Fueki, Yuka Inamochi, Eiko Yoshida-Kohno, Noriyuki Wakabayashi. Cost-effectiveness analysis of prosthetic treatment with thermoplastic resin removable partial dentures. J Prosthodont Res. 2021.02; 65(1); 52-55
- 1. Komada W. A case report of rehabilitation of esthetics and mastication by prosthodontic treatment in a patient with severely worm dentition 2021.07; 13(3); 265-268

[Misc]

- 1. Oliver Schierz, Kazuyoshi Baba, Kenji Fueki. Functional oral health-related quality of life impact: A systematic review in populations with tooth loss. J Oral Rehabil. 2021.03; 48(3); 256-270
- 2. M T John, B Häggman-Henrikson, S Sekulic, T Stamm, I Oghli, O Schierz, T List, K Baba, K Bekes, A van Wijk, N Su, D R Reissmann, K Fueki, P Larsson, N Theis-Mahon, M Omara, L Bondemark, C M Visscher. Mapping Oral Disease Impact with a Common Metric (MOM) - Project Summary and Recommendations. J Oral Rehabil. 2021.03; 48(3); 305-307

- YOSHIMATSU S., KOMADA W., NEMOTO R., OISHI S., TSUKAHARA R., OMORI S., NOZAKI K., MIURA H.. Effect of Glass Fiber Sleeve for Reinforcement of Flared Root. The 69th Annual Meeting of Japanese Association for Dental Research 2021.10.24
- 2. Shinya Oishi, Wataru Komada, Daiki Kondo, Ruri Tsukahara, Shu Yoshimatsu, Yusuke Yokosuka, Satoshi Omori, Kosuke Nozaki, Hiroyuki Miura. The Influence of Zirconia Tube for Stress in Endodontically-Treated Molar. The 69th Annual Meeting of Japanese Association for Dental Research 2021.10.24
- 3. Nozaki K, Komine K, Yanaka W, Matsumura M, Saleh O, Shin C, Matsumura M, Komada W, Miura H. Effect of repeated use of end mill on the internal fitness of complete crown. The 69th Annual Meeting of the Japanese Association for Dental Research 2021.10.24
- 4. Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Cho Too TD, Minakuchi S. Long-Term low-Temperature Degradation Behavior of High-Speed Sintered Zirconia. 2021 CED-IADR/NOF Oral Health Research congress 2021.09.16 hybrid (web, Brussels)
- 5. Inokoshi M, Liu H, Shimizubata M, Nozaki K, Minakuchi S. Translucency, Crystallography and Flexural Strength of Multi-Layered Highly Translucent Zirconia. 2021 CED-IADR/NOF Oral Health Research congress 2021.09.16 hybrid (web, Brussels)
- 6. Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Cho Too TD, Minakuchi S. Translucency and crystallography of speed-sintered highly translucent dental zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
- 7. Nakai H, Inokoshi M, Nozaki K, Kamijo S, Shimizubata M, Liu H, Minakuchi S. Crystallography and flexural strength of additive manufactured zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
- 1. Matsumura M, Nozaki K, Yanaka W, Uchida E, Komine K, Matsumura M, Miura H, Fueki K. Development of the cutting resistance measurement method during high-speed milling in dental CAD/CAM system. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2021.12.05
- 2. Highly functional titania for dental materials. 2021.11.30
- 3. Yuka Inamochi, Kenji Fueki, Eiko Yoshida-Kohno, Junichiro Wada, Natsuko Murakami, Atsushi Takaichi, Takeshi Ueno, Noriyuki Wakabayashi. The effect of remote flipped classroom under COVID-19 pandemic. The 24th Scientific Meeting of the Japanese Association for Dental Science, Japan 2021.09.23 online conference
- 4. Yuka Inamochi, Kenji Fueki, Eiko Yoshida-Kohno, Junichiro Wada, Natsuko Murakami, Atsushi Takaichi, Takeshi Ueno, Noriyuki Wakabayashi. A new masticatory performance scale to integrate food biting, comminution, and mixing ability in removable partial denture wearers.. The 24th Scientific Meeting of the Japanese Association for Dental Science, Japan 2021.09.23 online conference

- 5. Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Minakuchi S. Flexural strength of speed-sintered highly translucent dental zirconia. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19
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- 7. Randomized controlled clinical evaluation of ceramic crown restoration with press ceramics for premolar and molar teeth -short term follow-up study-. 2021.06.19
- 8. Yanaka W, Nozaki K, Matsumura M, Shin C, Saleh O, Takita M, Nemoto R, Matsumura M, Miura H. Optimized stage movement improves the marginal and internal fit of CAD/CAM crown. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19
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- 13. Komad W, Shinya A, Mine A. The future prospective of metal-free post and core design. 2021.06.19

[Social Contribution]

- 1. Associate editor of Annals of Dentistry University of Malaya, 2019.04 Now
- 2. Associate editor of Journal of Prosthodontic Research, the Japan Prosthodontic Society, 2019.07 Now

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, Yamamoto Mao, Ishida Naoya, Ishii Yoshitaka, Kurosawa Sayuri

(1) Research

Plastic and Reconstructive Surgery : MORI Hiroki

- 1. Pre and post operative breast or facial contour evaluation usning 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. Adipogenesis in a external negative pressure lymphedema model A new possibility of scaffold transplantation
- 5. Blood circulation study of the surgical flap using indocyanine green angioraphy 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 tisssue 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 remolding of nearly all external body structures.

(3) Clinical Performances

We cover the whole field of plastic surgery. In particular, we deal with the following field; congenital anormaly (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**

- 1. Ogawa K, Okazaki M, Mori H, Hidaka T, Tomioka Y, Tanaka K, Uemura N, Akiyama M. Comparative Blink Analysis in Patients With Established Facial Paralysis Using High-Speed Video Analysis. The Journal of craniofacial surgery. 2021.11;
- 2. Tanaka K,Sugawara T,Asakage T,Okazaki M. A Concept of "Boundary Determination" by the Combination of a Local Flap and Free Tissue Transfer Useful for the Prevention of Postoperative Complications After Complex and Widespread Skull Base Reconstruction. J Craniofac Surg. 2021.11; 32(8); e820-e822
- 3. Ogawa K, Okazaki M, Mori H, Hidaka T, Tomioka Y, Tanaka K, Uemura N, Akiyama M. Comparative Blink Analysis in Patients With Established Facial Paralysis Using High-Speed Video Analysis. The Journal of craniofacial surgery. 2021.11;
- 4. Nakamura Mayu, Mori Hiroki, Kubota Masashi, Uemura Noriko, Tanaka Kentaro. Influence of Marker Number and Position on Accuracy of Breast Measurement With Three-Dimensional Camera AESTHETIC PLASTIC SURGERY. 2021.10;
- 5. Oda Goshi, Nakagawa Tsuyoshi, Uemura Noriko, Mori Hiroki, Mori Mio, Fujioka Tomoyuki, Onishi Iichiroh, Uetake Hiroyuki. Immediate breast reconstruction is oncologically safe for node-positive patients: Comparison using propensity score matching. Medicine (Baltimore). 2021.09; 100(36); e27184
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- 8. Yoshino M, Oda G, Nakagawa T, Uemura N, Mori H, Mori M, Fujioka T. Higher body mass index is a more important risk factor than sarcopenia for complications in deep inferior epigastric perforator reconstruction. Asian journal of surgery. 2021.07; 45(1); 360-366
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- 11. Tanaka K,Suesada N,Homma T,Mori H,Okazaki M. Reliability of Temporal Vascular Anastomosis and Techniques for Better Outcomes JOURNAL OF RECONSTRUCTIVE MICROSURGERY. 2021.06; 38(1); 41-46
- 12. Nakagawa T, Oda G, Kato R, Shinohara H, Osanai T, Kumaki Y, Takiguchi N, Mori H, Oyama J, Okamoto K, Uetake H. A Case of Breast Cancer in a Patient with a Congenital Pectoralis Muscle Defect. Case reports in oncology. 2021.05; 14(2); 1092-1096
- 13. Oda G, Nakagawa T, Uemura N, Mori H, Mori M, Fujioka T, Onishi I, Uetake H. Axillary lymph node recurrence in patients with breast cancer who underwent breast reconstruction using a latissimus dorsi flap after mastectomy. Molecular and clinical oncology. 2021.03; 14(3); 49
- Ogawa K, Okazaki M, Tanaka K, Uemura N, Homma T. Chimeric Latissimus Dorsi Flap in One-Stage Reconstruction of Depressor Muscle Dysfunction and Depression Deformity in the Perimandibular Area. The Journal of craniofacial surgery. 2021.03;

- 1. Uami S,Inami K. Expand application of ulnar parametacarpal perforator flap for the converage of finger defect. The 5th Congress of Asian Pacific Federation of Societies for Reconstructive Microsurgery 2021.12.02 Tsukubashi
- 2. Usami S,Kawahara S,Takemitsu M,Inami K. Repair of ruptured extensor pollicis longus with running interlocking horizontal mattress suture technique. Federation of European Societies for Surgery of the Hand 2021 2021.06.16 Virtual congress

Head and Neck Surgery

Professor: Takahiro Asakage Junior Associate Professor: Yosuke Ariizumi, Kazuchika Ohno Assistant Professor: Akihisa Tasaki Specially Appointed Assistant Proffesor:Ryuhei Okada(2021.4 \sim), Yumiko Tateishi Senior Resident: Nobuaki Koide(\sim 2021.3), Hiroaki Kawabe, Ryosuke Takahashi Graduate Student: Masaharu Kishikawa(\sim 2021.7), Toshifumi Tomioka, Sadahiro Kishishita

(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**

- 1. Yoshimura Ryo-ichi, Toda Kazuma, Watanabe Hiroshi, Kaida Atsushi, Harada Hiroyuki, Asakage Takahiro, Miura Masahiko. Efficacy and Safety of Induction Chemotherapy and/or External Beam Radiotherapy Followed by Brachytherapy in Patients With Tongue Cancer ANTICANCER RESEARCH. 2021.12; 41(12); 6259-6266
- 2. Ohno Kazuchika, Kawada Kenro, Sugimoto Taro, Kiyokawa Yusuke, Kawabe Hiroaki, Takahashi Ryosuke, Koide Nobuaki, Tateishi Yumiko, Tasaki Akihisa, Ariizumi Yosuke, Asakage Takahiro. Evaluation of synchronous multiple primary superficial laryngo-pharyngeal cancers that were treated by endoscopic laryngo-pharyngeal surgery(和訳中) Auris· Nasus· Larynx. 2021.12; 48(6); 1162-1166
- 3. Kentaro Tanaka, Takashi Sugawara, Takahiro Asakage, Mutsumi Okazaki. A Concept of "Boundary Determination" by the Combination of a Local Flap and Free Tissue Transfer Useful for the Prevention of Postoperative Complications After Complex and Widespread Skull Base Reconstruction. J Craniofac Surg. 2021.11; 32(8); e820-e822
- 4. Ryuji Yasumatsu, Yasushi Shimizu, Nobuhiro Hanai, Shin Kariya, Tomoya Yokota, Takashi Fujii, Kiyoaki Tsukahara, Mizuo Ando, Kenji Hanyu, Tsutomu Ueda, Hitoshi Hirakawa, Shunji Takahashi, Takeharu Ono, Daisuke Sano, Moriyasu Yamauchi, Akihito Watanabe, Koichi Omori, Tomoko Yamazaki, Nobuya Monden, Naomi Kudo, Makoto Arai, Syuji Yonekura, Takahiro Asakage, Takahiro Nekado, Takayuki Yamada, Akihiro Homma. Outcomes of long-term nivolumab and subsequent chemotherapy in Japanese patients with head and neck cancer: 2-year follow-up from a multicenter real-world study. Int J Clin Oncol. 2021.11;
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- 6. Kiyoto Shiga, Ken-Ichi Nibu, Yasushi Fujimoto, Takahiro Asakage, Akihiro Homma, Hiroki Mitani, Takenori Ogawa, Kenji Okami, Shigeyuki Murono, Shigeru Hirano, Tsutomu Ueda, Nobuhiro Hanai, Kiyoaki Tsukahara, Ichiro Ota, Seiichi Yoshimoto, Takeshi Shinozaki, Shigemichi Iwae, Katsunori Katagiri, Daisuke Saito, Naomi Kiyota, Makoto Tahara, Fumiaki Takahashi, Ryuichi Hayashi. Sites of invasion of cancer of the external auditory canal predicting oncologic outcomes. Head Neck. 2021.10; 43(10); 3097-3105
- 7. Kato T, Okada R, Furusawa A, Inagaki F, Wakiyama H, Furumoto H, Okuyama S, Fukushima H, Choyke PL, Kobayashi H. Simultaneously Combined Cancer Cell- and CTLA4-Targeted NIR-PIT Causes a Synergistic Treatment Effect in Syngeneic Mouse Models. Molecular cancer therapeutics. 2021.09;
- 8. Tanaka K, Suesada N, Homma T, Mori H, Sugawara T, Tsutsumi T, Asakage T, Okazaki M. The different concepts of surgical managements between anterior and lateral skull base reconstructions based on surgical purposes. Auris, nasus, larynx. 2021.08;
- Okada R, Furusawa A, Inagaki F, Wakiyama H, Kato T, Okuyama S, Furumoto H, Fukushima H, Choyke PL, Kobayashi H. Endoscopic near-infrared photoimmunotherapy in an orthotopic head and neck cancer model. Cancer science. 2021.08; 112(8); 3041-3049
- 10. Kiyokawa Yusuke, Ariizumi Yousuke, Ohno Kazuchika, Ito Taku, Kawashima Yoshiyuki, Tsunoda Atsunobu, Kishimoto Seiji, Asakage Takahiro, Tsutsumi Takeshi. Indications for and extent of elective neck dissection for lymph node metastasis from external auditory canal carcinoma(和訳中) Auris: Nasus-Larynx. 2021.08; 48(4); 745-750
- 11. Kishikawa M, Inoue J, Hamamoto H, Kobayashi K, Asakage T, Inazawa J. Augmentation of lenvatinib efficacy by topical treatment of < i> miR-634< /i> ointment in anaplastic thyroid cancer. Biochemistry and biophysics reports. 2021.07; 26; 101009
- 12. Inoue J, Kishikawa M, Tsuda H, Nakajima Y, Asakage T, Inazawa J. Identification of PDHX as a metabolic target for esophageal squamous cell carcinoma. Cancer science. 2021.07; 112(7); 2792-2802

 Kurebayashi Y, Olkowski CP, Lane KC, Vasalatiy OV, Xu BC, Okada R, Furusawa A, Choyke PL, Kobayashi H, Sato N. Rapid Depletion of Intratumoral Regulatory T Cells Induces Synchronized CD8
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- 14. Shin Kariya, Yasushi Shimizu, Nobuhiro Hanai, Ryuji Yasumatsu, Tomoya Yokota, Takashi Fujii, Kiyoaki Tsukahara, Masafumi Yoshida, Kenji Hanyu, Tsutomu Ueda, Hitoshi Hirakawa, Shunji Takahashi, Takeharu Ono, Daisuke Sano, Moriyasu Yamauchi, Akihito Watanabe, Koichi Omori, Tomoko Yamazaki, Nobuya Monden, Naomi Kudo, Makoto Arai, Shuji Yonekura, Takahiro Asakage, Akinori Fujiwara, Takayuki Yamada, Akihiro Homma. Effectiveness of nivolumab affected by prior cetuximab use and neck dissection in Japanese patients with recurrent or metastatic head and neck cancer: results from a retrospective observational study in a real-world setting. Int J Clin Oncol. 2021.06; 26(6); 1049-1056
- 15. Yokokawa Taizo, Ariizumi Yosuke, Hiramatsu Mariko, Kato Yujin, Endo Kazuhira, Obata Kazufumi, Kawashima Kayoko, Sakata Toshifumi, Hirano Shigeru, Nakashima Torahiko, Sekine Tatsurou, Kiyuna Asanori, Uemura Saeko, Okubo Keisuke, Sugimoto Taro, Tateya Ichiro, Fujimoto Yasushi, Horii Arata, Kimura Yurika, Hyodo Masamitsu, Homma Akihiro. COVID-19 患者に対する気管切開の管理 日本での経験 (Management of tracheostomy in COVID-19 patients: The Japanese experience) Auris· Nasus· Larynx. 2021.06; 48(3); 525-529
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- 17. Okada R, Furusawa A, Vermeer DW, Inagaki F, Wakiyama H, Kato T, Nagaya T, Choyke PL, Spanos WC, Allen CT, Kobayashi H. Near-infrared photoimmunotherapy targeting human-EGFR in a mouse tumor model simulating current and future clinical trials. EBioMedicine. 2021.05; 67; 103345
- 18. Nobuhiro Hanai, Yasushi Shimizu, Shin Kariya, Ryuji Yasumatsu, Tomoya Yokota, Takashi Fujii, Kiyoaki Tsukahara, Masafumi Yoshida, Kenji Hanyu, Tsutomu Ueda, Hitoshi Hirakawa, Shunji Takahashi, Takeharu Ono, Daisuke Sano, Moriyasu Yamauchi, Akihito Watanabe, Koichi Omori, Tomoko Yamazaki, Nobuya Monden, Naomi Kudo, Makoto Arai, Daiju Sakurai, Takahiro Asakage, Issei Doi, Takayuki Yamada, Akihiro Homma. Correction to: Effectiveness and safety of nivolumab in patients with head and neck cancer in Japanese real- world clinical practice: a multicentre retrospective clinical study. Int J Clin Oncol. 2021.05; 26(5); 1005-1006
- 19. Ohno K, Kawada K, Sugimoto T, Kiyokawa Y, Kawabe H, Takahashi R, Koide N, Tateishi Y, Tasaki A, Ariizumi Y, Asakage T. Evaluation of synchronous multiple primary superficial laryngo-pharyngeal cancers that were treated by endoscopic laryngo-pharyngeal surgery. Auris, nasus, larynx. 2021.04;
- Wu S, Okada R, Liu Y, Fang Y, Yan F, Wang C, Li H, Kobayashi H, Chen Y, Tang Q. Quantitative analysis of vascular changes during photoimmunotherapy using speckle variance optical coherence tomography (SV-OCT). Biomedical optics express. 2021.04; 12(4); 1804-1820
- 21. Nobuhiro Hanai, Yasushi Shimizu, Shin Kariya, Ryuji Yasumatsu, Tomoya Yokota, Takashi Fujii, Kiyoaki Tsukahara, Masafumi Yoshida, Kenji Hanyu, Tsutomu Ueda, Hitoshi Hirakawa, Shunji Takahashi, Takeharu Ono, Daisuke Sano, Moriyasu Yamauchi, Akihito Watanabe, Koichi Omori, Tomoko Yamazaki, Nobuya Monden, Naomi Kudo, Makoto Arai, Daiju Sakurai, Takahiro Asakage, Issei Doi, Takayuki Yamada, Akihiro Homma. Effectiveness and safety of nivolumab in patients with head and neck cancer in Japanese real-world clinical practice: a multicenter retrospective clinical study. Int J Clin Oncol. 2021.03; 26(3); 494-506
- 22. Kiyoto Shiga, Ken-Ichi Nibu, Yasushi Fujimoto, Takahiro Asakage, Akihiro Homma, Hiroki Mitani, Takenori Ogawa, Kenji Okami, Shigeyuki Murono, Shigeru Hirano, Tsutomu Ueda, Nobuhiro Hanai, Kiyoaki Tsukahara, Ichiro Ota, Seiichi Yoshimoto, Takeshi Shinozaki, Shigemichi Iwae, Katsunori Katagiri, Daisuke Saito, Naomi Kiyota, Makoto Tahara, Fumiaki Takahashi, Ryuichi Hayashi. Multi-institutional Survey of Squamous Cell Carcinoma of the External Auditory Canal in Japan. Laryngoscope. 2021.03; 131(3); E870-E874
- 23. Inagaki FF, Fujimura D, Furusawa A, Okada R, Wakiyama H, Kato T, Choyke PL, Kobayashi H. Diagnostic imaging in near-infrared photoimmunotherapy using a commercially available camera for indocyanine green. Cancer science. 2021.03; 112(3); 1326-1330

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- 25. Atsuto Katano, Ryousuke Takenaka, Hideomi Yamashita, Mizuo Ando, Masafumi Yoshida, Yuki Saito, Takahiro Asakage, Osamu Abe, Keiichi Nakagawa. A retrospective analysis of radiotherapy in the treatment of external auditory canal carcinoma. Mol Clin Oncol. 2021.03; 14(3); 45
- 26. Okano S, Homma A, Kiyota N, Tahara M, Hanai N, Asakage T, Matsuura K, Ogawa T, Saito Y, Sano D, Kodaira T, Motegi A, Yasuda K, Takahashi S, Tanaka K, Onoe T, Yokota T, Imamura Y, Ariizumi Y, Akimoto T, Hayashi R. Induction chemotherapy in locally advanced squamous cell carcinoma of the head and neck. Japanese journal of clinical oncology. 2021.02; 51(2); 173-179
- 27. Baba Shunichi, Akashi Takumi, Kayamori Kou, Ohuchi Tomoyuki, Ogawa Ikuko, Kubota Nobuhisa, Nakano Keisuke, Nagatsuka Hitoshi, Hasegawa Hiromasa, Matsuzaka Kenichi, Tomii Shohei, Uchida Keisuke, Katsuta Noriko, Sekiya Takahiro, Ando Noboru, Miura Keiko, Ishibashi Hironori, Ariizumi Yousuke, Asakage Takahiro, Michi Yasuyuki, Harada Hiroyuki, Sakamoto Kei, Eishi Yoshinobu, Okubo Kenichi, Ikeda Tohru. ホメオボックス転写因子 engrailed homeobox 1 は腺様嚢胞癌および多形腺癌の診断 マーカーの可能性がある (Homeobox transcription factor engrailed homeobox 1 is a possible diagnostic marker for adenoid cystic carcinoma and polymorphous adenocarcinoma) Pathology International. 2021.02; 71(2); 113-123
- 28. Yokokawa T, Ariizumi Y, Hiramatsu M, Kato Y, Endo K, Obata K, Kawashima K, Sakata T, Hirano S, Nakashima T, Sekine T, Kiyuna A, Uemura S, Okubo K, Sugimoto T, Tateya I, Fujimoto Y, Horii A, Kimura Y, Hyodo M, Homma A. Management of tracheostomy in COVID-19 patients: The Japanese experience. Auris, nasus, larynx. 2021.01; 48(3); 525-529
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- 30. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. Am J Otolaryngol. 35(3); 402-404
- 31. Emi Yamaga, Tomoyuki Fujioka, Takahiro Asakage, Keiko Miura, Ukihide Tateishi. 18F-FDG-Detected Brown Tumor Confined to the Maxillary Bone With Parathyroid Adenoma. Clin Nucl Med. 2021.09;
- 1. Tohyama K, Kano Y, Noji R, Aoyagi Y, Matsudera S, Ohno K, Ariizumi Y, Michi Y, Tomioka H, Shimamoto H, Asakage T, Harada H, Yoshimura R, Miyake S, Miura M, and Ikeda S. The clinical utility of comprehensive genomic profiling for Recurrent / Metastatic Head and Neck Cancer Head and Neck Cancer. 2021.12; 47(4); 359-365

- Ryuhei Okada, Takuya Kato, Aki Furusawa, Fuyuki Inagaki, Hiroaki Wakiyama, Peter L. Choyke, Hisataka Kobayashi. Local Depletion of Immune Checkpoint Ligand CTLA4 Expressing Cells in Tumor Beds Enhances Antitumor Host Immunity. 第 59 回日本癌治療学会学術集会 2021.10.21
- 2. Asakage T. A personal experience of 100 cases of skull base surgery. International Symposium American Academy of Otolaryngology-Head and Neck Surgery 2021, Annual meeting & Oto experience 2021.10 Los Angeles, USA and WEB
- 3. 加納 嘉人, 野地 理夏, 山下 大和, 工藤 亮, 田崎 彰久, 大野 十央, 有泉 陽介, 平井 秀明, 富岡 寛文, 島本 裕 彰, 道 泰之, 三浦 雅彦, 吉村 亮一, 朝蔭 孝宏, 原田 浩之, 岡本 隆一, 三宅 智, 池田 貞勝. Clinical utility of tumor-profiling multiplex gene panel testing in advanced head and neck cancer at TMDU. 第 18 回日本臨 床腫瘍学会学術集会 2021.02.18

Radiation Therapeutics and Oncology

ProfessorRyoichi YoshimuraLecturersKazuma TodaResearch Associates Takuya NaganoHospital Staff membersDaigoro Matsubara,Aya UsamiGraduate StudentsYoshinao Takada,Masahiro Yoshida,Kazuma Sasamura

(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 619 patients, including 178 head and neck cancer patients, 75 prostate cancer patients, 54 breast cancer patients, 44 lung cancer patients, and 21 esophageal cancer patients, were treated at our hospital in 2020.

(6) Clinical Performances

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

(7) **Publications**

- 1. Matsuoka Y, Uehara S, Toda K, Fukushima H, Tanaka H, Yoshida S, Yokoyama M, Yoshimura R, Kihara K, Fujii Y. Focal brachytherapy for localized prostate cancer: 5.7-year clinical outcomes and a pair-matched study with radical prostatectomy. Urologic oncology. 2021.12;
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- 3. Yoshida S, Matsuoka Y, Toda K, Uehara S, Tanaka H, Yokoyama M, Saito K, Yoshimura R, Fujii Y. Nonmetastatic castration-resistant prostate cancer treated with salvage focal brachytherapy after external beam radiotherapy. IJU case reports. 2021.07; 4(4); 228-230
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- Yoshida Soichiro, Takahara Taro, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Can progressive site-directed therapy prolong the efficacy of subsequent androgen receptor axis-targeted drugs in oligometastatic castration-resistant prostate cancer? International Journal of Urology. 2021.02; 28(2); 241-242
- 9. Yoshida Soichiro, Takahara Taro, Arita Yuki, Toda Kazuma, Yamada Ichiro, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Genuine- and induced-oligometastatic castration-resistant prostate cancer: clinical features and clinical outcomes after progressive site-directed therapy INTERNATIONAL UROLOGY AND NEPHROLOGY. 2021.01;
- Saito Kazutaka, Matsuoka Yoh, Toda Kazuma, Yoshida Soichiro, Yokoyama Minato, Yoshimura Ryoichi, Kihara Kazunori, Fujii Yasuhisa. Medium-term oncological and functional outcomes of hemi-gland brachytherapy using iodine-125 seeds for intermediate-risk unilateral prostate cancer BRACHYTHERAPY. 2021; 20(4); 842-848
- Noji R, Kano Y*(*corresponding author), Hirai H, Onishi I, Nishii N, Yoshimura R, Miyake S, Ikeda S, Harada H. MYC-PDL1 axis reduces sensitivity to nivolumab in recurrent head and neck squamous cell carcinoma. Oral oncology. 2021.12; 124; 105666

- 1. Yuji Kabasawa, Kanade Ito, Shiori Tokura, Itsuki Takazawa,Rio Kimura, Tohko Nakanishi, Kikue Akiyama, Yuki Onuma, Toshiko Adachi, Ruri Komiya, Hiroyuki Harada, Hitomi Nojima, Masahiko Miura, Ryoichi Yoshimura. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. The 1st Annual Meeting of the International Society of Oral Care 2021.04.18 東京
- 1. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. 2021.04.18

Cognitive Neurobiology

Professor: Naofumi Uesaka Lecturer: Daisuke Tanaka Assistant Professor Atsuya Takeuchi

Graduate Students Moe Tanigawa Nozomi Utsumi Midori Wada Ryo Masumura Yang Sun Ibin Han

(1) Outline

Our goal is to understand how each brain cell or group of brain cells generates complex brain functions and how dysfunction of each cell causes brain diseases. To answer these questions, we use a variety of techniques, including neurophysiology, molecular biology, and genetics. We promote researches and aim to find novel concepts in brain development, brain function, and brain diseases.

(2) Research

1. Functional development of the brain

We are studying the mechanism of selective strengthening and elimination of synapses (synapse elimination) during postnatal development.

2. Glial function

We aim to discover novel functions of glial cells.

3. Crosstalk between oral function and brain function in the health and disease. We aim to elucidate the information processing of oral sensation in the brain and brain disease caused by oral dysfunction.

4) Brain diseases

We aim to elucidate the mechanisms by which brain diseases develop and become malignant.

(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

We plan to actively accept a diverse range of students and staff from various backgrounds, including biology, engineering, dentistry, and medicine, regardless of academic field. We will educate them to be able to either develop innovative methods, hit innovative hypotheses, or make innovative discoveries. For this reason, we place importance on creating an environment and atmosphere where staff and students can actively share their opinions in daily discussions and study sessions. By reading our papers and papers on the latest research findings and conducting research with staff and senior students, students can learn how to acquire and analyze data, conduct research, and write papers. Let's work together to make innovative discoveries by cooperating with each other and doing research every day toward the major goal of elucidating brain development, brain function, and brain diseases.

(5) Publications

[Original Articles]

- 1. Suzuki Honoka, Choo Myeongjeong, Watanabe Takaki, Sakimura Kenji, Uesaka Naofumi, Kato Masanobu. MEF2D は発達期の小脳において後期のシナプス刈り込みに関与する (Myocyte Enhancer Factor 2D(MEF2D) mediates late phase synapse elimination in the developing cerebellum) The Journal of Physiological Sciences. 2021.08; 71(Suppl.1); 110
- 2. Uesaka Naofumi, Akamatsu Tsubasa, Suzuki Honoka, Kato Masanobu. アストロサイト 2 型イノシ トール 3 リン酸受容体を介して発達期小脳のシナプス刈り込みを制御する (Astrocytes regulate synapse elimination in the developing cerebellum through type 2 inositol 1,4,5-trisphosphate receptor) The Journal of Physiological Sciences. 2021.08; 71(Suppl.1); 94
- Nagahama K, Fujino S, Watanabe T, Uesaka N, Kano M. Combining electrophysiology and optogenetics for functional screening of pyramidal neurons in the mouse prefrontal cortex. STAR protocols. 2021.06; 2(2); 100469
- 4. Tanaka DH, Li S, Mukae S, Tanabe T. Genetic recombination in disgust-associated bitter taste-responsive neurons of the central nucleus of amygdala in male mice. Neuroscience letters. 2021.01; 135456
- Fleck D, Kenzler L, Mundt N, Strauch M, Uesaka N, Moosmann R, Bruentgens F, Missel A, Mayerhofer A, Merhof D, Spehr J, Spehr M. ATP activation of peritubular cells drives testicular sperm transport. eLife. 2021.01; 10;

- 1. 上阪直史. Astrocytes regulate synapse elimination in the developing cerebellum.. 第 64 回日本神経化学会 大会 2021.10.01
- 2. 上阪 直史, 赤松 翼, 鈴木 穂香, 狩野 方伸. アストロサイトは2型イノシトール3リン酸受容体を介して発達 期小脳のシナプス刈り込みを制御する. 第98回 日本生理学会大会 2021.03.29日本(Web シンポジウム)

Molecular Craniofacial Embryology

Staffs and Students Professor Associate Professor Tenure Track Assistant Professor Part-time lecturers

Sachiko ISEKI Masa-Aki IKEDA Masaki TAKECHI 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 Yukiko HOSHINO

Research students

(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

- 1. Saadat KASM, Lestari W, Pratama E, Ma T, Iseki S, Tatsumi M, Ikeda MA. Distinct and overlapping roles of ARID3A and ARID3B in regulating E2F dependent transcription via direct binding to E2F target genes. International journal of oncology. 2021.04; 58(4);
- 2. Guo L, Iida A, Bhavani GS, Gowrishankar K, Wang Z, Xue J, Wang J, Miyake N, Matsumoto N, Hasegawa T, Iizuka Y, Matsuda M, Nakashima T, Takechi M, Iseki S, Yambe S, Nishimura G, Koseki H, Shukunami C, Girisha KM, Ikegawa S. Deficiency of TMEM53 causes a previously unknown sclerosing bone disorder by dysregulation of BMP-SMAD signaling. Nature Communications. 2021.04; 12(1); 2046
- 3. Takenoshita M, Takechi M (Co-first), Vu TH, Furutera T, Akagawa C, Namangkalakul W, Aoto K Kume T, Miyashin M, Iwamoto T, Iseki S. Cell lineage- and expression-based inference of the roles of forkhead box transcription factor Foxc2 in craniofacial development. Developmental Dynamics. 2021.03;

- 4. Shunya Kuroda, Noritaka Adachi, Rie Kusakabe, Shigeru Kuratani. Developmental fates of shark head cavities reveal mesodermal contributions to tendon progenitor cells in extraocular muscles. Zoological Lett. 2021.02; 7(1); 3
- 5. Vu TH, Takechi M (Co-first), Shimizu M, Kitazawa T, Higashiyama H, Iwase A, Kurihara H, Iseki S. Dlx5-augmentation in neural crest cells reveals early development and differentiation potential of mouse apical head mesenchyme. Scientific Reports. 2021.01; 11(1); 2092

- 1. Yukiko Hoshino, Masaki Takechi, Mehran Moazen, Daisuke Koyabu, Toshiko Furutera, Youichiro Ninomiya, Erwin Pauws, Takashi Nuri, Sachiko Iseki. Ontogenic trajectories of cranial growth in syndromic craniosynostosis mouse models. 2nd Advances in Craniosynostosis Basic Science to Clinical Practice 2021.08.27
- 2. Takechi Masaki, Vu Hoang Tri, Shimizu Miki, Kitazawa Taro, Higashiyama Hiroki, Iwase Akiyasu, Kurihara Hiroki, Iseki Sachiko. 神経堤細胞特異的に Dlx5 を強制発現させたマウスにより示された初期頭頂 部間葉の潜在的骨 · 軟骨分化能 (Forced expression of Dlx5 in mouse neural crest cells reveals differentiation potential of bone and cartilage in early apical cranial mesenchyme). The Journal of Physiological Sciences 2021.08.01
- 3. Worachat Namangkalakul, Shigenori Nagai, Ken-ichi Nakahama, Kazunari Akiyoshi, Masaki Takechi, Sachiko Iseki. Fibroblast Growth Factor18 Activity on Calvarial Bone Regeneration. 2021IADR/AADR/CADR General session & Exhibition 2021.07.21
- 4. 形づくり (頭蓋顎顔面形態形成). 2021.02.13
- 1. Takeuchi S, Okada M, Fukuba S, Matsuura T, Akizuki T, Nohara K, Sato R, Doi H, Imamura W, Iseki S, Aoki A. Effects of fibroblast growth factor 18 on periodontal regeneration in three-wall intrabony defects in dogs. The 64th Autumn Meeting of Japanese Society of Periodontology 2021.10.15 Nagoya Congress Center, Nagoya, Japan
- 2. Yamazaki S, Shimizu M, Yoda T, Ikeda MA. Investigation of culture conditions and scaffolds for human mesenchymal stem cells suitable for bone regeneration via endochondral ossification. The 42nd Annual Meeting of the Japanese Society of Inflammation and Regeneration 2021.07.07 Tokyo

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama

Junior Associate Professor Hiroshi Fujita, Hideto Kameda, Masahiro Shinohara

Research Student : Shiho Hidaka : Risa Kawakura :Rika Kodama (2022.1-)

Collaborator :Yuki Kasahara

(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

 $\label{eq:undergraduate} Undergraduate \ students \ should \ understand \ basic \ biochemistry \ and \ physiology \ under \ healthy/diseased \ conditions.$

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]

- Nagashima S, Maruyama J, Honda K, Kondoh Y, Osada H, Nawa M, Nakahama KI, Ishigami-Yuasa M, Kagechika H, Sugimura H, Iwasa H, Arimoto-Matsuzaki K, Nishina H, Hata Y. CSE1L promotes nuclear accumulation of transcriptional coactivator TAZ and enhances invasiveness of human cancer cells. The Journal of biological chemistry. 2021.05; 297(1); 100803
- 2. Fukuda S, Akiyama M, Niki Y, Kawatsura R, Harada H, Nakahama KI. Inhibitory effects of miRNAs in astrocytes on C6 glioma progression via connexin 43. Molecular and cellular biochemistry. 2021.03;
- 3. LIU Hongding, AKIYAMA Masako, NAKAHAMA Ken- ichi. Ogerin Accelerates Osteoclastogenesis via GPR68 in Neutral Conditions 口腔病学会雑誌. 2021.03; 88(1); 58-66

[Conference Activities & Talks]

1. Role of GJIC established among osteoblasts in osteoclast differentiation supported by osteoblasts. 2021.12.02

Maxillofacial Surgery

Professor: Tetsuya YODA

Associate Professor: Yoshiyuki SASAKI, (\sim Jul.) Eriko MARUKAWA, (Nov. \sim) Kei-ichi MORITA Junior Associate Professor: (\sim Oct.) Kei-ichi MORITA,

(Dec. \sim) Hiroyuki YOSHITAKE

Assistant Professor:, (~ Nov.) Hiroyuki YOSHITAKE, (~ Mar.) Kouichi NAKAKUKI,

Namiaki TAKAHARA, Nobuyoshi TOMOMATSU,

(Apr. \sim) Yosuke HARAZONO

Special Assistant Professor: Yasuhiro KURASAWA, Masahiko TERAUCHI, Hirokazu KACHI,

(Apr. \sim) Erina TONOUCHI, Takasuke INADA,

 $(\sim Mar.)$ Yosuke HARAZONO, Tasuku KIHARA

Hospital Staff: Erina NAKAMURA, Tomomi SAKUMA, Atsushi KIMURA

(Apr. \sim) Narumi OSHIBE, Shinpei TSUDA, Remi ISHIBASHI,

(\sim Mar.) Chie AKATSU, Takahiko YAMADA, Kentaro SUGIYAMA, Daisuke YAMAMOTO

Graduate Student: Hiroki MASUDA, Yu AKAIKE, Hongfei ZHU, Noboru MARUTA,

Shintarou YAMAZAKI, Rina TAJIMA,

 (Apr. \sim) Karen KUROYAMA, Taishi NAKAMURA, Koutaro YAMAZAKI

Social Graduate Student: Mari SHIBATA, Eri SHIBATA, Takuya IWASAKI

Student: Chizuko KOMURO, Souichi ROKUSHIMA, Junya KUMAGAI, Yuuko KATSUKI,

(\sim Mar.) Chika MIURA, Koutaro WACHI

Clinical professor: Hiroyuki WAKE

Part-time Lecturer: Masashi YAMASHIRO, Jin SATO, Hideo MIYACHI,

Akiko KOBAYASHI, Fumiaki SATO, Kazuhiro YAGIHARA, Yutaka SATO, Takashi MISHIMAGI,

Kazuto KUROHARA, Katuya AIKOU, Yoshio OHYAMA, Jyunichi TSUGAWA, Chieko MICHIKAWA,

Ryosuke NAGAOKA, Toshiyuki YAMADA, Katsuya HYODO,

(Apr. \sim) Takahiko YAMADA, Daisuke YAMAMOTO,

(Dec. $\sim)$ Tomohisa KITAMURA

(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**

- Chigasaki O, Aoyama N, Sasaki Y, Takeuchi Y, Mizutani K, Ikeda Y, Gokyu M, Umeda M, Izumi Y, Iwata T, Aoki A. Porphyromonas gingivalis, the most influential pathogen in red-complex bacteria: A cross-sectional study on the relationship between bacterial count and clinical periodontal status in Japan. Journal of Periodontology. 2021.12; 92(12); 1719-1729
- Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Delayed senescence of human vascular endothelial cells by molecular mobility of supramolecular biointerfaces Macromolecular Bioscience. 2021.12; 21(12); 2100216
- 3. ティーラウォン · チャンヤーヌット, 坂本 啓, 布川 裕規, 土谷 麻衣子, 栢森 高, 明石 巧, 濱垣 美和子, 富岡 博文, 黒嶋 雄志, 森田 圭一, 原田 浩之, 池田 通. 舌癌症例にみられるヒトパピローマウイルス (HPV) 感染 と無関係な p16 免疫染色陽性反応 口腔病学会雑誌. 2021.11; 88(2-3); 115-126
- 4. Okumura T, Hara K, Nakane A, Namiki C, Nakagawa K, Yamaguchi K, Yoshimi K, Toyoshima M, Sasaki Y, Tohara H. Can Videofluoroscopic Swallowing Kinematic Analysis Predict Recovery of Oral Intake in Postoperative Oral Cancer Patients Requiring Nasogastric Tube Feeding? Int J Environ Res Public Health. 2021.11; 18(22);
- 5. Tomomatsu N, Takahara N, Nakakuki K, Kimura A, Kurasawa Y, Terauchi M, Yoda T. A study of unfavorable splits in the sagittal ramus osteotomy with a short lingual cut. Int J Oral Maxillofac Surg. 2021.10; 50(10); 1329-1335
- 6. Shibata E, Morita KI, Kayamori K, Tange S, Shibata H, Harazono Y, Michi Y, Ikeda T, Harada H, Imoto I, Yoda T. Detection of novel fusion genes by next-generation sequencing-based targeted RNA sequencing analysis in adenoid cystic carcinoma of head and neck. Oral surgery, oral medicine, oral pathology and oral radiology. 2021.10; 132(4); 426-433
- 7. Tomomatsu N, Takahara N, Kurasawa Y, Terauchi M, Iwasaki T, Yoda T. Three-dimensional changes in cystic lesions of the mandible after marsupialization Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2021.10;
- 8. Hakariya M, Arisaka Y, Masuda H, Yoda T, Tamura A, Iwata T, Yui N. Tissue Adhesion-Anisotropic Polyrotaxane Hydrogels Bilayered with Collagen Gels. 2021.10; 7(4); 168
- Govitvattana N, Kaku M, Ohyama Y, Jaha H, Lin I, Mochida H, Pavasant P, Mochida Y. Molecular Cloning of Mouse Homologue of Enamel Protein C4orf26 and Its Phosphorylation by FAM20C. Calcif Tissue Int. 2021.10; 109(4); 445-454

- Mochizuki Y, Marukawa E, Harada H, Kinoshita N, Nakatani R, Oikawa Y, Hirai H, Tomioka H, Yoda T, Nakamura S, Kurabayashi T. Postoperative morphological changes over time of vascularized scapular bone used for mandibular reconstruction: A retrospective cohort study. Journal of plastic, reconstructive & aesthetic surgery : JPRAS. 2021.09; 74(9); 1984-1990
- 11. Iwanaga J, Kim HJ, Wysiadecki G, Obata K, Harazono Y, Ibaragi S, Tubbs SR.. Localizing the nerve to the mylohyoid using the mylohyoid triangle. Anat Cell Biol. 2021.09; 54(3); 304-307
- Enomoto A, Mano Y, Kawano Y, Nishikawa T, Aoyama T, Sasaki Y, Nagata M, Takahashi H. Comparison of the Safety and Effectiveness of Four Direct Oral Anticoagulants in Japanese Patients with Nonvalvular Atrial Fibrillation Using Real-World Data. Biological and Pharmaceutical Bulletin. 2021.09; 44(9); 1294-1302
- Kurasawa Y, Yoshitake H, Tomomatsu N, Yoda T. Long-term follow-up after arthroplasty for pediatric temporomandibular joint ankylosis performed before the critical period of mandibular growth: A case report. International journal of surgery case reports. 2021.09; 86; 106330
- Takahara N, Tomomatsu N, Hsieh D, Kurasawa Y, Morita KI, Yoda T. Short-Term Stability After Segmental Le Fort I Maxillary Impaction Surgery With Mandibular Autorotation in Seven High-Angle Class II Patients: A Case Series. J Craniofac Surg. 2021.08;
- 15. Yoshitake H, Kayamori K, Wake S, Sugiyama K, Yoda T. Biomarker expression related to chondromatosis in the temporomandibular joint. Cranio : the journal of craniomandibular & sleep practice. 2021.07; 39(4); 362-366
- 16. Harazono Y, Kayamori K, Sakamoto J, Akaike Y, Kurasawa Y, Tsushima F, Sasaki Y, Harada H, Yoda T. A retrospective analysis of schwannoma in the oral maxillofacial region: the clinicopathological characteristics and the specific pathology of ancient change British Journal of Oral & Maxillofacial Surgery. 2021.07;
- 17. Sekiya H, Kurasawa Y, Maruoka Y, Mukohyama H, Negishi A, Shigematsu S, Sugizaki J, Ohashi M, Hasegawa S, Kobayashi Y, Ueno M, Michiwaki Y. Cost-Effectiveness Analysis of Perioperative Oral Management after Cancer Surgery and an Examination of the Reduction in Medical Costs Thereafter: A Multicenter Study INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH. 2021.07; 18(14);
- 18. Kim Y, Yagihara K, Yagishita H, Ishii J, Kanda H, Ishikawa A. Basaloid squamous cell carcinoma of the floor of the mouth: A case report with review of the literature. Oral Science International. 2021.07;
- Kaida A, Yamamoto S, Parrales A, Young ED, Ranjan A, Alalem MA, Morita KI, Oikawa Y, Harada H, Ikeda T, Thomas SM, Diaz FJ, Iwakuma T. DNAJA1 promotes cancer metastasis through interaction with mutant p53. Oncogene. 2021.06;
- Masuda H, Arisaka Y, Hakariya M, Iwata T, Yoda T, Yui N. Synergy of molecularly mobile polyrotaxane surfaces with endothelial cell co-culture for mesenchymal stem cell mineralization RSC Advances. 2021.06; 11(30); 18685-18692
- 21. Sekiya H, Kurasawa Y, Kaneko K, Takahashi K, Maruoka Y, Michiwaki Y, Takeda Y, Ochiai R. Preventive Effects of Sustainable and Developmental Perioperative Oral Management Using the "Oral Triage" System on Postoperative Pneumonia after Cancer Surgery INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH. 2021.06; 18(12);
- 22. Kawasaki R, Sasaki Y, Nishimura T, Katagiri K, Morita KI, Sekine Y, Sawada S, Mukai S, Akiyoshi K. Magnetically Navigated Protein Transduction In Vivo using Iron Oxide-Nanogel Chaperone Hybrid ADVANCED HEALTHCARE MATERIALS. 2021.05; 10(9);
- 23. Miki K, Aizawa Y, Fujii S, Karakama J, Fujita K, Sasaki Y, Nemoto S, Sumita K. Combined Technique Thrombectomy with a Long Balloon-Guiding Catheter and Long Sheath Aids in Rapid and Stable Recanalization in Patients with Anterior Circulation Acute Ischemic Stroke JNET: Journal of Neuroendovascular Therapy. 2021.05; 15(5); 281-287
- 24. Arisaka Y, Hakariya M, Iwata T, Masuda H, Yoda T, Tamura A, Yui N. Surface-tethering of methylated polyrotaxanes with 4-vinylbenzyl groups onto poly(ether ether ketone) substrates for improving osteoblast compatibility. Dental materials journal. 2021.05; 40(3); 813-819

- 25. Ohyama Y, Yamashiro M, Michi Y, Uzawa N, Myo K, Sonoda I, Sumino J, Miura C, Mizutani M, Yamamoto D, Kayamori K, Yoda T. . Determination of Significant Prognostic Factors for Maxillary Gingival Squamous Cell Carcinoma in 90 Cases. Indian Journal of Otolaryngology and Head & Neck Surgery. 2021.04;
- 26. Iida T, Nakamura M, Inazawa M, Munetsugu T, Nishida M, Fujimoto T, Sasaki Y, Ohshima Y, Nakazato Y, Namiki T, Yokozeki H. Prognosis after steroid pulse therapy and seasonal effect in acquired idiopathic generalized anhidrosis. The Journal of Dermatology. 2021.03; 48(3); 271-278
- 27. Aragaki T, Tomomatsu N, Michi Y, Hosaka H, Fukai Y, Iijima M, Yoda T. Ramucirumab-related Oral Pyogenic Granuloma: A Report of Two Cases Internal Medicine. 2021.03;
- 28. Terauchi M, Michi Y, Hirai H, Sugiyama K, Wada A, Harada H, Yoda T. Prognostic factors in mucoepidermoid carcinoma of the minor salivary glands: A single-center retrospective study. Oral surgery, oral medicine, oral pathology and oral radiology. 2021.02; 131(2); 209-216
- 29. Sekiya-Aoyama R, Arisaka Y, Hakariya M, Masuda H, Iwata T, Yod T, Yui N. Dual effect of molecular mobility and functional groups of polyrotaxane surfaces on the fate of mesenchymal stem cells Biomaterials Science. 2021.02; 9(3); 675-684
- Kayamori K, Tsuchiya M, Michi Y, Kuribayashi A, Mikami T, Sakamoto K, Yoda T, Ikeda T. Primordial odontogenic tumor occurred in the maxilla with unique calcifications and its crucial points for differential diagnosis. Pathol Int. 2021.01; 71(1); 80-87
- 1. SHIBTA Eri, OKUYAMA Kohei, MICHI Yasuyuki, SAKAMOTO Kei, HATADA Hiroyuki, YODA Tetsuya. A case of osteosarcoma of the mandible treated with surgical resections for pulmonary metastases JAPANESE JOURNAL OF ORAL &MAXILLOFACIAL SURGERY. 2021.06; 67(6); 353-358

[Misc]

1. Masahiko Terauchi, Atsushi Tamura, Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Cyclodextrin-based supramolecular complexes of osteoinductive agents for dental tissue regeneration. Pharmaceutics. 2021.01; 13(2); 136

[Awards & Honors]

1. The 1st runner-up prize for the Oral Paper Competition, 14th Asian Congress on Oral & Maxillofacial Surgery, 2021.06

Maxillofacial Orthognathics

Professor and Chair Keiji MORIYAMA Associate Professor Takuya OGAWA Junior Associate Professor Norihisa HIGASHIHORI Assistant Professor Michiko TSUJI, Yukiho KOBAYASHI, Masayoshi UEZONO, Chiho KADOTA Specially Appointed Assistant Professor Takeshi OGASAWARA, Hiroyuki KAMIMOTO, Kenta FUNAHASHI, Hideyuki YOSHIZAWA Dental Resident Sonhwa KANG, Yumi INAGAKI, Atsuhiro INOUE, Riho YOKOUCHI Doctoral Program : Medical and Dental Sciences Track Kaori IWANAMI, Hidekazu MATSUMOTO, Takayuki MIYAZAKI, Phyo Thiha, Masaki INOUE, Yoshiya KAISAKA, Yuki NIKI, Badrakhkhuu Nomin Dulguun, Sakurako KANO, Yuki SAGAWA, Lin Tun Oo, Kyaw Min Soe, Faisal Alkherainej, Aina OKAWARA, Misato SHIMIZU, Ryoto MACHIDA, Aye Chan Myo, Hanae ARAI, Ayako SUZUKI, Yuri TAKAGIWA, Satoka TAKEUCHI, Shen Huiyu, Nao UKITA, Suzu CHIDA, Mikiko TERASHIMA, Daigo YAMAHARA, Yunaho YONEMITSU, Liu Yinan, Lu Yeming, Aung Thet Khine Doctoral Program : Joint Degree Program (Chulalongkorn University) Sansanee Wijarn Graduate International Research Student Program Nanase IGARASHI, Kota ANAN, Kanako HORI, Mayu Oiwa, Yuichiro OMORI, Yoshimitsu TAKAHASHI, Ami TSUNASHIMA, Shintaro ARIKATA, Shiori OKUBO, Konosuke YOSHITANI Cheng Shih-Wei Eric, Kenjiro MATSUMURA Part-time Lecturer Shoichi SUZUKI, Tatsuo KAWAMOTO, Naoto SUDA, Tamiko TERASHIMA, Yoshiyuki KATO, Yasuo ISHIWATA, Yoshiyuki BABA, Toshimoto TENGAN, Masahiko YOKOZEKI, Shigetoshi HIYAMA, Shigeki TAKAHASHI, Maristela Sayuri ARAI, Jun MIYAMOTO, Junichi TAKADA, Rina HIKITA, Tsutomu MATSUMOTO, Yuko YASUDA

(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**

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Maxillofacial Prosthetics

2021 April

Junior Associate Professor (~ 21 April) SUMITA Yuka Associate Professor (Career-up) (22 April $\sim)$ SUMITA Yuka

Assistant Professor HATTORI Mariko

Project Assistant Professor HARAGUCHI Mihoko MURASE Mai

Clinical Staff FUJITA Haruka (April \sim) TANABE Gen (April \sim March, 2022)

Graduate Student ZHANG Manjin (\sim September) LIU Rongguang (\sim September) TANI Hiroko (\sim March, 2022) GAO Yuan WANG Yujia TOWITHELERTKUL Cheewin YU Hongli CHUGH Anshul HAN Xuewei ALI Islam Elsayed BAI Ziyi (April \sim) WANG Jiangyu (April \sim) ZHANG Fan (April \sim) PRADHAN Nehasha (October \sim)

Part-time Special Student ALI Ahmed Sameir Mohamed (October \sim March, 2022)

Part-time Lecturer (Faculty of Dentistry) ARAI Takayuki ELBASHTI Mahmoud Ellarousi HATANO Noriko TERUYAMA Yuko

Part-time Lecturer (Graduated School) OZAWA Shogo TANIGAWA Chihiro INOHARA Ken (April \sim)

Speech-Language-Hearing Therapist MASAKI Keita

(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 delvelopment of new materials for facial prosthesis

(3) Publications

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- 7. Churei H, Hayashi K, Tanabe G, Sakai M, Shimizu S, Ueno T. Relationship between appropriate heating temperature and dropping distance of polyolefin-polystyrene sheet materials for mouthguard. The 32nd Annual Meeting of Japanese Academy of Sports Dentistry 2021.09.21 Yokohama (Japan)+Web
- 8. Tanabe G, Hasunuma T, Takeuchi Y, Kobayashi H, Shimizu S, Hayashi K, Churei H, Sumita YI, Suzuki K, Ueno T. Real-time assessment of dehydration during swim practice by oral mucosa moisture. The 76th Japanese Society of Physical Fitness and Sports Medicine 2021.09.17 (Web)
- 9. Tani H, Murase M, Sumita YI. Factors affecting resting energy expenditure in patients treated for head and neck cancer in the perioperative period. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19 (Web)
- Hattori M, Zhang M, Sumita YI. Fabrication of maxillofacial prostheses using a 3-dimensional printed record base. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19 (Web)
- 11. Haraguchi M, Michi Y, Sumita YI, Harada H. Aesthetic prosthetic rehabilitations for 2 patients with the deformity of lower lip caused by mandibulectomy. The 45th Annual Meeting of Japan Society for Head and Neck Cancer 2021.06.17 Urayasu (Japan)+Web
- 12. Murase M, Tani H, Sumita YI. A case of removable denture treatment in a patient with mouth opening disturbances coursed by Systemic Sclerosis. The 38th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2021.06.04 (Web)
- 13. Hattori M, Han X, Haraguchi M, Sumita YI. The use of a copied obturator as a radiotherapy prosthesis for the recurrence of maxillary cancer. The 38th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2021.06.04 (Virtual Meeting)
- 14. Zhang M, Hattori M, Sumita YI. Three-dimensional evaluation of teeth position in cleft lip and palate patients after prosthetic treatment. The 38th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2021.06.04 (Virtual Meeting)
- 15. Hattori M. Symposium I: For what kind of facial defect cases are facial prostheses effective?. The 38th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2021.06.04 (Virtual Meeting)
- 16. Liu R. Use of an occlusal ramp for rehabilitation after a mandibulectomy and its effects on mastication. Joint Symposium of Immunology and Pathological Biochemistry Units & Intractable Disease(Cancer) Unit Workshops 2021 2021.03.18 Tokyo (Japan) (by the Abstracts / Online)

[Awards & Honors]

- 1. The 2021 ICP Poster Award, Best Case Presentation (Sumita YI), 19th Biennial Meeting of the International College of Prosthodontists, 2021.09
- 2. The 2021 ICP Poster Award, Best Laboratory Research Presentations (Towithelertkul C), 19th Biennial Meeting of the International College of Prosthodontists, 2021.09
- 3. The 2021 AAMP Student Poster Competition, Research-2nd Place (Yu H), The 68th Annual Meeting of the American Academy of Maxillofacial Prosthetics, 2021.10

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. Tomoya Uchimura, Toshifumi Asano, Takao Nakata, Akitsu Hotta, Hidetoshi Sakurai. A muscle fatigue-like contractile decline was recapitulated using skeletal myotubes from Duchenne muscular dystrophy patient-derived iPSCs. Cell Reports Medicine. 2021.06; 2(6); 100298

2. Hironori Inaba, Qianqian Miao, Takao Nakata. Optogenetic control of small GTPases reveals RhoA mediates intracellular calcium signaling. J Biol Chem. 2021.01; 100290

[Misc]

- 1. Toshifumi Asano, Daniel Boon Loong Teh, Hiromu Yawo. Application of Optogenetics for Muscle Cells and Stem Cells Advances in Experimental Medicine and Biology. 2021.01; 1293; 359-375
- 1. Optogenetic manipulations of small GTP ases and observations of their intracellular functions 2021.08; 56(2); 59-63

- 1. Hironori Inaba, Tsuyoshi Imasaki, Kazuhiro Aoyama, Hiroko Takazaki, Takayuki Kato, Kaoru Mitsuoka, Ryo Nitta, Takoa Nakata. Cryo-electron tomogprahy of the actin cytoskelton in optogenetically induced lamellipodia. Grant-in-Aid for Transformative Research Areas(A) New cross scale biology, kickoff meeting 2021.12.13 Nagaragawa Convention Center
- 2. Hironori Inaba, Qianqian Miao, Takao Nakata. Optogenetic control of small GTPases reveals RhoA-mediated intracellular calcium signaling. the 126th Annual Meeting of The Japanese Association of Anatomists/ the 98th Annual Meeting of The Physiological Society of Japan 2021.03.29 Online

Medical Biochemistry

Professor Yutaka Hata

Assistant Professor Hiroaki Iwasa

Assistant Professor Kyoko Arimoto-Matsuzaki

Assistant Professor Junichi Maruyama

Technical Assistant Yuki Nakajima

(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 organaized the course of Biochemmistry for the undergraduate students.

2 : Master course

We organized the course of Biochemmistry 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. Kuleape JA, Hossain S, Sinclear CK, Shimizu T, Iwasa H, Maruyama J, Arimoto-Matsuzaki K, Nishina H, Hata Y. DNA damage triggers the nuclear accumulation of RASSF6 tumor suppressor protein < i> via< /i> CDK9 and BAF53 to regulate p53-target gene transcription. Molecular and cellular biology. 2021.12; MCB0031021
- Nagashima S, Maruyama J, Honda K, Kondoh Y, Osada H, Nawa M, Nakahama KI, Ishigami-Yuasa M, Kagechika H, Sugimura H, Iwasa H, Arimoto-Matsuzaki K, Nishina H, Hata Y. CSE1L promotes nuclear accumulation of transcriptional coactivator TAZ and enhances invasiveness of human cancer cells. The Journal of biological chemistry. 2021.05; 297(1); 100803
- 3. Jiang Xinliang, Maruyama Junichi, Iwasa Hiroaki, Arimoto-Matsuzaki Kyoko, Nishina Hiroshi, Hata Yutaka. Heat shock induces the nuclear accumulation of YAP1 via SRC (vol 399, 112439, 2021) EXPERIMENTAL CELL RESEARCH. 2021.04; 401(2); 112555
- 4. Yuxiong Lu, Junichi Maruyama, Haruhiko Sugimura, Yutaka Hata. Double
cortin-like kinase 1 expression is induced by alternative NF-
 κ B signaling in human lung cancer cells Journal of Medical and Dental Sciences. 2021.03; 68; 39-48
- 5. Xinliang Jiang, Junichi Maruyama, Hiroaki Iwasa, Kyoko Arimoto-Matsuzaki, Hiroshi Nishina, Yutaka Hata. Heat shock induces the nuclear accumulation of YAP1 via SRC. Exp Cell Res. 2021.02; 399(1); 112439
- 6. Lu Yuxiong, Maruyama Junichi, Sugimura Haruhiko, Hata Yutaka. Double
cortin-like kinase 1 expression is induced by alternative NF-
 κ B signaling in human lung cancer cells
(和訳中) Journal of Medical and Dental Sciences. 2021; 68; 39-48

[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 Appication of split-GFP reassembly assay to the study of the in vitro myogenesis and myofusion. Springer,

Joint Surgery and Sports Medicine

Hideyuki Koga Yusuke Nakagawa, Mai Katakura

Department of Cartilage Regeneration Tomomasa Nakamura, Kazumasa Miyatake

Kazumasa Kawata, Masaaki Isono, Aritoshi Yoshihara Tang Guo, Kei Sato, Yusuke Amano, Shoichi Hasegawa Tetsuya Tachibana, Zhu Ling, Qu Zhen, Yang Yang Riko Yamashita, Ryu Yoshida, Tatsunobu Ikeda

Miyoko Ojima, Miho Okada

(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

- Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Toshitaka Yoshii, Shigenori Kawabata, Atsushi Okawa. Does surgical body position influence the risk for neurovascular injury in total hip arthroplasty? A magnetic resonance imaging study. Orthop Traumatol Surg Res. 2021.12; 102817
- 2. Katsuaki Yanagisawa, Toshifumi Watanabe, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta, Tetsuya Jinno. Do the distal femur and the proximal tibia have narrower aspect ratios in smaller knees? : A morphological analysis of osteoarthritic knees in the Japanese population using computed tomography. Knee. 2021.12; 33; 84-92

- Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Yuji Kohno, Ichiro Sekiya. Surgical Repair of Symptomatic Wrisberg Variant Discoid Lateral Mensicus with Pull-Out Repair and Capsulodesis. Arthrosc Tech. 2021.12; 11(1); e61-e68
- 4. Mitsuru Mizuno, Kentaro Endo, Hisako Katano, Naoki Amano, Masaki Nomura, Yoshinori Hasegawa, Nobutake Ozeki, Hideyuki Koga, Naoko Takasu, Osamu Ohara, Tomohiro Morio, Ichiro Sekiya. Transplantation of human autologous synovial mesenchymal stem cells with trisomy 7 into the knee joint and 5 years of follow-up. Stem Cells Transl Med. 2021.11; 10(11); 1530-1543
- Tomomasa Nakamura, Brandon D Marshall, Taylor M Price, Yongtao Mao, Monica A Linde, Hideyuki Koga, Patrick Smolinski, Freddie H Fu. Arthroscopic Centralization for Lateral Meniscal Injuries Reduces Laxity in the Anterior Cruciate Ligament-Reconstructed Knee. Am J Sports Med. 2021.11; 49(13); 3528-3533
- 6. Masaki Amemiya, Yusuke Nakagawa, Hideya Yoshimura, Toru Takahashi, Kei Inomata, Tsuyoshi Nagase, Young-Jin Ju, Masayuki Shimaya, Sachiyuki Tsukada, Naoyuki Hirasawa, Hideyuki Koga. Comparison of tissue pharmacokinetics of esflurbiprofen plaster with flurbiprofen tablets in patients with knee osteoarthritis: A multicenter randomized controlled trial. Biopharm Drug Dispos. 2021.11; 42(9); 418-426
- 7. Naoki Yamamoto, Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Kazuyoshi Yagishita, Atsushi Okawa. Wear rate and osteolysis in two types of second-generation annealed highly cross-linked polyethylene in total hip arthroplasty: A retrospective comparative study with a minimum of five years. Orthop Traumatol Surg Res. 2021.11; 103147
- 8. Mai Katakura, Haruki Odagiri, Christel Charpail, James Calder, Stéphane Guillo, Ankle Instability Group. Arthroscopic treatment for anterolateral impingement of the ankle: Systematic review and exploration of evidence about role of ankle instability. Orthop Traumatol Surg Res. 2021.11; 103159
- Kentaro Endo, Kiyotaka Horiuchi, Hisako Katano, Nobutake Ozeki, Yuriko Sakamaki, Hideyuki Koga, Ichiro Sekiya. Intra-articular Injection of PDGF-BB Explored in a Novel in Vitro Model Mobilizes Mesenchymal Stem Cells From the Synovium Into Synovial Fluid in Rats. Stem Cell Rev Rep. 2021.10; 17(5); 1768-1779
- 10. Carola F van Eck, Tomomasa Nakamura, Taylor Price, Monica Linde, Patrick Smolinski. Suture tape augmentation improves laxity of MCL repair in the ACL reconstructed knee. Knee Surg Sports Traumatol Arthrosc. 2021.08; 29(8); 2545-2552
- Misaki Yagi, Mitsuru Mizuno, Ryota Fujisawa, Hisako Katano, Kentaro Endo, Nobutake Ozeki, Yuriko Sakamaki, Hideyuki Koga, Ichiro Sekiya. Optimal Pore Size of Honeycomb Polylactic Acid Films for In Vitro Cartilage Formation by Synovial Mesenchymal Stem Cells. Stem Cells Int. 2021.08; eCollection; 2021:9239728
- 12. Takashi Hoshino, Toshifumi Watanabe, Yusuke Nakagawa, Hiroki Katagiri, Nobutake Ozeki, Toshiyuki Ohara, Mikio Shioda, Yuji Kono, Ichiro Sekiya, Hideyuki Koga. Clinical outcomes of two-stage revision total knee arthroplasty in infected cases with antibiotic-loaded cement spacers produced using a handmade silicone mold. Knee Surg Relat Res. 2021.08; 33(1); 27
- 13. Toshifumi Watanabe, Kazuyoshi Gamada, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta, Tetsuya Jinno. Consistent femoral external rotation during weight-bearing knee flexion is associated with better patient-reported pain and mediolateral balance after total knee arthroplasty. Clin Biomech (Bristol, Avon). 2021.08; 88; 105438
- 14. Hiroko Ueki, Hiroki Katagiri, Kunikazu Tsuji, Kazumasa Miyatake, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Effect of transplanted mesenchymal stem cell number on the prevention of cartilage degeneration and pain reduction in a posttraumatic osteoarthritis rat model. J Orthop Sci. 2021.07; 26(4); 690-697
- 15. Hiroki Katagiri, Kaori Nakamura, Takeshi Muneta, Toshifumi Watanabe, Kazumasa Miyatake, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. Inflammatory and healing environment in synovial fluid after anterior cruciate ligament reconstruction: Granulocytes and endogenous opioids as new targets of postoperative pain. Biochem Biophys Rep. 2021.07; 26; 100981
- Ichiro Sekiya, Hisako Katano, Mitsuru Mizuno, Hideyuki Koga, Jun Masumoto, Makoto Tomita, Nobutake Ozeki. Alterations in cartilage quantification before and after injections of mesenchymal stem cells into osteoarthritic knees. Sci Rep. 2021.07; 11(1); 13832
- 17. Kazumasa Kawata, Hideyuki Koga, Kunikazu Tsuji, Kazumasa Miyatake, Yusuke Nakagawa, Takanori Yokota, Ichiro Sekiya, Hiroki Katagiri. Extracellular vesicles derived from mesenchymal stromal cells mediate endogenous cell growth and migration via the CXCL5 and CXCL6/CXCR2 axes and repair menisci. Stem Cell Res Ther. 2021.07; 12(1); 414
- Nobutake Ozeki, Yusuke Nakagawa, Mitsuru Mizuno, Yuji Kohno, Hisako Katano, Hideyuki Koga, Ichiro Sekiya. Ultrasound-Guided Harvesting of Synovium for Regenerative Medicine of Cartilage and Meniscus Using Synovial Mesenchymal Stem Cells. Arthrosc Tech. 2021.07; 10(7); e1723-e1727
- 19. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. The psychological readiness to return to sports of patients with anterior cruciate ligament reconstruction preoperatively and 6 months postoperatively PHYSICAL THERAPY IN SPORT. 2021.07; 50; 114-120
- Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Injury-related fear in athletes returning to sports after anterior cruciate ligament reconstruction
 A quantitative content analysis of an open-ended questionnaire. Asia Pac J Sports Med Arthrosc Rehabil Technol. 2021.07; 25; 1-7
- 21. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Tetsuya Jinno, Hideyuki Koga, Kazuyoshi Yagishita. Characteristics of landing impact in athletes who have not returned to sports at the pre-injury competition level after anterior cruciate ligament reconstruction. Asia Pac J Sports Med Arthrosc Rehabil Technol. 2021.07; 25; 47-52
- 22. Ichiro Sekiya, Yuji Kohno, Akinobu Hyodo, Hisako Katano, Keiichiro Komori, Hideyuki Koga, Makoto Tomita, Kenji Suzuki, Jun Masumoto, Nobutake Ozeki. Interscan measurement error of knee cartilage thickness and projected cartilage area ratio at 9 regions and 45 subregions by fully automatic three-dimensional MRI analysis. Eur J Radiol. 2021.06; 139; 109700
- 23. Christophe Jacquet, Caroline Mouton, Roland Becker, Hideyuki Koga, Matthieu Ollivier, Peter Verdonk, Philippe Beaufils, Romain Seil. Does practice of meniscus surgery change over time? A report of the 2021 'THE MENISCUS' Webinar. J Exp Orthop. 2021.06; 8(1); 46
- 24. Masato Takao, Danielle Lowe, Satoru Ozeki, Xavier M Oliva, Ryota Inokuchi, Takayuki Yamazaki, Yoshitaka Takeuchi, Maya Kubo, Kentaro Matsui, Mai Katakura, Mark Glazebrook. Strain patterns in normal anterior talofibular and calcaneofibular ligaments and after anatomical reconstruction using gracilis tendon grafts: A cadaver study. BMC Musculoskelet Disord. 2021.06; 22(1); 558
- 25. Kiyotaka Horiuchi, Nobutake Ozeki, Kentaro Endo, Mitsuru Mizuno, Hisako Katano, Masako Akiyama, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Thawed cryopreserved synovial mesenchymal stem cells show comparable effects to cultured cells in the inhibition of osteoarthritis progression in rats. Sci Rep. 2021.05; 11(1); 9683
- 26. Masanobu Hirao, Kazumasa Miyatake, Daisuke Koga, Ryohei Takada, Gaku Koyano, Atsushi Okawa, Tetsuya Jinno. Comparison of 5-year postoperative results between standard-length stems and short stems in one-stage bilateral total hip arthroplasty: a randomized controlled trial. Eur J Orthop Surg Traumatol. 2021.05; 31(4); 743-753
- 27. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Toshitaka Yoshii, Atsushi Okawa. Incidence of tensor fascia lata muscle atrophy after using the modified Watson-Jones anterolateral approach in total hip arthroplasty. Eur J Orthop Surg Traumatol. 2021.04; 31(3); 533-540
- 28. Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Correlations between isokinetic knee torques and single-leg hop distances in three directions in patients after ACL reconstruction. BMC Sports Sci Med Rehabil. 2021.04; 13(1); 38
- 29. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Sho Mitomo, Takehiro Ohmi, Tetsuya Jinno, Hideyuki Koga, Kazuyoshi Yagishita. Athletic identity and sport commitment in athletes after anterior cruciate ligament reconstruction who have returned to sports at their pre-injury level of competition. BMC Sports Sci Med Rehabil. 2021.04; 13(1); 37

- 30. Kiyotaka Horiuchi, Mitsuru Mizuno, Hisako Katano, Kentaro Endo, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Optimal initial cell density that yields the highest number of primary synovial mesenchymal stem cells in a clinical setting. J Med Dent Sci. 2021.04; 68; 17-26
- 31. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Tetsuya Jinno, Hideyuki Koga, Kazuyoshi Yagishita. Single-leg hop distance normalized to body height is associated with the return to sports after anterior cruciate ligament reconstruction. J Exp Orthop. 2021.04; 8(1); 26
- 32. J-S An, K Tsuji, H Onuma, N Araya, M Isono, T Hoshino, K Inomata, J Hino, M Miyazato, H Hosoda, K Kangawa, Y Nakagawa, H Katagiri, K Miyatake, I Sekiya, T Muneta, H Koga. Inhibition of fibrotic changes in infrapatellar fat pad alleviates persistent pain and articular cartilage degeneration in monoiodoacetic acid-induced rat arthritis model. Osteoarthritis Cartilage. 2021.03; 29(3); 380-388
- 33. Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Nobutake Ozeki, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya. Arthroscopic Centralization Using Knotless Anchors for Extruded Medial Meniscus. Arthrosc Tech. 2021.03; 10(3); e639-e645
- 34. Toshifumi Watanabe, Kazuyoshi Gamada, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta, Tetsuya Jinno. Characteristic kinematics of floor-sitting activities after posterior-stabilized total knee arthroplasty determined using model-based shape-matching techniques. Knee. 2021.03; 29; 571-579
- 35. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Single-leg hop can result in higher limb symmetry index than isokinetic strength and single-leg vertical jump following anterior cruciate ligament reconstruction. Knee. 2021.03; 29; 160-166
- 36. Weiding Cui, Yusuke Nakagawa, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Takashi Hoshino, Aritoshi Yoshihara, Ichiro Sekiya, Hideyuki Koga. Knee laxity, lateral meniscus tear and distal femur morphology influence pivot shift test grade in ACL injury patients. Knee Surg Sports Traumatol Arthrosc. 2021.02; 29(2); 633-640
- 37. Yoshitaka Takeuchi, Ryota Inokuchi, Masato Takao, Mark Glazebrook, Xavier Martin Oliva, Takayuki Yamazaki, Maya Kubo, Danielle Lowe, Kentaro Matsui, Mai Katakura, Satoru Ozeki, Ankle Instability Group. Three-dimensional analysis of anterior talofibular ligament strain patterns during cadaveric ankle motion using a miniaturized ligament performance probe. BMC Musculoskelet Disord. 2021.02; 22(1); 208
- 38. Nobutake Ozeki, Yuji Kohno, Yoshihisa Kushida, Naoto Watanabe, Mitsuru Mizuno, Hisako Katano, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Synovial mesenchymal stem cells promote the meniscus repair in a novel pig meniscus injury model. J. Orthop. Res. 2021.01; 39(1); 177-183
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- 41. Mai Katakura, Yasuyuki Jujo, Kazuaki Okugura, Yukinori Mori, Keisuke Hayashi, Hideyuki Koga, Masato Takao. Simultaneous reconstruction of the bilateral chronic achilles tendon rupture with early functional rehabilitation: A case report Foot & Ankle Surgery: Techniques, Reports & Cases. 2021; 1(4);

[Books etc]

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- 2. Hideyuki Koga . Les ostéotomies autour du genou (Osteotomies around the knee) . 2021

- 1. Hideyuki Koga. Round table Case-based discussion. 1st Japanese Knee Osteotomy & Joint Preservation meeting 2021.12.18 Kobe, Japan
- 2. Hideyuki Koga. How I treat a degenerative meniscus tear. Singapore Orthopaedic meeting 2021.12.15 Singapole (web)
- 3. Hideyuki Koga. Meniscus centralization. EU Arthrex webinar 2021.12.03
- 4. Mai Katakura. Arthroscopic treatment for anterolateral impingement of the ankle : Systematic review and exploration of evidence about role of ankle instability. 2021 ISAKOS 2021.11.27 CapeTown(web)
- 5. Hideyuki Koga. The Tibial Slope in ACL Deficient Knees -The State of the Art- How I do it? asymmetric and hybrid closing –. ESSKA Core Curriculum Webinar 2021.11.10
- 6. Hideyuki Koga. Meniscus centralization. Malaysian Arthroscopy Society meeting 2021.10.15 Malaysia (web)
- 7. Hideyuki Koga. Minimum correction of HTO with medial meniscus centralization. Knee Joint Symposium-Myongji Knee Arthroscopy:An Up-to-date Guide 2021.08.21 Seoul, Korea (web)
- 8. Hideyuki Koga. Meniscus preservation. Taiwan JuggerStitch seminar 2021.07.31 Taipei, TAIWAN (web)
- 9. Hideyuki Koga. Treatment strategies for MMPRT -pull out repair + centralization augmentation-. 2021 SMC Knee Arthroscopy Cadaver Workshop 2021.06.20 Seoul, Korea (web)
- 10. Tomomasa Nakamura, Hideyuki Koga, Nobutake Ozeki, Ichiro Sekiya. Synovial MSC therapy for knee OA and establishment of objective quantitative MRI evaluation using AI. 2021 JOSKAS (web) 2021.06.17
- 11. Yuko Segawa, Reiko Yamaguchi, Kazumasa Miyatake, Atsushi Okawa. Four-years experience with new screening system on developmental dysplasia of the hip. The 13th Combined Meeting of Asia Pacific Spine Society & Asia Pacific Paediatric Orthopaedic Society (online) 2021.06.09
- 12. Tetsuya Jinno, Yutaka Inaba, Tamon Kabata, Tomohiro Goto, Kazumasa Miyatake, Shigeru Mitani. Clinical results of bipolar hemiarthroplasty for femoral neck fractures: A multicenter prospective observational study. The 94th Annual Meeting of the Japanese Orthopaedic Association 2021.05.20
- 13. Hideyuki Koga. Ramp lesions -Which lesions I fix and how. 19th ESSKA (web) 2021.05.11
- 14. Tomomasa Nakamura, Price TM, DiNenna M, Linde MA, van Eck C, Smolinski P, Fu FH. Graft Augmentation Combined with MCL Suture Repair Provides Sufficient Knee Kinematic Restoration in Concomitant ACL Reconstruction and MCL Grade 3 Injury. 19th ESSKA (web) 2021.05.11
- 15. Tomomasa Nakamura, Price TM, DiNenna M, Linde MA, van Eck C, Smolinski P, Fu FH. The Effect of Different MCL Repairs on Medial Tissue Forces in the ACL/MCL Injured Knee. 19th ESSKA (web) 2021.05.11
- 16. Hiroki Katagiri, Yoshie Seki, Yusuke Nakagawa, Ichiro Sekiya , Hiedyuki Koga . Validity of the preoperative intra-articular anesthetic test as the predictive factor of persistent pain after TKA. 19th ESSKA (web) 2021.05.11
- 17. Hiroki Katagiri, Yusuke Nakagawa, Ichiro Sekiya , Hiedyuki Koga . Effect of the autograft source on the knee joint stability and patient-reported outcomes in revision anterior cruciate ligament reconstruction. 19th ESSKA (web) 2021.05.11
- 18. Hideyuki Koga. Meniscus -how to preserve?. 2nd International Knee Day (web) 2021.03.18
- 19. Hideyuki Koga. Meniscus centralization. 2nd International Knee Day (web) 2021.03.18
- 20. Yusuke Nakagawa, Kunikazu Tsuji, Tomomasa Nakamura, Hiroki Katagiri, Nobutake Ozeki, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Jae-Sung An, Hideyuki Koga. IFP fibrosis delays functional recovery and is associated with elevation of inflammatory cytokines level in the synovial fluid in ACLR. 2nd International Knee Day (web) 2021.03.18

- 21. Aritoshi Yoshihara, Hiroki Katagiri, Yusuke Nakagawa, Kazumasa Miyatake, Tomomasa Nakamura, Kunikazu Tsuji, Ichiro Sekiya, Hideyuki Koga. Synovial superficial cells proliferate toward deeper layer in a rat monoiodoacetic acid-induced arthritis model. ORS 2021 Virtual 2021.02.12
- 22. Masaaki Isono, Kunikazu Tsuji, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Ichiro Sekiya, Atsushi Okawa, Hideyuki Koga. Hyaluronic acid/CD44 signal axis plays important roles during the formation and in the maintenance of mesenchymal stem cell (MSC) antigen-positive cells in vitro. ORS 2021 Virtual 2021.02.12
- 23. Zhu Ling, Shuhei Kajikawa, Kunikazu Tsuji, Yoshinori Asou, Hideyuki Koga, Yoichi Ezura. Alendronate Improves the Osteolytic Bone Phenotype of the Osteoclast-specific Mutant Pfn1-cKOOCL Mouse as a Model for Recently Identified Severe Form of Paget's Disease of Bone. ORS 2021 Virtual 2021.02.12
- 24. Guo Tang, Kunikazu Tsuji, Keiichiro Komori, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Ichiro Sekiya, Yoshinori Asou, Atsushi Okawa, Hideyuki Koga. IL-1 β Enhances The Proliferation fo Human Synovial Mesenchymal Stem Cells By Extending The Phosphorylation of Extracellular Signal-regulated Kinase 1/2(erk1/2)). ORS 2021 Virtual 2021.02.12
- 25. Kazumasa Kawata, Hiroki Katagiri, Kunikazu Tsuji, Kazumasa Miyatake, Yusuke Nakagawa, Ichiro Sekiya, Hideyuki Koga. Exosomes derived from mesenchymal stem cells regenerate meniscus and enhance endogenous cells proliferation and migration. ORS 2021 Virtual 2021.02.12
- 26. Hideyuki Koga. Practice change over time: MENISECTOMY VS REPAIR: a Japanese point of view. The Meniscus webinar 2021.01.30

Pharmacology

Staffs and Students

Assistant Professor Yukihiko TAMURA

Researchers

Tomoki UEHARA (Pediatric Dentistry) Noriko HIRAISHI (Cariology and Operative Dentistry) Yasuka KUSUMOTO (Pediatric Dentistry) Shinji Kuroda(Regenerative Dental Medicine) Hidemi Nakata(Regenerative Dental Medicine) Graduate Students Kenya YONEDA (Regenerative Dental Medicine) Michiko OZAWA C.Supachatwong (Regenerative Dental Medicine) Jason Hou (Regenerative Dental Medicine) Meng Sikun (Regenerative Dental Medicine) Rizwangul Ali(Regenerative Dental Medicine) Hsin-Ying Lu(Regenerative Dental Medicine) Gonndou Tadamu(Cariology and Operative Dentistry) Lecturers Yoshihiro WAKI Etsuko TAKAHASHI Kenichi NAGANO Hiroyuki 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. Supachatwong Chayapong, Hidemi Nakata, Yukihiko Tamura, Shohei Kasugai, Shinji Kuroda. Static Magnetic Fields Promote the Differentiation of MC3T3-E1 Cells Via the Transforming Growth Factor- β Pathway Journal of Oral and Dental Health Research. 2021.11; 3(3); 1-7
- 2. Gao Jing, Muroya Ryusuke, Huang Fei, Nagata Kengo, Shin Masashi, Nagano Ryoko, Tajiri Yudai, Fujii Shinsuke, Yamaza Takayoshi, Aoki Kazuhiro, Tamura Yukihiko, Inoue Mayuko, Chishaki Sakura, Kukita Toshio, Okabe Koji, Matsuda Miho, Mori Yoshihide, Kiyoshima Tamotsu, Jimi Eijiro. Bone morphogenetic protein induces bone invasion of melanoma by epithelial-mesenchymal transition via the Smad1/5 signaling pathway LABORATORY INVESTIGATION. 2021.09; 101(11); 1475-1483
- 3. Tamura Yukihiko, Fuangtharnthip Pornpoj, Uehara Tomoki, Iwamoto Tsutomu, Waki Yoshihiro. Metallothionein expression in zinc-treated cartilage precursor ATDC5 cells Biomedical Research on Trace Elements. 2021.06; 32(1); 23-29
- 4. Kim S, Nassar M, Tamura Y, Hiraishi N, Jamleh A, Nikaido T, Tagami j. The Effect of Reduced Glutathione on the Toxicity of Silver Diamine Fluoride in Rat Pulpal Cells Journal of Applied Oral Science. 2021.04; 29(e20200859); 1-8
- 5. Nishimaki Mayuri, Nassar Mohannad, Tamura Yukihiko, Hiraishi Noriko, Dargham Ahmad, Nikaido Toru, Tagami Junji. The effect of surface pre-reacted glass-ionomer filler eluate on dental pulp cells and mineral deposition on dentin: In vitro study EUROPEAN JOURNAL OF ORAL SCIENCES. 2021.03; 129(3); e12777

- 1. Yukihiko Tamura, Pornpoj Fuangtharnthip. Regulation of metallothionein gene expression in dental pulp cells. ADA FDI 2021 World Dental Congress 2021.09.26 オンライン (Sydney, Australia)
- 2. 田村幸彦, Pornpoj Fangtharnthip, 小野真一, 脇能広. アムロジピンによる歯肉細胞におけるメタロチオネインの発現誘導. 第 48 回日本毒性学会学術年会 2021.07.07 Hybrid Meeting
- 3. Supachatwong Chayapong, Hidemi Nakata, Yukihiko Tamura, Shinji Kuroda. Effect of Static Magnetic Field on MC3T3-E1 Cells Differentiation via TGF- β Pathway. Academic of Osseointegration 36th Annual Meeting 2021 2021.03.12 $\exists \nu \exists \ell \nu$
- 4. Jason Hou, Yukihiko Tamura, Yuta Takahashi, Shinji Kuroda, Hidemi Nakata. Effects of Selenium Nanoparticles on Osteoblastic Differentiation and Antimicrobial Effects on Pathogen of Peri-Implantitis. Academic of Osseointegration 36th Annual Meeting 2021 2021.03.12 オンライン

Biochemistry

Professor Testuro Watabe Associate Professor Miki Yokoyama Assistant Professor Katarzyna Anna Podyma-Inoue, Miho Kobayashi Technical staff Megumi Naito Part-time Lecturer Yasuhiro Yoshimatsu, Jun Ishihara, Kazuki Takahashi (2020/3/31) Collaborative Researcher Kazuki Takahashi (2020/4/1) Graduate student Hitomi Takahashi, Ikumi Wakabashi, Maki Saito, Kashio Fujiwara, Hisae Katsumata, Noriko Shibao

(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 lympangiognesis

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 antiogenesis and lymphaniogenesis 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 detyrosination enzyme

VASH1, which is induced expression by VEGF stimulation in endothelial cells, was re-identified as a enzyme of detyrosination. Detyrosination is one of the post-translational modification of microtubules, It is known that detyrosinated microtubules play 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 detyrosination enzyme in physiological function of VASH1.

(5) Structural basis for chaperone-mediated autophagy

A mechanism for appropriately removing unnecessary proteins is indispensable for maintaining intracellular homeostasis. Intracellular proteolytic reactions can be broadly divided into lysosome-mediated pathways and proteasome-mediated pathways. In the lysosome-mediated pathway, lysosomes often fuse with vesicles containing target proteins (endosomes, phagosomes, autophagosomes, etc.). In contrast, chaperone-mediated autophagy (hereinafter abbreviated as CMA) has a unique mode in which the target protein is recruited by the chaperone onto the lysosomal membrane and directly incorporated into the lysosome. CMA was discovered as a phenomenon that is activated by serum removal, but in recent years it has been reported that CMA plays an important role in maintaining pluripotency of embryonic stem cells and maintaining the function of hematopoietic stem cells. On the other hand, it has been pointed out that CMA dysfunction causes neurodegenerative diseases or myopathy, and conversely, excessive CMA causes malignant transformation in cancer. However, while research on the functional importance of CMA is progressing, many unclear points remain in the molecular mechanism of CMA.

Lysosomal-associated membrane protein 2A (LAMP2A) provides a scaffold for the substrate protein chaperone to bind to the lysosomal membrane in CMA. LAMP2A is a single-transmembrane glycoprotein that is abundant in the lysosomal membrane. Most of the LAMP2A protein resides on the luminal side of the lysosome, and the short peptide portion of only 11 amino acid residues protruding to the cytoplasm side serves as a scaffold. The lumen side of LAMP2A is composed of two homologous subdomains, and we have reported by crystallographic analysis that the subdomains have a unique triangular prism structure (\Box -prism) (BBRC, 2016). However, it was unclear what structure the entire molecule of LAMP2A would take to provide a scaffold.

We analyzed the homophilic interaction of LAMP2A molecules, using expanded genetic code technologies that generate photo-crosslinking and/or steric hindrance at specified interfaces. As a result, it was clarified that LAMP2A has a structure in which specific faces of the triangular prisms of the subdomain close to the membrane face each other, and that CMA activity decreases when this structure cannot be obtained. This result suggests that the interaction between LAMP2A within the lysosomal lumen defines the proper arrangement of the short peptide moiety on the lysosomal membrane, which is a great clue to elucidate the molecular mechanism of CMA centered on LAMP2A (Autophagy, 2021).

(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. Shingo Kodama, Katarzyna A Bdyma-Inoue, Toshihiro Uchihashi, Kyoko Kurioka, Hitomi Takahashi, Akinari Sugauchi, Kazuki Takahashi, Toshihiro Inubushi, Mikihiko Kogo, Susumu Tanaka, Tetsuro Watabe. Progression of melanoma is suppressed by targeting all transforming growth factor β isoforms with an Fc chimeric receptor. Oncol Rep. 2021.09; 46(3);
- 2. Yoshiya Asano, Daisuke Okano, Michiya Matsusaki, Tetsuro Watabe, Yasuhiro Yoshimatsu, Mitsuru Akashi, Hiroshi Shimoda. Construction of transplantable artificial vascular tissue based on adipose tissuederived mesenchymal stromal cells by a cell coating and cryopreservation technique. Scientific Reports. 2021.09; 11(1); 17989
- 3. Fujimoto M, Kamiyama M, Fuse K, Ryuno H, Odawara T, Furukawa N, Yoshimatsu Y, Watabe T, Prchal-Murphy M, Sexl V, Tahara H, Hayakawa Y, Sato T, Takeda K, Naguro I, Ichijo H. ASK1 suppresses NK cell-mediated intravascular tumor cell clearance in lung metastasis. Cancer science. 2021.04; 112(4); 1633-1643
- 4. Terasawa K, Kato Y, Ikami Y, Sakamoto K, Ohtake K, Kusano S, Tomabechi Y, Kukimoto-Niino M, Shirouzu M, Guan JL, Kobayashi T, Iwata T, Watabe T, Yokoyama S, Hara-Yokoyama M. Direct homophilic interaction of LAMP2A with the two-domain architecture revealed by site-directed photo-crosslinks and steric hindrances in mammalian cells. Autophagy. 2021.04; 1-19
- 5. Nishino K, Yoshimatsu Y, Muramatsu T, Sekimoto Y, Mitani K, Kobayashi E, Okamoto S, Ebana H, Okada Y, Kurihara M, Suzuki K, Inazawa J, Takahashi K, Watabe T, Seyama K. Isolation and characterisation of lymphatic endothelial cells from lung tissues affected by lymphangioleiomyomatosis. Scientific reports. 2021.04; 11(1); 8406
- 6. Shintaro Sakakitani, Katarzyna A Podyma-Inoue, Rina Takayama, Kazuki Takahashi, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiroyuki Harada, Tetsuro Watabe. Activation of β 2adrenergic receptor signals suppresses mesenchymal phenotypes of oral squamous cell carcinoma cells. Cancer Science. 2021.01; 112(1); 155-167
- 7. Iwasaki K, Akazawa K, Nagata M, Komaki M, Peng Y, Umeda M, Watabe T, Morita I. Angiogenic Effects of Secreted Factors from Periodontal Ligament Stem Cells. Dentistry journal. 2021.01; 9(1);
- 8. Kobayashi M, Wakabayashi I, Suzuki Y, Fujiwara K, Nakayama M, Watabe T, Sato Y. Tubulin carboxypeptidase activity of vasohibin-1 inhibits angiogenesis by interfering with endocytosis and trafficking of pro-angiogenic factor receptors Angiogenesis. 2021.02; 24(1); 159-176

[Misc]

1. The novel anti-angiogenic mechanism: the role of vasohibin-1 in suppression of angiogenic-receptor endocytosis via the post-translational modification of microtubules 2021.12; 44(2); 65-69

[Conference Activities & Talks]

1. Tetsuro Watabe. Roles of signaling and transcriptional networks during maintenance of vascular systems. 第 44 回日本分子生物学会 2021.12.02 Yokohama

- 2. Tet
suro Watabe. Roles of TGF- β family signals during progression of oral cancer.
. 13th BMP Conference 2021.10.27 web
- 3. Yasuhiro Yoshimatsu, Kentaro Maeda, Naoya Takahashi, Ikumi Wakabayashi, Shiori Kimuro, Kazuki Takahashi, Miho Kobayashi, Katarzyna A. Inoue, Masanori Hirashima, Kohei Miyazono, Tetsuro Watabe . Role of an ETS family transcription factor in endothelial mesenchymal transition (EndoMT)-driven EMT. 第 80 回日本癌学会学術総会 2021.10.01
- 4. Katarzyna A. Inoue, Kazuki Takahashi, Sakakitani Shintaro, Daizo Koinuma, Akinari Sugauchi, Maki Saito, Atsushi Kaida, Yasuhiro Yoshimatsu, Toshihiro Uchihashi, Masahiko Miura, Kohei Miyazono, Tetsuro Watabe. Activation of epithelial-mesenchymal transition program in oral cancer cells under TGF- β -induced cell cycle arrest. TGF- β Superfamily Conference: Signaling in Development and Disease (FASEB) 2021.07.20
- 5. Miho Kobayashi, Kashio Fujiwara, Ikumi Wakabayashi, Yasuhiro Suzuki, Masanori Nakayama, Yasufumi Sato, Tetsuro Watabe. Novel anti-angiogenic mechanism of VASH1 through the modification of microtubules. CVMW2020 心血管代謝週間(第 28 回日本血管生物医学会学術集会) 2021.03.12 Web
- 1. Maki Saito, Kazuki Takahashi, Katarzyna A. Inoue, Shintaro Sakakitani, Toru Konishi, Akinari Sugauchi, Atsushi Kaida, Daizo Koinuma, Toshihiro Uchihashi, Masahiko Miura, Kohei Miyazono, Tetsuro Watabe. Oral cancer cells under TGF- β -induced cell cycle arrest exhibit motile phenotypes through induction of epithelial-mesenchymal transition (EMT). The 44th Annual Meeting of the Molecular Biology Society of Japan 2021.12.02
- 2. The regulatory mechanism of signaling through the modulating intracellular trafficking by vasohibin-1 and its role in angiogenesis. 2021.12.01
- 3. The mechanism of malignant transformation through oral cancer derived exosomes. 2021.12
- 4. Katarzyna A Podyma-Inoue, Shintaro Sakakitani, Kazuki Takahashi, Hiroyuki Harada and Tetsuro Watabe. Development of novel therapeutic agents targeting epithelial-mesenchymal transition of oral squamous cell carcinoma cells. The 66th Congress of the Japanese Society of Oral and Maxillofacial Surgeons 2021.11.13
- 5. Kazuki Takahashi, Katarzyna A. Inoue, Shintaro Sakakitani, Toru Konishi, Akinari Sugauchi, Maki Saito, Atsushi Kaida, Daizo Koinuma, Yasuhiro Yoshimatsu, Toshihiro Uchihashi, Mikihiko Kogo, Masahiko Miura, Kohei Miyazono, Tetsuro Watabe . Oral cancer cells under TGF- β -induced cell cycle arrest exhibit motile phenotypes through induction of EMT. The 80th Annual Meeting of the Japanese Cancer Society 2021.10.01
- 6. The novel anti-angiogenic mechanism: the role of vasohibin-1 in suppression of angiogenic-receptor endocytosis via the post-translational modification of microtubules. JSL2021 2021.06.04
- 7. Yuta Ikami, Hiroyuki Harada, Tetsuro Watabe, Miki Yokoyama. Role of chaperone-mediated autophagy in migration of oral squamous cell carcinoma cells. The 39th Annual Meeting of Japanese Society of Oral Oncology 2021.01.28 WEB

Cell Signaling

Professor(Principal Investigator)Tomoki NAKASHIMA Assistant Professor Mikihito 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]

- Lin Liu, Hiroyuki Koike, Takehito Ono, Shinichiro Hayashi, Fujimi Kudo, Atsushi Kaneda, Hiroyuki Kagechika, Ichiro Manabe, Tomoki Nakashima, Yumiko Oishi. Identification of a KLF5-dependent program and drug development for skeletal muscle atrophy. Proc Natl Acad Sci U S A. 2021.08; 118(35);
- Guo L, Iida A, Bhavani GS, Gowrishankar K, Wang Z, Xue J, Wang J, Miyake N, Matsumoto N, Hasegawa T, Iizuka Y, Matsuda M, Nakashima T, Takechi M, Iseki S, Yambe S, Nishimura G, Koseki H, Shukunami C, Girisha KM, Ikegawa S. Deficiency of TMEM53 causes a previously unknown sclerosing bone disorder by dysregulation of BMP-SMAD signaling. Nature Communications. 2021.04; 12(1); 2046
- 3. Noriko Komatsu, Stephanie Win, Minglu Yan, Nam Cong-Nhat Huynh, Shinichiro Sawa, Masayuki Tsukasaki, Asuka Terashima, Warunee Pluemsakunthai, George Kollias, Tomoki Nakashima, Hiroshi Takayanagi. Plasma cells promote osteoclastogenesis and periarticular bone loss in autoimmune arthritis. J Clin Invest. 2021.03; 131(6);

4. Sasaki Fumiyuki, Hayashi Mikihito, Ono Takehito, Nakashima Tomoki. The regulation of RANKL by mechanical force(和訳中) Journal of Bone and Mineral Metabolism. 2021.01; 39(1); 34-44

[Misc]

1. Fumiyuki Sasaki, Mikihito Hayashi, Takehito Ono, Tomoki Nakashima. The regulation of RANKL by mechanical force. J Bone Miner Metab. 2021.01; 39(1); 34-44

Periodontology

From January. 2021 [Professor] Takanori Iwata [Photoperiodontics Professor] Akira Aoki [Associate Professor] Sayaka Katagiri (Apr~) [Junior Associate Professor] Yasuo Takeuchi [Assistant Professor] Koji Mizutani, Yuichi Ikeda, Takahiko Shiba [Specially appointed Assistant Professor] Risako Tanimoto(~Oct), Hideyuki Takamatsu [Clinical Fellow] Shunsuke Fukuba, Kohei Takeda, Yujin Ohsugi, Yosuke Tsuchiya, Munehiro Okada, Hiromi Niimi (Apr~), Tomoaki Kariya (Nov~), Ayako Kawada(Nov~)

[Graduate Students] Yutaro Kitanaka (~Mar), Kohei Nohara (~Mar), Kazuki Watanabe (~Mar), Keiji Komatsu (~Mar), Ryo Satou, Daiki Tanaka, Takashi Nemoto, Hiromi Kominato, Natsumi Saito, Ryo Mikami, Tsuyoshi Shimohira, Shunsuke Takeuchi, Masahiro Hatasa, Anhao Liu, Shu Takemura, Keita Nakagawa, Takahiko Nagai, Masahiro Hakariya, Kazuki Morita, Lisa Yagasaki, Mako Yokose, Sumiko Yoshida, Sakura Hayashi, Jiacheng Wang, Peiya Lin, Shiwei Sun(Apr~), Ryota Kobayashi (Apr~), Airi Sakaniwa (Apr~), Tatsuro Seike (Apr~), Kanji Tabata (Apr~), Keita Toyoshima (Apr~), Daichi Yamaki (Apr~)

【Adult graduate student】
Fumihoko Kimura (Apr ~), Ito Hirasawa (Apr ~)
【Graduate Research Student】
Takeshi Iida (~Mar), Mai Kitamura, Yuri Ito, Aiko Fujino, Kazuki Miyata, Miki Dobashi,
Akane Ochiai(Apr~), Sakurako Kawamoto Yumine Kiuchi, Hiroe Nakashima, Yuya Hamada,
Takahiro Naito (Apr~)
【Clinical Professor】 Hiroaki Kobayashi, Shigenari Kikuchi, Hiroaki Tsutioka
【Adjunct Lecturer】 42
【Registered dentist】 71
【Assistant Administrative Staff】 Saori Hashimoto (~ May), Hiroka Watanabe (Aug~)

(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 application of lasers/LEDs in periodontal therapy

(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]

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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 improtant 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. Wang Yunting, Yoshida Yutaka, Kamiie Junichi, Shiwaku Yukari, Suzuki Osamu, Furuya Maiko, Yokota Kotone, Kanetaka Hiroyasu, Yokoi Taishi, Kawashita Masakazu. Proteomic identification of serum proteins to induce osteoconductivity of hydroxyapatite(和訳中) Dental Materials Journal. 2021.11; 40(6); 1428-1436
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- 2. H. Chigama, M. Kawashita, M. Furuya, K. Yokota, H. Kanetaka. Effect of antibacterial metal-doped raw silk fabric on proliferation and differentiation of pre-osteoblast. The 16th International Workshop on Biomaterials in Interface Science 2021.09.28
- 1. Taishi Yokoi, Masakazu Kawashita. Synthesis of octacalcium phosphate with incorporated fluorescent molecules. The 78th General Session of the Japanese Society for Dental Materials and Devices 2021.10.17
- 2. Masakazu Kawashita. Research on ceramic-based dental materials. The 78th General Session of the Japanese Society for Dental Materials and Devices 2021.10.16
- 3. T. Yokoi, M. Kawashita. Hydroxyapatite mesocrystal formation from octacalcium phosphate with incorporated carboxylate ions. The 16th International Workshop on Biomaterials in Interface Science 2021.09.28

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 Education Research and Development)

Research Fellow of Japan Society for the Promotion of Science: Aya Isumi, PhD; Satomi Doi, PhD Project Assistant Professor: Yui Yamaoka, PhD

(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 indiviual factors (e.g., genetic factor) and environmental factors, especially social detreminants, their inter actions; 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 writeing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or preogran to prevent diseases in a real life setting.

(2) Research

The main focus of the department is as follows:

Social epidemiology (impact of social inequality, social capital, social network, and social support on health)
 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)
- 8. Infectious Disease Epidemiology (descriptive epidemiology about COVID-19, research on behavioral change)

(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 indiviual factors (e.g., genetic factor) and environmental factors, especially social detreminants, their inter actions; make causal inference applying a life-course perspective on diseease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statics; acquire attitudes toward social contribution through writeing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or preogram 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 adnvaced analysis (multilevel analysis, propensity score moathcing, multiple imputation, etc)

- 7. justify the research question logically, in scientific writing in English.
- 8. develop an intervention (policy or program) and design a study protocol to assess its effectiveness.

(4) Publications

[Original Articles]

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- 5. Tani Y, Isumi A, Doi S, Fujiwara T^{*}. Associations of Caregiver Cooking Skills with Child Dietary Behaviors and Weight Status: Results from the A-CHILD Study. Nutrients. 2021.12; 13(12);
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- 11. Ishii E, Nawa N, Matsui H, Otomo Y, Fujiwara T. Response to the Letter to the Editor on "Comparison of disease patterns and outcomes between non-Japanese and Japanese patients at a single tertiary emergency care center in Japan". Journal of epidemiology. 2021.11;
- 12. Sagawa Y, Ogawa T, Matsuyama Y, Nakagawa Kang J, Yoshizawa Araki M, Unnai Yasuda Y, Tumurkhuu T, Ganburged G, Bazar A, Tanaka T, Fujiwara T, Moriyama K. Association between Smoking during Pregnancy and Short Root Anomaly in Offspring. International Journal of Environmental Research and Public Health. 2021.11; 18(21); 11662

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Department of Parasitology & Tropical Medicine

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(1) Outline

Parasitic diseases continue to have a significant impact on people's lives in many countries of the world, and their control is an important public health challenge. Malaria, one of the world's major infectious diseases, is a parasitic disease that infects more than 200 million people worldwide and kills 600,000 people annually, mainly in Africa. The mortality rate is particularly high among infants under the age of five, with one child dying every two minutes. Although more than 200 million people are infected with schistosomiasis worldwide, the disease is regarded as a "neglected tropical disease" for which no effective countermeasures have been taken. We will continue our research on these parasitic diseases with the goal of elucidating the mechanisms of infection and their interactions with the host. These basic research will also lead to the development of vaccines and drugs in collaboration with researchers around the world, including those in endemic areas.

This department was established primarily to conduct research in the field of zoology, and has a long history of active research on helminths, among other parasitic diseases. In 2021, Dr. Ishino joined this department as a professor and focus on malaria research, together with other important parasitic diseases, such as schistosomiasis. Our aim of malaria research is the elucidation of the molecular mechanisms of parasite infection via specific interaction between parasite and host molecules. To achieve this, research will be conducted on Plasmodium berghei, a rodent malaria parasite, and Plasmodium falciparum, which cause lethal symptoms in humans, by reverse genetics, live imaging techniques, and transcriptome analyses. In addition, the mechanisms of drug resistance acquisition and the development of new vaccines will also be conducted. In the case of schistosomiasis, we are studying the mechanism of small RNAs transfer between parasites by extracellular vesicles. In addition, field studies are being conducted in endemic areas such as Ghana and Laos, with the aim of developing new diagnostic tools and vaccines for parasitic diseases.

(2) Research

(1) Elucidation of the host cell infection mechanism of Plasmodium:

Plasmodium efficiently invades and infects variously different cells in its life cycle. In particular, we will focus on elucidating the mechanism of sporozoites, which are responsible for malaria transmission from mosquitoes to humans, reach and infect hepatocytes. We have previously identified several secreted proteins involved in sporozoite infection of the liver by reverse-genetic technology of Plasmodium berghei, and have elucidated part of the mechanisms how sporozoites reach the hepatocytes. In the future, we aim to comprehensively understand the infection mechanism from the viewpoint of host-parasite interaction. The same approach will lead to the elucidation of the mechanisms of infection of erythrocytes and sexual reproduction in the mosquito body. Based on the knowledge obtained from research, we aim to develop methods to prevent infection/transmission in collaboration with researchers in endemic areas.

(2) Research on drug resistance mechanisms of Plasmodium falciparum:

egg laying by RNAi knockdown of the calpain gene family.

Artemisinin combination therapy, which combines artemisinin as the main drug and a partner drug with a different mechanism of action and half-life, is the first choice for malaria drug therapy. However, parasite resistant to artemisinin and/or partner drugs is widespread in endemic areas, and is a major obstacle to malaria eradication. We have been searching for drug-resistant genes by whole genome sequencing of clinical isolates from endemic areas. Furthermore, we are utilizing genome editing technology to analyze the function of these drug resistance genes in order to elucidate the mechanism of drug resistance acquisition. The findings obtained are expected to be useful for the development of drug treatment strategies in malaria-endemic areas.

(3) Elucidation of the egg-laying induction mechanism through extracellular vesicles of the schistosome: Schistosoma japonicum is a vasoactive species that lays eggs through the conjugation of males and females within the blood vessels. We are studying extracellular vesicles as a ways of communication for reproduction between males and females. Parasites treated with calpeptin, an inhibitor of extracellular vesicle secretion, showed a decrease in the number of egg laying as well as extracellular vesicle secretion. Based on this finding, we are currently analyzing the function of calpeptin in the secretion of extracellular vesicles and induction of

(4) Research Support for the Noguchi Memorial Institute for Medical Research in Ghana:

We will conduct parasite research focusing on malaria as a member of collaboration teams between TMDU and NMIMR. In Ghana, about 5 million people, corresponding to 1/6 of the total population, are infected with malaria annually. In order to tackle problems that have large social impacts, we will focus particularly on the transmission stage via mosquitoes, and aim to develop novel vaccines based on the basic research. In addition, the knowledge, experience and resources from endemic areas will be returned to basic research and to the education of medical students. We also accept young researchers from the NMIMR as PhD students and conducting research with them for the continuous future collaboration.

(3) Education

The number of cases of parasite infection in Japan has decreased significantly since the end of World War II due to various efforts, including the implementation of testing and drug administration by local communities, schools, and workplaces. On the other hand, recent dramatic changes in the social environment, changing dietary habits, and advances in refrigeration technology have led to major changes in the types of parasitic diseases detected in Japan. In addition, with the increase in logistics and human immigration and travel, the increase in imported cases from endemic regions of parasitic diseases has had a significant impact on the safety and security of our country. It is critical to keep our knowledge and clinical treatments up-to-date to prepare for emerging and re-emerging infectious diseases. Furthermore, the fact that the majority of neglected tropical diseases are parasitic diseases clearly indicates that parasitic diseases are an issue that needs to be addressed internationally.

In order to promote the students' ability to understand, think and discuss health and welfare in the world, this department gives lectures on Parasitology, Medical Zoology, and Tropical Medicine. In addition, during the project semester at the School of Medicine, we teach the "basis" of basic research on malaria topics. Through these educational efforts, we aim to develop future clinicians and researchers who can take leadership positions internationally in the field of health and medical care.

- 1. The actual situation of parasitic diseases in Japan and their diagnosis, treatment, etc.
- 2. The situation of parasitic diseases in the world and preventive tools
- 3. Biological understanding of the mechanism of parasite infection, together with its life cycle
- 4. Basic knowledge of tropical diseases and international health initiatives
- 5. Neglected tropical diseases and strategies taken by the international community

(4) Lectures & Courses

Lectures on parasitology and medical zoology will be given in a systematic manner. The history of the discovery and conquest of each parasitic disease will be introduced in order to foster the ability to deal with emerging and reemerging infectious diseases in the future. By observing actual parasite specimens on their own, students will spontaneously promote understanding of parasites from a biological perspective.

Through practical training, the course aims to cultivate the ability to find questions and solve them on one's own. Students are encouraged to participate in practical training and field research to cultivate the ability to find real problems and solve them.

(5) Clinical Services & Other Works

We provide advice on the diagnosis of parasitic diseases in collaboration with medical institutions both on and off campus.

Research aimed at developing diagnostic methods, therapeutics and vaccines for parasitic infections is being conducted. In addition, as part of international collaboration research, we conduct surveys as well as basic research in endemic areas to contribute to disease control, development of new vaccines, and elucidation of the mechanisms to acquire the resistance against drugs.

(6) Publications

[Original Articles]

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- Nishi Tsubasa, Shinzawa Naoaki, Yuda Masao, Iwanaga Shiroh. Highly efficient CRISPR/Cas9 system in Plasmodium falciparum using Cas9-expressing parasites and a linear donor template SCIENTIFIC REPORTS. 2021.09; 11(1); 18501
- Tachibana M, Iriko H, Baba M, Torii M, Ishino T. PSOP1, putative secreted ookinete protein 1, is localized to the micronemes of Plasmodium yoelii and P. berghei ookinetes. Parasitology international. 2021.06; 84; 102407
- 4. Taku Izumi, Hirai Tomohiro, Makiuchi Takashi, Shinzawa Naoaki, Iwanaga Shiroh, Annoura Takeshi, Nagamune Kisaburo, Nozaki Tomoyoshi, Saito-Nakano Yumiko. Rab5b-Associated Arf1 GTPase Regulates Export of N-Myristoylated Adenylate Kinase 2 From the Endoplasmic Reticulum in Plasmodium falciparum FRONTIERS IN CELLULAR AND INFECTION MICROBIOLOGY. 2021.02; 10; 610200

[Misc]

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- 1. Tomoko Ishino. Molecular mechanisms of sporozoite transmission to mammals, the target of the first malara vaccine. 難病のプロテオ医学研究 2021 The Genetics, Biology and Epidemiology of Diseases of Poverty 2021.12.11 東温市、愛媛県
- 1. Tomoko Ishino. Investigation of molecular mechanisms of Plasmodium transmission via mosquito vector. 2021.11.16

Forensic Medicine

Professor Koichi UEMURA

Associate Professor Toshihiko AKI Kana UNUMA

Assistant Professor Takeshi FUNAKOSHI

Specially Appointed Assistant Professor Ryo WATANABE

Graduate Student Tomomi SANO Shuheng Wen Sho Aoki Moeka NOMURA Miu Kajihara Miyu Komatsu Hasumi Matsuyama

(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]

- Shuheng Wen, Kana Unuma, Takeshi Funakoshi, Toshihiko Aki, Koichi Uemura. Altered cardiac mitochondrial dynamics and biogenesis in rat after short-term cocaine administration. Sci Rep. 2021.12; 11(1); 24129
- Shuheng Wen, Kana Unuma, Ryo Watanabe, Yohsuke Makino, Koichi Uemura. Forensic evaluation of fatal-suffocating retropharyngeal haematoma secondary to cervical fractures: Report of two cases. J Forensic Leg Med. 2021.11; 85; 102274
- 3. Atsushi Yamada, Kana Unuma, Nobutaka Arai, Osamu Kitamura, Koichi Uemura. Inappropriate diet and fatal malnutrition in a 10-year-old child fed only infant formula throughout life: Novel pathological diagnostic criterion for starvation via lipophagy. Forensic Sci Int. 2021.07; 325; 110896
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- 5. Momoka Ota, Takeshi Funakoshi, Toshihiko Aki, Kana Unuma, Koichi Uemura. Oxcarbazepine induces mitotic catastrophe and apoptosis in NRK-52E proximal tubular cells. Toxicol Lett. 2021.07; 350; 240-248
- 6. Shuheng Wen, Kana Unuma, Ryo Watanabe, Koichi Uemura. Diagnosis by forensic autopsy of cannula malposition resulting in fatal tension pneumothorax after attempted percutaneous tracheostomy: A short communication. J Forensic Leg Med. 2021.05; 81; 102177
- Tatsuya Norii, Yohsuke Makino, Kana Unuma, Natalie L Adolphi, Danielle Albright, David P Sklar, Cameron Crandall, Darren Braude. CT imaging of extraglottic airway device-pictorial review. Emerg Radiol. 2021.02;
- 8. Tatsuya Norii, Yohsuke Makino, Kana Unuma, Gary M Hatch, Natalie L Adolphi, Sarah Dallo, Danielle Albright, David P Sklar, Darren Braude. Extraglottic Airway Device Misplacement: A Novel Classification System and Findings in Postmortem Computed Tomography. Ann Emerg Med. 2021.01;
- 9. Tatsuhiko Murata, Kanako Noritake, Toshihiko Aki, Koichi Uemura. Possible roles of AMPK and macropinocytosis in the defense responses against Δ 9-THC toxicity on HL-1 cardiomyocytes Toxicol Rep. 2021; 8; 980-987
- 10. Moeka Nomura, Kana Unuma, Toshihiko Aki, Koichi Uemura. Sustained splenic contraction after daily cocaine administration in rats. PLoS One. 2021; 16(6); e0252853

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Molecular Epidemiology

Professor: Masaaki MURAMATSU Associate Professor : Noriko SATO Assistant Professor : Chihiro Imai

Adjunct Instructor : Sumio Sugano, Tomio Arai

Graduate Student: Hiroo Fujitani, Tadaaki Katsuta, Tong Daike Master Student: Fuko Yamada

(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. Developmental Origin of Health and Diseases
- 3. Role of nutrition on epigenetic modification and health
- 4. Genetic factors that affect the severity of pathological atherosclerosis and the development of cancer
- 5. Severe cutaneous adverse response (Stevens-Jhonson' s Syndrome) and HLA genotypes.
- 6. Application of personal genome to preemptive & preventive medicine.

(3) Education

[Doctor course] Noriko Sato: Biomedical Science

[Master course] Masaaki Muramatsu: Environmental Social Health Masaaki Muramatsu: Health Care Informatics

Noriko Sato: Molecular and Cellular Biology Noriko Sato: Introduction to Human Molecular Genetics

[Undergraduate] Noriko Sato: Bioinformatics Noriko Sato: Diet and Health

(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]

- Sato N, Fudono A, Imai C, Takimoto H, Tarui I, Aoyama T, Yago S, Okamitsu M, Mizutani S, and Miyasaka N. Placenta mediates the effect of maternal hypertension polygenic score on offspring birth weight: a study of birth cohort with fetal growth velocity data BMC Medicine. 2021.11; 19(1); 260
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- 3. Imai C, Takimoto H, Fudono A, Tarui I, Aoyama T, Yago S, Okamitsu M, Sasaki S, Mizutani S, Miyasaka N, Sato N. Application of the Nutrient-Rich Food Index 9.3 and the Dietary Inflammatory Index for assessing maternal dietary quality in Japan: a single-center birth cohort study Nutrients. 2021.08; 13; 2854
- 4. Zong Y, Tanaka M, Muramatsu M, Arai T. D-amino acid oxidase (DAO) rare genetic missense variant p.Pro103Leu and gastric cancer. Molecular and clinical oncology. 2021.03; 14(3); 58

[Works]

1. DOHaD study for preemptive medicine (Noriko Sato), Other, http://www.tmd.ac.jp/ppepi/index.html, 2019.04 - Now

[Others]

- 1. Maternal genetic risk of hypertension associated with reduced placental weight, 2021.11 2 Minute Medicine
- 2. The Placenta the Smoking Gun in Cardiovascular Disease, 2021.12 AAAS EurekAlert! The Global Source for Science News
- 3. New the rapeutic targets for the treatment and prevention of hypertension, cardiov ascular diseases, 2021.12 The Medical News.
Health Policy and Informatics

Professor:Kiyohide FUSHIMI Associate Professor:Daisuke SHINJO Graduate Student : Akira HOMMA, Kyoko HIRANO, Mihoko OTA, Risa SUZUKI, Sayomi TSUKADA, Kyunghee LEE, Graduate Research Student:Masahiro INOUE, Tomonori TAKEUCHI

(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

- Akira Honda, Nobuaki Michihata, Yoichi Iizuka, Tokue Mieda, Eiji Takasawa, Sho Ishiwata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Hirotaka Chikuda. Clinical features and early post-operative complications of isolated C2 odontoid fractures: a retrospective analysis using a national inpatient database in Japan. Eur Spine J. 2021.12; 30(12); 3631-3638
- Taisuke Jo, Nobuaki Michihata, Hayato Yamana, Kojiro Morita, Miho Ishimaru, Yasuhiro Yamauchi, Wakae Hasegawa, Hirokazu Urushiyama, Kazuaki Uda, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Takahide Nagase. Risk of drug-induced interstitial lung disease in hospitalised patients: a nested case-control study. Thorax. 2021.12; 76(12); 1193-1199
- Hiroyuki Nagano, Jung-Ho Shin, Tetsuji Morishita, Daisuke Takada, Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. Hospitalization for ischemic stroke was affected more in independent cases than in dependent cases during the COVID-19 pandemic: An interrupted time series analysis. PLoS One. 2021.12; 16(12); e0261587
- Takuaki Tani, Shinobu Imai, Kiyohide Fushimi. Impact of the COVID-19 pandemic on emergency admission for patients with stroke: a time series study in Japan. Neurol Res Pract. 2021.12; 3(1); 64

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- 6. Hayato Yamana, Shinobu Imai, Kazumi Yamasaki, Hiromasa Horiguchi, Keisuke Ario, Tatsuji Komatsu, Rie Sugimoto, Shinji Katsushima, Atsushi Naganuma, Yutaka Mano, Tsutomu Yamashita, Hiroshi Kamitsukasa, Satoru Tsuruta, Taisuke Jo, Hideo Yasunaga, Kiyohide Fushimi, Hiroshi Yatsuhashi. Prognosis of patients with liver cirrhosis: A multi-center retrospective observational study. Hepatol Res. 2021.12; 51(12); 1196-1206
- Takahisa Ogawa, Haggai Schermann, Hiroki Kobayashi, Kiyohide Fushimi, Atsushi Okawa, Tetsuya Jinno. Age and clinical outcomes after hip fracture surgery: do octogenarian, nonagenarian and centenarian classifications matter? Age Ageing. 2021.11; 50(6); 1952-1960
- Takanori Suzuki, Nobuaki Michihata, Shotaro Aso, Tetsushi Yoshikawa, Kazuyoshi Saito, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Sodium-containing versus sodium-trace preparations of IVIG for children with Kawasaki disease in the acute phase. Eur J Pediatr. 2021.11; 180(11); 3279-3286
- Yusuke Ugata, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Impact of proton pump inhibitors on mortality and severe esophageal injury after catheter ablation for atrial fibrillation: a nationwide retrospective study using propensity score matching. Heart Vessels. 2021.11; 36(11); 1730-1738
- Yutaka Kondo, Hiroyuki Ohbe, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hiroshi Tanaka, Hideo Yasunaga. Efficacy of Prophylactic Antibiotics during Extracorporeal Membrane Oxygenation: A Nationwide Cohort Study. Ann Am Thorac Soc. 2021.11; 18(11); 1861-1867
- 11. Kensuke Nakamura, Hiroyuki Ohbe, Kazuaki Uda, Kiyohide Fushimi, Hideo Yasunaga. Early rehabilitation after acute myocardial infarction: A nationwide inpatient database study. J Cardiol. 2021.11; 78(5); 456-462
- Takaaki Konishi, Michimasa Fujiogi, Nobuaki Michihata, Ryosuke Kumazawa, Hiroki Matsui, Kiyohide Fushimi, Masahiko Tanabe, Yasuyuki Seto, Hideo Yasunaga. Outcomes of Nonoperative Treatment for Gastroduodenal Ulcer Perforation: a Nationwide Study of 14,918 Inpatients in Japan. J Gastrointest Surg. 2021.11; 25(11); 2770-2777
- Hiroyuki Ohbe, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Effect of Daikenchuto for Mechanically Ventilated Patients With Enteral Feeding Intolerance: A Propensity Score-Matched Analysis Using a Nationwide Administrative Inpatient Database. JPEN J Parenter Enteral Nutr. 2021.11; 45(8); 1703-1713
- 14. Yukiyo Sakamoto, Yasuhiro Yamauchi, Taisuke Jo, Nobuaki Michihata, Wakae Hasegawa, Hideyuki Takeshima, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Takahide Nagase. In-hospital mortality associated with community-acquired pneumonia due to methicillin-resistant Staphylococcus aureus: a matched-pair cohort study. BMC Pulm Med. 2021.11; 21(1); 345
- 15. Shintaro Mandai, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Shinichi Uchida, Kiyohide Fushimi, Tatemitsu Rai. Burden of kidney disease on the discrepancy between reasons for hospital admission and death: An observational cohort study. PLoS One. 2021.11; 16(11); e0258846
- 16. Sachie Shirane, Nobuaki Michihata, Kazuhiro Yoshiuchi, Keisuke Ariyoshi, Satoru Iwase, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Evaluation of quality indicators near death in older adult cancer decedents in Japan: A nationwide retrospective cohort study. Jpn J Clin Oncol. 2021.11; 51(11); 1643-1648
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- Nishimura H, Nawa N, Ogawa T, Fushimi K, Fujiwara T. Association of ambient temperature and sun exposure with hip fractures in Japan: A time-series analysis using nationwide inpatient database. Sci Total Environ. 2021.10; 807(Pt 1); 150774
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- 22. Hiroyuki Ohbe, Yusuke Sasabuchi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Resource-rich Intensive Care Units vs. Standard Intensive Care Units on Patient Mortality: A Nationwide Inpatient Database Study. JMA J. 2021.10; 4(4); 397-404
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- 26. Takaaki Konishi, Michimasa Fujiogi, Nobuaki Michihata, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Masahiko Tanabe, Yasuyuki Seto, Hideo Yasunaga. Comparisons of postoperative outcomes after breast cancer surgery in patients with and without renal replacement therapy: a matched-pair cohort study using a Japanese nationwide inpatient database. Breast Cancer. 2021.09; 28(5); 1112-1119
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- 32. Natsuko Kanazawa, Sumio Yamada, Kiyohide Fushimi. Trends in the Use of Cardiac Rehabilitation in Japan Between 2010 and 2017 An Epidemiological Survey. Circ Rep. 2021.09; 3(10); 569-577
- Kenji Fujimori, Kunio Tarasawa, Kiyohide Fushimi. Effectiveness of polymyxin B hemoperfusion for sepsis depends on the baseline SOFA score: a nationwide observational study. Ann Intensive Care. 2021.09; 11(1); 141
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- 39. Shingo Morishita, Toshitaka Yoshii, Hiroyuki Inose, Takashi Hirai, Masato Yuasa, Yu Matsukura, Takahisa Ogawa, Kiyohide Fushimi, Atsushi Okawa, Takeo Fujiwara. Comparison of Perioperative Complications in Anterior Decompression With Fusion and Posterior Decompression With Fusion for Cervical Spondylotic Myelopathy: Propensity Score Matching Analysis Using a Nationwide Inpatient Database. Clin Spine Surg. 2021.08; 34(7); E425-E431
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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

- Ishisaka Y, Nosaka N, Mishima Y, Masuda T, Nagashima M, Tanaka Y, Yamamoto K, Yoshida M, Shigemitsu H. COVID-19 case of ventilator-induced lung injury on extracorporeal membrane oxygenation: Physicians' clinical struggle and ethical conflict in a novel pandemic. Clinical case reports. 2021.12; 9(12); e05223
- Aoyama J, Osaka M, Deushi M, Hosoya S, Ishigami A, Maehara T, Yoshida M. CXCL1-Triggered PAD4 Cytoplasmic Translocation Enhances Neutrophil Adhesion through Citrullination of PDIA1. Journal of atherosclerosis and thrombosis. 2021.12;
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- 4. Yusuke Ebana, Sou Hee Yang, Megumu Yokono, Masayuki Yoshida. Establishment of the Certified Research Ethics Professionals: An Ethical Review Expert -Translated in English from Japanese Version. JMA J. 2021.10; 4(4); 405-408
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- 9. Ikeda Sadakatsu, Kudo Ryo, Yamashita Yamato, Noji Rika, Yokobori Jyunko, Ohki Mika, Takamine Eriko, Kobayashi Yumi, Egawa Makiko, Ebana Yusuke, Kimura Koichiro, Yokoyama Kohta, Onishi Iichiro, Takemoto Akira, Kirimura Susumu, Kinowaki Yuko, Tanimoto Kosuke, Miya Fuyuki, Kano Yoshihito, Yoshida Masayuki, Miyake Satoshi. Clinical utility of multi-disciplinary expert panel discussion in precision cancer medicine ANNALS OF ONCOLOGY.. 2021.07;
- 10. Myunghee Hong, Yusuke Ebana, Jaemin Shim, Eue-Keun Choi, Hong Euy Lim, Inseok Hwang, Hee Tae Yu, Tae-Hoon Kim, Jae-Sun Uhm, Boyoung Joung, Seil Oh, Moon-Hyoung Lee, Young-Hoon Kim, Sun Ha Jee, Hui-Nam Pak. Ethnic similarities in genetic polymorphisms associated with atrial fibrillation: Far East Asian vs European populations. Eur J Clin Invest. 2021.05; e13584
- Nagaoka E, Arai H, Ugawa T, Masuda T, Ochiai K, Tamaoka M, Kurashima N, Oi K, Fujiwara T, Yoshida M, Shigemitsu H, Otomo Y. Efficacy of Multidisciplinary Team Approach with Extracorporeal Membrane Oxygenation for COVID-19 in Low Volume ECMO center. Artificial organs. 2021.03;
- 12. Dewan SMR, Osaka M, Deushi M, Yoshida M. Complement C5a-triggered differentiated HL-60 stimulates migration of THP-1 monocytic leukocytes via secretion of CCL2. FEBS open bio. 2021.03;
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- 14. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. Complement Factor D Facilitates the Development of Fatty Liver under Long-term but not Short-term High-fat Diet-feeding Conditions(和訳中) 日本循環器学 会学術集会抄録集. 2021.03; 85 回; OE113-3
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1. Yusuke Ebana, Tetsushi Furukawa. Up-to-date knowledge for genetic diagnosis of inherited arrhythmia syndrome Heart View. 2021.07; 25(7); 648-651

[Conference Activities & Talks]

- 1. 青山 二郎, 大坂 瑞子, 吉田 雅幸. CXCL1 誘導性好中球接着亢進に好中球 Peptidylarginine deiminase 4 に よる細胞 質シトルリン化を介する integrin 活性化が 関与する. 第 29 回日本血管生物医学会学術集会 (心血 管代謝週間 2021) 2021.12.10 web
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- 3. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. 補体 D 因子は長期高脂肪食条件下で脂肪肝の発生を 促進する (Complement Factor D Facilitates the Development of Fatty Liver under Long-term but not Short-term High-fat Diet-feeding Conditions). 日本循環器学会学術集会抄録集 2021.03.01

Forensic Dentistry

Professor Koichi SAKURADA Assistant Professor Hajime UTSUNO Assistant Professor Saki MINEGISHI Graduate Student Shuuji NAMIKI Graduate Student Maiko TOYA Graduate Student Nozomi SUMI

(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]

- Ohta J, Konishi-Kato Y, Minegishi S, Sakurada K. Oral bacterial DNA-based discrimination of human and canine saliva for the analysis of indistinct bite marks. Forensic science international Genetics. 2021.07; 54; 102566
- 2. Rutsuko Yamaguchi, Koichi Sakurada, Hisako Saitoh, Maiko Yoshida, Yohsuke Makino, Suguru Torimitsu, Satomi Mizuno, Hirotaro Iwase. Fatal airway obstruction due to Ludwig's angina from severe odontogenic infection during antipsychotic medication: A case report and a literature review. J Forensic Sci. 2021.04;
- 1. Jun Ohta, Masako Ohmura, Saki Minegishi, Koichi Sakurada. Evaluation of a saliva presumptive test using the α -amylase assay kit Japanese Journal of Forensic Science and Technology. 2021.07; 26(2); 231-238

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1. Koichi Sakurada. Crimes in Heisei and forensic dentistry for Reiwa Acta Criminologiae et Medicinae Legalis Japonica. 2021.06; 87(1 & 2); 20-23

[Conference Activities & Talks]

- 1. Jun Ohta, Masako Ohmura, Saki Minegishi, Koichi Sakurada. Evaluation of a saliva presumptive test using the α -amylase assay kit . 27th Annual Meeting of Japanese Association of Forensic Science and Technology 2021.11.11 Online
- 2. Tomoko Akutsu, Isao Yokota, Ken Watanabe, Kochi Toyomane, Takayuki Yamagishi, Koichi Sakurada. Development of a multiplex RT-PCR procedure for the comprehensive discrimination of forensically relevant body fluids. 27th Annual Meeting of Japanese Association of Forensic Science and Technology 2021.11.11 Online
- 3. Saki Minegishi, Syuji Namiki, Jun Ohta, Maiko Toya, Nozomi Sumi, Hajime Utsuno, Hisako Saitoh, Koichi Sakurada. Comparison of racemization rates of vital and non-vital teeth used for age estimation. 15th Annual Scientific Meeting of Japanese Society of Forensic Dental Science 2021.07.31 Kyoto
- 4. Syuji Namiki, Hajime Utsuno, Yosuke Makino, Saki Minegishi, Maiko Toya, Nozomi Sumi, Koichi Sakurada. Establishment of a method for estimating a defective mandible from skulls using postmortem CT images in a Japanese population. 15th Annual Scientific Meeting of Japanese Society of Forensic Dental Science 2021.07.31 Kyoto
- 5. Saki Minegishi, Jun Ohta, Syuji Namiki, Maiko Toya, Hajime Utsuno, Jyoji Funakoshi, Hisako Saitoh, Hirotaro Iwase, Koichi Uemura, Koichi Sakurada. Effect of non-vital teeth on age estimation by dentin racemization method. The 105th Congress of the Japanese Society of Legal Medicine 2021.06.11 In the journal
- 6. Maiko Toya, Masayoshi Kamata. Cases in which improvement of dietary intake was observed by multidisciplinary collaboration through NST intervention. 32nd Annual Meeting of the Japanese Society of Gerodontology 2021.06.11
- 7. Hajime Utsuno, Syuji Namiki, Yosuke Makino, Hisako Saitoh, Saki Minegishi, Maiko Toya, Hirotaro Iwase, Koichi Sakurada . Development of a method for estimating the nasal wing in the Japanese skull. The 105th Congress of the Japanese Society of Legal Medicine 2021.06.10 In the journal
- 8. Koichi Sakurada, Takashi Zaitsu, Naoko Seki. Unit (Society / Education) 5-year research report and future plans . Project for Promoting Leading-edge Research in Oral Science 2021.02.13 Online

[Social Contribution]

- 1. Personal identification using dental findings and others (37 cases), 2021.01.01 2021.12.31
- 2. Suginami Dental Association Lecture (Koichi Sakurada) , Suginami Dental Association, Online , 2021.04.28
- 3. Arakawa Dental Association Lecture (Koichi Sakurada) , Arakawa Dental Association , Online , 2021.12.01
- 4. 2021 Personal Identification training program (First) (Koichi Sakurada) , Tokyo Dental Association, Japan Dental Association Building , 2021.12.10

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 pharmaceutics 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

Dental Education Development

Professor: Ikuko MORIO Junior Associate Professor: Naoko SEKI Graduate Student: Mio NAITO Graduate Student: Ai OHSATO 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. Discussion Cafe (online, TMDU Global Education). April 3.
- 2. Essential Expertise for Clinical Dentistry 7 (TMDU) Aug.17-27.
- 3. International Course for Clinical Dentistry (ICCD) Sept. 1 Dec. 22.
- 4. Essential Expertise for Clinical Dentistry 7 online session for treatment planning- (TMDU)Dec. 15.

(4) Publications

- Cheng Hsin-Chung, Chang Yan-Ju, Liao Shin-Ru, Siewchaisakul Pallop, Chen Sam Li-Sheng. The impact of COVID-19 on knowledge, attitude, and infection control behaviors among dentists BMC ORAL HEALTH. 2021.11; 21(1); 584
- Seki N, Moross J, Kanamori Y, Sunaga M, Kinoshita A, Morio I. Including clinic-based English education in dental curriculum, supplemented by e-learning Journal of Medical and Dental Sciences. 2021.05; 68; 55-61

[Conference Activities & Talks]

- 1. Pravitharangul N, Matsumoto T, Suzuki S, Yoshizawa H, Miyamoto J, Chantarawaratit P, Moriyama K. Sound difference between skeletal class III malocclusion and normal groups: a preliminary study. The 80th Annual Meeting of the Japanese Orthodontic Society & The 5th International Congress 2021.11.03 Kanagawa / ondemand
- 2. Sireerat K, Seki N, Akiyama M, Araki K, Kinoshita A, Morio I. Current Status of Critical Thinking Disposition in Thai Dental Students. The 2021 IADR/AADR/CADR General Session & Exhibition / 99th General Session and Exhibition of the IADR 2021.07.23 Virtual Experience
- 1. Yuna Kanamori, Naoko Seki, Kanako Noritake, Janelle Moross, Masayo Sunaga, Ikuko Morio, Atsuhiro Kinoshita, Hiroshi Nitta. Trial of online English medical interview training for TMDU trainee residents. The 86th annual meeting of the Stomatological Society 2021.12.04 Tokyo

Oral Health Promotion

Professor Assistant Professor

Office administrator Registered Resident Graduate Student Jun Aida Takashi Zaitsu Shiho Kino Akiko Oshiro Miho Ishimaru Kotomi Ito Hiromi Nishiyama Takashi Tanemura Jin Aoki Tomoya Saito Srinarupat Jarassri Yuko Inoue Duc Ho Satomi Shimada Masuko Sayo

(1) Outline

In "clinical practice," patients are diagnosed and treated, but "epidemiology" is used to diagnose people in society, and "public health" is used to maintain and promote the health of population in society through this process. The Department of Health Promotion Dentistry aims to promote people's health through epidemiology, public health, and the clinical and field activities of Fresh Breath Clinic.

Epidemiology" is also useful for future clinicians. Epidemiology is indispensable to determine the characteristics of one's own clinic and the condition of patients objectively from data, and to provide evidence-based prevention and treatment.

Public health" is an essential study for those who work in public administration at the national, prefectural, and municipal levels. Public health dentists work to maintain and promote the health of society. It is important to acquire a public health knowledge in order to contribute to the population health.

We also conduct dental examinations at health centers and companies, as well as at the "Fresh Breath Clinic," which specializes in the treatment of halitosis. Halitosis is the third most common dental and oral health concern, and is a factor that hinders people's communication in the workplace and in the community. As a department of a university hospital specializing in halitosis treatment, which is rare in the world, we provide state-of-the-art halitosis treatment equipped with measuring instruments, which are few in Japan, to contribute to well-being. Here, as dentists and dental hygienists, we are able to acquire a few special skills.

By acquiring such special expertise, we are training people who can contribute to the promotion of people's health as "epidemiological researchers," "administrative professionals," and "clinicians who can use epidemiology to understand their own patients' conditions and determine the best treatment based on data and evidence, and who can also provide halitosis treatment," as one-of-a-kind human resources.

(2) Research

Major research themes in the field

- \cdot ~ Research on causal inference between oral and general health
- \cdot ~ Research on health inequalities and social determinants of health
- \cdot ~ Research on the construction of a diagnosis and treatment system for halitosis

(3) Education

1) Graduate education

Doctoral Course Health Promotion Dentistry Advanced Theory (1st year), Seminar (1-2 years), Research Practice (2-3 years)

Graduate School of Medical and Dental Sciences Course Advanced Theory Health Science Course

Master's Course Environmental and Social Medicine and Dentistry

2) Undergraduate education

For first-year students of the School of Dentistry Module 01 "Introduction to Dentistry": Unit 03 "Current Dentistry", Unit 04 "Early Clinical Experience Practicum

For second-year students of the School of Dentistry Module 04 "Society and Environment": Unit 02 "Lifestyle and Health

For third-year students of the School of Dentistry Module 10 "Prevention and Health Care": Unit 01 "Prevention of Oral Diseases (Lecture and Practice)", Unit 02 "Prevention of Oral Diseases (Practical Training)

For fourth-year students of the School of Dentistry Module 19 "Research Experience Practicum

For 5th and 6th year students of the School of Dentistry Module 29 "Comprehensive Clinical Practice

For fourth-year students of the Department of Oral Health Sciences Module 29: Clinical Practice

(4) Lectures & Courses

1) Graduate education

The program will train dental professionals who can conduct research and regional diagnosis from epidemiology, statistics, and public health. To this end, cutting-edge research will be conducted in an international network with an understanding of international research context.

In the advanced course, basic, clinical, and epidemiological studies on oral disease prevention and oral health promotion will be reviewed. Lectures and discussions will be held on prevention of oral diseases, dental public health, epidemiology of oral diseases, social aspects of oral diseases, primary health care and health promotion, and the relationship between health care systems and educational systems and oral health promotion.

2) Undergraduate Education

Lifestyle and Health": To help students understand the relationship between health and social systems and the environment, and to acquire the knowledge, skills, and attitudes necessary to become dentists who can help people promote their health.

Prevention of Oral Diseases I & II": To acquire the knowledge, skills, and attitudes necessary for students to

become dentists who practice prevention and health management of oral diseases.

(5) 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.

(6) Publications

- Inoue Yuko, Zaitsu Takashi, Akiko Oshiro, Ishimaru Miho, Taira Kento, Takahashi Hideto, Aida Jun, Tamiya Nanako. Association between exposure to secondhand smoking at home and tooth loss in Japan: A cross-sectional analysis of data from the 2016 National Health and Nutrition Survey Tobacco Induced Diseases. 2021.12; 19; 1-7
- 2. Upul Cooray, Richard G Watt, Georgios Tsakos, Anja Heilmann, Masanori Hariyama, Takafumi Yamamoto, Isuruni Kuruppuarachchige, Katsunori Kondo, Ken Osaka, Jun Aida. Importance of socioeconomic factors in predicting tooth loss among older adults in Japan: Evidence from a machine learning analysis. Soc Sci Med. 2021.12; 291; 114486
- Koichiro Shiba, Adel Daoud, Hiroyuki Hikichi, Aki Yazawa, Jun Aida, Katsunori Kondo, Ichiro Kawachi. Heterogeneity in cognitive disability after a major disaster: A natural experiment study. Sci Adv. 2021.10; 7(40); eabj2610
- 4. Hazem Abbas, Jun Aida, Sakura Kiuchi, Katsunori Kondo, Ken Osaka. Oral status and homebound status: A 6-year bidirectional exploratory prospective cohort study. Oral Dis. 2021.10;
- 5. Atsuhide Takesue, Yoshimune Hiratsuka, Akira Inoue, Katsunori Kondo, Akira Murakami, Jun Aida. Is social participation associated with good self-rated health among visually impaired older adults?: the JAGES cross-sectional study. BMC Geriatr. 2021.10; 21(1); 592
- 6. Mikami R, Mizutani K, Shioyama H, Matsuura T, Aoyama N, Suda T, Kusunoki Y, Takeda K, Izumi Y, Aida J, Aoki A, Iwata T. Influence of aging on periodontal regenerative therapy using enamel matrix derivative: A 3-year prospective cohort study. Journal of clinical periodontology. 2021.09; 49(2); 123-133
- Nguyen Vy Thi Nhat, Furuta Michiko, Zaitsu Takashi, Oshiro Akiko, Shimazaki Yoshihiro, Ando Yuichi, Miyazaki Hideo, Kambara Masaki, Fukai Kakuhiro, Aida Jun. Periodontal health predicts self-rated general health: A time-lagged cohort study COMMUNITY DENTISTRY AND ORAL EPIDEMIOLOGY. 2021.08;
- Maki Nii, Nobuhiro Yoda, Ramadhan Hardani Putra, Jun Aida, Keiichi Sasaki. Evaluation of the optimal hardness and thickness of music splints for wind instrument players. J Prosthet Dent. 2021.08;
- Jarassri Srinarupat, Akiko Oshiro, Takashi Zaitsu, Piyada Prasertsom, Kornkamol Niyomsilp, Yoko Kawaguchi, Jun Aida. Inequalities in Periodontal Disease According to Insurance Schemes in Thailand. Int J Environ Res Public Health. 2021.06; 18(11);
- Nishioka D, Ueno K, Kino S, Aida J, Kondo N. Sociodemographic inequities in dental care utilisation among governmental welfare recipients in Japan: a retrospective cohort study Int J Equity Health. 2021.06; 20(1); 141

- Miyaguni Y, Tabuchi T, Aida J, Saito M, Tsuji T, Sasaki Y, Kondo K. Community social support and onset of dementia in older Japanese individuals: a multilevel analysis using the JAGES cohort data BMJ Open. 2021.06; 11(6); e044631
- 12. Kusama T, Nakazawa N, Kiuchi S, Kondo K, Osaka K, Aida J. Dental prosthetic treatment reduced the risk of weight loss among older adults with tooth loss J Am Geriatr Soc. 2021.06;
- 13. Hirosaki M, Ohira T, Shirai K, Kondo N, Aida J, Yamamoto T, Takeuchi K, Kondo K. Association between frequency of laughter and oral health among community-dwelling older adults: a population-based cross-sectional study in Japan Qual Life Res. 2021.06;
- 14. Matsuyama Y, Aida J, Takeuchi K, Koyama S, Tabuchi T. Dental Pain and Worsened Socioeconomic Conditions Due to the COVID-19 Pandemic J Dent Res. 2021.06; 100(6); 591-598
- 15. Matsuyama Y, Listl S, Jurges H, Watt RG, Aida J, Tsakos G. Causal Effect of Tooth Loss on Functional Capacity in Older Adults in England: A Natural Experiment J Am Geriatr Soc. 2021.05; 69(5); 1319-1327
- 16. Takahashi A, Chiba M, Tanahara A, Aida J, Shimizu Y, Suzuki T, Murakami S, Koarai K, Ono T, Oka T, Ikeyama J, Kaneko O, Unno M, Hirose K, Ohno T, Kino Y, Sekine T, Osaka K, Sasaki K, Shinoda H. Radioactivity and radionuclides in deciduous teeth formed before the Fukushima-Daiichi Nuclear Power Plant accident Sci Rep. 2021.05; 11(1); 10335
- 17. Kusama T, Kiuchi S, Umehara N, Kondo K, Osaka K, Aida J. The deterioration of oral function and orofacial appearance mediated the relationship between tooth loss and depression among community-dwelling older adults: A JAGES cohort study using causal mediation analysis J Affect Disord. 2021.05; 286; 174-179
- Zhang W, Tsuji T, Yokoyama M, Ide K, Aida J, Kawachi I, Kondo K. Increased frequency of participation in civic associations and reduced depressive symptoms: Prospective study of older Japanese survivors of the Great Eastern Japan Earthquake Soc Sci Med. 2021.05; 276; 113827
- 19. Tashiro A, Nakaya T, Nagata S, Aida J. Types of coastlines and the evacuees' mental health: A repeated cross-sectional study in Northeast Japan Environ Res. 2021.05; 196; 110372
- 20. Koyama S, Saito M, Cable N, Ikeda T, Tsuji T, Noguchi T, Abbas H, Miyashiro I, Osaka K, Kondo K, Watt RG, Aida J. Examining the associations between oral health and social isolation: A cross-national comparative study between Japan and England Soc Sci Med. 2021.05; 277; 113895
- 21. Takashi Zaitsu, Mari Ohnuki, Yuichi Ando, Yoko Kawaguchi. Evaluation of occlusal status of Japanese adults based on functional tooth units. Int Dent J. 2021.05; 72(1); 100-105
- Masashige Saito, Naoki Kondo, Jun Aida, Junko Saito, Hisataka Anezaki, Toshiyuki Ojima, Katsunori Kondo. Differences in Cumulative Long-Term Care Costs by Community Activities and Employment: A Prospective Follow-Up Study of Older Japanese Adults. Int J Environ Res Public Health. 2021.05; 18(10);
- 23. Iwai-Saito K, Shobugawa Y, Aida J, Kondo K. Frailty is associated with susceptibility and severity of pneumonia in older adults (A JAGES multilevel cross-sectional study) Sci Rep. 2021.04; 11(1); 7966
- 24. Kino S, Aida J, Kondo K, Kawachi I. Persistent mental health impacts of disaster. Five-year follow-up after the 2011 great east Japan earthquake and tsunami: Iwanuma Study J Psychiatr Res. 2021.04; 136; 452-459
- 25. Vy Thi Nhat Nguyen, Takashi Zaitsu, Akiko Oshiro, Tai Tan Tran, Yen Hoang Thi Nguyen, Yoko Kawaguchi. Impact of School-Based Oral Health Education on Vietnamese Adolescents: A 6-Month Study International Journal of Environment Research and Public Health. 2021.03; 18(5);
- 26. Inoue Yuko Shimazaki Yoshihiro Oshiro Akiko Zaitsu Takashi Furuta Michiko Ando Yuichi Miyazaki Hideo Kambara Masaki Fukai Kakuhiro Aida Jun. Multilevel Analysis of the Association of Dental-Hygienist-Related Factors on Regular Dental Check-Up Behavior International Journal of Environment Research and Public Health. 2021.03; 18(6);
- 27. Shiba K, Kawahara T, Aida J, Kondo K, Kondo N, James P, Arcaya M, Kawachi I. Causal Inference in Studying the Long-term Health Effects of Disasters: Challenges and Potential Solutions Am J Epidemiol. 2021.03;

- Nguyen VTN, Zaitsu T, Oshiro A, Tran TT, Nguyen YHT, Kawaguchi Y, Aida J. Impact of School-Based Oral Health Education on Vietnamese Adolescents: A 6-Month Study Int J Environ Res Public Health. 2021.03; 18(5);
- Inoue Y, Shimazaki Y, Oshiro A, Zaitsu T, Furuta M, Ando Y, Miyazaki H, Kambara M, Fukai K, Aida J. Multilevel Analysis of the Association of Dental-Hygienist-Related Factors on Regular Dental Check-Up Behavior Int J Environ Res Public Health. 2021.03; 18(6);
- Igarashi A, Aida J, Yamamoto T, Hiratsuka Y, Kondo K, Osaka K. Associations between vision, hearing and tooth loss and social interactions: the JAGES cross-sectional study J Epidemiol Community Health. 2021.03; 75(2); 171-176
- Igarashi A, Aida J, Kusama T, Tabuchi T, Tsuboya T, Sugiyama K, Yamamoto T, Osaka K. Heated Tobacco Products Have Reached Younger or More Affluent People in Japan J Epidemiol. 2021.03; 31(3); 187-193
- Gero K, Aida J, Shirai K, Kondo K, Kawachi I. Dispositional Optimism and Disaster Resilience: A natural experiment from the 2011 Great East Japan Earthquake and Tsunami Social Science & Medicine. 2021.03; 273; 113777
- 33. Noguchi T, Saito M, Aida J, Cable N, Tsuji T, Koyama S, Ikeda T, Osaka K, Kondo K. Association between social isolation and depression onset among older adults: a cross-national longitudinal study in England and Japan BMJ Open. 2021.03; 11(3); e045834
- 34. Masato Nagai, Tetsuya Ohira, Masaharu Maeda, Seiji Yasumura, Itaru Miura, Shuntaro Itagaki, Mayumi Harigane, Kanae Takase, Hirooki Yabe, Akira Sakai, Kenji Kamiya. The association between body mass index and recovery from post-traumatic stress disorder after the nuclear accident in Fukushima. Sci Rep. 2021.03; 11(1); 5330
- 35. Saito M, Aida J, Cable N, Zaninotto P, Ikeda T, Tsuji T, Koyama S, Noguchi T, Osaka K, Kondo K. Cross-national comparison of social isolation and mortality among older adults: A 10-year follow-up study in Japan and England Geriatr Gerontol Int. 2021.02; 21(2); 209-214
- 36. Inoue Y, Stickley A, Yazawa A, Aida J, Koyanagi A, Kondo N. Childhood adversities, late-life stressors and the onset of depressive symptoms in community-dwelling older adults Aging Ment Health. 2021.02; 1-6
- Kiuchi S, Kusama T, Sugiyama K, Yamamoto T, Cooray U, Yamamoto T, Kondo K, Osaka K, Aida J. Longitudinal association between oral status and cognitive decline by fixed-effects analysis J Epidemiol. 2021.01;
- 38. Hikichi H, Aida J, Kondo K, Kawachi I. Six-year follow-up study of residential displacement and health outcomes following the 2011 Japan Earthquake and Tsunami Proc Natl Acad Sci U S A. 2021.01; 118(2);
- 39. Koyama T, Takeuchi K, Tamada Y, Aida J, Koyama S, Matsuyama Y, Tabuchi T. Prolonged sedentary time under the state of emergency during the first wave of coronavirus disease 2019: Assessing the impact of work environment in Japan. Journal of occupational health. 2021.01; 63(1); e12260
- 40. Masato Nagai, Tetsuya Ohira, Kokoro Shirai, Katsunori Kondo. Does variety of social interactions associate with frequency of laughter among older people? The JAGES cross-sectional study. BMJ Open. 2021.01; 11(1); e039363
- 41. Inoue Y, Zaitsu T, Akiko O, Ishimaru M, Taira K, Takahashi H, Aida J, Tamiya N. Association between exposure to secondhand smoking at home and tooth loss in Japan: A cross-sectional analysis of data from the 2016 National Health and Nutrition Survey. Tobacco induced diseases. 2021; 19; 96

[Books etc]

- 1. Kondo N, Aida J. Health in japan: Social epidemiology of japan since the 1964 tokyo olympics. Oxford University Press, 2021.01
- 2. Aida J. Oral epidemiology a textbook on oral health conditions, research topics and methods. Springer International Publishing, 2021.01

[Misc]

1. Jun Aida, Kakuhiro Fukai, Richard G Watt. Global Neglect of Dental Coverage in Universal Health Coverage Systems and Japan's Broad Coverage Int Dent J. 2021.02;

[Conference Activities & Talks]

- 1. Akiko OSHIRO, Masako Okada, Naomi yoshida, Jun aida, Kayoko Shinada. Approaches at training for dental hygienists reinstatement and new graduate in Japan. The 14th International Conference AAPD 2021 2021.11.02
- 2. Jun Aida. Causal Inference of the Relation between Oral and General Health: Beyond the Critiques. The 14th International Conference of Asian Academy of Preventive Dentistry(AAPD) 2021.10.01 オンライン
- 3. Jarassri Srinarupat, 財津 崇, 大城 暁子, 相田 潤. 成人における社会的不平等および歯数 (Social inequalities and number of teeth in adult). 日本歯科医師会雑誌 2021.07.01
- 4. Jarassri Srinarupat, 財津 崇, 大城 暁子, 相田 潤. 成人における社会的不平等および歯数 (Social inequalities and number of teeth in adult). 日本歯科医師会雑誌 2021.07.01
- 5. Nguyen Thi Nhat Vy, 財津 宗, 大城 暁子, 古田 美智子, 深井 穫博, 相田 潤, 8020 推進財団. 歯周炎は自己 評価健康状態が不良となる一因である (Periodontitis contributes to poor self-rated health). 日本歯科医師 会雑誌 2021.07.01
- 6. 相田潤. Researches in Department of Oral Health Promotion (OHP). King' s-TMDU London-Tokyo Research Exchange Event 2021.06.05 オンライン
- 8. Jun Aida. Dental public health issues relating to COVID-19. Japan-Mongolia Special Forum on COVID-19 2021.01.12 オンライン

Sports Medicine and Dentistry

[Associate Professor] Toshiaki Ueno
[Assistant Professor] Hiroshi Churei
[Specially Appointed Assistant Professor] Kairi Hayashi
[Graduate Student] Rio Kinjo, Thet Khaing Aung, Yuumi Takahashi, Chenyuan Li, Masato Sakai, Shintaro Shimizu, Thida Aung, Zhu Qiushuang, Li Zequn
[Research Student] Kaito Togawa, Akihito Kumagai, Koushiro Watanabe, Liu Chang
[Part-time Instructor] Goshi Kondo, Yukio Sasaki, Ryo Sato, Takuto Yamanaka, Sachiko Fujino, Takefumi Negoro, Kazushi Watanabe, Shintarou Fukasawa, Takahiro Shirako, Chiho Shibata, Mai Ikegawa, Misaki Suzaka
[Part-time Resident] Takaaki Fukuda, Chie Ichihara, Yoko Ohara, Akira Nagai, Asami Sakuma, Nana Kamiya-Shiota

(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/dentistryin 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 Dentitry
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 Meddicne/Dentistry: Mouthguard training facility certified by Japanese Academy of Sports Dentistry(JASD)

Clinic of Sports Dentistry in University Hospital: Medical Check-up Facility cerfitaied 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 Dentl Materials and Devices), 4.Dental specialist certified by Japanese Academy of Dental Truamatology, 7.JPSA Sports Doctor 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)

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

Rio Kinjo (MG technical instructor certified by JASD)

Yuumi Takahashi(MG technical instructor certified by JASD) Kaito Togawa (MG technical instructor certified by JASD)

(7) Publications

- 1. Hiroshi Churei, Ruman Uddin Chowdhury, Yuriko Yoshida, Gen Tanabe, Shintaro Fukasawa, Takahiro Shirako, Takahiro Wada, Motohiro Uo, Hidekazu Takahashi, Toshiaki Ueno. Use of the fiberglass reinforcement method in thermoplastic mouthguard materials to improve flexural properties for enhancement of functionality. Dent Mater J. 2021.12; 40(6); 1338-1344
- Gonda T, Yasui T, Maeda Y, Ishigami K, Ueno T, Matsumoto M, Takamata T, Koide K, Kawara M. Application of sensors to oral appliances: possibilities, problems and prospects International Journal of Sports Dentistry. 2021.10; 14(1); 34-37
- 3. Gonda T, Yasui T, Maeda Y, Ishigami K, Ueno T, Matsumoto M, Takamata T, Koide K, Kawara M. Literature review on relationship between body balance and occlusal status International Journal of Sports Dentistry. 2021.10; 14(1); 38-58
- 4. Gonda T, Yasui T, Maeda Y, Ishigami K, Ueno T, Matsumoto M, Takamata T, Koide K, Kawara M. Proposal for social insurance coverage of sports mouthguards in Japan: survey of oral health professionals International Journal of Sports Dentistry. 2021.10; 14(1); 59-62
- 5. Kairi Hayashi, Ruman Uddin Chowdhury, Nafees Uddin Chowdhury, Abhishekhi Shrestha, Ishan Pradhan, Sharika Shahrin, Yukako Toyoshima, Gen Tanabe, Yuriko Yoshida, Kaito Togawa, Hiroshi Churei, Toshiaki Ueno. Thickness change and deformation of custom-made mouthguards after two years of use by Bangladeshi field hockey players. Dent Traumatol. 2021.08; 37(4); 617-622
- 6. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Correction: Aung et al. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications. Polymers 2021, 13, 1879 POLYMERS. 2021.07; 13(14); 2280
- 7. Tanabe G, Hasunuma T, Inai Y, Takeuchi Y, Kobayashi H, Hayashi K, Shimizu S, Kamiya N, Churei H, Sumita Y, Suzuki K, Moriya N, Ueno T. Potential assessment of dehydration during high-intensity training using a capacitance sensor for oral mucosal moisture: evaluation of elite athletes in a field-based survey. Chemosensors. 2021.07; 9(8); 196
- 8. Tanabe G, Churei H, Takeuchi Y, Hayashi K, Kanasaki A, Yoshida Y, Toma J, Araie Y, Ueno T. Antibacterial effect of a disinfectant spray for sports mouthguards on Streptococcus sobrinus Dental research journal. 2021.07; 18; 59
- 9. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications POLYMERS. 2021.06; 13(11); 1879
- Hayashi K, Churei H, Shrestha A, Suzuki T, Matsubara H, Otomaru T, Sumita YI, Uddin Chowdhury R, Uddin Chowdhry N, Ueno T. Fabrication technique of obturator-type sports mouthguard for a patient who had undergone maxillectomy and its speech intelligibility assessment: A case report. Journal of Prosthodontic Research. 2021.06; 65(2); 261-265
- 11. Toshiaki Ueno, Yukako Toyoshima. The Relationship Between the State of Engagement in Exercise/ Sports and Medical Evaluations: Dental Evaluations Japan Sport Association/ Follow up study on the TOKYO1964 Olympians. 2021.03; 26-27
- Kinjo Rio, Wada Takahiro, Churei Hiroshi, Ohmi, Takehiro, Hayashi Kairi, Yagishita Kazuyoshi, Uo Motohiro, Ueno Toshiaki. Development of a Wearable Mouth Guard Device for Monitoring Teeth Clenching during Exercise Sensors. 2021.02; 21(4); 1503

13. Nana Shiota, Atsuhiro Kinoshita, Masayo Sunaga, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tomoko Fukai, Masaru Matsumoto, Toshikazu Yasui, Toshiaki Ueno. Effectiveness of computer-assisted learning in sports dentistry: Studies over a multiple-year period and at two universities. Eur J Dent Educ. 2021.01; Online ahead of print;

[Conference Activities & Talks]

- 1. Aung TK, Churei H, Tanabe G, Kinjo R, Li C, Tun PS, Ueno T. Shock absorption of 3D-printed ABS and fabric for sports faceguard. FDI 2021 World Dental Congress 2021.09.26 Virtual online
- Tanabe G, Hattori M, Obata S, Takahashi Y, Sumita YI, Ueno T. Psychoacoustic analysis of a clarinet performance with soft type custom-made lip shield to prevent mucosal erosion of lower lip: A case study. 39th Annual PAMA International Symposium 2021.06.24 Live Event on Virtual Platform
- 3. Hattori M, Tanabe G, Nishiyama A, Churei H, Tanase R, Sumita YI. Use of 4D facial scanner in dentistry for musician: Facial surface analysis while recorder playing. 39th Annual PAMA International Symposium 2021.06.24 Live Event on Virtual Platform

Educational System in Dentistry

Chair of Department Jun TSURUTA Associate Professor Jun TSURUTA Part time lecturer Richard Foxton

(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.

Another topics for our department are XR education and Ineterprofessional education.

Implementing these subject and activities, we try to find the most appropriate use of educational tools and evaluation system.

(2) Research

1) Development of evaluation method for dental education curriculum

- 2) Development of the program for dental clinical skills improvement by the virtual reality simulation system
- 3) Development of evaluation system for Dental education system

4) The development of inspection method of the validity and reliability of the evaluation system for dental education

(3) Clinical Performances

none

(4) **Publications**

[Original Articles]

1. Akitaka Hattoria, Ken-ichi Tonami, JunTsuruta, Masayuki Hideshima, Yasuyuki Kimura, Hiroshi Nitta, Kouji Araki. Effect of the haptic 3D virtual reality dental training simulator on assessment of tooth preparation Journal of Dental Sciences . 2022.01; 17(1); 514-520

[Books etc]

1. White paper on Medical Education 2022(Japan). 2022.07 (ISBN : 978-4867058169)

[Conference Activities & Talks]

1. Mitsuyuki Numasawa, Nobutoshi Nawa, Kumiko Yamaguchi, Kanako Noritake, Jun Tsuruta, Mina Nakagawa. Comparison of readiness for interprofessional learning among medical, dental, and nursing students before the start of clinical practice. AMEE 2022 2022.08.29 The Virtual Conference

- 2. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Kanako Noritake, Janelle Moross, Jun Tsuruta. Remote interprofessional learning during the COVID-19 pandemic for younger undergraduate students' early exposure to medicine . AMEE 2022 2022.08.27
- 1. Remote interprofessional learning for younger undergraduate students' early exposure. 2022.08.05
- 2. Y2021 report of university facility for self-development of dental clinical skills. 2022.07

Educational Media Development

Professor KINOSHITA Atsuhiro Assistant Professor SUNAGA Masayo Graduate Student AKIYAMA Kyoko Graduate Student HARADA Yusuke(~ March) Graduate Student TAKENOUCHI Akane(~ March) Graduate Student URAKAWA Ayaka(~ March)

(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. In 2021, live broadcast lectures were implemented using zoom between clinics and students' homes. 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.

 \cdot We examine the effects of utilization and evaluation method with SIMROID, a patient robot for attitude education and communication education with patients in dentistry.

(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. Seki Naoko , Moross Janelle , Kanamori Yuna , Sunaga Masayo , Kinoshita Atsuhiro , Morio Ikuko. Including clinic-based English education in dental curriculum, supplemented by e-learning J. Med. Dent. Sci.. 2021.05; 68; 55-61
- Yusuke Harada, Masayo Sunaga, Yasuo Takeuchi, Koji Mizutani, Sayaka Katagiri, Yuichi Ikeda, Akira Aoki, Takanori Iwata, Atsuhiro Kinoshita. Standardization of examiners using a dental model for pocket probe training: Adequacy of evaluation with model and standard accuracy rate of skilled examiners J. Med. Dent. Sci.. 2021.02; 68; 49-54
- 3. Nana Shiota, Atsuhiro Kinoshita, Masayo Sunaga, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tomoko Fukai, Masaru Matsumoto, Toshikazu Yasui, Toshiaki Ueno. Effectiveness of computer-assisted learning in sports dentistry: Studies over a multiple-year period and at two universities. Eur J Dent Educ. 2021.01; Online ahead of print;

[Conference Activities & Talks]

1. Kittichai Sireerat, Naoko Seki, Masako Akiyama, Kouji Araki, Atsuhiro Kinoshita, Ikuko Morio. Current Status of Critical Thinking Disposition in Thai Dental Students. The 2021 IADR/AADR/CADR General Session & Exhibition, July 21-24 2021.07.23 Online

Insured Medical Care Management

Professor Masumi AI Associate Professor Minato YOKOYAMA Graduate Student Masako ARIMOTO

(1) Outline

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

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

(2) Research

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

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

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

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

(3) Education

The staff has been in charge for education of social health insurance system and rules for insured medical treatment at the TMDU medical hospital.

A doctor course student is in her third year.

(4) Lectures & Courses

*Providing practical supports for an appropriate insured medical care in the clinical fields. Providing individual support for an appropriate billing for medical service fees at the medical hospital. We also focus on development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

(5) Clinical Services & Other Works

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

(6) Clinical Performances

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

(7) **Publications**

[Original Articles]

- Yokoyama Minato, Ishioka Junichiro, Toba Mikayo, Fukushima Hiroshi, Tanaka Hajime, Yoshida Soichiro, Matsuoka Yoh, Ai Masumi, Fushimi Kiyohide, Fujii Yasuhisa. Trends and safety of robot-assisted partial nephrectomy during the initial 2-year period after government approval in Japan: A nationwide database study from 2016 to 2018(和訳中) International Journal of Urology. 2021.12; 28(12); 1268-1272
- 2. Morimoto Nobuhisa, Urayama Kevin, Tanaka Akira, Ai Masumi. Relationship between dietary fibre to carbohydrate ratio and mortality risk in the NHANES INTERNATIONAL JOURNAL OF EPIDEMIOLOGY. 2021.09; 50;
- 3. Yokoyama Minato, Ishioka Junichiro, Toba Mikayo, Fukushima Hiroshi, Tanaka Hajime, Yoshida Soichiro, Matsuoka Yoh, Ai Masumi, Fushimi Kiyohide, Fujii Yasuhisa. Trends and safety of robot-assisted partial nephrectomy during the initial 2-year period after government approval in Japan: A nationwide database study from 2016 to 2018 INTERNATIONAL JOURNAL OF UROLOGY. 2021.09; 28(12); 1268-1272
- 4. Yokoyama Shinji, Remaley Alan T., Sampson Maureen, Ai Masumi, Okazaki Mitsuyo. Validation by HPLC analyses of new equations for estimating cholesterol in plasma lipoprotein subfractions BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR AND CELL BIOLOGY OF LIPIDS. 2021.09; 1866(9); 158986
- Nakamura Marie, Yamamoto Yasushi, Imaoka Wataru, Kuroshima Toshio, Toragai Ryoko, Ito Yasuki, Kanda Eiichiro, Schaefer Ernst J., Ai Masumi. Relationships between Smoking Status, Cardiovascular Risk Factors, and Lipoproteins in a Large Japanese Population Journal of Atherosclerosis and Thrombosis. 2021.09; 28(9); 942-953
- 6. Ikezaki H., Nakashima R., Ai M., Okazaki M., Kohzuma T., Schaefer E. J.. RELATIONSHIP BETWEEN DIETARY VITAMIN D INTAKE, OBESITY, AND TWENTY LIPOPROTEIN SUBCLASSES: RESULTS FROM THE KYUSHU AND OKINAWA POPULATION STUDY (KOPS) ATHEROSCLEROSIS. 2021.08; 331; E163-E164
- 7. Kayamori Y, Nakamura M, Kishi K, Miida T, Nishimura K, Okamura T, Hirayama S, Ohmura H, Yoshida H, Ai M, Tanaka A, Sumino H, Murakami M, Inoue I, Teramoto T, Yokoyama S. Comparison of the Japan Society of Clinical Chemistry reference method and CDC method for HDL and LDL cholesterol measurements using fresh sera. Practical laboratory medicine. 2021.05; 25; e00228
- 8. Nakamura Marie, Yamamoto Yasushi, Imaoka Wataru, Kuroshima Toshio, Toragai Ryoko, Ito Yasuki, Kanda Eiichiro, Schaefer Ernst J., Ai Masumi. Relationships between Smoking Status, Cardiovascular Risk Factors, and Lipoproteins in a Large Japanese Population JOURNAL OF ATHEROSCLEROSIS AND THROMBOSIS. 2021; 28(9); 942-953

[Others]

1. IRB Member, Sony Corporation 2012-

Department of Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD Junior Associate Professor: Kaoruko Seino, PhD Research Fellow: Yuri Tashiro, MPharm, MPH, PhD; AL-SOBAIHI Saber, RN, MPH, PhD;

Graduate Student: 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; Kouki Akahoshi, MD; Ayano Miyashita, MSc; Yasushi Sakuramoto MD, MPH, MPA; Hideko Sato, RN, MPH; Anderson Bendera, MD; Kamila Dost, MD; Eugene Meshi, MSc; Zia-ul-haq Safi, MD; Minh Tri Tran Xuan, MD; Thao Vi, MD; Iftikhar Halimza, MD; Angelica Latorre, MPH; Ana Kriselda Rivera, MPH Jobir Khan, PD; Uyanga Munkhdavaa; Nalusha Quadros, DMD; Pichaya Jaroongjittanusonti, MD

(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 covrage 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

- 1. Vo MTH, Nakamura K, Seino K, Vo TV.. Greater risk of negative health outcomes of older adults living alone in Vietnam: A community survey. Int J Environ Res Public Health. 2021.10; 18; 11115
- 2. Siongco KLL, Nakamura K, Seino K, Moncatar TJRT, Tejero LMS, De La Vega SAF, Bonito SR, Javier R, Tsutsui T, Tashiro Y, Al-Sobaihi S, Lorenzo FME, Canila CC. Improving Community Health Workers' Attitudes toward Collaborative Practice in the Care of Older Adults: An In-Service Training Intervention Trial in the Philippines. International journal of environmental research and public health. 2021.09; 18(19);

- 3. Alojaimy RS, Nakamura K, Al-Sobaihi S, Tashiro Y, Watanabe N, Seino K. Infection prevention and control standards and associated factors: Case study of the level of knowledge and practices among nurses in a Saudi Arabian hospital Journal of Preventive Medicine and Hygiene. 2021.07; 62; E501-E507
- 4. Alemi S, Nakamura K, Arab AS, Mashal MO, Tashiro Y, Seino K, Hemat S.. Gender-specific prevalence of risk factors for non-communicable diseases by health service use among schoolteachers in Afghanistan. International Journal of Environmental Research and Public Health. 2021.06; 18(11); 5729
- 5. Lee A, Nakamura K. Engaging diverse community groups to promote population health through Healthy City approach: analysis of successful cases in Western Pacific Region. International Journal of Environmental Research and Public Health. 2021.06; 18; 6617
- 6. Moncatar TRT, Nakamura K, Siongco KLL, Seino K, Carlson R, Canila CC, Javier RS, Lorenzo FME. Interprofessional collaboration and barriers among health and social workers caring for older adults: a Philippine case study. Human Resources for Health. 2021.04; 19; 52
- 7. Moncatar TJRT, Nakamura K, Siongco KLL, Seino K, Carlson R, Canila CC, Javier RS, Lorenzo FME. Interprofessional collaboration and barriers among health and social workers caring for older adults: a Philippine case study. Human resources for health. 2021.04; 19(1); 52
- Hasan S. M. Mahmudul, Rahman Mosiur, Nakamura Keiko, Tashiro Yuri, Miyashita Ayano, Seino Kaoruko. Relationship between diabetes self-care practices and control of periodontal disease among type2 diabetes patients in Bangladesh PLOS ONE. 2021.04; 16(4); e0249011
- 9. Shayo FK, Nakamura K, Al-Sobaihi S, Seino K. Is the source of domestic water associated with the risk of malaria infection? Spatial variability and a mixed-effects multilevel analysis. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2021.03; 104; 224-231
- Hasan SMM, Rahman M, Nakamura K, Tashiro Y, Miyashita A, Seino K. Relationship between diabetes self-care practices and control of periodontal disease among type2 diabetes patients in Bangladesh Plos ONE. 2021.03; 16(4); e0249011
- 11. Nakamura K, Seino K. Multidisciplinary, cross-sector, and transborder approach in planetary health education: a pilot-program at a graduate school. Japanese Journal of Hygiene. 2021.03; 76(1);
- 12. 中村 桂子, 清野 薫子. 大学院におけるプラネタリーヘルス教育プログラム 分野横断アプローチ 日本衛生 学雑誌. 2021.03; 76(Suppl.); S149
- Han TDT, Nakamura K, Seino K, Duc VNH, Vo TV.. Do communication patterns affect the association between cognitive impairment and hearing loss among older adults in Vietnam? Int J Environ Res Public Health. 2021.02; 18; 1603
- 14. Tran Dai Tri Han, Nakamura Keiko, Seino Kaoruko, Vo Nu Hong Duc, Thang Van Vo. Do Communication Patterns Affect the Association between Cognitive Impairment and Hearing Loss among Older Adults in Vietnam? INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH. 2021.02; 18(4);
- Shayo FK, Nakamura K, Al-Sobaihi S, Seino K.. Is the source of domestic water associated with the risk of malaria infection? Spatial variability and a mixed-effects multilevel analysis. Int J Infectious Diseases. . 2021.01; 104; 224-231
- Sumino K, Sato N, Nakashiba K, Ohisa K, Fujii K, Hashimoto A, Kataoka M, Sato H, Kobayashi Y, Masuda R, Zhang J, Kijima Y, Nakamura K, Hashimoto H.. Collaboration between acadmic institutes and public health centers under public health emergecy; lessons learnt through COVID-19 epidemic. 2021.03; 68(3); 186-194

[Books etc]

- 1. Nakajima T, Nakamura K, Nohara K, Kondoh A.. Overcoming Environmental Risks to Achieve Sustainable Development Goals. Springer Nature, 2021.11 (ISBN : 978-981-16-6249-2)
- 2. Nakamura K.. An Initiative of an Environmental Model City: Featuring Sustainable and Healthy Cities.. Springer Nature, 2021.11
3. Nakajima T, Nakamura K, Nohara K, Kondo A. Overcoming Environmental Risks to Achieve Sustainable Development Goals. 2021.09

[Misc]

1. Nakamura K. Healthy Cities as a model of value-based urban regeneration Planning and Public Management. 2021.07; 44(3); 45-50

[Conference Activities & Talks]

- 1. Nakamura K. Promoting health and well-being in cities during the COVID-19 pandemic and beyond.. 10th Global Conference on Health Promotion 2021.12.14 Geneva
- 2. Nakamura K. Evaluation of Healthy Cities around the World. Healthy City Workshop, Mongolia 2021.11.29
- 3. Nakamura K, Kiyu A, Moncatar TR. Re-Imaging Healthy Cities beyond COVID-19. The 9th Global Conference of the Alliance for Healthy Cities 2021.11.03
- 4. Nakamura K. Healthy Cities Initiatives in Japan for Today and the Future. Technical Deep Drive: Healthy Cities for All 2021.04.20 online
- 5. Nakamura K. Smarter Healthy Cities beyond COVID-19. Annual E-meeting of Healthy Cities Mongolia 2021.01.28 Ulannbaatar, online

[Others]

1. Vertual research conference on interprofessional education to advance care for older adults, 2021.09 WHO Centre for Health Development reported virtual research conference hosted by Department of Global Health Entrepreneurship, TMDU https://extranet.who.int/kobe_centre/en/news/TMDU_conference

Rehabilitation Medicine

Professor Associate Professor Adjunct Lecturer Assistant Professor Assistant Professor

Atsushi OKAWA Tomoko SAKAI Tetsuya JINNO Chisato HOSHINO Reiko YAMAGUCHI

Graduate Student

Kazuko ISSHIKI Shunsuke OHJI Ryo ONUMA Yuji TAKAHASHI Kenji HIROHATA Tomoko KAWASAKI Keigo NANJO Koji IKEMATSU Megumi NAKANO

(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

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

- Kazuko Isshiki, Tetsuya Jinno, Junya Aizawa, Ryohei Takada, Tomoko Sakai, Tetsuya Tachibana, Atsushi Okawa. Asymmetry of the Cross-sectional Area of the Gluteus Medius Muscle Persists Eight Years after Total Hip Arthroplasty for Osteoarthritis of the Hip. Prog Rehabil Med. 2021.12; 6; 20210052
- Hirohata K, Aizawa J, Ohmi T, Ohji S, Yagishita K. Characteristics of ground reaction force and frontal body movement during failed trials of single-leg lateral drop jump-landing task. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.10; 26; 8-14

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- Ryo Onuma, Tadashi Masuda, Fumihiko Hoshi, Tadamitsu Matsuda, Tomoko Sakai, Atsushi Okawa, Tetsuya Jinno. Separated center-of-pressure measurements reveal new characteristics of reduced anticipatory postural adjustments during gait initiation in patients with Parkinson's disease. Physiother Theory Pract. 2021.06; 1-10
- Aizawa Junya, Hirohata Kenji, Ohji Shunsuke, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Correlations between isokinetic knee torques and single-leg hop distances in three directions in patients after ACL reconstruction BMC SPORTS SCIENCE MEDICINE AND REHABILITATION. 2021.04; 13(1); 38
- 11. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Jinno T, Koga H, Yagishita K. Single-leg hop distance normalized to body height is associated with the return to sports after anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2021.04; 8(1); 26
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- Tomoko Sakai, Chisato Hoshino, Masanobu Hirao, Reiko Yamaguchi, Rui Nakahara, Atsushi Okawa. Rehabilitation for Patients with COVID-19: A Japanese Single-center Experience. Prog Rehabil Med. 2021.03; 6; 20210013
- 14. Tomoko Sakai, Tokumitsu Shirai, Tsutomu Oishi. Vitamins K and D deficiency in severe motor and intellectually disabled patients. Brain Dev. 2021.02; 43(2); 200-207
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Gerodontology and Oral Rehabilitation

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(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) Stress analyses of implant overdenture
- 9) Factorial analysis of complete denture prosthesis
- 10) Resilient denture lining material
- 11) CAD/CAM system for fabricating complete dentures
- 12) Evaluations of masticatory performance using color-changeable chewing gum
- 13) Development of novel restorative materials for root caries
- 14) Development of novel aesthetic, strong and ageing resistant highly translucent zirconia
- 15) 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.

(3) Clinical Performances

We manage the prosthodontic and special care departments.

(4) **Publications**

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- 3. Suzuki H, Furuya J, Hidaka R, Miyajima S, Matsubara C, Ohwada G, Asada T, Akazawa C, Sato Y, Tohara H, Minakuchi S.. Patients with mild cognitive impairment diagnosed at dementia clinic display decreased maximum occlusal force: a cross-sectional study. BMC Oral Health. 2021.12; 21(1); 665
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- 8. Tangpothitham S, Pongprueksa P, Inokoshi M, Mitrirattanakul S. Effect of post-polymerization with autoclaving treatment on monomer elution and mechanical properties of 3D-printing acrylic resin for splint fabrication. J Mech Behav Biomed Mater. 2021.11; 126; 105015
- 9. Ohara Y, Kawai H, Shirobe M, Iwasaki M, Motokawa K, Edahiro A, Kim H, Fujiwara Y, Ihara K, Watanabe Y, Obuchi S, Hirano H. Association between dry mouth and physical frailty among community-dwelling older adults in Japan: The Otassha Study. Gerodontology. 2021.11;
- Sayaka Tada, Manabu Kanazawa, Anna Miyayasu, Maiko Iwaki, Murali Srinivasan, Shunsuke Minakuchi, Gerald McKenna. Patient preferences for different tooth replacement strategies for the edentulous mandible: A willingness-to-pay analysis. J Prosthodont Res. 2021.10; 65(4); 535-540
- 11. Hatanaka Y, Furuya J, Sato Y, Uchida Y, Osawa T, Shichita T, Suzuki H, Minakuchi S. Impact of oral health guidance on the tongue-lip motor function of outpatients at a dental hospital. Gerodontology. 2021.10;
- 12. Iwasaki M, Hirano H, Motokawa K, Shirobe M, Edahiro A, Ohara Y, Kawai H, Kojima M, Obuchi S, Murayama H, Fujiwara Y, Ihara K, Shinkai S, Kitamura A. Interrelationships among whole-body skeletal muscle mass, masseter muscle mass, oral function, and dentition status in older Japanese adults. BMC geriatrics. 2021.10; 21(1); 582
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- Nakai H, Inokoshi M, Nozaki K, Komatsu K, Kamijo S, Liu H, Shimizubata M, Minakuchi S, Van Meerbeek B, Vleugels J, Zhang F. Additively Manufactured Zirconia for Dental Applications. Materials (Basel). 2021.07; 14(13); 3694

- 22. Furuya J, Suzuki H, Hidaka R, Akatsuka A, Nakagawa K, Yoshimi K, Nakane A, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Oral health status and its association with nutritional support in malnourished patients hospitalised in acute care. Gerodontology. 2021.07;
- 23. Negoro M, Kanazawa M, Sato D, Shimada R, Miyayasu A, Asami M, Katheng A, Kusumoto Y, Abe Y, Baba K, Minakuchi S. Patient-reported outcomes of implant-assisted removable partial dentures with magnetic attachments using short implants: A prospective study. Journal of prosthodontic research. 2021.07;
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- 25. Shirobe M, Watanabe Y, Tanaka T, Hirano H, Kikutani T, Nakajo K, Sato T, Furuya J, Minakuchi S, Iijima K. Effect of an Oral Frailty Measures Program on Community-Dwelling Elderly People: A Cluster-Randomized Controlled Trial. Gerontology. 2021.07; 1-10
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- Hada T, Kanazawa M, Iwaki M, Katheng A, Minakuchi S. Comparison of Mechanical Properties of PMMA Disks for Digitally Designed Dentures. Polymers. 2021.05; 13(11);
- 35. Inokoshi M, Kubota K, Yamaga E, Ueda K, Minakuchi S. Postoperative bleeding after dental extraction among elderly patients under anticoagulant therapy. Clin Oral Investig. 2021.04; 25(4); 2363-2371
- 36. Atsushi Oishi,Yohei Hama,Emi Kanai,Michiyo Miyashin. Color-changeable chewing gum to motivate chewing training with complete dentures for a male patient with hypohidrotic ectodermal dysplasia and oligodontia Pediatric Dental Journal. 2021.04; 31(1); 123-127
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- 46. Yamamoto K, Motokawa K, Yoshizaki T, Yano T, Hirano H, Ohara Y, Shirobe M, Hayakawa M, Inagaki H, Awata S, Shinkai S, Watanabe Y. Dietary variety is associated with sleep efficiency in urban-dwelling older adults: A longitudinal study. Clinical nutrition ESPEN. 2021.02; 41; 391-397
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- 54. Ryo Shimada, Manabu Kanazawa, Anna Miyayasu, Mari Asami, Thuy V. Lam, Khaing M. Thu, Daisuke Sato, Shunsuke Minakuchi. A preliminary comparison of marginal bone-level changes, survival rates, and prosthodontic maintenances between immediately and conventionally loaded two-implant overdentures with magnetic attachments. Journal of Medical and Dental Sciences. 2021.01; 68; 9-16
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- 57. Yumika Soeda, Manabu Kanazawa, Tamaki Hada, Toshio Arakida, Maiko Iwaki, Shunsuke Minakuch. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. 2021;
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[Conference Activities & Talks]

- 1. Minakuchi S. Punch-lines on Paving the Gerodontologic Strategies to a Happy Longevity. TAGD: 2021 Fall-&-Winter CE Session-2 of "Gerodontology on Overall Health & Longevity" 2021.11.21 Taiwan
- 2. Manabu Kanazawa. Scan in digital denture. Japan Denture Professional 2021.11.18
- 3. Inokoshi M. Zirconia ceramics aesthetic, strong and aging resistant restorative materials. 19th Biennial Meeting of the ICP 2021.09.22 web
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- 5. Yamamoto M, Inokoshi M, Tamura M, Yoshihara K, Minakuchi S. Long-Term Antimicrobial Effects of 4-META/MMA-TBB Resin Containing Antibacterial Agents. 2021 CED-IADR/NOF Oral Health Research congress 2021.09.16 hybrid (web, Brussels)
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- 8. Inokoshi M, Liu H, Shimizubata M, Nozaki K, Minakuchi S. Translucency, Crystallography and Flexural Strength of Multi-Layered Highly Translucent Zirconia. 2021 CED-IADR/NOF Oral Health Research congress 2021.09.16 hybrid (web, Brussels)

- 9. Bui Ngoc Huyen Trang, Manabu Kanazawa, Natsuko Murakami, Noriyuki Wakabayashi, Awutsadaporn Katheng, Sai Tun Naing, Sahaprom Namano, Maiko Iwaki, Shunsuke Minakuchi. Stress Distribution of One-Piece and Two-Piece Mini-Implant Overdentures (Various Attachments). CED-IADR/NOF Oral Health Research Congress in Brussels 2021.09.16
- 10. Manabu Kanazawa. Applied concepts & digital advancements in implantology. The Roundtable 2021.08.17
- 11. Manabu Kanazawa. One day direct denture restorations using hard and soft relining materials. Essential Expertise for Clinical Dentistry 7 2021.08.17
- 12. Sai Tun Naing, Manabu Kanazawa, Tamaki Hada, Shunsuke Minakuchi. Effect of implant position on the stress distribution of IARPD. IADR general session, Boston, 2021 2021.07.21
- Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Cho Too TD, Minakuchi S. Translucency and crystallography of speed-sintered highly translucent dental zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
- Nakai H, Inokoshi M, Nozaki K, Kamijo S, Shimizubata M, Liu H, Minakuchi S. Crystallography and flexural strength of additive manufactured zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
- 15. Minakuchi S. Gerodontology for achieving healthy longevity society. New challenge of JSG. ECG 2021 Annual Meeting 2021.04.09 Bern
- 1. Effect of high-speed sintering protocols on the microstructure of highly translucent zirconia. The 78th General Session of the Japanese Society for Dental Materials and Devices (JSDMD) 2021.10.16
- 2. Nakai H, Inokoshi M, Liu H, Minakuchi S. Grain size distribution of additively manufactured zirconia. The 78th General Session of the Japanese Society for Dental Materials and Devices (JSDMD) 2021.10.16
- 3. Inokoshi M. Current status of dental materials containing S-PRG filler and its future perspectives in prosthodontics. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.20
- 4. Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Minakuchi S. Flexural strength of speed-sintered highly translucent dental zirconia. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19
- 5. Inokoshi M. Latest evidence of dental zirconia ceramics from material science. The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.19
- 6. Otake R, Kanazawa M, et al.. A prospective study of digital complete dentures using customized disc method.. 2021.06.19 online
- Minakuchi S, Inokoshi M. Application of S-PRG filler-containing materials in the super-aged society to improve the oral environment of the elderly. The 32nd Annual Meeting of Japanese Society of Gerodontology 2021.06.13 web
- Inokoshi M, Ueda K, Shimizubata M, Motomura K, Yamamoto M, Onuma H, Watanabe M, Shimizu K, Kubota K, Minakuchi S. Online elderly simulation training program during the COVID-19 pandemic. The 32nd Annual Meeting of Japanese Society of Gerodontology 2021.06.12 web
- 9. Mitsuzumi Okada, Kazumasa Kubota. A case of oral management including tooth extraction in a patient with COVID-19 infection. The 32nd Annual Meeting of the Japanese Society of Gerodontology 2021.06.12 Online held
- Hara Yoshiko, Nakane Ayako. A case in which swallowing function was improved by stimulating interferential current transcutaneous electrical sensory stimulation in a patient with severe dementia. Japanese Society of Gerodontology 2021.06.11 Web
- Soeda Y, Kanazawa M, Iwaki M, Arakida T, Hada T, Otake R, Katheng A, Akiyama Y, Ando K, Minakuchi S. Trueness and precision of artificial teeth in CAD/CAM milled complete dentures with custom disks of prefabricated frame. 2021.04.24

12. Yamamoto M, Inokoshi M, Shimizubata M, Nozaki K, Takahashi R, Yoshihara K, Minakuchi S. Shear bond strength to root dentin of 4-META/MMA-TBB resin containing antibacterial agents. The 77th General Session of the Japanese Society for Dental Materials and Devices 2021.04.10

[Awards & Honors]

1. MINAKUCHI Shunsuke, the Robin Heath Award for the most-cited paper in Gerodontology, Gerodontology, 2021.09

[Others]

1. Yamaga Eijiro Grant-in-Aid for for Young Scientists, 2021.04 Strucrural 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

Dysphagia Rehabilitation

(1) Publications

- Suzuki H, Furuya J, Hidaka R, Miyajima S, Matsubara C, Ohwada G, Asada T, Akazawa C, Sato Y, Tohara H, Minakuchi S.. Patients with mild cognitive impairment diagnosed at dementia clinic display decreased maximum occlusal force: a cross-sectional study. BMC Oral Health. 2021.12; 21(1); 665
- Furuya J, Suzuki H, Hidaka R, Nakagawa K, Yoshimi K, Nakane A, Yamaguchi K, Shimizu Y, Itsui Y, Saito K, Sato Y, Tohara H, Minakuchi S. Factors Related to Oral Intake of Food by Hospitalized Patients with Malnutrition under the Care of a Nutrition Support Team. Int J Environ Res Public Health. 2021.11; 18(21); 11725
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- 4. Hasegawa S, Nakagawa K, Yoshimi K, Yamaguchi K, Nakane A, Ishii M, Okumura T, Hara K, Minakuchi S, Tohara H. Jaw-retraction exercise increases anterior hyoid excursion during swallowing in older adults with mild dysphagia. Gerodontology. 2021.10;
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- 6. Nomoto Akiko, Shimizu Akio, Ohno Tomohisa, Tohara Haruka, Hashidume Momoyo, Hatano Machiko, Fujishima, Ichiro. Poor oral health and anorexia in older rehabilitation patients Gerodontology. 2021.10;
- Furuya J, Suzuki H, Hidaka R, Koshitani N, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Minakuchi S, Miyake S. Factors affecting the oral health of inpatients with advanced cancer in palliative care. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2021.09;
- Nakane A, Hasegawa S, Ishii M, Tamai T, Moritoyo R, Saito M, Ando M, Tohara H. Swallowing Function Evaluation in a Patient with Gerstmann-Sträussler-Scheinker Disease with Pro105Leu: A Case Report. International journal of environmental research and public health. 2021.09; 18(18);
- 9. Miki Ishii, Kazuharu Nakagawa, Kanako Yoshimi, Takuma Okumura, Shohei Hasegawa, Kohei Yamaguchi, Ayako Nakane, Tomoe Tamai, Yuki Nagasawa, Akira Yoshizawa, Haruka Tohara. Higher Activity and Quality of Life Correlates with Swallowing Function in Older Adults with Low Activities of Daily Living Gerontology. 2021.09;
- Yamaguchi K, Nakagawa K, Yoshimi K, Chantaramanee A, Nakane A, Furuya J, Tohara H. Age-related changes in swallowing muscle intramuscular adipose tissue deposition and related factors Experimental Gerontology. 2021.08;

- 11. Daisuke Takagi, Tomohisa Ohno, Motoki Moriwaki, Norimasa Katagiri, Yoshiko Umeda, Haruka Tohara, Akiko Nomoto, Ichiro Fujishima. Effect of dentures on pharyngeal swallowing function in patients with dysphagia. Geriatr Gerontol Int. 2021.08;
- Yamaguchi K, Nakagawa K, Yoshimi K, Ariya C, Nakane A, Furuya J, Tohara H. Age-related changes in swallowing muscle intramuscular adipose tissue deposition and related factors. Experimental gerontology. 2021.08; 153; 111505
- 13. Furuya J, Suzuki H, Hidaka R, Akatsuka A, Nakagawa K, Yoshimi K, Nakane A, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Oral health status and its association with nutritional support in malnourished patients hospitalised in acute care. Gerodontology. 2021.07;
- 14. Furuya J, Suzuki H, Hidaka R, Akatsuka A, Nakagawa K, Yoshimi K, Nakane A, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Oral health status and its association with nutritional support in malnourished patients hospitalised in acute care. Gerodontology. 2021.07;
- 15. Yoshimi K, Nakagawa K, Momosaki R, Yamaguchi K, Nakane A, Tohara H. . Effects of Oral Management on Elderly Patients with Pneumonia. The journal of nutrition, health & aging.. 2021.07;
- Takano S, Yamaguchi K, Nakagawa K, Yoshimi K, Nakane A, Okumura T, Tohara H. Author Correction: Effect of isometric exercises on the masseter muscle in older adults with missing dentition: a randomized controlled trial. Scientific reports. 2021.04; 11(1); 9086
- Hidaka R, Furuya J, Nishiyama A, Suzuki H, Aoyagi M, Matsubara C, Yoshizumi Y, Yoshimi K, Nakane A, Tohara H, Sato Y, Minakuchi S. Structural Equation Modeling of Tongue Function and Tongue Hygiene in Acute Stroke Patients. International journal of environmental research and public health. 2021.04; 18(9); 4567
- 18. Yamaguchi Kohei, Hara Koji, Nakagawa Kazuharu, Yoshimi Kanako, Ariya Chantaramanee, Nakane Ayako, Furuya Junichi, Tohara Haruka. Ultrasonography Shows Age-related Changes and Related Factors in the Tongue and Suprahyoid Muscles JOURNAL OF THE AMERICAN MEDICAL DIRECTORS ASSOCIATION. 2021.04; 22(4); 766-772
- Satoru Takano, Kohei Yamaguchi, Kazuharu Nakagawa, Kanako Yoshimi, Ayako Nakane, Takuma Okumura, Haruka Tohara. Effect of isometric exercises on the masseter muscle in older adults with missing dentition: A randomized controlled trial Scientific reports. 2021.03;
- 20. Tamura A, Yamaguchi K, Ariya C, Totoki H, Tohara H. Dysphagia in a persistently vegetative patient improved by orthodontic treatment of severe dental misalignment. Special care in dentistry : official publication of the American Association of Hospital Dentists, the Academy of Dentistry for the Handicapped, and the American Society for Geriatric Dentistry. 2021.03; 41(2); 271-276
- 21. Katagiri Sayaka, Watanabe Kazuki, Maekawa Shogo, Hatasa Masahiro, Shiba Takahiko, Komatsu Keiji, Ohsugi Yujin, Tohara Haruka, Iwata Takanori. Porphyromonas gingivalis impairs glucose uptake in skeletal muscle associated with altering gut microbiota(和訳中) 口腔病学会雑誌. 2021.03; 88(1); 71
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- 23. Watanabe K, Katagiri S, Takahashi H, Sasaki N, Maekawa S, Komazaki R, Hatasa M, Kitajima Y, Maruyama Y, Shiba T, Komatsu K, Ohsugi Y, Tanaka K, Matsuzawa A, Hirota T, Tohara H, Eguchi Y, Anzai K, Hattori A, Iwata T. Porphyromonas gingivalis impairs glucose uptake in skeletal muscle associated with altering gut microbiota FASEB JOURNAL. 2021.02; 35(2); e21171
- 24. Yoshiko Hara, Ayako Nakane, Haruka Tohara, Kazumasa Kubota , et al.. Cervical Intervention Current Transcutaneous Electrical Sensory Stimulation for Patients with Dysphagia and Dementia in Nursing Homes Clinical Intervention s in Aging. 2021.01; 2020(15); 2431-2437
- 25. Hara Y, Nakane A, Tohara H, Kubota K, Nakagawa K, Hara K, Yamaguchi K, Yoshimi K, Minakuchi S. Cervical Interferential Current Transcutaneous Electrical Sensory Stimulation for Patients with Dysphagia and Dementia in Nursing Homes. Clinical interventions in aging. 2021.01; 5(15); 2431-2437

- 26. Mori T, Wakabayashi H, Ogawa N, Fujishima I, Oshima F, Itoda M, Kunieda K, Shigematsu T, Nishioka S, Tohara H, Yamada M, Ogawa S. The Mass of Geniohyoid Muscle Is Associated with Maximum Tongue Pressure and Tongue Area in Patients with Sarcopenic Dysphagia. J Nutr Health Aging. 2021.01;
- 27. Hatasa M, Ohsugi Y, Katagiri S, Yoshida S, Niimi H, Morita K, Tsuchiya Y, Shimohira T, Sasaki N, Maekawa S, Shiba T, Hirota T, Tohara H, Takahashi H, Nitta H, Iwata T. Endotoxemia by Porphyromonas gingivalis alters endocrine functions in brown adipose tissue Frontiers in Cellular and Infection Microbiology. 2021.01; 19(10); 580577
- 28. Ogawa Nami, Wakabayashi Hidetaka, Mori Takashi, Fujishima Ichiro, Oshima Fumiko, Itoda Masataka, Kunieda Kenjiro, Shigematsu Takashi, Nishioka Shinta, Tohara Haruka, Ohno Tomohisa, Nomoto Akiko, Shimizu Akio, Yamada Minoru, Ogawa Sumito. Digastric muscle mass and intensity in older patients with sarcopenic dysphagia by ultrasonography GERIATRICS & GERONTOLOGY INTERNATIONAL. 2021.01; 21(1); 14-19
- 29. Ogawa Nami, Wakabayashi Hidetaka, Mori Takashi, Fujishima Ichiro, Oshima Fumiko, Itoda Masataka, Kunieda Kenjiro, Shigematsu Takashi, Nishioka Shinta, Tohara Haruka, Ohno Tomohisa, Nomoto Akiko, Shimizu Akio, Yamada Minoru, Ogawa Sumito. Digastric muscle mass and intensity in older patients with sarcopenic dysphagia by ultrasonography(和訳中) Geriatrics & Gerontology International. 2021.01; 21(1); 14-19
- 30. Nakayama Enri, Tohara Haruka, Sato Mitsuyasu, Abe Kimiko, Kimura Masanori, Watanabe Mao, Iida Masato, Ueda Koichiro. Relationship between oral intake level and oral health assessment tool scores in the convalescent ward JOURNAL OF ORAL SCIENCE. 2021.01; 63(1); 79-82
- 31. Nakayama Enri, Tohara Haruka, Sato Mitsuyasu, Abe Kimiko, Kimura Masanori, Watanabe Mao, Iida Masato, Ueda Koichiro. Relationship between oral intake level and oral health assessment tool scores in the convalescent ward(和訳中) Journal of Oral Science. 2021.01; 63(1); 79-82
- 32. Ayako Nakane, Shohei Hasegawa, Miki Ishii, Tomoe Tamai, Rieko Moritoyo, Mitsuko Saito, Mariko Ando, Haruka Tohara. Swallowing Function Evaluation in a Patient with Gerstmann – Sträussler – Scheinker Disease with Pro105Leu : A Case Report International Journal of Environment Research and Public Health. 2021; 18;

[Conference Activities & Talks]

- 1. 齋木章乃, 吉見佳那子, 中川量晴, 長谷川翔平, 柳田陵介, 中根綾, 山口浩平, 戸原玄. とろみ付き炭酸飲料が 嚥下動態に与える効果の検証. 第86回 口腔病学会学術大会 2021.12.03
- 2. Kazuharu Nakagawa, Yuki Nagasawa, Kanako Yoshimi, Haruka Tohara. Effects of Thickened Food Products on Nutrient Absorption When Used for Preventing Aspiration in Dysphagia: A study using the rat model. biennial iADH research competition online 2021.11.27 web 開催
- 3. Akira Yoshizawa, Shinya Saito, Sirinthip Amornsuradech, Kazuharu Nakagawa, Kohei Yamaguchi, Kanako Yoshimi, Haruka Tohara . Online swallowing evaluation can be an effective modality for bed bounded patient considering prevention of COVID-19 infection . World Dysphagia Summit 2021 2021.08.21
- 4. Taishi Yamada, Kohei Yamaguchi, Kazuharu Nakagawa, Ayako Nakane, Kanako Yoshimi,Sirinthip Amornsuradech,Haruka Tohara. Inventing new type of denture shaped alternative vocalization. World Dysphagia Summit 2021.08.21 Nagoya
- 5. Shohei Hasegawa, Kazuharu Nakagawa, Kanako Yoshimi, Kohei Yamaguchi, Ayako Nakane, Miki Ishii, Takuma Okumura, Haruka Tohara. The jaw-retraction exercise improves the anterior displacement of the hyoid bone during swallowing in elderly patients with mild dysphagia.. World Dysphagia Summit 2021 2021.08.20 Nagoya, Japan / Online
- 6. Takuma Okumura, Ayako Nakane, Kazuharu Nakagawa, Kohei Yamaguchi, Knakako Yoshimi, Haruka Tohara. The Development of multiple angle endoscope for swallowing examination. World Dysphagia Summit 2021 2021.08.20 Nagoya, Japan / Online

- 7. Miki Ishii, Kazuharu Nakagawa, Kanako Yoshimi, Takuma Okumura, Shohei Hasegawa, Kohei Yamaguchi, Ayako Nakane, Tomoe Tamai, Yuki Nagasawa, Akira Yoshizawa, Haruka Tohara. Time Spent Away from Bed to Maintain Swallowing Function in Older Adults. World Dysphagia Summit 2021 2021.08 Nagoya, Japan and Online
- 8. Akino Saiki, Kanako Yoshimi, Kazuharu Nakagawa, Shohei Hasegawa, Ryosuke Yanagida, Ayako Nakane, Kohei Yamaguchi, Haruka Tohara. THE EFFECT OF THICKENED CARBONATED BEVERAGE ON SWALLOWING DYNAMICS. 2nd World Dysphagia Summit 2021.08
- 9. 奥村拓真, 中根綾子, 中川量晴, 石井美紀, 吉田早織, 吉見佳那子, 山口浩平, 戸原玄. 訪問診療研修にオン ラインを用いた学生教育 · リカレント教育の有用性. 日本老年歯科医学会第 32 回学術大会 2021.06.15 ウェ ブLive
- 10. Haruka Tohara. Comprehensive research focusing on oral and swallowing function-oral function unit-. TMDU Research Online Exchange Event 2021.06.05
- 11. 2. Haruka Tohara. Outline of dysphagia and our recent researches. FDCU International Symposium and the 33rd research day 2021.05.24
- 12. Haruka Tohara. Dysphagia Rehabilitation in Home Care. Concept and clinical trial of dental treatment for the elderly in Germany and Japan 2021.04.26
- 1. Rieko Moritoyo,Kazuharu Nakagawa,Haruka Tohara. The Effects of Telemedicine in Dysphagia Rehabilitation. 2021.10.09
- 2. Kinematic analysis of swallowing function pre/post surgery for patients with cervical spine disease. 2021.08.20
- 3. Akino Saiki, Kanako Yoshimi, Kazuharu Nakagawa, Yuki Nagasawa, Akira Yoshizawa, Kota Aritaki, Ayako Nakane, Kohei Yamaguchi, Haruka Tohara. How effective are carbonated beverages for patients with dysphagia?. 26th and 27th Joint Annual Meetings of the Japanese Society of Dysphagia Rehabilitation 2021.08.20
- 4. Akira Yoshizawa, Kazuharu Nakagawa, Kanako Yoshimi, Kota Aritaki, Rei Horiuchi, Tomoko Odani, Ayako Nakane, Haruka Tohara . A study on the safety of rehydration jelly intake in patients with dysphagia. 26th & 27th Joint Meeting of Japanese Society of Dysphagia Rehabilitation 2021.08.19
- 5. Susa C, Michiwaki Y, Kikuchi T, Ijiri T, Kobayashi T, Sahara Y, Tohara H. Visualization of tongue movement during mastication and swallowing using segmentation of 4-dimensional CT. 26th&27th Joint Meeting of Japanese Society of Dysphagia Rehabilitation 2021.08.19 Nagoya, Japan
- 6. Mitsuko Saito, Ayako Nakane, Yuko Kagifuku, Kanako Yoshimi, Kohei Yamaguchi, Kazuharu Nakagawa, Haruka Tohara. Relationship between reconstructed tongue volume changes and nutritional status in patients with tongue cancer. 26th & 27th Joint Meeting of Japanese Society of Dysphagia Rehabilitation 2021.08.19
- 7. The Effects of Telemedicine in Patients with Dysphagia during the COVID-19 Pandemic. 2021.08
- 8. Akira Yoshizawa, Kazuharu Nakagawa, Kanako Yoshimi, Kohei Yamaguchi, Yuki Nagasawa, Ayako Nakane, Kota Aritaki, Haruka Tohara. Characteristics of dysphagia according to surgical procedure in patients with cervical spine disease . THE 36TH ANNUAL MEETING OF JAPANESE SOCIETY FOR CLINICAL NUTRITION AND METABOLISM 2021.07.21
- 9. Akira Yoshizawa, Kazuharu Nakagawa, Kanako Yoshimi, Miki Ishii, Chizuru Namiki, Yosuke Kawai, Nakane Ayako, Haruka Tohara . A case of dysphagia after Anterior Cervical Discectomy and Fusion-Kinematic analysis before and after surgery-. The 32nd Annual Meeting of the Japanese Society of Gerodontology 2021.06.13
- 10. Hara Yoshiko, Nakane Ayako. A case in which swallowing function was improved by stimulating interferential current transcutaneous electrical sensory stimulation in a patient with severe dementia. Japanese Society of Gerodontology 2021.06.11 Web
- 11. A case in which swallowing rehabilitation for the elderly at home and evaluation by the KT balance chart were useful. 2021.06

12. Akino Saiki, Kanako Yoshimi, Kazuharu Nakagawa, Yuki Nagasawa, Akira Yoshizawa, Taishi Yamada, Kota Aritaki, Ayako Nakane, Kohei Yamaguchi, Haruka Tohara. The effect of thickened carbonated beverages on swallowing function in patients with dysphagia. The 32nd Annual Meeting of the Japanese Society of Gerodontology 2021.06

Laboratory Medicine

Professor Shuji TOHDA Assistant Professor Mai ITOH Graduate Students Tatsuya SAITO, Salwa MOHAMMAD, Chisuzu ITO, Kotomi NOGUCHI

(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 thepapy

- 2) Molecular diagnostic tests for cancer and detection of minimal residual cancer cells
- 3) Mechanism of abnormal growth of lymphoma cells
- 4) Molecular diagnostic tests for infectious diseases

(3) Education

To graduates students, we provide opportunity to study and develop novel diagnostic tests using cellular and molecular biological techeque 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. Takahiro Kameda, Yuna Horiuchi, Shitsuko Shimano, Kouji Yano, Shao-Jui Lai, Naoya Ichimura, Shuji Tohda, Yuriko Kurihara, Minoru Tozuka, Ryunosuke Ohkawa. N-homocysteinylation of high-density lipoprotein on endothelial repair function. Biol Chem. 2021.08;
- Nagano K, Tani-Sassa C, Iwasaki Y, Takatsuki Y, Yuasa S, Takahashi Y, Nakajima J, Sonobe K, Ichimura N, Nukui Y, Takeuchi H, Tanimoto K, Tanaka Y, Kimura A, Tohda S. SARS-CoV-2 R.1 lineage variants prevailed in Tokyo in March 2021. Journal of medical virology. 2021.07;
- 3. Takahiro Mitsumura, Tsukasa Okamoto, Tsuyoshi Shirai, Yuki Iijima, Rie Sakakibara, Takayuki Honda, Masahiro Ishizuka, Junichi Aiboshi, Tomoya Tateishi, Meiyo Tamaoka, Hidenobu Shigemitsu, Hirokuni Arai, Yasuhiro Otomo, Shuji Tohda, Tatsuhiko Anzai, Kunihiko Takahashi, Shinsuke Yasuda, Yasunari Miyazaki. Predictors associated with clinical improvement of SARS-CoV-2 pneumonia. J Infect Chemother. 2021.06; 27(6); 857-863
- 4. Azusa Yamazaki, Ryunosuke Ohkawa, Yuka Yamagata, Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Naoya Ichimura, Shuji Tohda, Minoru Tozuka. Apolipoprotein C-II and C-III preferably transfer to both high-density lipoprotein (HDL)2 and the larger HDL3 from very low-density lipoprotein (VLDL). Biol Chem. 2021.05; 402(4); 439-449
- 5. Sonoda Y, Itoh M, Tohda S. Effects of HOXA9 Inhibitor DB818 on the Growth of Acute Myeloid Leukaemia Cells. Anticancer Research. 2021.04; 41(4); 1841-1847
- 6. Yamazaki Azusa, Ohkawa Ryunosuke, Yamagata Yuka, Horiuchi Yuna, Lai Shao-Jui, Kameda Takahiro, Ichimura Naoya, Tohda Shuji, Tozuka Minoru. Apolipoprotein C-II and C-III preferably transfer to both high-density lipoprotein (HDL)(2) and the larger HDL3 from very low-density lipoprotein (VLDL) BIOLOGICAL CHEMISTRY. 2021.03; 402(4); 439-449
- 7. Shitsuko Shimano, Ryunosuke Ohkawa, Mayu Nambu, Mai Sasaoka, Azusa Yamazaki, Yuki Fujii, Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Naoya Ichimura, Koji Fujita, Shuji Tohda, Minoru Tozuka. Marked Changes in Serum Amyloid A Distribution and High-Density Lipoprotein Structure during Acute Inflammation. Biomed Res Int. 2021; 2021; 9241259

[Conference Activities & Talks]

- 1. 野上 彩子, 岡田 啓五, 本村 鷹多朗, 吉藤 康太, 東田 修二, 長尾 俊景. Inhibition of USP14 induces apoptosis in FLT3-ITD-positive AML cells through upregulation of Nrf-2(和訳中). 日本血液学会学術集会 2021.09.01
- 2. 吉藤 康太, 本村 鷹多朗, 野上 彩子, 岡田 啓五, 東田 修二, 長尾 俊景. Involvement of TPL2/p105/STAT3 axis in tumorigenesis of ABC-DLBCL(和訳中). 日本血液学会学術集会 2021.09.01
- 3. 木村 萌, 西山 優, 上田 浩樹, 有松 朋之, 久保木 麻衣, 高畑 篤, 斎藤 真貴子, 東田 修二, 野上 彩子. Perioperative management of a PNH patient treated with ravulizumab: in case of gallstone disease(和訳中). 日本血液 学会学術集会 2021.09.01
- 1. Inhibition of USP14 induces apoptosis in FLT3-ITD-positive AML cells through upregulation of Nrf-2. 2021.09.23
- 2. Moyu KIMURA,Yu NISHIYAMA,Hiroki UEDA,Tomoyuki ARIMATSU,Mai KUBOKI,Atsushi TAKAHATA,Makiko SAITO,Shuji TOHDA,Ayako NOGAMI. Perioperative management of a PNH patient treated with ravulizumab: in case of gallstone disease. The 83rd Annual Meeting of the Japanese Society of Hematology 2021.09.23 Sendai

Intensive Care Medicine

Professor and Chairman Kenji Wakabayashi (2021.10.1 -)

Specially Appointed Professor Hideo Takahashi(2017.4.1 -)

Associate Professor Toyomu Ugawa (2018.11.1 -)

Junior Associate Professor Michio Nagashima (2017.4.1 -) Hideo Yamauchi (2019.4.1 -)

Assistant Professor Takahiro Masuda (Intensive Care Unit) (2014.4.1 -) Fumi Maruyama (Intensive Care Unit) (2017.2.1 -) Nobuyuki Nosaka (2020.4.1 -)

Specially Appointed Assistant Professor Nobuhiro Shiota (2017.4.1 -) Ryo Uchimido (Intensive Care Unit) (2020.4.1 -) Yuka Mishima (Intensive Care Unit) (2017.4.1 -) Toshihiro Kubo (Intensive Care Unit) (2019.10.1 -)

Fellow: Taiga Nagase (Anesthesiology) (2020.4.1 -)

Postgraduate students: Shotaro Matsumoto (2016.4.1 -) Nobuhiro Shiota (2017.4.1 -) Yoichi Iki (2018.4.1 -) Michiko Abe (2019.4.1 -) Yuka Mishima (2019.4.1 -) Ryo Uchimido (2020.4.1 -) Toshihiro Kubo(2021.4.1-)

Adjunct lecturer Yoshito Ujike (2017.4.1 -) Eriko Takezawa (2017.4.1 -)

(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 liaise 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)

6)Development of a program method to support appropriate use of antimicrobial agents in ICUs(Mishima, 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, pharmarcist, 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

- 1. Nobuyuki Nosaka, Takahiro Masuda. Sedation and Ventilator Liberation Protocol vs Usual Care and Duration of Invasive Ventilation in Pediatric Intensive Care Units. JAMA. 2021.12; 326(22); 2328-2329
- Yoshiko Ishisaka, Nobuyuki Nosaka, Yuka Mishima, Takahiro Masuda, Michio Nagashima, Yosuke Tanaka, Kouhei Yamamoto, Masayuki Yoshida, Hidenobu Shigemitsu. COVID-19 case of ventilator-induced lung injury on extracorporeal membrane oxygenation: Physicians' clinical struggle and ethical conflict in a novel pandemic. Clin Case Rep. 2021.12; 9(12); e05223
- 3. Osawa I, Tsuboi N, Nosaka N, Nishimura N, Nakagawa S. Impact of extensive negative pressure wound therapy on neonatal respiration: A case report. Clinical case reports. 2021.10; 9(10); e05008
- Noda K, Nosaka N, Hara N, Yokota T, Shigemitsu H, Takahashi H. We Should Pay Attention to "Referred Pain" - A Case of Acute Myocardial Infarction that Masked and Delayed the Diagnosis of Esophageal Perforation. Internal medicine (Tokyo, Japan). 2021.09;
- Masuda T, Nosaka N, Nagashima M. Intubation Practices and Adverse Peri-intubation Events in Critically Ill Patients. JAMA. 2021.08; 326(6); 568-569
- Masuda T, Uchimido R, Nosaka N, Akiyama H, Kamisato A, Yoshida M. Concerns in Methodology for Self-Administered Questionnaire: Needs for Involvement of Social Scientists. Chest. 2021.07; 160(1); e92-e93
- 7. Takahiro Masuda, Nobuyuki Nosaka, Ryo Uchimido, Michio Nagashima. Use of stylet and airway management procedure in critically ill patients. Intensive Care Med. 2021.07; 47(12); 1497-1498
- Yoshihiko Sano, Kentaro Sato, Ryusei Iida, Narut oshi Kabashima, Toyomu Ugawa. Analytical Solutions of a Two-Compartment Model Based on the Volume-Average Theory for Blood Toxin Concentration during and after Dialysis membranes. 2021.07; 11(7), 506(11(7), 506);
- 9. Yoshihiko Sano, Toyomu Ugawa, Ayato Takeda, Toru Hyakutake, Takashi Nakazawa, Shinichiro Yanase, Hidenobu Shigemitsu, Hirokuni Arai. Hydrodynamic approach for revealing venous anastomotic stenosis formation within a dialysis arteriovenous graft ASAIO. 2021.05;
- Tsuboi Kaoru, Tsuboi Norihiko, Nosaka Nobuyuki, Nishimura Nao, Nakagawa Satoshi. Neonatal Harlequin color change associated with Prostaglandin E-1 administration PEDIATRICS INTERNATIONAL. 2021.05; 63(5); 610-611
- Nagaoka E, Arai H, Ugawa T, Masuda T, Ochiai K, Tamaoka M, Kurashima N, Oi K, Fujiwara T, Yoshida M, Shigemitsu H, Otomo Y. Efficacy of Multidisciplinary Team Approach with Extracorporeal Membrane Oxygenation for COVID-19 in Low Volume ECMO center. Artificial organs. 2021.03;
- 12. Saito J, Shoji K, Oho Y, Kato H, Matsumoto S, Aoki S, Nakamura H, Ogawa T, Hasegawa M, Yamatani A, Miyairi I. Integration of Continuous Renal Replacement Therapy in a Meropenem Population Pharmacokinetics Model in Critically Ill Children Antimicrob Agents Chemother. 2021.03; 65(4);
- Noda K, Nosaka N, Sai Y, Nagaoka E, Nagashima M, Arai H, Shigemitsu H. A laceration of a wired silastic tracheostomy tube: A case report and review of the literature. Clinical case reports. 2021.03; 9(3); 1500-1503

- 14. Saito J, Shoji K, Oho Y, Kato H, Matsumoto S, Aoki S, Nakamura H, Ogawa T, Hasegawa M, Yamatani A, Miyairi I. Population Pharmacokinetics and Pharmacodynamics of Meropenem in Critically Ill Pediatric Patients Antimicrob Agents Chemother. 2021.01; 65(2); e1909-e1920
- 15. Tsuboi N, Tsuboi K, Nosaka N, Nishimura N, Nakagawa S. The Ventilatory Strategy to Minimize Expiratory Flow Rate in Ventilated Patients with Chronic Obstructive Pulmonary Disease. International journal of chronic obstructive pulmonary disease. 2021; 16; 301-304
- 16. Oba S, Hosoya T, Amamiya M, Mitsumura T, Kawata D, Sasaki H, Kamiya M, Yamamoto A, Ando T, Shimada S, Shirai T, Okamoto T, Tateishi T, Endo A, Aiboshi J, Nosaka N, Yamanouchi H, Ugawa T, Nagaoka E, Oi K, Tao S, Maejima Y, Tanaka Y, Tanimoto K, Takeuchi H, Tohda S, Hirakawa A, Sasano T, Arai H, Otomo Y, Miyazaki Y, Yasuda S. Arterial and Venous Thrombosis Complicated in COVID-19: A Retrospective Single Center Analysis in Japan. Frontiers in cardiovascular medicine. 2021; 8; 767074

[Misc]

1. Yoichi Iki, Kenji Wakabayashi. Update of research and investigation of ECMO-induced injury for improving prognosis of critically ill patients Pediatrics of Japan. 2021.08; 62(8); 807-814

[Conference Activities & Talks]

 Hinoshita Takuga, Noda Koutaro, Kubo Toshihiro, Mishima Yuka, Uchimido Ryo, Shiota Nobuhiro, Nosaka Nobuyuki, Masuda Takahiro, Yamanouchi Hideo, Shigemitsu Hidenobu. PAI-1 of COVID-19 patients in ICU(和訳中). 日本集中治療医学会雑誌 2021.09.01

Pharmacokinetics and Pharmacodynamics

Associate Professor Masashi Nagata Postgraduate student Xue Bingyang, Tsubura Noda, Shotaro Mizuno, Tatsuki Akahoshi

(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

- Kawasumi K, Kawano Y, Kujirai A, Mano Y, Matsui R, Maeda-Minami A, Yamamoto Y, Negishi K, Shimada S, Yamaguchi M, Nagata M, Aoyama T. Risk Factors Associated With Unplanned Acute Care in Outpatient Chemotherapy With Oral Anticancer Drugs as Monotherapy or Combination Therapy With Injectable Anticancer Drugs. Anticancer research. 2021.11; 41(11); 5827-5834
- Ishiwata Y, Nagata M, Kiuchi S, Ippongi C, Takeda H, Takahashi H. Intravenous Infusion of Fentanyl Has No Effect on Blood Concentration of Tacrolimus In Patients Receiving Hematopoietic Stem Cell Transplantation. Therapeutic drug monitoring. 2021.10; 43(5); 688-691
- 3. Aya Enomoto, Yasunari Mano, Yohei Kawano, Tomoki Nishikawa, Takao Aoyama, Yoshiyuki Sasaki, Masashi Nagata, Hiromitsu Takahashi. Comparison of the Safety and Effectiveness of Four Direct Oral Anticoagulants in Japanese Patients with Nonvalvular Atrial Fibrillation Using Real-World Data. Biological and Pharmaceutical Bulletin. 2021.09; 44(9); 1294-1302
- 4. Kawano Y, Nagata M, Nakamura S, Akagi Y, Suzuki T, Tsukada E, Hoshiko M, Kujirai A, Nakamatsu S, Nishikawa T, Enomoto A, Negishi K, Shimada S, Aoyama T, Mano Y. Comprehensive Exploration of Medications That Affect the Bleeding Risk of Oral Anticoagulant Users. Biological & pharmaceutical bulletin. 2021.05; 44(5); 611-619
- Asada M, Nagata M, Mizuno T, Uchida T, Takahashi H, Makita K, Arai H, Kijima S, Echizen H, Yasuhara M. Population pharmacokinetics of cefazolin before, during and after cardiopulmonary bypass in adult patients undergoing cardiac surgery. European journal of clinical pharmacology. 2021.04; 77(5); 735-745
- 6. Kawano Y, Katsuyama M, Nagata M, Obana M, Nakamatsu S, Mori A, Sakamoto N, Mano Y, Negishi K, Shimada S, Aoyama T. Antiplatelet Effect of Mirtazapine via Co-blocking of the 5-HT_{2A} and α ₂-Adrenergic Receptors on Platelets. Biological & pharmaceutical bulletin. 2021.02; 44(2); 238-244

7. Yanagie H, Fujino T, Yanagawa M, Terao T, Imagawa T, Fujihara M, Morishita Y, Mizumachi R, Murata Y, Dewi N, Ono Y, Ikushima I, Seguchi K, Nagata M, Nonaka Y, Furuya Y, Hisa T, Nagasaki T, Arimori K, Nakashima T, Sugihara T, Kakimi K, Ono M, Nakajima J, Eriguchi M, Higashi S, Takahashi H. Tumor Growth Suppression With Novel Intra-arterial Chemotherapy Using Epirubicin-entrapped Water-in-oil-in-water Emulsion In Vivo. In vivo. 2021.01; 35(1); 239-248

[Conference Activities & Talks]

1. Masatoshi Takagi, Chitose Ogawa, Tomoko Iehara, Yuki Aoki-Nogami, Eri Isibashi, Minoru Imai, Toshimi Kimura, Masashi Nagata, Masato Yasuhara, Mitsuko Masutani, Kenichi Yoshimura, Daisuke Tomizawa, Atsushi Ogawa, Kan Yonemori, Tetsuro Kihara, Kiyoshi Nobori, Kazuhisa Hasebe, Shuki Mizutani, Tomohiro Morio, Hajime Hosoi, Ryuji Koike. First In Children Phase I Clinical Study Of Oral Olaparib In Pediatric Patients With Refractory Solid Tumors. SIOP2021 2021.10.24 Honolulu (Web)

Medical Education Research and Development

Professor Masanaga YAMAWAKI Junior Associate Professor Eriko OKADA Junior Associate Professor Yasuhiro ITSUI Assistant Professor Nobutoshi NAWA Attending Staff Ayako KASHIMADA

(1) Outline

Our aim is to carry out the mission of the university, "cultivating professionals with knowledge and humanity, thereby contributing to people's well-being," from the perspective of educational management. The basis of our department is to contribute to the education, research, clinical practice, and management & operation of the university in cooperation with other departments and sections. Medical education will continue from undergraduate education to lifelong learning. Our department is in charge of "coordination and support" of education for 6 years of undergraduate and 2 years of junior residency period, and of cultivating future Clinician Scientific Clinicians.

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

We are developing the following research from the perspective of medical education.

 $\cdot\,$ Study on evaluation for clinical ability acquisition

We are studying educational and evaluation system on how to learn and continue to practice in under- and post-graduate clinical training.

· Research on career education

Research on career education for doctors is being conducted with development of entrepreneurship education program for doctors.

· Research on research ethics education of medical students and residents

Development and verification of a model evaluation program for research ethics education by an interdisciplinary approach.

· Research on patient medication and drug swallowing using design thinking

Research on patient medication and drug swallowing using design thinking is being conducted in search for new treatment strategy for dysphagia.

 $\cdot\,$ Research on team medical care and multidisciplinary education

We are conducting research on team medical care and multidisciplinary collaborative education.

 $\cdot\,$ Research on health prevention and patient education

We are conducting research on the development of patient education programs related to

health promotion for the super-elderly. In addition, we are also conducting preventive research on lifestyle-related diseases in Kyo-tango Longevity Cohort Study.

 $\cdot~$ Other research on medical education

We are also conducting research on cognitive mechanism and cerebral processing in clinical reasoning, on competence evaluation in pre- and post-graduate clinical medical education, on multifaceted evaluation in medical communication and research on community-based medicine.

(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, our education program revealed one of the most competitive among all national teaching hospitals.

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

- 1. Tomohiro Tago, Tomonori Suzuki, Ayako Kashimada, Masatoshi Takagi, Tomoko Mizuno. Two case reports of KBG syndrome with Dandy-Walker variant. Pediatr Int. 2021.12; 63(12); 1530-1532
- 2. Ishii T, Nawa N, Morio T, Fujiwara T. Association between nationwide introduction of public-access defibrillation and sudden cardiac death in Japan: An interrupted time-series analysis. International journal of cardiology. 2021.12;

- 3. Suzuki E, Nawa N. US Sick Leave In Global Context. HEALTH AFFAIRS. 2021.12;
- Katagiri A, Nawa N, Fujiwara T. Association Between Paternal Separation During Early Childhood and Pubertal Timing Among Girls Using Longitudinal Birth Cohort in Japan. Frontiers in Endocrinology. 2021.12; 12; 766728
- Kawahara T, Ueki Y, Nawa N, Miyamae S, Hanafusa M, Goto Y, Tohda S, Fujiwara T. Characteristics of SARS-CoV-2 super-spreaders in Japan. The Journal of infection. 2021.12; 84(2); e6-e9
- Ishii E, Nawa N, Matsui H, Otomo Y, Fujiwara T. Response to the Letter to the Editor on "Comparison of disease patterns and outcomes between non-Japanese and Japanese patients at a single tertiary emergency care center in Japan". Journal of epidemiology. 2021.11;
- Nawa N, Trude ACB, Black MM, Richiardi L, Surkan PJ. Associations between Paternal Anxiety and Infant Weight Gain. CHILDREN-BASEL. 2021.11;
- 8. Masakatsu Yanagimachi, Sayaka Fukuda, Fumiko Tanaka, Mari Iwamoto, Chiho Takao, Kunihiro Oba, Natsuko Suzuki, Koji Kiyohara, Dai Kuranobu, Norimasa Tada, Ayako Nagashima, Taku Ishii, Yoko Ino, Yayoi Kimura, Nobutoshi Nawa, Takeo Fujiwara, Takuya Naruto, Tomohiro Morio, Shouzaburo Doi, Masaaki Mori. Leucine-rich alpha-2-glycoprotein 1 and angiotensinogen as diagnostic biomarkers for Kawasaki disease. PLoS One. 2021.09; 16(9); e0257138
- Yohei Furumoto, Akihiro Araki, Taichi Matsumoto, Takahito Nozaka, Masato Yauchi, Katsumasa Kobayashi, Sayuri Nitta, Eriko Okada. Experience of disruption of capsule endoscopy after prolonged retention DEN open. 2021.09; 2(1);
- Nawa N, Tebi D, Kuramochi J, Fujiwara T. Estimation of the Total Number of SARS-CoV-2-infected Individuals and the Necessary Tests and Cost during the First Wave of the COVID-19 Pandemic in Japan. Journal of epidemiology. 2021.08;
- Numasawa M, Nawa N, Funakoshi Y, Noritake K, Tsuruta J, Kawakami C, Nakagawa M, Yamaguchi K, Akita K. A mixed methods study on the readiness of dental, medical, and nursing students for interprofessional learning. PloS one. 2021.07; 16(7); e0255086
- 12. Tsuboi H, Kasamatsu Y, Matsubara S, Sasao A, Kunimitsu K, Munakata N, Ito T, Tsuchido Y, Yamawaki M, Fujita N. Two cases of novel coronavirus infection (COVID-19) with transient viral elevation using semi-quantitative real-time reverse transcription PCR and symptom relapse after completion of 10 days of favipiravir treatment. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy. 2021.07; 27(7); 1072-1075
- 13. Kawatani K, Nambara T, Nawa N, Yoshimatsu H, Kusakabe H, Hirata K, Tanave A, Sumiyama K, Banno K, Taniguchi H, Arahori H, Ozono K, Kitabatake Y. A human isogenic iPSC-derived cell line panel identifies major regulators of aberrant astrocyte proliferation in Down syndrome. Communications biology. 2021.06; 4(1); 730
- Khin YP, Nawa N, Fujiwara T, Surkan PJ. Access to contraceptive services among Myanmar women living in Japan: A qualitative study. Contraception. 2021.05;
- Mitani Y, Kobayashi Z, Hattori E, Numasawa Y, Ishihara S, Tomimitsu H, Shintani S. Successful treatment of ischemic stroke associated with brachiocephalic artery stenosis using alteplase. Journal of rural medicine : JRM. 2021.04; 16(2); 123-125
- Nawa N, Yamaoka Y, Koyama Y, Nishimura H, Sonoda S, Kuramochi J, Miyazaki Y, Fujiwara T. Association between Social Integration and Face Mask Use Behavior during the SARS-CoV-2 Pandemic in Japan: Results from U-CORONA Study. International journal of environmental research and public health. 2021.04; 18(9);
- 17. Mitani Yuta, Kobayashi Zen, Hattori Eijiro, Numasawa Yoshiyuki, Ishihara Shoichiro, Tomimitsu Hiroyuki, Shintani Shuzo. Successful treatment of ischemic stroke associated with brachiocephalic artery stenosis using alteplase(和訳中) Journal of Rural Medicine. 2021.04; 16(2); 123-125
- Koyama Y, Nawa N, Yamaoka Y, Nishimura H, Sonoda S, Kuramochi J, Miyazaki Y, Fujiwara T. Interplay between social isolation and loneliness and chronic systemic inflammation during the COVID-19 pandemic in Japan: Results from U-CORONA Study. Brain, behavior, and immunity. 2021.03;

- 19. Kanaya T, Miyagawa S, Kawamura T, Sakai Y, Masada K, Nawa N, Ishida H, Narita J, Toda K, Kuratani T, Sawa Y. Innovative therapeutic strategy using prostaglandin I₂ agonist (ONO1301) combined with nano drug delivery system for pulmonary arterial hypertension. Scientific reports. 2021.03; 11(1); 7292
- 20. Sakagami Junichi, Sogame Yoshio, Yasuda Hiroaki, Sakai Takamitsu, Kitano Satomi, Yamawaki Masanaga, Itoh Yoshito, Kagawa Keizo. A case of hereditary hemorrhagic telangiectasia complaining of shunt encephalopathy diagnosed by fast Fourier transform and contrast-enhanced ultrasonography Journal of Hospital General Medicine. 2021.03; 3(2); 49-53
- Miyamura K, Nawa N, Isumi A, Doi S, Ochi M, Fujiwara T. The association of passive smoking and dyslipidemia among adolescence in Japan: Results from A-CHILD Study. The Journal of clinical endocrinology and metabolism. 2021.02;
- Nawa N, Yamaguchi K, Kawakami C, Nakagawa M, Fujiwara T, Akita K. Differential effects of interprofessional education by gender and discipline among medical and dental students in Japan. MedEdPublish. 2021.02; 10(1);
- 23. Takizawa M, Kawachi I, Fujiwara T, Kizuki M, Nawa N, Kino S. Association Between Maternal Working Status and Unintentional Injuries Among 3 to 4-Month-Old Infants in Japan. Maternal and child health journal. 2021.01;
- 24. Kobayashi Zen, Sakai Sawako, Itaya Sakiko, Numasawa Yoshiyuki, Ota Kiyobumi, Akaza Miho, Ueda Yasuhiro, Ogawa Shinichi, Ishihara Shoichiro, Tomimitsu Hiroyuki, Shintani Shuzo. Distribution of Deep Gray Matter Lesions on Magnetic Resonance Imaging in Lymphomatosis Cerebri INTERNAL MEDICINE. 2021; 60(4); 623-627
- 25. Yashiro D, Nawa N, Okada E, Kato H, Yonemori-Matsumoto S, Kashimada A, Itsui Y, Tanaka Y. Facilitators and barriers to physicians' entrepreneurial ventures in major Japanese cities: A qualitative study. PloS one. 2021; 16(10); e0258957
- Hanafusa M, Kuramochi J, Ishihara K, Honda M, Nawa N, Fujiwara T. Clinical characteristics of patients with SARS-CoV-2 N501Y variants in general practitioner clinic in Japan. Journal of Clinical Medicine. 2021; (in press);

[Conference Activities & Talks]

- 1. Mitsuyuki Numasawa, Nobutoshi Nawa, Yu Funakoshi, Kumiko Yamaguchi, Chiharu Kawakami, Mina Nakagawa. Comparison of the readiness of medical, dental, and nursing students for interprofessional learning. AMEE 2021 2021.08.27 The Virtual Conference
- 2. Yu Funakoshi, Nobutoshi Nawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Takeo Fujiwara, Keiichi Akita. The association between social capital and succeeding academic performance: A multilevel analysis. The Association for Medical Education in Europe (AMEE) Conference 2021 2021.08.27 Online
- 3. Kumiko Yamaguchi, Nobutoshi Nawa, Mitsuyuki Numasawa, Yu Funakoshi, Keiichi Akita. Evaluation of the effectiveness of multiple terminology test and e-learning materials in a human anatomy course. The Association for Medical Education in Europe (AMEE) Conference 2021 2021.08.27 Online
- 4. Mitsuyuki Numasawa, Nobutoshi Nawa, Yu Funakoshi, Kumiko Yamaguchi, Chiharu Kawakami, Mina Nakagawa. Comparison of the readiness of medical, dental, and nursing students for interprofessional learning. The Association for Medical Education in Europe (AMEE) Conference 2021 2021.08.27 Online
- 1. Development of Excel macro to automatically output files showing questionnaire data graphically. The 53rd Annual Meeting of the Japan Society for Medical Education 2021.07.30

General Dentistry

Professor Hiroshi NITTA Associate Professor Akira NISHIYAMA Junior Associate Professor Masayuki HIDESHIMA Junior Associate Professor Ken-ichi TONAMI Junior Associate Professor Kanako NORITAKE Assistant Professor Sachi UMEMORI Project Assistant Professor Maiko IWAKI Project Assistant Professor Yasuyuki KIMURA Project Assistant Professor Naoko HARADA Hospital Staff Hiraku OONUMA Hospital Staff Yuna KANAMORI Hospital Staff Yutaro KITANAKA Hospital Staff Daisuke KIDO Hospital Staff Yukako KUSUNOKI Hospital Staff Naoki SASAKI Hospital Staff Shogo TAKEUCHI Hospital Staff Akitaka HATTORI Hospital Staff Hirohito MIKI Hospital Staff Mai MIYACHI Graduate student Ayako SEKIGUCHI

(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

- 1. Suzuki H, Sugimoto K, Kubota-Miyazawa A, Noritake K, Umemori S, Araki K, Adachi N, Otsuka H, Yoshida N. A survey of oral health status, subjective oral symptoms and oral health behaviors among first-year dental students at a Japanese university. Journal of oral science. 2021.12; 64(1); 85-90
- 2. Sayaka Tada, Manabu Kanazawa, Anna Miyayasu, Maiko Iwaki, Murali Srinivasan, Shunsuke Minakuchi, Gerald McKenna. Patient preferences for different tooth replacement strategies for the edentulous mandible: A willingness-to-pay analysis. J Prosthodont Res. 2021.10; 65(4); 535-540
- 3. Mikami R, Mizutani K, Shioyama H, Matsuura T, Aoyama N, Suda T, Kusunoki Y, Takeda K, Izumi Y, Aida J, Aoki A, Iwata T. Influence of aging on periodontal regenerative therapy using enamel matrix derivative: A 3-year prospective cohort study. Journal of clinical periodontology. 2021.09; 49(2); 123-133
- 4. Hiroyuki Saida, Shunsuke Fukuba, Takahiko Shiba, Keiji Komatsu, Takanori Iwata, Hiroshi Nitta. Two-stage approach for class II mandibular furcation defect with insufficient keratinized mucosa: a case report with 3 years' follow-up. J Int Med Res. 2021.09; 49(9); 3000605211044595
- 5. Kataoka A, Katagiri S, Kawashima H, Nagura F, Nara Y, Hioki H, Nakashima M, Sasaki N, Hatasa M, Maekawa S, Ohsugi Y, Shiba T, Watanabe Y, Shimokawa T, Iwata T, Kozuma K. Association between Periodontal Bacteria and Degenerative Aortic Stenosis: A Pilot Study Journal of Periodontal and Implant Science. 2021.08; 51(4); 226-238

- Yasuyuki Kimura, Ken-ichi Tonami, Akira Toyofuku, Hiroshi Nitta . Analysis of Incident Reports of a Dental University Hospital. International Journal of Environmental Research and Public Health. 2021.08; 18(16); 8350
- Rumi Tano, Hiroko Miura, Katsuo Oshima, Kanako Noritake and Hideki Fukuda. Relationship between career education experience among final year dental hygiene students and their perspective towards work and profession: a nationwide survey in dental hygiene schools of Japan. International Journal of Dental Hygiene. 2021.07; 0(00); 1-6
- Numasawa M, Nawa N, Funakoshi Y, Noritake K, Tsuruta J, Kawakami C, Nakagawa M, Yamaguchi K, Akita K. A mixed methods study on the readiness of dental, medical, and nursing students for interprofessional learning. PloS one. 2021.07; 16(7); e0255086
- 9. Shiba T, Watanabe T, Komatsu K, Koyanagi T, Nemoto T, Ohsugi Y, Michi Y, Katagiri S, Takeuchi Y, Ishihara K, Iwata T. Non-surgical treatment for periodontitis and peri-implantitis: longitudinal clinical and bacteriological findings-A case report with a 7-year follow-up evaluation. SAGE open medical case reports. 2021.07; 9; 2050313X211029154
- Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S.. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. Journal of Dental Sciences. 2021.07;
- Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S. Patient-reported outcomes with immediate-loaded two-implant-supported mandibular overdentures: Results of a 5-year prospective study. Journal of Dental Sciences. 2021.06;
- 12. Noritake Kanako, Kanamori Yuna, Nitta Hiroshi. A remote program for residents to solve clinical questions and improve presentation skills. JOURNAL OF DENTAL EDUCATION. 2021.06; 85; 998-999
- Onuma H, Inokoshi M, Hirayama D, Inoue M, Minakuchi S. Stress distribution analysis of oral mucosa under soft denture liners using smoothed particle hydrodynamics method. J Mech Behav Biomed Mater. 2021.05; 117; 104390
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- 15. Hidaka R, Furuya J, Nishiyama A, Suzuki H, Aoyagi M, Matsubara C, Yoshizumi Y, Yoshimi K, Nakane A, Tohara H, Sato Y, Minakuchi S. Structural Equation Modeling of Tongue Function and Tongue Hygiene in Acute Stroke Patients. International journal of environmental research and public health. 2021.04; 18(9); 4567
- 16. Hiroyuki Ishiyama, Masayuki Hideshima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki. Evaluation of Respiratory Resistance as a Predictor for Oral Appliance Treatment Response in Obstructive Sleep Apnea: A Pilot Study. Journal of Clinical Medicine. 2021.03; 10(6); 1255-1268
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- Soeda Y, Kanazawa M, Hada T, Arakida T, Iwaki M, Minakuchi S. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. The Journal of prosthetic dentistry. 2021.03;
- 19. Nour Ammar, Nourhan M. Aly, Morenike O. Folayan, Yousef Khader, Simin Z. Mohebbi, Sameh Attia, Hans-Peter Howaldt, Sebastian Boettger, Jorma Virtanen, Marwa Madi, Diah A. Maharani, Anton Rahardjo, Imran Khan, Ola B. Al-Batayneh, Maher Rashwan, Verica Palvic, Smiljka Cicmil, Kanako Noritake, Gabriella Galluccio, Antonella Polimeni, Anas A. Shamala, Arheiam Aarheiam, Davide Mancino, Prathip Phantumvanit, Jin-Bom Kim, Youn-Hee Choi, Mai A. Dama, Maha M. Abdelsalam, Jorge L. Castillo, Myat Nyan, Iyad Hussein, Easter Joury, Ana P. Vukovic, Alfredo Iandolo, Arthur M. Kemoli, Maha El Tantawi . Preparedness of Dental Academic Institutions to Cope with the COVID-19. International journal of Environmental Research and Public Health. 2021.02; 18(4); 1445-1459

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- 22. Inagaki K, Kikuchi T, Noguchi T, Mitani A, Naruse K, Matsubara T, Kawanami M, Negishi J, Furuichi Y, Nemoto E, Yamada S, Yoshie H, Tabeta K, Tomita S, Saito A, Katagiri S, Izumi Y, Nitta H, Iwata T, Numabe Y, Yamamoto M, Yoshinari N, Fujita T, Kurihara H, Nishimura F, Nagata T, Yumoto H, Naito T, Noguchi K, Ito K, Murakami S, Nishimura R, Tajima N. A large-scale observational study to investigate the current status of diabetic complications and their prevention in Japan (JDCP study 6): baseline dental and oral findings. Diabetology international. 2021.01; 12(1); 52-61
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- Inokoshi M, Onuma H, Hirayama D, Inoue M, Minakuchi S. Application of the particle method simulation to dental materials. The Journal of the Japanese Society for Dental Materials and Devices. 2021.01; 40(1); 17-20

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- 1. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part12 PSG/OCST for The Objective Effect Measurement of Oral Appliance and The Instructive and Coaching Methods for Its Habit Training. the Quintessence. 2021.12; 40(12); 212-219
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part11 Jaw Exercises, Subjective Assessments of Oral Appliance, and Mandibular Advancement Titration. the Quintessence. 2021.11; 40(11); 190-199
- 3. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part10 The Fabrication, Adjustment and Delivery of the OA. the Quintessence. 2021.10; 40(10); 212-221
- 4. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part9 Protrusive Bite Fundamentals in Preparation of Oral Appliance. the Quintessence. 2021.09; 40(9); 204-211
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part8 Perfect Techniques for Impression Taking in Preparation of Oral Appliances. the Quintessence. 2021.08; 40(8); 196-201
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part7 The Treatment Planning and Consultation in Dental Sleep Medicine. the Quintessence. 2021.07; 40(7); 220-227
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part6 The Preprocedural Testing of Sleep-Related Breathing Disorders Necessary to Make Oral Appliances. the Quintessence. 2021.06; 40(6); 228-239
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part5 The Testing of Sleep Apnea Syndrome and the Exploratory Data Analysis Method for Its Outcomes. the Quintessence. 2021.05; 40(5); 250-260

- 9. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part4 How to Counsel Someone with Sleep Disorders. the Quintessence. 2021.04; 40(4); 254-264
- 10. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part3 The Definition and Description of Sleep and of sleep disorders. the Quintessence. 2021.03; 40(3); 224-231
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part2 The Screening and Clinical Diagnosis of Obstructive Sleep Apnea and Its Treatment Options. the Quintessence. 2021.02; 40(2); 192-199
- 12. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part1 Significance and Prospects of Dental Sleep Medicine. the Quintessence. 2021.01; 40(1); 194-199

[Conference Activities & Talks]

- Bui Ngoc Huyen Trang, Manabu Kanazawa, Natsuko Murakami, Noriyuki Wakabayashi, Awutsadaporn Katheng, Sai Tun Naing, Sahaprom Namano, Maiko Iwaki, Shunsuke Minakuchi. Stress Distribution of One-Piece and Two-Piece Mini-Implant Overdentures (Various Attachments). CED-IADR/NOF Oral Health Research Congress in Brussels 2021.09.16
- Kay Thwe Ye Min Soe, Akira Nishiyama. Effect of different Upper Oral Appliance designs on sleep-associated-respiratory status. 2021 ADR/AADR/CADR General Session & Exhibition 2021.07.24 (online)
- 3. Ken-ichi Tonami, Sachi Umemori, Yasuyuki Kimura, Kanako Noritak, Kouji Araki, Hiroshi Nitta. Effects of Online Education on Students' Self-Reflection About Inter-Personal Relationship. 99th General Session & Exhibition of the IADR 2021.07.14 online
- 4. Kay Thwe Ye Min Soe, Akira Nishiyama. Effect of palatal width and vertical dimension of the upper oral appliance on respiratory status during sleep. The 75th Annual Meeting of Japanese Stomatological Society 2021.05.13 (online)
- Dalia Kaisarly, Yuna Kanamori, Daniel Meierhofer, Ruth Langenegger, Moataz El Gezawi, Peter Rösch, Karl-Heinz Kunzelmann. Shrinkage Vectors In Bulk-fill Composites Restoring Endodontic Access Cavities. 10th online CONSEURO 2021 2021.04.22 (online)
- 6. Jun Tsuruta, Ken-ichi Tonami, Kanako Noritake, Kumiko Yamaguchi, Mina Nakagawa. New approach for IPE for dental and medical clinical students with restriction of educational setting under the COVID-19 pandemic. ADEE Strasbourg Online Annual Meeting 2021 2021 (online)
- 1. Yuna Kanamori, Naoko Seki, Kanako Noritake, Janelle Moross, Masayo Sunaga, Ikuko Morio, Atsuhiro Kinoshita, Hiroshi Nitta. Trial of online English medical interview training for TMDU trainee residents. The 86th annual meeting of the Stomatological Society 2021.12.04 Tokyo
- 2. Ken-ichi Tonami, Jun Tsuruta, Kanako Noritake, Sachi Umemori, Yasuyuki Kimura, Hiroshi Nitta. Analysis of reports of dental students attending to a palliative care Krusus. 2021.12.04
- 3. Mai Miyachi. Approach for the side effects of Mandibular Advanced Device treatment for Obstructive Sleep Apnea in the United States. The 20th Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2021.11.28 Kitakyuusyuu Convention Center
- 4. NORITAKE Kanako, SUNAGA Masayo, EBIHARA Arata, HIDESHIMA Masayuki, TONAMI Ken-ichi, UMEMORI Sachi, KANAMORI Yuna, KINOSHITA Atsuhiro, NITTA Hiroshi. A Trial of Online Examination for Recruitment of Dental Residents at Dental Hospital, Tokyo Medical and Dental University. 2021.11.20
- 5. UMEMORI Sachi, TONAMI Ken-ichi, NORITAKE Kanako, KIMURA Yasuyuki, KANAMORI Yuna, NITTA Hiroshi. The Analysis of professionalism education for Dental students in the online classes of behavioral science in Tokyo Medical and Dental University . 2021.11.20
- 6. TONAMI Ken-ichi, UMEMORI Sachi, NORITAKE Kanako, KIMURA Yasuyuki, KANAMORI Yuna, NITTA Hiroshi. Perception of behavioral science in the second-year dental students, TMDU. 2021.11.20

- 7. KANAMORI Yuna, NORITAKE Kanako, KIMURA Yasuyuki, KIDO Daisuke, EBIHARA Arata, HIDESHIMA Masayuki, TONAMI Ken-ichi, UMEMORI Sachi, NITTA Hiroshi. TMDU dental trainee residents' ability to evaluate abutment tooth preparation. The 40th General and Scientific Meeting of the Japanese Dental Education Association 2021.11.20 online
- 8. Yuna KANAMORI, Rena TAKAHASHI, Masaomi IKEDA, Shingo KAMIJO, Shin ROZAN, Kanako NORITAKE, Ken-ichi TONAMI, Hiroshi NITTA, Toru NIKAIDO, Yasushi SHIMADA, Junji TAGAMI. The effect of resin coating technique on internal fit of CAD/CAM composite resin crowns. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Web
- 9. Mai Miyachi. Medical and dental cooperation in sleep apnea treatment, Practice and problems of medical and dental cooperation: Perspective of general dentistry. Japanese Society of Sleep Research 46th Annual Meeting 2021.09.23 Fukuoka Convention Center
- 10. Mai Miyachi. Approach for the side effects of Mandibular Advanced Device treatment for Obstructive Sleep Apnea in the United States. Japanese Society of Sleep Research 46th Annual Meeting 2021.09.23 Fukuoka Convention Center
- 11. Kanako Noritake, Kumiko Yamaguchi, Yuna Kanamori, Makoto Kikukawa, Hiroshi Nitta. The characteristics of a good clinical teacher for dental trainees. 2021.07.30
- 12. Masayuki Hideshima, Takeshi Suganuma, Kentaro Okuno, Eri Makihara. Symposium "Oral appliance therapy for obstructive sleep apnea (OSA)". The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.20
- 13. Otake R, Kanazawa M, et al.. A prospective study of digital complete dentures using customized disc method.. 2021.06.19 online
- 14. Inokoshi M, Ueda K, Shimizubata M, Motomura K, Yamamoto M, Onuma H, Watanabe M, Shimizu K, Kubota K, Minakuchi S. Online elderly simulation training program during the COVID-19 pandemic. The 32nd Annual Meeting of Japanese Society of Gerodontology 2021.06.12 web
- 15. Soeda Y, Kanazawa M, Iwaki M, Arakida T, Hada T, Otake R, Katheng A, Akiyama Y, Ando K, Minakuchi S. Trueness and precision of artificial teeth in CAD/CAM milled complete dentures with custom disks of prefabricated frame. 2021.04.24

[Others]

Prognosis model of treatment effect for sleep apnea - Non-contacting evaluation of oral appliance therapy

 , 2021.04
 Masayuki HIDESHIMA
 Grant-in-Aid for Scientific Research(C) 2018
 Research No. 18K09678
 Research Period 2018-2021
 Principal Investigator Masayuki HIDESHIMA
 Research Fund \3,500,000

Psychosomatic Dentistry

Professor

Akira Toyofuku

Assistant Professor

Motoko Watanabe

Hospital Staff

Takayuki Suga, Chihiro Takao, Chizuko Maeda

Graduate Student

Atsushi Ito, Kazuya Watanabe, Mitsuhiro Asami, Chaoli Hong,

Chihiro Takao, Liu Zhenyan Kiyokazu Iwawaki, Gayatri Nayanar

Lecturer (part-time) Haruhiko Motomura, Jiro Kurata, Takahiko Naganine

(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 trough 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**

- 1. Kazuya Watanabe, Motoko Watanabe, Chihiro Takao, Chaoli Hong, Zhenyan Liu, Takayuki Suga, Trang Thi Huyen Tu, Junichiro Sakamoto, Yojiro Umezaki, Tatsuya Yoshikawa, Miho Takenoshita, Akihito Uezato, Haruhiko Motomura, Tohru Kurabayashi, Yoshihiro Abiko, Akira Toyofuku. Clinical Characteristics of Predominantly Unilateral Oral Cenesthopathy With and Without Neurovascular Contact. Front Neurol. 2021.10; 12; 744561
- 2. C Takao, G Nayanar, A Toyofuku. COVID-19 'syndemic'. Br Dent J. 2021.10; 231(8); 426
- Miho Takenoshita, Haruhiko Motomura, Akira Toyofuku. Olfactory Reference Syndrome (Halitophobia) With Oral Cenesthopathy Treated With Low-Dose Aripiprazole: A Case Report. Clin Neuropharmacol. 2021.09;
- 4. Motoko Watanabe, Chaoli Hong, Zhenyan Liu, Chihiro Takao, Takayuki Suga, Trang Thi Huyen Tu, Tatsuya Yoshikawa, Miho Takenoshita, Yusuke Sato, Norihisa Higashihori, Keiji Moriyama, Haruhiko Motomura, Akira Toyofuku. Case Report: Iatrogenic Dental Progress of Phantom Bite Syndrome: Rare Cases With the Comorbidity of Psychosis. Front Psychiatry. 2021.08; 12; 701232
- Yasuyuki Kimura, Ken-ichi Tonami, Akira Toyofuku, Hiroshi Nitta . Analysis of Incident Reports of a Dental University Hospital. International Journal of Environmental Research and Public Health. 2021.08; 18(16); 8350
- Takayuki Suga, Trang T H Tu, Junichiro Sakamoto, Akira Toyofuku. A case of vestibular schwannoma with oral burning sensation: surgical complication or burning mouth syndrome? Biopsychosoc Med. 2021.08; 15(1); 13
- Trang Thi Huyen Tu, Motoko Watanabe, Takayuki Suga, Chaoli Hong, Chihiro Takao, Miho Takenoshita, Haruhiko Motomura, Akira Toyofuku. Personality Traits in Burning Mouth Syndrome Patients With and Without a History of Depression. Front Psychiatry. 2021.07; 12; 659245
- 8. Takayuki Suga, Trang Thi Huyen Tu, Miho Takenoshita, Lou Mikuzuki, Yojiro Umezaki, Hiroaki Shimamoto, Yasuyuki Michi, Chaoli Hong, Yoshihiro Abiko, Tohru Ikeda, Narikazu Uzawa, Hiroyuki Harada, Akira Toyofuku. Case Report: Hidden Oral Squamous Cell Carcinoma in Oral Somatic Symptom Disorder. Front Psychiatry. 2021.04; 12; 651871
- 9. Takayuki Suga, Miho Takenoshita, Trang T H Tu, Takashi Sugawara, Susumu Kirimura, Akira Toyofuku. A case of vestibular schwannoma mimicking burning mouth syndrome. Biopsychosoc Med. 2021.03; 15(1); 7
- 10. Takayuki Suga, Trang T H Tu, Takahiko Nagamine, Akira Toyofuku. Careful use of clonazepam and alpha lipoid acid in burning mouth syndrome treatment. Oral Dis. 2021.01;

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- Trang Thi Huyen Tu, Motoko Watanabe, Gayatri Krishnakumar Nayanar, Yojiro Umezaki, Haruhiko Motomura, Yusuke Sato, Akira Toyofuku. Phantom bite syndrome: Revelation from clinically focused review. World J Psychiatry. 2021.11; 11(11); 1053-1064
- Yoshihiro Abiko, Durga Paudel, Hirofumi Matsuoka, Mitsuru Moriya, Akira Toyofuku. Psychological Backgrounds of Medically Compromised Patients and Its Implication in Dentistry: A Narrative Review. Int J Environ Res Public Health. 2021.08; 18(16);
- 3. Yojiro Umezaki, Haruhiko Motomura, Akihito Uezato, Toru Naito, Akira Toyofuku. The similarities and differences between oral cenesthopathy and burning mouth syndrome in the elderly. Gerodontology. 2021.05;

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

- $\cdot\,$ Needs assessment in health care and in professional development in health science fields
- $\cdot~$ Curriculum development for professionals of the future needs in health sciences

(3) Education

Undergraduate schools

Courses

- \cdot School of medicine (1st year): Medical Introductory Courses
- · Schools of medicine/dentistry (2nd/3rd years): Global Communication for Health Professionals
- \cdot School of medicine (4th year): Preparation for Clinical Clerkship
- \cdot School of medicine (5th/6th years): Clinical Clerkship
- \cdot 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
- · [Master level] Health Systems Management

(4) Clinical Services & Other Works

Medical Hospital Kazuki TAKADA (Rheumatology)

(5) **Publications**

[Original Articles]

1. Wang Z, Kohno EY, Fueki K, Ueno T, Inamochi Y, Takada K, Wakabayashi N. Multilevel factor analysis of flipped classroom in dental education: A 3-year randomized controlled trial. PloS one. 2021.09; 16(9); e0257208

Family Medicine

Masanaga Yamawaki Toru Yamada Masashi Beppu Suguru Mabuchi Yu Akaishi Shoko Yoshida Risa Suzuki Yuki Goto Takahiro Shinohara Mari Fukuhara

Masako Sugihara Yuya Ando Akane Futami Hiroshi Koike Kota Hada Kaname Dateoka Mari Miya

Shuji Ouchi Hiroki Nin Hiroki Sekiguchi Maki Goto Risa Narita Kouki Kiyama Azusa Aoshima Seiya Sato Ryota Takaishi Tsukasa Tabuchi Rio Tsuruwaka Hironori Yamada

(1) **Outline**

"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.

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. Uchihara M, Ehara J, Iwanami K, Kitamura K, Suzuki T, Ishizuka N, Yamada T, Hiraoka E. Chylous Ascites Due to Hyperthyroidism and Heart Failure. Internal medicine (Tokyo, Japan). 2021.12;
- 2. Kawahara T, Ueki Y, Nawa N, Miyamae S, Hanafusa M, Goto Y, Tohda S, Fujiwara T. Characteristics of SARS-CoV-2 super-spreaders in Japan. The Journal of infection. 2021.12;
- 3. Yuya Ando, Yosuke Ono, Azusa Sano, Naoya Fujita, Sachiko Ono. Posterior Reversible Encephalopathy Syndrome: A Review of the Literature. Intern Med. 2021.07;
- 4. Yuya Ando, Sachiko Ono, Yosuke Ono, Jinghua Yin. Sister Mary Joseph's Nodule from Pancreatic Cancer. Intern Med. 2021.05;
- 5. Ando Y, Hashimoto K, Sano A, Fujita N, Yanagawa R, Ono Y, Obuchi Y, Tatsushima D, Watanabe S, Tomifuji M, Tanaka Y. Frequent occurrence of postbreakfast syncope due to carotid sinus syndrome after surgery for hypopharyngeal cancer: A case report. Medicine. 2021.05; 100(20); e25959
- 6. Yuya Ando, Yosuke Ono, Sachiko Ono. Diphyllobothriasis from Eating Sushi. Am J Trop Med Hyg. 2021.04;
- Yamada T, Hiraoka E, Takemura Y. Predictive Validity of Past-Behavioral Versus Situational Questions in Postgraduate Medical Admissions. Academic medicine : journal of the Association of American Medical Colleges. 2021.02; 96(2); 164-165

Infectious Diseases

Professor GU Yoshiaki Assistant professor TAGASHIRA Yasuaki Assistant professor KURITA Takashi Assistant professor (Division of Infection Control and Prevention) IDE Satoshi Secretary FUNADA Eriko

(1) **Outline**

The Department of Infectious Diseases is in charge of research and education with a focus on clinical infectious diseases. We are in charge of clinical practice of infectious diseases and infection prevention and control at Tokyo Medical and Dental University Hospital. We conduct epidemiological research on infectious diseases and other researches, as well as educational activities on infectious diseases in general.

In addition, as the core of TMDU's "Platform Project for Multilayered Efforts to Conquer Infectious Disease Pandemics," the department plays a role in promoting infectious disease research and education at the university.

(2) Research

We conduct clinical and epidemiological research on infectious diseases from various perspectives, with a focus on research on the proper use of antimicrobials and the control of hospital-acquired infections.

Among these, we are focusing on hospital epidemiology research related to antimicrobial resistance (AMR), which has become a major problem in Japan and worldwide, and research aimed at changing the behavior of healthcare workers and the general public by investigating their awareness of AMR.

In collaboration with the Tokyo Metropolitan Government, we are also conducting research on the response of medical institutions and public health to the COVID-19 pandemic.

(3) Education

We are committed to training the infectious disease specialists who will lead the future. Since infectious diseases are related to all aspects of healthcare, it is also important to increase the number of physicians who are trained in basic infectious disease treatment and infection prevention and control. Education for multiple professions is also important. We are committed to human resource development by providing education at various stages.

Pre-graduate education

We are in charge of lectures and practical training related to clinical infectious disease treatment and infection prevention and control, focusing on lectures for third-year medical students. We devise ways for students to learn with interest the basics of clinical infectious diseases that all physicians and health care workers should learn.

Post-graduate education

We offer programs that match your previous experience and career plans, including initial residency , major residency, and fellowship to become a specialist.

Graduate Education

We aim to train professionals to tackle infectious diseases from multiple perspectives, with a focus on clinical

infectious diseases and infectious disease epidemiology.

Topics include AMR control, hospital epidemiology, and control of hospital acquired infections.

Continuing Education

In all areas of clinical practice, you will be involved in the treatment of infectious diseases to a greater or lesser extent. We contribute to lifelong education by providing information on the diagnosis and treatment of infectious diseases.

We are also involved in education for pharmacists, nurses, clinical laboratory technicians, and other professionals.

(4) Lectures & Courses

The program aims to train professionals to tackle infectious diseases from multiple perspectives, with a focus on clinical infectious diseases and infectious disease epidemiology.

(5) Clinical Services & Other Works

We are in charge of the Department of Infectious Diseases and the Division of Infection Control and Prevention at Tokyo Medical and Dental University Hospital.

The Department of Infectious Diseases is a new department established in October 2021. Focusing on consultations from various departments, our department diagnoses and treats a variety of infectious diseases that occur mainly in inpatients. The department identifies the microorganisms that are causing symptoms of infections such as fever and other suspected infectious diseases, and selects the most appropriate treatment according to the microorganisms and the patient's condition.

The Division of Infection Control and Prevention is responsible for preventing infectious diseases that occur in the hospital, preventing their spread, and providing a safe environment for patients to receive medical care. We work as a multidisciplinary team in cooperation with all related departments.

We are working to promote the proper use of antimicrobial agents to prevent antimicrobial resistance (AMR), which has become a major problem in recent years. The Department of Infectious Diseases and the Department of Infection Control are working together to monitor the use of antimicrobials and to improve AMR control and treatment outcomes by optimizing the treatment of infectious diseases.

Outside of the university, we have a project with the Tokyo Metropolitan Government for the "Project for Strengthening the Capacity of Small and Medium-Sized Hospitals to Respond to Infectious Disease Health Crises in the Post-Coronary Era" as a three-year plan starting in FY2022. We are also involved in a variety of other activities, including academic conferences and public activities.

(6) Clinical Performances

The Department of Infectious Diseases provides clinical consultation services in response to consultations from various departments. It provides support to each department by dealing with various infectious diseases regardless of the organ, and contributes to the diagnosis and treatment of infectious diseases throughout the University Hospital. The Division of Infection Control and Prevention focuses on the prevention of infectious diseases. Through these activities, the department plays a role in supporting advanced medical care at the university hospital.

(7) Publications

[Original Articles]

- Inoue K, Kobayashi S, Sato K, Kanno H, Kantou R, Naganuma Y, Kawamura N, Oike Y, Kobayashi M, Yanai M, Suzuki A, Kurai H, Miyairi I, Kutsuna S, Gu Y. Regional antimicrobial stewardship program in a provincial medical zone in Japan: A multifaceted approach. Japanese journal of infectious diseases. 2021.12;
- 2. Koizumi R, Kusama Y, Asai Y, Yoshiaki G, Muraki Y, Ohmagari N. Effects of the cefazolin shortage on the sales, cost, and appropriate use of other antimicrobials. BMC health services research. 2021.10; 21(1); 1118

- 3. Takamatsu A, Kano Y, Tagashira Y, Kirikae T, Honda H. Current in-hospital management for patients with tuberculosis in a high-income country: a retrospective cohort study. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2021.07;
- 4. Tagashira Yasuaki, Takamatsu Akane, Hasegawa Shinya, Uenoyama Yuki, Honda Hitoshi. A survey of preparedness against coronavirus disease 2019 (COVID-19) in hospitals in Tokyo, Japan, with healthcare personnel with COVID-19 and in-facility transmission INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY. 2021.06; 42(6); 746-750
- Hasegawa S, Tagashira Y, Murakami S, Urayama Y, Takamatsu A, Nakajima Y, Honda H. Antimicrobial Time-Out for Vancomycin by Infectious Disease Physicians Versus Clinical Pharmacists: A Before-After Crossover Trial. Open forum infectious diseases. 2021.06; 8(6); ofab125
- Honda N., Tagashira Y., Kawai S., Kobayashi T., Yamamoto M., Shimada K., Yokogawa N.. Reduction of Pneumocystis jirovecii pneumonia and bloodstream infections by trimethoprim-sulfamethoxazole prophylaxis in patients with rheumatic diseases SCANDINAVIAN JOURNAL OF RHEUMATOLOGY. 2021.03;
- 7. Yamagishi T, Ohnishi M, Matsunaga N, Kakimoto K, Kamiya H, Okamoto K, Suzuki M, Gu Y, Sakaguchi M, Tajima T, Takaya S, Ohmagari N, Takeda M, Matsuyama S, Shirato K, Nao N, Hasegawa H, Kageyama T, Takayama I, Saito S, Wada K, Fujita R, Saito H, Okinaka K, Griffith M, Parry AE, Barnetson B, Leonard J, Wakita T. Corrigendum to: Environmental Sampling for Severe Acute Respiratory Syndrome Coronavirus 2 During a COVID-19 Outbreak on the Diamond Princess Cruise Ship. The Journal of infectious diseases. 2021.02; 223(3); 540
- 8. Morioka Shinichiro, Gu Yoshiaki, Tsuzuki Shinya, Fujitomo Yumiko, Soeda Hiroshi, Nakahama Chikara, Hasegawa Naoki, Maesaki Shigefumi, Maeda Masayuki, Matsumoto Tetsuya, Miyairi Isao, Ohmagari Norio. Determinants of clinic doctors' attitudes concerning antimicrobial prescription for patients with common colds or bronchitis: Additional analysis of a nationwide survey conducted by the Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases(和訳中) Journal of Infection and Chemotherapy. 2021.02; 27(2); 131-138
- 9. Morioka S, Gu Y, Tsuzuki S, Fujitomo Y, Soeda H, Nakahama C, Hasegawa N, Maesaki S, Maeda M, Matsumoto T, Miyairi I, Ohmagari N. Determinants of clinic doctors' attitudes concerning antimicrobial prescription for patients with common colds or bronchitis: Additional analysis of a nationwide survey conducted by the Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy. 2021.02; 27(2); 131-138
- Shin JH, Mizuno S, Okuno T, Itoshima H, Sasaki N, Kunisawa S, Kaku M, Yoshida M, Gu Y, Morii D, Shibayama K, Ohmagari N, Imanaka Y. Nationwide multicenter questionnaire surveys on countermeasures against antimicrobial resistance and infections in hospitals. BMC infectious diseases. 2021.02; 21(1); 234
- 11. Yao Kenta, Hasegawa Shinya, Tagashira Yasuaki, Takamatsu Akane, Uenoyama Yuki, Shimizu Keiki, Honda Hitoshi. Experience of 101 patients with coronavirus infectious disease 2019 (COVID-19) at a tertiary care center in Japan JOURNAL OF INFECTION AND CHEMOTHERAPY. 2021.02; 27(2); 413-417
- 12. Yao Kenta, Hasegawa Shinya, Tagashira Yasuaki, Takamatsu Akane, Uenoyama Yuki, Shimizu Keiki, Honda Hitoshi. Experience of 101 patients with coronavirus infectious disease 2019(COVID-19) at a tertiary care center in Japan(和訳中) Journal of Infection and Chemotherapy. 2021.02; 27(2); 413-417
- Tagashira Y, Goto M, Kondo R, Honda H. Multifaceted intervention for improving antimicrobial prescription at discharge in the emergency department. Infection control and hospital epidemiology. 2021.02; 1-4
- 14. Jindai Kazuaki, Kusama Yoshiki, Gu Yoshiaki, Honda Hitoshi, Ohmagari Norio. Narrative Review: The Process of Expanding the Manual of Antimicrobial Stewardship by the Government of Japan(和訳中) Internal Medicine. 2021.01; 60(2); 181-190
- Jindai K, Kusama Y, Gu Y, Honda H, Ohmagari N. Narrative Review: The Process of Expanding the Manual of Antimicrobial Stewardship by the Government of Japan. Internal medicine (Tokyo, Japan). 2021.01; 60(2); 181-190

1. Yoshiaki Gu, Yumiko Fujitomo, Norio Ohmagari. Outcomes and Future Prospect of Japan's National Action Plan on Antimicrobial Resistance (2016-2020). Antibiotics (Basel, Switzerland). 2021.11; 10(11);

[Social Contribution]

1. Self-Isolation Handbook for COVID-19 Patients , Tokyo iCDC Expert Board, 2021.01 $\,$

Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio Lecturer : SAITO Kenta Assistant Professor: KAWAGISHI Masahiko 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]

 Nori Nakai, Keisuke Sato, Masahiko Kawagishi, Hiromasa Ka, Kenta Saito, Sumio Terada. Development of nanobody-based POLArIS orientation probes enabled multi-color/multi-target orientation imaging in living cells. Biochemical and biophysical research communications. 2021.08; 565; 50-56 2. Ayana Sugizaki, Keisuke Sato, Kazuyoshi Chiba, Kenta Saito, Masahiko Kawagishi, Yuri Tomabechi, Shalin B Mehta, Hirokazu Ishii, Naoki Sakai, Mikako Shirouzu, Tomomi Tani, Sumio Terada. POLArIS, a versatile probe for molecular orientation, revealed actin filaments associated with microtubule asters in early embryos Proceedings of the National Academy of Sciences of the United States of America. 2021.03; 118(11);

[Misc]

1. TERADA Sumio, KAWAGISHI Masahiko. axon Brain Science Dictionary . 2021.06;

[Conference Activities & Talks]

- 1. 佐藤啓介, 杉﨑 綾奈, 齊藤 健太, Shalin B. Mehta, 白水 美香子, 谷 知己, 寺田 純雄. F-actin 特異的分子配向 プローブ POLArIS^{act}の開発と評価. 第 126 回日本解剖学会総会 · 全国学術集会 2021.03.29 オンライン開催
- 2. 杉崎 綾奈, 佐藤 啓介, 千葉 和義, 川岸 将彦, 寺田 純雄. ヒトデ初期発生の有糸分裂においてアクチン繊維は 微小管星状体と関連して放射状に伸長する. 第 126 回日本解剖学会総会 · 全国学術集会 2021.03.29 オンライ ン開催
- 1. Keisuke Sato, Ayana Sugizaki, Kazuyoshi Chiba, Kenta Saito, Masahiko Kawagishi, Shalin B. Mehta, Mikako Shirouzu, Tomomi Tani, Sumio Terada. Development of POLArIS, a versatile probe for molecular orientation, and its application to the analysis of actin dynamics in living cells. The 44th Annual Meeting of the Molecular Biology Society of Japan 2021.12.03 Yokohama
- 2. Terada Sumio. Development of POLArIS, a versatile and genetically encoded fluorescent probe for molecular orientation, and its application in live-cell imaging. the 126th Annual Meeting of The Japanese Association of Anatomists 2021.03.31 JAPAN

[Others]

1. The Stars Align: New Imaging Technology Reveals Architecture in Dividing Starfish Cells, 2021.04 Seeing how the building blocks of cells align over time is important for understanding how cells are built, move, grow and divide. Recently, researchers from Japan collaborated with imaging scientists at the Marine Biological Laboratory (MBL) to develop a new cellular probe, POLArIS, that allows real-time imaging of molecular orientations in live cells.

The study, led by researchers at Tokyo Medical and Dental University (TMDU), was published in Proceedings of the National Academy of Sciences.

Systems Neurophysiology

Professor Izumi Sugihara Associate Professor Yuriko Sugiuchi Lecturer Yoshiko Izawa Lecturer Mayu Takahashi JSPS Postdoctoral fellow Yuanjun Luo Students (dorcor) 7

(1) Outline

Department of Systems Neurophysiology, formarly 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]

- Malhotra Shreya, Banumurthy Gokulakrishna, Pennock Reagan L., Vaden Jada H., Sugihara Izumi, Overstreet-Wadiche Linda, Wadiche Jacques I. Climbing Fiber-Mediated Spillover Transmission to Interneurons Is Regulated by EAAT4 JOURNAL OF NEUROSCIENCE. 2021.09; 41(39); 8126-8133
- 2. Zhang Yongquan, Luo Yuanjun, Sasamura Kazuma, Sugihara Izumi. Single axonal morphology reveals high heterogeneity in spinocerebellar axons originating from the lumbar spinal cord in the mouse JOURNAL OF COMPARATIVE NEUROLOGY. 2021.08; 529(18); 3893-3921

[Books etc]

- 1. Sugihara I, (2021) Cerebellar lobules and stripes, viewed from development, topographic axonal projections, functional localization, and interspecies homology. In: Mizusawa H and Kakei S, eds, Cerebellum as a CNS Hub, pp 93-119. Springer. . Springer, 2021 (ISBN : 978-3-030-75816-5)
- Voogd J, Shinoda Y, Ruigrok TJ, Sugihara I. Voogd J, Shinoda Y, Ruigrok TJ, Sugihara I (2021) Cerebellar Nuclei and the Inferior Olivary Nuclei: Organization and Connections. In: Ed. M. Manto, D. Gruol, J. Schmahmann, N Koibuchi, R. Sillitoe eds, Handbook of the Cerebellum and Cerebellar Disorders, 2nd Ed. New York, Springer.. Springer, 2021 (ISBN : 978-3-030-23809-4)
- 3. Shinoda Y, Sugihara I. Shinoda Y, Sugihara I (2021) Axonal Trajectories of Single Climbing and Mossy Fiber Neurons in the Cerebellar Cortex and Nucleus. In: Ed. M. Manto, D. Gruol, J. Schmahmann, N Koibuchi, R. Sillitoe eds, Handbook of the Cerebellum and Cerebellar Disorders, 2nd Ed.. Springer, 2021 (ISBN : 978-3-030-23809-44)
- 1. Izumi Sugihara. Color Illustrated Normal Structure and Function of the Human Body 4th Edition. 2021.01 (ISBN : 978-4-7849-3181-1)

[Misc]

- 1. Mayu Takahashi, Yoshikazu Shinoda. Fastigial nucleus input/output related to motor control 2021;
- 1. Yuriko Sugiuchi. Anatomy and Physiology of the Vestibulospinal System 2021.08; 80(4); 303-310

[Conference Activities & Talks]

1. Sugihara I, Luo Y. Single axon morphology to classify neuronal populations and understand brain organization.. The joint Meeting of the 126th Annual Meeting of the Japanese Association of Anatomists and the 98th Annual Meeting of the Physiological Society of Japan. 2021.03.30 Online

Pharmacology and Neurobiology

Assistant professor:Hironao SAEGUSA Assistant professor:Makoto FUJIKAWA

(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. Molecular basis of Calcium channelopathy

6. 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 recombination in disgust-associated bitter taste-responsive neurons of the central nucleus of amygdala in male mice. Neuroscience letters. 2021.01; 135456

Molecular Neuroscience

Professor Kohichi Tanaka Assistant Professor Yuichi Hiraoka Assistant Professor Tetsuo Ohnishi

Graduate Student (doctor course) Bi Haining Zhao Di

Graduate Student (master course) Akira Kawai Mahito Mitumasa

(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. Attention-deficit/hyperactivity disorder (ADHD) is a common neuropsychiatric disorder in children. Although animal models and human brain imaging studies indicate a significant role for glutamatergic dysfunction in ADHD, there is no direct evidence that glutamatergic dysfunction is sufficient to induce ADHD-like symptoms. The glial glutamate transporter GLT1 plays a critical role in glutamatergic neurotransmission. We report the generation of mice expressing only 20% of normal levels of the GLT1. Unlike conventional GLT1 knockout mice, these mice survive to adulthood and exhibit ADHD-like phenotypes, including hyperactivity, impulsivity and impaired memory. These findings indicate that glutamatergic dysfunction due to GLT1 deficiency, a mechanism distinct from the dopaminergic deficit hypothesis of ADHD, underlies ADHD-like symptoms.

2. Novel mouse models for focal epilepsy

The most frequent genetic cause of focal epilepsies is variations in the GAP activity toward RAGs 1 complex genes DEP domain containing 5 (DEPDC5), nitrogen permease regulator 2-like protein (NPRL2) and nitrogen permease regulator 3-like protein (NPRL3). Because these variations are frequent and associated with a broad spectrum of focal epilepsies, a unique pathology categorized as GATORopathy can be conceptualized. Animal

models recapitulating the clinical features of patients are essential to decipher GATORopathy. Although several genetically modified animal models recapitulate DEPDC5-related epilepsy, no models have been reported for NPRL2- or NPRL3-related epilepsies. Here, we conditionally deleted Nprl2 and Nprl3 from the dorsal telencephalon in mice [Emx1cre/+; Nprl2f/f (Nprl2-cKO) and Emx1cre/+; Nprl3f/f (Nprl3-cKO)] and compared their phenotypes with Nprl2+/-, Nprl3+/- and Emx1cre/+; Depdc5f/f (Depdc5-cKO) mice. Nprl2-cKO and Nprl3-cKO mice recapitulated the major abnormal features of patients-spontaneous seizures, and dysmorphic enlarged neuronal cells with increased mechanistic target of rapamycin complex 1 signaling-similar to Depdc5-cKO mice. Chronic postnatal rapamycin administration dramatically prolonged the survival period and inhibited seizure occurrence but not enlarged neuronal cells in Nprl2-cKO and Nprl3-cKO mice. Further studies using these conditional knockout mice will be useful for understanding GATORopathy and for the identification of novel therapeutic targets.

3. Analysis of a novel gene expression regulatory system related to the pathophysiology of mental disorders Patients with schizophrenia, one of severe mental disorders, suffer from a variety of symptoms including hallucination, delusion, affective flattening and cognitive deficits. Although the genetic predisposition contributes to the pathogenesis of this illness, its genetic architecture remains still to be elucidated. We have reported on a schizophrenia patient who harbored a balanced chromosomal translocation, and identified the gene LDB2 (Lim Domain-Binding 2), which locates proximately to the chromosomal breakpoint. Ldb2 KO mice exhibited multiple deficits related to schizophrenia, strongly supporting that LDB2 is a causal gene in the proband patient. On a basis of the fact that LDB2 is a potential transcription regulator, we conducted ChIP-seq analyses with an LDB2-specific antibody. Of interest, we found that LDB2 binds to 10,000 genomic sites in human neurosphreres, and that its DNA binding is indirectly mediated by the EGR (early growth response) transcription factors, which are implicated in the pathophysiology of schizophrenia. Taken together, we proposed that a novel gene expression regulatory system, which we named the 'LDB2-EGR axis', regulates synapse dynamics via controlling expressions of downstream genes.

(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. Ishida S, Zhao D, Sawada Y, Hiraoka Y, Mashimo T, Tanaka K. Dorsal telencephalon-specific Nprl2- and Nprl3-knockout mice: novel mouse models for GATORopathy. Human molecular genetics. 2021.11;

- 2. Ai Minamidate, Michio Onizawa, Chikako Saito, Rie Hikichi, Tomoaki Mochimaru, Mai Murakami, Chiharu Sakuma, Takehito Asakawa, Yuichi Hiraoka, Shigeru Oshima, Takashi Nagaishi, Kiichiro Tsuchiya, Hiromasa Ohira, Ryuichi Okamoto, Mamoru Watanabe. A potent endocytosis inhibitor Ikarugamycin up-regulates TNF production. Biochem Biophys Rep. 2021.09; 27; 101065
- 3. Uchida M, Noda Y, Hasegawa S, Hida H, Taniguchi M, Mouri A, Yoshimi A, Nabeshima T, Yamada K, Aida T, Tanaka K, Ozaki N. Early postnatal inhibition of GLAST causes abnormalities of psychobehaviors and neuronal morphology in adult mice. Neurochemistry international. 2021.09; 150; 105177
- 4. Hiraoka Yuichi, Sugiyama Kaori, Nagaoka Daiki, Tsutsui-Kimura Iku, Tanaka Kenji F., Tanaka Kohichi. Mice with reduced glutamate transporter GLT1 expression exhibit behaviors related to attention-deficit/hyperactivity disorder BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 2021.08; 567; 161-165
- Guo Xinzheng, Zhou Jing, Starr Christopher, Mohns Ethan J., Li Yidong, Chen Earnest P., Yoon Yonejung, Kellner Christopher P., Tanaka Kohichi, Wang Hongbing, Liu Wei, Pasquale Louis R., Demb Jonathan B., Crair Michael C., Chen Bo. Preservation of vision after CaMKII-mediated protection of retinal ganglion cells CELL. 2021.08; 184(16); 4299-+
- 6. Eshiba Sally, Namiki Takeshi, Mohri Yasuaki, Aida Tomomi, Serizawa Naotaka, Shibata Takakazu, Morinaga Hironobu, Nanba Daisuke, Hiraoka Yuichi, Tanaka Kohichi, Miura Keiko, Tanaka Masaru, Uhara Hisashi, Yokozeki Hiroo, Saida Toshiaki, Nishimura Emi K.. Stem cell spreading dynamics intrinsically differentiate acral melanomas from nevi CELL REPORTS. 2021.08; 36(5); 109492
- 7. Shabeesh Balan, Tetsuo Ohnishi, Akiko Watanabe, Hisako Ohba, Yoshimi Iwayama, Manabu Toyoshima, Tomonori Hara, Yasuko Hisano, Yuki Miyasaka, Tomoko Toyota, Chie Shimamoto-Mitsuyama, Motoko Maekawa, Shusuke Numata, Tetsuro Ohmori, Tomomi Shimogori, Yoshiaki Kikkawa, Takeshi Hayashi, Takeo Yoshikawa. Role of an Atypical Cadherin Gene, Cdh23 in Prepulse Inhibition, and Implication of CDH23 in Schizophrenia. Schizophr Bull. 2021.07; 47(4); 1190-1200
- 8. Nagaishi T, Watabe T, Kotake K, Kumazawa T, Aida T, Tanaka K, Ono R, Ishino F, Usami T, Miura T, Hirakata S, Kawasaki H, Tsugawa N, Yamada D, Hirayama K, Yoshikawa S, Karasuyama H, Okamoto R, Watanabe M, Blumberg RS, Adachi T. Immunoglobulin A-specific deficiency induces spontaneous inflammation specifically in the ileum. Gut. 2021.05;
- 9. Mariko Onodera, Jan Meyer, Kota Furukawa, Yuichi Hiraoka, Tomomi Aida, Kohichi Tanaka, Kenji F Tanaka, Christine R Rose, Ko Matsui. Exacerbation of epilepsy by astrocyte alkalization and gap junction uncoupling. J Neurosci. 2021.01; 41; 2106-2118
- 10. Chie Shimamoto-Mitsuyama, Akihiro Nakaya, Kayoko Esaki, Shabeesh Balan, Yoshimi Iwayama, Tetsuo Ohnishi, Motoko Maekawa, Tomoko Toyota, Brian Dean, Takeo Yoshikawa. Lipid Pathology of the Corpus Callosum in Schizophrenia and the Potential Role of Abnormal Gene Regulatory Networks with Reduced Microglial Marker Expression. Cereb Cortex. 2021.01; 31(1); 448-462
- 11. Tanaka K. Astroglia and Obsessive Compulsive Disorder. Advances in neurobiology. 2021; 26; 139-149
- 12. Tetsuo Ohnishi, Yuji Kiyama, Fumiko Arima-Yoshida, Mitsutaka Kadota, Tomoe Ichikawa, Kazuyuki Yamada, Akiko Watanabe, Hisako Ohba, Kaori Tanaka, Akihiro Nakaya, Yasue Horiuchi, Yoshimi Iwayama, Manabu Toyoshima, Itone Ogawa, Chie Shimamoto-Mitsuyama, Motoko Maekawa, Shabeesh Balan, Makoto Arai, Mitsuhiro Miyashita, Kazuya Toriumi, Yayoi Nozaki, Rumi Kurokawa, Kazuhiro Suzuki, Akane Yoshikawa, Tomoko Toyota, Toshihiko Hosoya, Hiroyuki Okuno, Haruhiko Bito, Masanari Itokawa, Shigehiro Kuraku, Toshiya Manabe, Takeo Yoshikawa. Cooperation of LIM domain-binding 2 (LDB2) with EGR in the pathogenesis of schizophrenia. EMBO Mol Med. 2021.04; 13(4); e12574
- Tadashi Shin, Yuichi Hiraoka, Tokiwa Yamasaki, Jamey D Marth, Josef M Penninger, Masami Kanai-Azuma, Kohichi Tanaka, Satoshi Kofuji, Hiroshi Nishina. MKK7 deficiency in mature neurons impairs parental behavior in mice. Genes Cells. 2021.01; 26(1); 5-17
- 14. Shabeesh Balan, Yoshimi Iwayama, Tetsuo Ohnishi, Mikiko Fukuda, Atsuko Shirai, Ayumi Yamada, Sara Weirich, Maren Kirstin Schuhmacher, Kalarickal Vijayan Dileep, Toshihiro Endo, Yasuko Hisano, Kaoru Kotoshiba, Tomoko Toyota, Takeshi Otowa, Hitoshi Kuwabara, Mamoru Tochigi, Akiko Watanabe, Hisako Ohba, Motoko Maekawa, Manabu Toyoshima, Tsukasa Sasaki, Kazuhiko Nakamura, Masatsugu Tsujii, Hideo Matsuzaki, Kam Y J Zhang, Albert Jeltsch, Yoichi Shinkai, Takeo Yoshikawa. A loss-of-function

variant in SUV39H2 identified in autism-spectrum disorder causes altered H3K9 trimethylation and dysregulation of protocadherin β -cluster genes in the developing brain. Mol Psychiatry. 2021.07;

Neuropathology

Professor: Hitoshi Okazawa Practical Professor: Kazuhiko Tagawa(~ 2021.3) Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone Junior Associate Professor: Kyota Fujita Specially Appointed Junior Associate Professor: Hidenori Homma Assistant Professor: Hikari Tanaka Assistant Administrative Staff: Shigemi Sato(~ 2021.3), Xuemei Zhang(2021.6 ~) Secretary: Marie Tanaka Graduate Student : Kanoh Kondo, 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

[Outline]

Following studies have been intensively carried out in our laboratory with various techniques including molecular biology, cell biology, biochemistry, Drosophila models, and mice models.

- 1)Investigation of molecular pathologies of neurodegenerative disease.
- 2)Development of new therapies for neurodegeneration.
- 3)Development of new seed drug for mental retardation.
- 4)Investigation of molecular function of Oct3/4.

[This year's progress]

1. DNA damage in embryonic neural stem cell determines FTLDs' fate via early-stage neuronal necrosis The early-stage pathologies of frontotemporal lobal degeneration (FTLD) remain largely unknown. In VCPT262A-KI mice carrying VCP gene mutation linked to FTLD, insufficient DNA damage repair in neural stem/progenitor cells (NSCs) activated DNA-PK and CDK1 that disabled MCM3 essential for the G1/S cell cycle transition. Abnormal neural exit produced neurons carrying over unrepaired DNA damage and induced early-stage transcriptional repression-induced atypical cell death (TRIAD) necrosis accompanied by the specific markers pSer46-MARCKS and YAP. In utero gene therapy expressing normal VCP or non-phosphorylated mutant MCM3 rescued DNA damage, neuronal necrosis, cognitive function, and TDP43 aggregation in adult neurons of VCPT262A-KI mice, whereas similar therapy in adulthood was less effective. The similar early-stage neuronal necrosis was detected in PGRNR504X-KI, CHMP2BQ165X-KI, and TDPN267S-KI mice, and blocked by embryonic treatment with AAV–non-phospho-MCM3. Moreover, YAP-dependent necrosis occurred in neurons of human FTLD patients, and consistently pSer46-MARCKS was increased in cerebrospinal fluid (CSF) and serum of these patients. Collectively, developmental stress followed by early-stage neuronal necrosis is a potential target for therapeutics and one of the earliest general biomarkers for FTLD.

2. Hepta-Histidine Inhibits Tau Aggregation

Tau aggregation is a central hallmark of tauopathies such as frontotemporal lobar degeneration and progressive supranuclear palsy as well as of Alzheimer's disease, and it has been a target for therapeutic development. Herein, we unexpectedly found that hepta-histidine (7H), an inhibitor of the interaction between Ku70 and Huntingtin proteins, suppresses aggregation of Tau-R3 peptides in vitro. Addition of the trans-

activator of transcription (TAT) sequence (YGRKKRRQRRR) derived from the TAT protein to 7H increased its permeability into cells, and TAT-7H treatment of iPS cell-derived neurons carrying Tau or APP mutations suppressed Tau phosphorylation. These results indicate that 7H is a promising lead compound for developing anti-aggregation drugs against Tau-related neurodegenerative diseases including Alzheimer's disease (AD).

3. Prediction and verification of the AD-FTLD common pathomechanism based on dynamic molecular network analysis

Multiple gene mutations cause familial frontotemporal lobar degeneration (FTLD) while no single gene mutations exists in sporadic FTLD. Various proteins aggregate in variable regions of the brain, leading to multiple pathological and clinical prototypes. The heterogeneity of FTLD could be one of the reasons preventing development of disease-modifying therapy. We newly develop a mathematical method to analyze chronological changes of PPI networks with sequential big data from comprehensive phosphoproteome of four FTLD knock-in (KI) mouse models (PGRNR504X-KI, TDP43N267S-KI, VCPT262A-KI and CHMP2BQ165X-KI mice) together with four transgenic mouse models of Alzheimer's disease (AD) and with APPKM670/671NL-KI mice at multiple time points. The new method reveals the common core pathological network across FTLD and AD, which is shared by mouse models and human postmortem brains. Based on the prediction, we performed therapeutic intervention of the FTLD models, and confirmed amelioration of pathologies and symptoms of four FTLD mouse models by interruption of the core molecule HMGB1, verifying the new mathematical method to predict dynamic molecular networks.

4. HMGB1 signaling phosphorylates Ku70 and impairs DNA damage repair in Alzheimer's disease pathology DNA damage is increased in Alzheimer's disease (AD), while the underlying mechanisms are unknown. Here, we employ comprehensive phosphoproteome analysis, and identify abnormal phosphorylation of 70 kDa subunit of Ku antigen (Ku70) at Ser77/78, which prevents Ku70- DNA interaction, in human AD postmortem brains. The abnormal phosphorylation inhibits accumulation of Ku70 to the foci of DNA double strand break (DSB), impairs DNA damage repair and eventually causes transcriptional repression-induced atypical cell death (TRIAD). Cells under TRIAD necrosis reveal senescence phenotypes. Extracellular high mobility group box 1 (HMGB1) protein, which is released from necrotic or hyper-activated neurons in AD, binds to toll-like receptor 4 (TLR4) of neighboring neurons, and activates protein kinase C alpha (PKC α) that executes Ku70 phosphorylation at Ser77/78. Administration of human monoclonal anti-HMGB1 antibody to post-symptomatic AD model mice decreases neuronal DSBs, suppresses secondary TRIAD necrosis of neurons, prevents escalation of neurodegeneration, and ameliorates cognitive symptoms. TRIAD shares multiple features with senescence. These results discover the HMGB1-Ku70 axis that accounts for the increase of neuronal DNA damage and secondary enhancement of TRIAD, the cell death phenotype of senescence, in AD.

5. Tau activates microglia via the PQBP1-cGAS-STING pathway to promote brain inflammation

Brain inflammation generally accompanies and accelerates neurodegeneration. Here we report a microglial mechanism in which polyglutamine binding protein 1 (PQBP1) senses extrinsic tau 3R/4R proteins by direct interaction and triggers an innate immune response by activating a cyclic GMP-AMP synthase (cGAS)-Stimulator of interferon genes (STING) pathway. Tamoxifen-inducible and microglia-specific depletion of PQBP1 in primary culture in vitro and mouse brain in vivo shows that PQBP1 is essential for sensing-tau to induce nuclear translocation of nuclear factor kB (NFkB), NFkB-dependent transcription of inflammation genes, brain inflammation in vivo, and eventually mouse cognitive impairment. Collectively, PQBP1 is an intracellular receptor in the cGAS-STING pathway not only for cDNA of human immunodeficiency virus (HIV) but also for the transmissible neurodegenerative disease protein tau. This study characterizes a mechanism of brain inflammation that is common to virus infection and neurodegenerative disorders.

(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 nerurodegenerative diseases.

(5) **Publications**

[Original Articles]

- 1. Jin M, Shiwaku H, Tanaka H, Obita T, Ohuchi S, Yoshioka Y, Jin X, Kondo K, Fujita K, Homma H, Nakajima K, Mizuguchi M, Okazawa H. Tau activates microglia via the PQBP1-cGAS-STING pathway to promote brain inflammation. Nat Commun. 2021.11; 12(1); 6565
- 2. Tanaka H, Kondo K, Fujita K, Homma H, Tagawa K, Jin X, Jin M, Yoshioka Y, Takayama S, Masuda H, Tokuyama R, Nakazaki Y, Saito T, Saido T, Murayama S, Ikura T, Ito N, Yamamori Y, Tomii K, Bianchi ME, Okazawa H. HMGB1 signaling phosphorylates Ku70 and impairs DNA damage repair in Alzheimer's disease pathology. Commun Biol. 2021.10; 4(1); 1175
- 3. Kondo K, Ikura T, Tanaka H, Fujita K, Takayama S, Yoshioka Y, Tagawa K, Homma H, Liu S, Kawasaki R, Huang Y, Ito N, Tate SI, Okazawa H. Hepta-Histidine Inhibits Tau Aggregation. ACS Chem Neurosci. 2021.08; 12(16); 3015-3027
- 4. Jin M, Jin X, Homma H, Fujita K, Tanaka H, Murayama S, Akatsu H, Tagawa K, Okazawa H. Prediction and verification of the AD-FTLD common pathomechanism based on dynamic molecular network analysis. Commun Biol. 2021.08; 4(1); 961
- 5. Homma H, Tanaka H, Jin M, Jin X, Huang Y, Yoshioka Y, Bertens CJ, Tsumaki K, Kondo K, Shiwaku H, Tagawa K, Akatsu H, Atsuta N, Katsuno M, Furukawa K, Ishiki A, Waragai M, Ohtomo G, Iwata A, Yokota T, Inoue H, Arai H, Sobue G, Sone M, Fujita K, Okazawa H. DNA damage in embryonic neural stem cell determines FTLDs' fate via early-stage neuronal necrosis. Life Sci Alliance. 2021.06; 4(7); e202101022
- 6. Saito M, Nakayama M, Fujita K, Uchida A, Yano H, Goto S, Okazawa H, Sone M. Role of the Drosophila YATA protein in the proper subcellular localization of COPI revealed by in vivo analysis. Genes Genet Syst. 2021.03; 95(6); 303-314

[Misc]

- 1. Hitoshi Okazawa. Intracellular amyloid hypothesis for ultra-early phase pathology of Alzheimer's disease. Neuropathology. 2021.04; 41(2); 93-98
- 2. Daniel J. Klionsky, et al. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). Autophagy. 2021.02; 17(1); 1-382

[Conference Activities & Talks]

- 1. Hitoshi Okazawa. Big data-driven research of neurodegenerative diseases. 62nd Annual Meeting of the Japanese Society of Neurology 2021.05.20 ICCKyoto(Kyoto)
- 2. Hitoshi Okazawa. Deciphering and tacking the ultra-early phase pathology of Alzheimer's disease. The 15th International Conference on Alzheimer's and Parkinson's Diseases (online) 2021.03.11

Pathophysiology

[Patents]

1. Methods for treating spinocerebellar ataxia type I using RPA1, Patent Number : US10989719

Ophthalmology and Visual Science

Professor;Kyoko Ohno-Matsui Associate Professor;Takeshi Yoshida Junior Associate Professor;Hiroshi Takase, Koju Kamoi, Shintaro Horie Assistant Professor; Tae Igarashi, Hiroyuki Takahashi, Kengo Uramoto, Takashi Watanabe Graduate student; keijia Cao, Yuxin Fang, Ran Du, Xie Shi Qi, Xuejiao Li

(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 immunoregulartion 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 in 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]

- Modjtahedi BS, Abbott RL, Fong DS, Lum F, Tan D; Task Force on Myopia(Abbott R, Tan D, Ang M, Cotter SA, Fernandez AM, Fong DS, Grzybowski A, He M, Jacobs DS, Jonas JB, Lee KA, Modjtahedi B, Molinari AD, Morgan I, Ohno-Matsui K, Repka MS, Salim S, Wu PC, Yao K, Zadnik K, Kemper A, Chiarito S). Reducing the Global Burden of Myopia by Delaying the Onset of Myopia and Reducing Myopic Progression in Children: The Academy's Task Force on Myopia. Ophthalmology. 2021.12; 128(6); 816-826
- Zhixi Li, Wei Wang, Ran Liu, Decai Wang, Jian Zhang, Ou Xiao, Xinxing Guo, Monica Jong, Padmaja Sankaridurg, Ohno-Matsui K, Mingguang He. Choroidal thickness predicts progression of myopic maculopathy in high myopes: a 2-year longitudinal study. Br J Ophthalmol. 2021.12; 105(12); 1744-1750
- 3. Kyoko Ohno-Matsui, Hiroyuki Takahashi, Zaixing Mao, Noriko Nakao. Determining posterior vitreous structure by analysis of images obtained by AI-based 3D segmentation and ultrawidefield optical coherence tomography. Br J Ophthalmol. 2021.12;
- 4. Shymaa K Hady, Shiqi Xie, K Bailey Freund, Emmett T Cunningham, Chee Wai Wong, Chui Ming Gemmy Cheung, Koju Kamoi, Tae Igarashi, Omar M Ali, Ehab I Wasfi, Mahmoud F Rateb, Kyoko Ohno-Matsui. Prevalence and characteristics of multifocal choroiditis /punctate inner choroidopathy in pathologic myopia eyes with patchy atrophy. Retina. 2021.12;
- 5. Ran Du, Shiqi Xie, Yuxin Fang, Shinichi Hagino, Shinji Yamamoto, Muka Moriyama, Takeshi Yoshida, Tae Igarashi-Yokoi, Hiroyuki Takahashi, Natsuko Nagaoka, Kengo Uramoto, Yuka Onishi, Takashi Watanabe, Noriko Nakao, Tomonari Takahashi, Yuichiro Kaneko, Takeshi Azuma, Ryoma Hatake, Takuhei Nomura, Tatsuro Sakura, Mariko Yana, Jianping Xiong, Changyu Chen, Kyoko Ohno-Matsui. Validation of Soft Labels in Developing Deep Learning Algorithms for Detecting Lesions of Myopic Maculopathy From Optical Coherence Tomographic Images. Asia Pac J Ophthalmol (Phila). 2021.12;

- Lillian Liu, Yuxin Fang, Tae Igarashi-Yokoi, Hiroyuki Takahashi, Ohno-Matsui K. Clinical and morphologic features of posterior staphyloma edges by ultra-widefield imaging in pathologic myopia. Retina. 2021.11; 41(11); 2278-2287
- Qiurong Lin, Junjie Deng, Ohno-Matsui K, Xiangui He, Xian Xu. The Existence and Regression of Persistent Bergmeister's Papilla in Myopic Children Are Associated With Axial Length. Transl Vis Sci Technol. 2021.11; 10(13); 4
- 8. Francesco Pichi, Rosa Dolz-Marco, Jasmine H Francis, Adrian Au, Janet L Davis, Amani Fawzi, Sarra Gattousi, Debra A Goldstein, Pearse A Keane, Elisabetta Miserocchi, Alessandro Marchese, Kyoko Ohno-Matsui, Mandeep S Sagoo, Scott D Smith, Ethan K Sobol, Anastasia Tasiopoulou, Xiaolu Yang, Carol L Shields, K Bailey Freund, David Sarraf. Advanced OCT Analysis of Biopsy-proven Vitreoretinal Lymphoma. Am J Ophthalmol. 2021.11; 238; 16-26
- Takashi Ono, Hiroshi Goto, Tsutomu Sakai, Fumihiko Nitta, Nobuhisa Mizuki, Hiroshi Takase, Yutaka Kaneko, Junko Hori, Satoko Nakano, Nobuhisa Nao-I, Nobuyuki Ohguro, Kazunori Miyata, Makoto Tomita, Manabu Mochizuki, . Comparison of combination therapy of prednisolone and cyclosporine with corticosteroid pulse therapy in Vogt-Koyanagi-Harada disease. Jpn J Ophthalmol. 2021.10;
- 10. Jorge Ruiz-Medrano, Ignacio Flores-Moreno, Ohno-Matsui Κ, Ming Gemmy Chui Rufino Silva, José CORRELATION BETWEEN Cheung, Μ Ruiz-Moreno. ATROPHY-TRACTION-NEOVASCULARIZATION GRADE FOR MYOPIC MACULOPATHY AND CLINICAL SEVERITY. Retina. 2021.09; 41(9); 1867-1873
- 11. Xiaotong Han, Tianzi Liu, Xiaohu Ding, Jialin Liu, Xingyan Lin, Decai Wang, Moeen Riaz, Paul N Baird, Zhi Xie, Yuan Cheng, Yi Li, Yuki Mori, Masahiro Miyake, Hengtong Li, Ching-Yu Cheng, Changqing Zeng, Kyoko Ohno-Matsui, Xiangtian Zhou, Fan Liu, Mingguang He. Identification of novel loci influencing refractive error in East Asian populations using an extreme phenotype design. J Genet Genomics. 2021.09;
- Hiroyuki Takahashi, Noriko Nakao, Kosei Shinohara, Keigo Sugisawa, Kengo Uramoto, Tae Igarashi-Yokoi, Takeshi Yoshida, Ohno-Matsui K. Posterior vitreous detachment and paravascular retinoschisis in highly myopic young patients detected by ultra-widefield OCT. Sci Rep. 2021.08; 11(1); 17330
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[Books etc]

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- 2. Lin S, Ohno-Matsui K, Salim S. How to spot glaucoma in the myopic patients. EyeNet, 2021.05
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- 4. Ohno-Matsui K, Wu PC, Yamashiro K, Vutipongsatorn K, Fang Y, Cheung CMG, Lai TYY, Ikuno Y, Cohen SY, Gaudric A, Jonas JB. Invest Ophthalmol Vis Sci. 2021.04
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[Misc]

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- 2. Hiroshi Takase. Characteristics and management of ocular sarcoidosis. Immunol Med. 2021.07; 1-10
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- 4. Sunao Sugita, Hiroshi Takase, Satoko Nakano. Practical use of multiplex and broad-range PCR in ophthalmology. Jpn J Ophthalmol. 2021.03; 65(2); 155-168

[Conference Activities & Talks]

- 1. Ohno-Matsui K.. AI-based diagnosis of myopic maculopathy. The 2nd International Summit on High Myopia & Complications 2021.12.18 WEB
- Naoko N, Igarashi-Yokoi T, Takahashi H, Shinohara K, Ohno-Matsui k. Quantitative Evaluations of Posterior Staphylomas in Highly Myopic Eyes by Ultra-Widefield Optical Coherence Tomography . 14th Asia-Pacific Vitreo-retina Society (APVRS) Congress 2021.12.12 WEB
- 3. Ohno-Matsui K.. Punctate Inner Choroidopathy in Pathologic Myopia. 14th Asia-Pacific Vitreo-retina Society (APVRS) Congress 2021.12.11 WEB
- 4. Hiroshi Takase. Diagnostic criteria for acute retinal necrosis based on ocular findings and virological testing for intraocular fluids. International Ocular Inflammation Society (IOIS) 2021 2021.12.05 Web
- 5. Hiroshi Takase. Management of complications in ocular sarcoidosis . International Ocular Inflammation Society (IOIS) 2021 2021.12.05 Web
- 6. Ohno-Matsui K.. Pathologic myopia. Retina Festival 2021 2021.12.04
- 7. Stanga PE, Moussa MS, Sadda SR, Ohno-Matsui K, Staurenghi G, Fawzi A, Papayannis A. Vitreous-Macular-Choroidal and Peripheral OCT: Cross-Sectional, En Face, Angio 3-D, Widefield and Intraoperative Imaging, AAO 2021 2021.11.14 WEB
- 8. Grzybowski A, Saw SM, Ohno-Matsui K, Koffler BH, Repka MX. New Approaches to the Prevention and Treatment of Myopia : Update 2021. AAO 2021 2021.11.14 WEB
- 9. Ohno-Matsui K.. Visualization of Posterior Vitreous by Ultra widefield OCT and AI-based 3D Imaging. AAO 2021 2021.11.13 WEB
- Uramoto K, Azuma T, Watanabe T, Takahashi H, Igarashi T, Shimada N, Ohno-Matsui K. Pseudo macular hole retinal detachment in eyes with pathologic myopia. The 2nd Asia-Pacific Ocular Imaging Society Meeting 2021.10.30 WEB
- 11. Ohno-Matsui K.. 3D visualization of posterior vitreous . Japan myopia retina club joint webinar 2021.10.23 WEB
- 12. Ohno-Matsui K.. Deep Learning approach for automated detection of myopia maculopathy and pathologic myopia in fundus images. EURETINA2021 2021.09.11 WEB
- 13. Ohno-Matsui K.. High myopia and its complications. EURETINA2021 2021.09.11 WEB
- 14. Ohno-Matsui K.. Pathologic myopia. APAO2021 2021.09.09 WEB
- 15. Ohno-Matsui K.. Complications of pathologic myopia. APAO2021 2021.09.07 WEB
- 16. Hiroshi Takase. Management of ocular sarcoidosis. Uveitis Webinar 9 2021.09.04 Web
- 17. Ohno-Matsui K.. Potentially longer acting agents should be considered for myopic neovascularization over currently available agents. Controversies of ophthalmology 2021.08.21 WEB

- Kamoi K, MD, Iwakiri Y, Ohno-Matsui K. Long-Term Follow-up of the Incidence of Posterior Capsular Opacification and Nd:YAG Capsulotomy in Patients with Uveitis. American Society of Cataract and Refractive Surgery (ASCRS) 2021.07.23 WEB
- 19. Koju Kamoi, Yuki Iwakiri, Kyoko Ohno-Matsui.. Long-Term Follow-up of the Incidence of Posterior Capsular Opacification and Nd:YAG Capsulotomy in Patients with Uveitis. American Society of Cataract and Refractive Surgery (ASCRS) Annual Meeting 2021.07.23
- 20. Ohno-Matsui K. Punctate Inner choroid
opathy in pathologic myopia.. Asia Pacific Retina Imaging Society (APRIS) 2021.07.03 WEB
- 21. Ohno-Matsui K. Pathologic myopia.. Wilmer Eye Institute science seminar 2021.06.10 WEB
- 22. Ohno-Matsui K. Utility of AI and 3D modeling of posterior vitreous.. Ophthalmic AI Summit 2021.06.06 WEB
- 23. Ohno-Matsui K, Takahashi H. A role of paravascular vitreal adhesions for development of myopic macular retinoschisis.. International Retinal Imaging Society 2021.06.05 WEB
- 24. Ohno-Matsui K, Jong M, Morgan I, Logan N, Jonas J, Wolffsohn J, Resnikoff S. Are we being myopic about myopia? Updated evidence for a change in clinical practice.. ARVO2021 2021.05.02 WEB
- 25. Ohno-Matsui K.. State-of-the-art imaging of pathologic myopia. 2021 International Conference on Clinical Research in Ophthalmology 2021.04.09 WEB
- 26. Ohno-Matsui K. Panel 1: Is Myopia prevention a viable business opportunity?. . Asian Retina Forum 2021.03.25 WEB
- 27. Ohno-Matsui K. Dilated choroidal veins in myopic macular neovascularization. . International swept-source OCT conference 2021.02.10 WEB
- 28. Ohno-Matsui K. Novel paravascular lesions with abnormal autofluorescence in eyes with pathologic myopia.. The Macula Society 2021.02.07 WEB
- 29. Shiqi Xie, Ohno-Matsui K. Full thickness scleral defect within an area of myopic patchy atrophy. Atlantic Coast Retina Club 2021.01.21 web

Otorhinolaryngology

Professor: Takeshi Tsutsumi Associate Professor: Yoshiyuki Kawashima Junior Associate Professor: Yasuhiro Suzuki Assistant Professor: Taku Itou, Tarou Fujikawa, Keiji Honda Hospital Staff: Hiroki Watanabe, Tomoki Ooka, Natsuko Kurata, Ayako Nishio Graduate Student: Ayako Maruyama, Bai Jing, Ayame Yamazaki, Hiroki Watanabe, Natsuki Aoki, Tomoki Ooka, Kaori Mohri

(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 clerkshipIII, 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, Yamazaki A, Tsutsumi T. Application of a virtual and mixed reality-navigation system using commercially available devices to the lateral temporal bone resection. Annals of medicine and surgery (2012). 2021.12; 72; 103063
- 2. Takeda Takamori, Ito Taku, Onishi Iichiroh, Yokomura Masaru, Kawashima Yoshiyuki, Fujikawa Taro, Tsutsumi Takeshi. Denosumab-induced osteonecrosis of external auditory canal(和訳中) Auris· Nasus-Larynx. 2021.12; 48(6); 1199-1203
- 3. Yamazaki Ayame, Ito Taku, Sugimoto Maki, Yoshida Soichiro, Honda Keiji, Kawashima Yoshiyuki, Fujikawa Taro, Fujii Yasuhisa, Tsutsumi Takeshi. Patient-specific virtual and mixed reality for immersive, experiential anatomy education and for surgical planning in temporal bone surgery(和訳中) Auris- Nasus-Larynx. 2021.12; 48(6); 1081-1091
- 4. Ito T, Kawashima Y, Yamazaki A, Tsutsumi T. Application of a virtual and mixed reality-navigation system using commercially available devices to the lateral temporal bone resection. Annals of medicine and surgery (2012). 2021.12; 72; 103063
- 5. Takeda Takamori, Ito Taku, Onishi Iichiroh, Yokomura Masaru, Kawashima Yoshiyuki, Fujikawa Taro, Tsutsumi Takeshi. デノスマブで誘発された外耳道の骨壊死 (Denosumab-induced osteonecrosis of external auditory canal) Auris· Nasus· Larynx. 2021.12; 48(6); 1199-1203
- 6. Mohri Kaori, Tanaka Kentaro, Sugawara Takashi, Asakage Takahiro, Tsutsumi Takeshi. 外耳道癌の切 除術後に生じる側頭骨欠損の管理法 (Management of the temporal bone defect after resection of external auditory canal cancer) Auris· Nasus· Larynx. 2021.12; 48(6); 1157-1161
- 7. Yamazaki Ayame, Ito Taku, Sugimoto Maki, Yoshida Soichiro, Honda Keiji, Kawashima Yoshiyuki, Fujikawa Taro, Fujii Yasuhisa, Tsutsumi Takeshi. 没入体験式の解剖教育への利用および側頭骨手術時 の手術計画への利用を目的とする、患者ごとに構築した仮想現実および複合現実 (Patient-specific virtual and mixed reality for immersive, experiential anatomy education and for surgical planning in temporal bone surgery) Auris Nasus Larynx. 2021.12; 48(6); 1081-1091
- 8. Ito Taku, Fujikawa Taro, Honda Keiji, Makabe Ayane, Watanabe Hiroki, Bai Jing, Kawashima Yoshiyuki, Miwa Toru, Griffith Andrew J., Tsutsumi Takeshi. Cochlear Pathomorphogenesis of Incomplete Partition Type II in Slc26a4-Null Mice JARO-JOURNAL OF THE ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY. 2021.10; 22(6); 681-691
- 9. Kurata N, Kawashima Y, Ito T, Ooka T, Tsutsumi T. Four-Hour Delayed Gadolinium-Enhanced 3D-FLAIR MR Imaging Highlights Intralabyrinthine Micro-Schwannomas. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2021.08; 42(10); e1444-e1448
- 10. Kiyokawa Yusuke, Ariizumi Yousuke, Ohno Kazuchika, Ito Taku, Kawashima Yoshiyuki, Tsunoda Atsunobu, Kishimoto Seiji, Asakage Takahiro, Tsutsumi Takeshi. Indications for and extent of elective neck dissection for lymph node metastasis from external auditory canal carcinoma(和訳中) Auris: Nasus-Larynx. 2021.08; 48(4); 745-750
- 11. Kiyokawa Yusuke, Ariizumi Yousuke, Ohno Kazuchika, Ito Taku, Kawashima Yoshiyuki, Tsunoda Atsunobu, Kishimoto Seiji, Asakage Takahiro, Tsutsumi Takeshi. 外耳道癌由来のリンパ節転移例に対 する選択的頸部郭清術の適応とその郭清範囲 (Indications for and extent of elective neck dissection for lymph node metastasis from external auditory canal carcinoma) Auris. Nasus. Larynx. 2021.08; 48(4); 745-750
- Ito T, Yamazaki A. Authors' reply to: Comment on the article by Dr. Georgios P. Skandalakis: Patient-specific virtual and mixed reality for immersive, experiential anatomy education and for surgical planning in temporal bone surgery. Auris, nasus, larynx. 2021.07;

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- 14. Ohno K, Kawada K, Sugimoto T, Kiyokawa Y, Kawabe H, Takahashi R, Koide N, Tateishi Y, Tasaki A, Ariizumi Y, Asakage T. Evaluation of synchronous multiple primary superficial laryngo-pharyngeal cancers that were treated by endoscopic laryngo-pharyngeal surgery. Auris, nasus, larynx. 2021.04;
- 15. Mori K, Tanaka K, Sugawara T, Asakage T, Tsutsumi T. Management of the temporal bone defect after resection of external auditory canal cancer. Auris, nasus, larynx. 2021.02; 48(6); 1157-1161
- 16. 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. 白 静, 伊藤 卓, 川島 慶之, 藤川 太郎, 本田 圭司, 渡邊 浩基, 倉田 奈都子, 堤 剛. マウスの生後における耳嚢 石灰化過程のマイクロ CT による可視化 (Calcification Process of the Otic Capsule in Postnatal Stage of Mice Visualized with Micro-CT). 日本耳科学会総会 · 学術講演会抄録集 2021.10.01
- 白静, 伊藤卓, 川島慶之, 藤川太郎, 本田圭司, 渡邊浩基, 倉田奈都子, 堤剛. マウスの生後における耳嚢 石灰化過程のマイクロ CT による可視化 (Calcification Process of the Otic Capsule in Postnatal Stage of Mice Visualized with Micro-CT). 日本耳科学会総会 · 学術講演会抄録集 2021.10.01

Neurology and Neurological Science

Professor YOKOTA Takanori Associate Professor NISHIDA Yoichiro Junior Associate Professor KUWAHARA Hiroya, HATTORI Takaaki Assistant Professor ISHIGURO Taro, YAGI Yohsuke, ONO Daisuke Project Professor SANJO Nobuo, UCHIHARA Toshiki Project Junior Associate Professor NAGATA Tetsuya Project Junior Associate Professor HARA Rintaro Project Assistant Professor YOSHIOKA Kotaro, HIRATA Kosei, ASAMI Yutaro Project Assistant Professor HIGASHI Miwa, SAKAUE Fumika Project Researcher AMANO Akiko, SU SU Lei Mon Graduate Student HASEGAWA Jyuri, MIYASHITA Akiko, SANO Tatsuhiko, ISHINOSE Keiko, MARUOKA Hiroyuki, NISHI Rieko, SUZUKI Motohiro, YAMADA Akane, KINA Satoko, SATO Takefumi, IIDA Shintaro, TAKAHASHI Yuko, OHARA Masahiro, MIURA Motoki, AOKI Hanako, YAMADA Hiroki, MATSUDA Sakino, YANAGIDAIRA Mitsugu, OHTANI Tai, SHINYA Akiko, TOIDE Nozomi, TAMAKI Kana, IWASE Ryo, MATSUBAYASHI Taiki, SHIMANO Kaoru, AMANO Eiichiro, JIA Chunyan, CHEN Qingmeng, THUNYARUT Bannawongsil, YASUDA Eiji, MORITO Koji, KURODA Takayuki, KUROIWA Nobuaki, YASUURA Asuka, HAMADA Meiko, KATO Tomotaka, YASUDA Kazuma, KATSUYAMA Maho, MOCHIZUKI Erika Resident SAGAWA Hirotaka, MINOMO Shogo, ADACHI Saori, KAWAI Honami, NAKATANI Natsuki, HUJINO Masaki, KYOYA Mitsuki, ENOMOTO Masayuki, SAKAMAKI Ayumi, SHIMIZU Saori

(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 32 in-patients, and offer in- and out-patient consultation services through the weekday and on weekends. We diagnose and treat patients with stroke, multiple sclerosis, Parkinson's disease, spinocerebellar ataxia, ALS, myopathies, neuropathies, meningitis/encephalitis, and hundreds of other neurological issues. We also have the "out-patients clinic specialized to patients with amnesia." Our patients will be reliably evaluated and diagnosed with some skillful techniques, such as the electrophysiological, neuroradiological, and neuropsychological tests and pathological diagnosis of biopsied nerves and muscles.

(4) **Publications**

[Original Articles]

- 1. Kotaro Noda, Yohsuke Yagi, Takanori Yokota. Evaluation of the risk factors predicting thrombotic complications associated with intravenous immunoglobulin therapy in neuroimmunological diseases. Neurol Sci. 2021.12; 42(12); 5321-5326
- 2. Eiichiro Amano, Tomokatsu Yoshida, Ikuko Mizuta, Jun Oyama, Shingo Sakashita, Syunsuke Ueyama, Akira Machida, Takanori Yokota. Activation of a Cryptic Splice Site of GFAP in a Patient With Adult-Onset Alexander Disease. Neurol Genet. 2021.12; 7(6); e626
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[Patents]

- 1. CHIMERIC DOUBLE-STRANDED NUCLEIC ACID, Patent Number : ZL201280062110.X
- 2. DOUBLE-STRANDED AGENTS FOR DELIVERING THERAPEUTIC OLIGONUCLEOTIDES, Patent Number : US11028387
- 3. DOUBLE-STRANDED AGENTS FOR DELIVERING THERAPEUTIC OLIGONUCLEOTIDES, Patent Number : US11028387
- 4. DOUBLE-STRANDED ANTISENSE NUCLEIC ACID WITH EXON-SKIPPING EFFECT, Patent Number : EP3010514
- 5. DOUBLE-STRANDED ANTISENSE NUCLEIC ACID WITH EXON-SKIPPING EFFECT, Patent Number : EP3010514
- 6. CARRIER FOR USE IN DELIVERING DRUG, CONJUGATE, COMPOSITION COMPRISING SAME, AND METHOD FOR ADMINISTRATING SAME, Patent Number : US10912838
- 7. CARRIER FOR USE IN DELIVERING DRUG, CONJUGATE, COMPOSITION COMPRISING SAME, AND METHOD FOR ADMINISTRATING SAME, Patent Number : US10912838

[Awards & Honors]

- 1. Best Presentation Award, 2021.06
- 2. Dr. Alan M. Gewirtz Memorial Scholarship Award, Oligonucleotide Therapeutics Society (OTS), 2021.09

[Social Contribution]

1. DRUG DESIGN, DRUG DELIVERY & TECHNOLOGIES NEWS , 2021.08.18

Psychiatry and Behavioral Sciences

Professor, Chair Hidehiko TAKAHASHI Professor Takayuki OKADA Associate Professor Genichi SUGIHARA Associate Professor Takashi TAKEUCHI Junior Associate Professor Daisuke JITOKU Assistant Professor Takehiro TAMURA, Shunsuke TAKAGI, Hiroki SHIWAKU, Yukiko MATSUMOTO, Junya FUJINO, Miho MIYAJIMA Junior Assistant Professor Nanase KOBAYASHI(-2021.3), Masanori ICHIHASHI, Takayuki WAKUI (2021.4-) Senior Resident Yuki SHIDEI(-2021.3), Kyoji MARUO(-2021.3), Saori TOYODA(2021.4-), Yukiko MOTOKAWA(2021.4-), Mao SHIMIZU(2021.4-) **Clinical Psychologist** Kazunori MURAKAMI, Takako ONO (-2021.3), Hisahi YAMADA, Ryoko NAKAJIMA, Hikaru TANIGUCHI, Ayako KUSANO **Psychiatric Social Worker** Yoshifumi KANEKO, Noriko NUMAGUCHI (-2021.3), Akinori MONTA, Mai KUDO(2021.4-), Masae NAKANISHI **Occupational Therapist** Tomoko SHIRATO Graduate Students (Doctoral Course) Asami ISHIZUYA, Yoshiko NOMURA, Masaki OHYA, Hironobu NAKAMURA, Marino KAWAMOTO, Kazushige HIRAKAKAWA, Takao KANAI, Yuki SHIDEI, Mariko SUNAHARA, Kouichi TABATA, Kyoji MARUO, Kentaro NAGAO, Shiori NOGUCHI, Yoritsugu IIDA, Chenyu QIAN, Nanase KOBAYASHI, Hidetoshi KINOSHITA, Yosuke SEKIGUCHI, Ikuko ARAKAWA, Takehiro IBARAKI, Marika OKAMURA, Yoshinori SASAKI, Wataru NAKAGAWA, Mayo FUHIWARA, Kanako AMANO, Sayaka OZAKA, Shiho MATSUOKA, Kazuhiro KOSUGI, Mayuko IIJIMA, Kensuke KOMTATSU, Hiroyuki TANAKA, Takahiro KAWATA, Yuka BANDO, Takehiro TAMURA (Diagnostic Radiology and Nuclear Medicine) Graduate Students (Master Course)

Masaaki SHIMIZU, Sayuri ISHII

(1) Outline

The theme of our research is to investigate the pathogenesis of psychiatric disorders such as schizophrenia, mood disorders, and addiction based on brain science, to develop objective diagnostic methods and novel treatments and establish psychosocial therapeutic approaches based on objective and scientific techniques and evidence. Our investigation focuses on the pathophysiology of psychiatric disorders using functional magnetic resonance imaging, nuclear medicine, and other modalities. We are also performing research to investigate the role of neurofeedback as a therapeutic strategy for mental disorders. Brain imaging studies are the most interesting

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and well-skilled lesion. Our study involves processing a large volume of brain data using machine learning and computational psychiatry to explore prospects for new discoveries and to predict pathological conditions through modeling. We are exploring neurofeedback as a novel therapeutic approach for psychiatric diseases and the role of artificial intelligence (AI) and computational psychiatry. Moreover, we are actively designing studies that can establish evidence-based approaches to address issues observed in routine clinical practice.

(2) Research

1) Studies in biological psychiatry

(i) Molecular and cellular studies to clarify the etiology and conditions of neuropsychiatric diseases We have performed translational and reverse translational research together with molecular, cellular, and behavioral analyses using animal models and clinical samples of DNA, serum, cerebrospinal fluid, and postmortem brain tissue obtained from patients with psychiatric disorders.

(ii) Study of sleep stages and behavior in neuropsychiatric diseases

Using an automatic analysis device (polysomnography), a study is being performed to investigate sleep stages and behavior in patients with various psychiatric disorders.

(iii) Neuroimaging in psychiatric disorders

We are actively incorporating AI technology in our research on brain structure and function and molecular imaging using magnetic resonance imaging and positron emission tomography to elucidate the pathogenesis of mental disorders, identify subtypes, and predict treatment response.

(iv) We are performing an observational study to retrospectively analyze information regarding electroconvulsive therapy (ECT). These data are submitted as performance reports from multi-institutional "ECT Training Facilities" accredited by the Japanese Society of General Hospital Psychiatry. Despite its long history in psychiatric clinical practice, the actual implementation of ECT in daily clinical practice remains unclear. This study will clarify the status of ECT in real-world Japanese medical facilities.

2) Psychopathological studies

Based on a psychotherapeutic approach, we are performing psychological studies of neuropsychiatric diseases with regard to phenomenology, anthropology, and linguistics. Other research activities include a review of fundamental psychiatric concepts and a basic study to establish a diagnostic classification of psychiatric disorders, which are important issues currently being widely recognized in clinical practice. In addition to studies on endogenous psychosis observed in schizophrenia and bipolar disorder, we are involved in psychoanalytical studies to better understand and develop psychotherapeutic modalities for neurosis and borderline personality disorder, which have gained increasing attention in recent times.

3) Research on liaison psychiatry and psycho-oncology

(i) Liaison psychiatry

In collaboration with dental hospitals, we are involved in research on the prevention of postoperative delirium. We are also performing research on delirium prevention in patients admitted to the physical department. We intend to perform research on perinatal mental health in the future.

(ii) Psycho-oncology

The concept of cancer disease is an important factor in the process by which a child accepts and adapts to cancer in his/her family. Therefore, we are analyzing textbooks used in elementary and junior high schools that could affect the development of the concept of cancer. Based on these data, from the perspective of psycho-oncology, we are attempting to prepare user-friendly home-based educational materials for parents to complement educational material available at school. We will verify the effects of these tools once they are operational.

4) Forensic psychiatry research

Our research includes projects for the development of forensic psychiatric evaluation methodology, risk assessment and management in forensic settings, and an investigation of the associations and mechanisms of criminal behavior. Our research encompasses a wide range of topics including the development of a method to assess the capacity to act for appraisal in the adult guardianship system.

(3) Education

Following the 2-year period of mandatory clinical training, during the second term of training, they will acquire knowledge and clinical experience necessary for neuropsychiatrists and will undergo practical training at affiliated medical facilities to qualify as psychiatrists. Undergraduate education, which emphasizes clinical clerkship training after a systematic series of lecture courses and seminar-based classes, is designed to develop students' problem-solving skills and improve their motivation to learn neuropsychiatry, with support from external facilities.

(4) Lectures & Courses

During the first term (two years) of postgraduate training, residents will learn basic laboratory procedures and diagnostic techniques, psychotherapy and drug treatment, laws and regulations related to clinical practice and will acquire other general knowledge, all of which are essential for a comprehensive understanding of the biopsychosocial approaches to neuropsychiatric diseases.

(5) Clinical Services & Other Works

Clinical practice

Among all new outpatients who visit our department, based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10), approximately 30% are diagnosed with "mood disorders" (F3), 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 from other departments. Patients with senile dementia, child and adolescent psychiatric disorders, substance, dependence, and neurosis, necessitating intensive psychotherapy are often referred to related and advanced facilities for specialized treatment. This facility is the psychiatric department of a general hospital and is involved with university education and training; therefore, most inpatients are diagnosed as F2, followed by F4 and F3 categories per ICD-10 codes. We also provide care and treatment for patients with sleep rhythm and neurological disorders, including epilepsy and senile dementia. In addition to drug treatment, we have introduced and provided modified ECT for inpatients and individual and group psychotherapy for patients admitted to our psychiatric ward, clinic, and day care center in close collaboration with rehabilitation facilities in the community. The day care (partial hospitalization) is a transitional element between inpatient and outpatient care and is indicated in a wide range of psychiatric disorders, such as schizophrenia, depression, bipolar disorder, adjustment disorder, and personality disorders.

Each member has its own aim, and the team provides care utilizing different types of frameworks. Our day care team places emphasis on the potentiality of the group and in our opinion, the collective efforts of the group could contribute to the therapeutic effect. This experience promotes good communication skills in patients and readaptation to social situations and social reintegration become easier.

(6) Clinical Performances

Per our policy, patients with schizophrenia are treated with clozapine, which is approved for the treatment of refractory schizophrenia. Following effective coordination with the Dental Hospital, we currently treat patients with oral pain or dysesthesia; this collaboration is a characteristic of our university. Our faculty includes board-certified specialists to treat patients who present with sleep disorders and epilepsy. In 2014, we introduced a psychoeducational program for patients with bipolar disorder, which focuses on relapse prevention. Additionally, we ensure close cooperation with the staff for an increasing number of liaison activities implemented for delirium prevention (particularly in surgical wards), interventions for patients with suicide attempts in the emergency room, and mental support for peripartum patients.

(7) Publications

[Original Articles]

- Sasaki Y, Usami M, Sasaki S, Sunakawa H, Toguchi Y, Tanese S, Saito K, Shinohara R, Kurokouchi T, Sugimoto K, Hakoshima Y, Inazaki K, Yoshimura Y, Mizumoto Y, Okada T. Case-control study on clinical characteristics of child and adolescent psychiatric outpatients with child-to-parent violence. BMJ open. 2021.12; 11(12); e048222
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- 3. Kuroda Naoto, Kubota Takafumi, Horinouchi Toru, Ikegaya Naoki, Kitazawa Yu, Kodama Satoshi, Matsubara Teppei, Nagino Naoto, Neshige Shuichiro, Soga Temma, Sone Daichi, Takayama Yutaro, Kuramochi Izumi, Kanemoto Kousuke, Ikeda Akio, Terada Kiyohito, Goji Hiroko, Ohara Shinji, Hagiwara Koichi, Kamada Takashi, Iida Koji, Ishikawa Nobutsune, Shiraishi Hideaki, Iwata Osato, Sugano Hidenori, Iimura Yasushi, Higashi Takuichiro, Hosoyama Hiroshi, Hanaya Ryosuke, Shimotake Akihiro, Kikuchi Takayuki, Yoshida Takeshi, Shigeto Hiroshi, Yokoyama Jun, Mukaino Takahiko, Kato Masaaki, Sekimoto Masanori, Mizobuchi Masahiro, Aburakawa Yoko, Iwasaki Masaki, Nakagawa Eiji, Iwata Tomohiro, Tokumoto Kentaro, Nishida Takuji, Takahashi Yukitoshi, Kikuchi Kenjiro, Matsuura Ryuki, Hamano Shin-ichiro, Yamanouchi Hideo, Watanabe Satsuki, Fujimoto Ayataka, Enoki Hideo, Tomoto Kyoichi, Watanabe Masako, Takubo Youji, Fukuchi Toshihiko, Nakamoto Hidetoshi, Inaji Motoki, Takagi Shunsuke, Enokizono Takashi, Masuda Yosuke, Hayashi Takahiro. Risk factors for psychological distress in electroencephalography technicians during the COVID-19 pandemic: A national-level cross-sectional survey in Japan EPILEPSY & BEHAVIOR. 2021.12; 125;
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- 5. Sugihara G, Hirai N, Takei N, Takahashi H. COVID-19 vaccination and mental health in hospital workers. Brain and behavior. 2021.11; 11(11); e2382
- 6. Uda M, Hashimoto M, Uozumi R, Torii M, Fujii T, Tanaka M, Furu M, Ito H, Terao C, Yamamoto W, Sugihara G, Nakagami Y, Mimori T, Nin K. Factors associated with anxiety and depression in rheumatoid arthritis patients: a cross-sectional study. Advances in rheumatology (London, England). 2021.10; 61(1); 65
- 7. Mayumi Echizen, Maiko Satomoto, Miho Miyajima, Yushi Adachi, Eisuke Matsushima. Preoperative heart rate variability analysis is as a potential simple and easy measure for predicting perioperative delirium in esophageal surgery Ann Med Surg (Lond) . . 2021.09; 70;
- 8. Tanaka SC, Yamashita A, Yahata N, Itahashi T, Lisi G, Yamada T, Ichikawa N, Takamura M, Yoshihara Y, Kunimatsu A, Okada N, Hashimoto R, Okada G, Sakai Y, Morimoto J, Narumoto J, Shimada Y, Mano H, Yoshida W, Seymour B, Shimizu T, Hosomi K, Saitoh Y, Kasai K, Kato N, Takahashi H, Okamoto Y, Yamashita O, Kawato M, Imamizu H. A multi-site, multi-disorder resting-state magnetic resonance image database. Scientific data. 2021.08; 8(1); 227
- 9. Katayama S, Kubota T, Takahashi H, Shiwaku H. Anti-rods/rings autoantibodies in a patient with pancreatic injury. Autoimmunity reviews. 2021.08; 102922
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- 14. Shisei Tei, Junya Fujino, Takashi Itahashi, Yuta Y. Aoki, Haruhisa Ohta, Manabu Kubota, Shuji Sawajiri, Ryu-ichiro Hashimoto, Hidehiko Takahashi, Nobumasa Kato, Motoaki Nakamura. The right temporoparietal junction during a cooperation dilemma: An rTMS study Neuroimage: Reports . 2021.07; 1; 100033
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[Books etc]

1. Takayuki Okada, Alan Felthous (Editor), Henning Sass (Editor). The Wiley International Handbook on Psychopathic Disorders and the Law, 2nd Edition. 2021.02 (ISBN : 978-1-119-15928-5)

- 1. Miho Sakuma, Miho Miyajima, Motoki Inaji, Masato Serino, Koichi Fujiwara, Manabu Kano, Taketoshi Maehara. Epileptic Seizure Prediction Based on Heart Rate Variability in a Patient with Intractable Epilepsy Due to Trauma under Electrocorticogram Monitoring: A Case Report. American Epilepsy Society 2021.12.03
- Junya Fujino, Shisei Tei, Hidehiko Takahashi, Motoaki Nakamura. A preliminary investigation of individual differences in attentional function and ventral attention network. 21st World Congress of Psychiatry 2021.10
- 3. Junya Fujino, Shisei Tei, Nobumasa Kato, Hidehiko Takahashi. A study of cognitive flexibility and theory of mind in autism spectrum disorder. 7th Congress of Asian College of Neuropsychopharmacology 2021.10

- 4. Junya Fujino, Shisei Tei, Takashi Itahashi, Yuta Y. Aoki, Haruhisa Ohta, Takuji Izuno, Hironobu Nakamura, Masaaki Shimizu, Ryu-ichiro Hashimoto, Hidehiko Takahashi, Nobumasa Kato, Motoaki Nakamura. Role of the right anterior temporoparietal junction in cognitive function in autism spectrum disorder. 7th Congress of Asian College of Neuropsychopharmacology 2021.10
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- 7. Miho Miyajima, Hiroki Shiwaku, Yukiko Matsumoto, Shiori Noguchi, Takashi Maruo, Yuki Shidei, Nanase Kobayashi, Masanori Ichihashi, Kanako Oohashi, Hidehiko Takahashi. Development of Tokyo Metropolitan Distress Scale for Pandemic (TMDP), for assessing mental and social stress of medical personnel in COVID-19 pandemic. 19th International Congress of the Pacific Rim College of Psychiatrists (PRCP 2021) 2021.04.08 Seoul, Korea
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- 10. Manabu Kubota, Junya Fujino, Shisei Tei, Keisuke Takahata, Kiwamu Matsuoka, Kenji Tagai, Yasunori Sano, Yasuharu Yamamoto, Hitoshi Shimada, Yuhei Takado, Chie Seki, Takashi Itahashi, Yuta Y. Aoki, Haruhisa Ohta, Ryu-ichiro Hashimoto, Ming-Rong Zhang, Motoaki Nakamura, Hidehiko Takahashi, Nobumasa Kato, Makoto Higuchi. Binding of Dopamine D1 Receptor and Noradrenaline Transporter in Individuals with Autism Spectrum Disorder: A PET Study with [11C] SCH23390 and (S,S)-[18F] FMeNER-D2. International College of Neuropsychopharmacology (CINP) 2021 Virtual World Congress 2021.02
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- Shota Kashiwazaki,Masanori Ichihashi,Miho Miyajima,Daisuke Jitoku,TakehiroTamura,Takashi Takeuchi,Genichi Sugihara,Hidehiko Takahashi. A Case of Psychogenic Non-epileptic Seizures Complicated by Epilepsy. The 123rd Academic Conference of the Tokyo Psychiatric Association 2021.11.06
- 3. Chisato Urui. A case of suspected chronic progressive neuro-Behçet's disease in a woman in her 40s with severe cognitive impairment. The 123rd Academic Conference of the Tokyo Psychiatric Association 2021.11.06
- 4. Prediction of epileptic seizures using heart rate variability analysis during chronic intracranial EEG recording, A case of a patient with traumatic intractable epilepsy. The 80th Annual Meeting of the Japanese Neurosurgical Society 2021.10.27
- 5. Miho Miyazima. Lessons from a multiinstitutional joint research based on medical-engineering collaboration:Development of epileptic prediction system utilizing heart rate variability analysis. Journal of the Japan Epilepsy Society 2021.09.23 Nagoya International Convention Center

Cognitive and Behavioral Medicine

6. Daisuke Jitoku. E-sports and gaming disorder.. The 19th Annual Meeting of Japanese Association of Sports Psychiatry 2021.09.04 Online

Neurosurgery

Professor: Taketoshi Maehara Associate Professor: Yoji Tanaka Assistant Professors: Motoki Inaji and Takashi Sugawara Hospital stuffs: Kaoru Tamura, Jun Karakama and Shoko Hara Graduate Students: Jiro Aoyama, Tomoyuki Nakano, Motoshige Yamashina Asumi Orihara, Satoru Takahashi, Yusuke Ebiko, Satoshi Kaneko, Daisu Abe Tadahiro Ishiwada, Kei Ito, Toshihiro Yamamura, Naoki Taira Masae Kuroha, Akihito Sato and Shoko Fujii

(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) Publications

[Original Articles]

- Hara S, Mukawa M, Akagawa H, Thamamongood T, Inaji M, Tanaka Y, Maehara T, Kasuya H, Nariai T. Absence of the RNF213 p.R4810K variant may indicate a severe form of pediatric moyamoya disease in Japanese patients. Journal of neurosurgery. Pediatrics. 2021.10; 1-9
- Chiba K, Sugawara T, Kobayashi D, Sato A, Murota Y, Maehara T. Atypical Histological Features as Risk Factors for Recurrence in Newly Diagnosed WHO Grade I Meningioma. Neurologia medico-chirurgica. 2021.09;
- 3. Shoko Hara, Yoji Tanaka, Motoki Inaji, Shihori Hayashi, Kenji Ishii, Tadashi Nariai, Taketoshi Maehara. Spatial coefficient of variation of arterial spin labeling MRI for detecting hemodynamic disturbances measured with 15O-gas PET in patients with moyamoya disease Neuroradiology. 2021.09;
- 4. Fujimoto Kenji, Arita Hideyuki, Satomi Kaishi, Yamasaki Kai, Matsushita Yuko, Nakamura Taishi, Miyakita Yasuji, Umehara Toru, Kobayashi Keiichi, Tamura Kaoru, Tanaka Shota, Higuchi Fumi, Okita Yoshiko, Kanemura Yonehiro, Fukai Junya, Sakamoto Daisuke, Uda Takehiro, Machida Ryunosuke, Kuchiba Aya, Maehara Taketoshi, Nagane Motoo, Nishikawa Ryo, Suzuki Hiroyoshi, Shibuya Makoto, Komori Takashi, Narita Yoshitaka, Ichimura Koichi. TERT promoter mutation status is necessary and sufficient to diagnose IDH-wildtype diffuse astrocytic glioma with molecular features of glioblastoma ACTA NEUROPATHOLOGICA. 2021.08; 142(2); 323-338
- 5. Tanaka K, Suesada N, Homma T, Mori H, Sugawara T, Tsutsumi T, Asakage T, Okazaki M. The different concepts of surgical managements between anterior and lateral skull base reconstructions based on surgical purposes. Auris, nasus, larynx. 2021.08;
- Hara S, Nariai T, Inaji M, Tanaka Y, Maehara T. Imaging Pattern and the Mechanisms of Postoperative Infarction After Indirect Revascularization in Patients with Moyamoya Disease. World neurosurgery. 2021.08;
- 7. Hirai Sakyo, Tanaka Yoji, Sato Hirotaka, Kato Koichi, Kim Yongson, Yamamura Toshihiro, Sumita Kazutaka, Arai Toshinari. Quantitative collateral assessment evaluated by cerebral blood volume measured by CT perfusion in patients with acute ischemic stroke JOURNAL OF STROKE & CEREBROVASCULAR DISEASES. 2021.07; 30(7); 105797
- 8. Takayuki Suga, Miho Takenoshita, Trang T H Tu, Takashi Sugawara, Susumu Kirimura, Akira Toyofuku. A case of vestibular schwannoma mimicking burning mouth syndrome. Biopsychosoc Med. 2021.03; 15(1); 7
- 9. Takahashi Satoshi, Takahashi Masamichi, Kinoshita Manabu, Miyake Mototaka, Kawaguchi Risa, Shinojima Naoki, Mukasa Akitake, Saito Kuniaki, Nagane Motoo, Otani Ryohei, Higuchi Fumi, Tanaka Shota, Hata Nobuhiro, Tamura Kaoru, Tateishi Kensuke, Nishikawa Ryo, Arita Hideyuki, Nonaka Masahiro, Uda Takehiro, Fukai Junya, Okita Yoshiko, Tsuyuguchi Naohiro, Kanemura Yonehiro, Kobayashi Kazuma, Sese Jun, Ichimura Koichi, Narita Yoshitaka, Hamamoto Ryuji. Fine-Tuning Approach for Segmentation of Gliomas in Brain Magnetic Resonance Images with a Machine Learning Method to Normalize Image Differences among Facilities CANCERS. 2021.03; 13(6);
- 10. Suga Takayuki, Takenoshita Miho, Tu Trang T.H., Sugawara Takashi, Kirimura Susumu, Toyofuku Akira. A case of vestibular schwannoma mimicking burning mouth syndrome(和訳中) Biopsychosocial Medicine. 2021.03; 15; 1 of 4-4 of 4
- 11. Mori K, Tanaka K, Sugawara T, Asakage T, Tsutsumi T. Management of the temporal bone defect after resection of external auditory canal cancer. Auris, nasus, larynx. 2021.02;

- 12. Inaji Motoki, Yamamoto Takamichi, Kawai Kensuke, Maehara Taketoshi, Doyle Werner K.. Responsive Neurostimulation as a Novel Palliative Option in Epilepsy Surgery NEUROLOGIA MEDICO-CHIRURGICA. 2021.01; 61(1); 1-11
- 13. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. Am J Otolaryngol. 35(3); 402-404
- 1. Murota Y, Tamura K, Tanaka Y, Aizawa Y, Kobayashi D, Matsuoka Y, Hashimoto S, Inaji M, Nariai T, Maehara T. A Case of Cerebral Tuberculoma 2021.05; 49(3); 683-688

- 1. 田村 郁, 稲次 基希, 小林大輔, 菅原 貴志、田中洋次, 成相 直, 石井 賢二、前原 健寿. 分子診断に基づ いて再分類したグリオーマにおける Methionine PET と臨床経過の検討. 第 44 回日本脳神経 C I 学会総会 2021.04.09
- 2. Takashi Sugawara. Surgical Strategy for Lesion in and around Cavernous Sinus. Fujita Health University Bantane Alumni Association Webinar 2021.03.07 Nagoya, Web

Endovascular Surgery

Professor Kazutaka Sumita Assistant Professor Sakyo Hirai, Kyohei Fujita Clinical Fellow Shoko Fujii, Mariko Ishikawa 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. Kuroda T, Akaza M, Miki K, Fujii S, Yagi Y, Kanouchi T, Sanjo N, Sumita K, Yokota T. Sacral dural arteriovenous fistula mimicking multiple mononeuropathy. Clinical neurology and neurosurgery. 2021.11; 210; 106993
- Ayabe Fuga, Sumita Kazutaka, Fujii Shoko, Fujita Kyohei, Miki Kazunori, Aizawa Yuki, Karakama Jun, Maehara Taketoshi, Nemoto Shigeru. Simulation Model of Arteriovenous Malformation Embolization Using Onyx Journal of Neuroendovascular Therapy. 2021.11; 15(11); 741-746
- Hiroto Yamaoka, Kyohei Fujita, Shoko Fujii, Fuga Ayabe, Jun Karakama, Sakyo Hirai, Masataka Yoshimura, Shinji Yamamoto, Shigeru Nemoto, Kazutaka Sumita. Clinical Course of Abducens Nerve Palsy in Patients with Ruptured Vertebral Artery Dissecting Aneurysms Journal of Neuroendovascular Therapy. 2021.10;
- 4. Miki Kazunori, Sumita Kazutaka, Fujii Shoko, Fujita Kyohei, Aizawa Yuki, Karakama Jun, Yoshino Yoshikazu, Emoto Hirofumi, Nemoto Shigeru. A Case of Idiopathic Intracranial Hypertension Treated by Transverse Sinus Stenting Journal of Neuroendovascular Therapy. 2021.10; 15(10); 653-658
- Fujii S, Fujita K, Yamaoka H, Miki K, Hirai S, Nemoto S, Sumita K. Refractory in-stent stenosis after flow diverter stenting associated with delayed cobalt allergic reaction. Journal of neurointerventional surgery. 2021.08;
- Kyohei Fujita,Shoko Fujii,Hiroto Yamaoka,Fuga Ayabe,Sakyo Hirai,Kittipong Srivatanakul,Kazutaka Sumita. Results of an International Questionnaire Investigating Changes in Acute Stroke Management between Before and During the COVID-19 Pandemic Journal of Neuroendovascular Therapy. 2021.08; 15(8); 498-504
- Masataka Yoshimura, Kazutaka Sumita, Shoko Fujii, Kazunori Miki, Yuki Aizawa, Kyohei Fujita, Shinji Yamamoto, Shigeru Nemoto, Taketoshi Maehara. Periprocedural Variability of Platelet Functions in Carotid Artery Stenting: An Analysis Using VerifyNow Journal of Neuroendovascular Therapy. 2021.08; 15(8); 505-516
- 8. Hirai Sakyo, Tanaka Yoji, Sato Hirotaka, Kato Koichi, Kim Yongson, Yamamura Toshihiro, Sumita Kazutaka, Arai Toshinari. Quantitative collateral assessment evaluated by cerebral blood volume measured by CT perfusion in patients with acute ischemic stroke JOURNAL OF STROKE & CEREBROVASCULAR DISEASES. 2021.07; 30(7); 105797
- 9. Miki K, Aizawa Y, Fujii S, Karakama J, Fujita K, Sasaki Y, Nemoto S, Sumita K. Combined Technique Thrombectomy with a Long Balloon-Guiding Catheter and Long Sheath Aids in Rapid and Stable Recanalization in Patients with Anterior Circulation Acute Ischemic Stroke JNET: Journal of Neuroendovascular Therapy. 2021.05; 15(5); 281-287
- Fujii Shoko, Miki Kazunori, Aizawa Yuki, Karakama Jun, Fujita Kyohei, Maehara Taketoshi, Nemoto Shigeru, Sumita Kazutaka. Mid-/Long-Term Outcome of Neuroendovascular Treatment for Chronic Carotid Artery Total Occlusion Journal of Neuroendovascular Therapy. 2021.05; 15(5); 288-294

[Conference Activities & Talks]

1. Association between P2Y12 reaction unit and ischemic complications after endovascular treatment. 2021.03.12

NCNP Brain Physiology and Pathology

1. Staffs

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Yu-ichi GOTO
Collaborative Professor	Noritaka ICHINOHE
Collaborative Professor	Yoshitsugu AOKI
Collaborative Associate Professor	Yuichi YAMASHITA
Collaborative Associate Professor	Shinji Oki

(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 molecular machinery for the cerebellar development (eNeuro, 2021).

2) Molecular genetic and genomic study for intellectual disability in Japan.

(Yu-ichi Goto, Department of Mental Retardation and Birth Defect Research, National Institute of Neuroscience, NCNP)

One of the major causes of intellectual disability (ID) is based on mutations in the related genes, which are timely and locally expressed in concert with one another in central nervous system. ID is a phenotype derived from the inappropriate expression of these genes. Recent advances in molecular genetics and genome medicine have pushed us on with systematic analysis of ID patients, especially on X-linked MR. Since 2013, we investigated the genetic causes and pathophysiology of mitochondrial disease, Rett syndrome, and diseases with cortical and white matter dysplasia. We detected pathogenic mutations in LIG3 gene in mitochondrial neurogastrointestinal encephalomyopathy (Borora T, et al. Brain. 2021) and pathogenic repeat expansions in SAMD12 and TNRC6A genes in familial benign myoclonic epilepsy (Terasaki A, et al. J. Human Genet. 202), and detect pathogenic mutations in 11 genes in 45 Japanese patients with intellectual disability (J. Human Genet. 2021).

3) Autism research using a primate model marmoset

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

Autism is a neurodevelopmental disorder characterized by impaired social skills and perseverance. Although autism has been studied in rodent models, no treatment for autism has yet been developed. New World monkey, marmosets are expected to be suitable for autism research because they are evolutionarily close to humans, and have advanced social skills and a well-developed prefrontal cortex. We have developed an autism model of marmosets to elucidate the pathogenesis of autism and to develop treatments. In particular, we are analyzing the marmoset autism model from multiple perspectives using molecular and cell biological methods, systems neuroscience approaches (electrophysiology, structural MRI, etc.), and behavioral techniques. This year, we showed that the transcriptome of the marmoset autism model is closer to human data than previous rodent models, objectively demonstrating the superiority of the primate model (Nature Commun, 2021). We also showed that the brain may be immature in children with autism.

4) Development of state-of-the-art genetic therapies using human 3D tissue models for neuromuscular diseases

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

Our research group 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. Primarily, our research focuses on novel genetic therapies targeting messenger RNA and DNA. We also investigate RNA interference-based and genome editing therapies for several neuromuscular disorders. We have successfully shown the proof of concept of exon skipping 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. Recently, we have successfully developed an exon 53-skipping drug (viltolarsen: NS-065/NCNP-01) in collaboration with a Japanese pharmaceutical company (conditional approval in Japan and the US FDA).

Additionally, our group has drawn on research worldwide to create a picture of the current state-of-the-art 3D tissue platform using human urine-derived stem cells and induced pluripotent stem cell (iPSC) for pre-clinical investigations in gene therapy. Our research entails several promising discoveries and offers hope to patients afflicted with the potentially life-limiting condition of neuromuscular diseases, including DMD.

5) Computational approach for psychiatric disorders

(Yuchi Yamashita, Department of Information Medicine, National, National Institute of Neuroscience, NCNP)

Computational approach for psychiatric disorders, referred to as "Computational psychiatry (CPSY)", is a new research field which seeks to understand mental disorders as aberrant computation by using mathematical modeling of information processing in the brain. Our laboratory conducted series of experiments in which behavioral control mechanisms with hierarchical predictive process were implemented by the physical (or simulated) actions of a humanoid robot driven by a hierarchical recurrent neural network. These experimental results provided a mechanistic explanation that unifies the various levels of observations in ASD, including behavioral level (hyper/hypo-sensitivity, reduced cognitive inflexibility, impaired emotional recognition), neurophysiological level (altered E/I balance, functional disconnections) and computational level (altered precision in predictive processing) (Idei et al. Neural Networks, 2021, Takahashi et al. 2021). In addition, we developed novel analysis methods of MRI images using deep learning technique for structural MRI (Yamaguchi et al. 2021) and restring state functional MRI (Hashimoto et al. 2021), successfully extracting features effective for predicting clinical symptoms and diagnosis of schizophrenia.

6) Translational research on immune dysregulation-mediated CNS diseases

(Shinji Oki, Department of Immunology, National Institute of Neuroscience, NCNP) Many diseases of central nervous system (CNS) are prone to be intractable, possibly due to pathogenic involvement of external components that may cause disease-associated chronic inflammation and subsequent CNS dyshomeostasis. We have been investigating pathogenesis of the immune dysregulation-mediated intractable CNS diseases such as multiple sclerosis (MS) and neuromyelitis optica (NMO) and searching for establishment of therapeutic interventions. We have identified a novel functional helper T cell subset that cause dysregulation of immune responses (Raveney et al. Proc Natl Acad Sci USA 2021) and have been analyzing environmental disease modifier such as gut microbiota, resulted in identification of novel bacterial species that is intimately associated with MS pathology (Takewaki et al. Proc Natl Acad Sci USA 2020). Recently, we have revealed that immune-mediated neurotoxicity plays a pivotal role on pathological propagation of neuronal cell death in mouse models of neurodegenerative diseases (Takahashi et al. iScience in press). Pathogenic significance of immune dysregulation keeps expanding beyond ordinary autoimmune CNS diseases. In this respect, we keep paying much efforts of elucidation of previously-unappreciated pathogenesis of CNS diseases that is not able to be resolved via existing research approach.

(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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- 6. Tarasaki A, Nakamura M, Urata Y, Hiwatahi H, Yokoyama I, Yasuda T, Onuma T, Wada K, Kaneko S, Kan R, Niwa S, Hashimoto O, Komure O, <u>Goto Y</u>, Yamagishi Y, Nakano M,

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- 15. Nogami K, Maruyama Y, Sakai-Takemura F, Motohashi N, Elhussieny A, Imamura M, Miyashita S, Ogawa M, Noguchi S, Tamura Y, Kira JI, <u>Aoki Y</u>, Takeda S, Miyagoe-Suzuki Y.: Pharmacological activation of SERCA ameliorates dystrophic phenotypes in dystrophin-deficient mdx mice. Hum Mol Genet. 30(11): 1006-1019, 2021
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[Review Articles • Books]

- 1. <u>Yamashita Y</u> (2021), Psychiatric disorders as failures in the prediction machine. Psychiatry Clin. Neurosci., 75: 1-2.
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Molecular Virology

Professor : Shoji YAMAOKA Associate Professor : Hiroaki TAKEUCHI Project Junior Associate Professor: Takaya HAYASHI Assistant Professor: Takeshi YOSHIDA sayaka SUKEGAWA Medical Technologist : Yoshio INAGAKI Secretary : Kumiko THORPE-MATSUI

-Students-Ph.D. course: Haruki KITAMURA,Kei TAGA Master course: Saki ECHIGOYA

(1) Outline

Microbiology covers several aspects of bacteriology, immunology and virology. Through the studies on various microbes it is expected to understand host-parasite relationship and mechanisms of pathogenicity. Unlike the past, microbiology has rapidly been drawn to the center of the biological stage.

Our laboratory mainly deals with viral oncogenesis and immunodeficiency in humans. Several projects are carried out with particular emphasis on investigation into the mechanisms of viral replication and pathogenesis induced by human retroviruses (HIV-1 and HTLV-I) and human herpes viruses. The purpose of many of the studies being undertaken is to identify critical events and molecules responsible for the efficient replication of these viruses, and in case of human retroviruses, those for transformation or destruction of normal lymphocytes. Virological, immunological and molecular approaches are being applied for this purpose.

(2) Research

The following studies have been extensively carried our in out laboratory with various biological and molecular biological techniques:

- Pathogenesis of HIV and HTLV (mutation, virulence,

apoptosis, polymorphism).

- Studies on signal transduction pathways targeted by

viral proteins.

- Molecular cloning by genetic approaches of components

essential for virus replication in mammalian cells.

- Virological approaches for robust increase in lentiviral titer.

(3) Education

We are engaged in the lectures and practices on the basic aspects of infections for the 2nd year medical students and in the pre-clinical clerkship for the 4th year medical students. Students are also accepted in the Project Semester Program. Graduate course students carry out research on virology and oncology in the laboratory and join seminars and progress meetings.

(4) Lectures & Courses

Students can learn the structure, replication, function and genetics of micro-organisms as well as the host-pathogen interactions based on the front-line molecular and microbiological sciences.

(5) **Publications**

[Original Articles]

- 1. Chihiro Tani-Sassa, Yumi Iwasaki, Naoya Ichimura, Katsutoshi Nagano, Yuna Takatsuki, Sonoka Yuasa, Yuta Takahashi, Jun Nakajima, Kazunari Sonobe, Yoko Nukui, Hiroaki Takeuchi, Kousuke Tanimoto, Yukie Tanaka, Akinori Kimura, Shuji Tohda. Viral loads and profile of the patients infected with SARS-CoV-2 Delta, Alpha, or R.1 variants in Tokyo. J Med Virol. 2021.11;
- 2. Deletsu Selase D., Kitamura Haruki, Ishida Takaomi, Gohda Jin, Yamaoka Shoji, Takeuchi Hiroaki. Identification and characterization of Stathmin 1 as a host factor involved in HIV-1 latency BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 2021.08; 567; 106-111
- 3. Akasu M, Shimada S, Kabashima A, Akiyama Y, Shimokawa M, Akahoshi K, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Intrinsic activation of β -catenin signaling by CRISPR/Cas9-mediated exon skipping contributes to immune evasion in hepatocellular carcinoma. Scientific reports. 2021.08; 11(1); 16732
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[Misc]

1. Sayaka SUKEGAWA, Hiroaki TAKEUCHI. Genomics and epidemiology of SARS-CoV-2 lineage Current update on SARS-CoV-2 Variants of Interest (VOIs) and Variants of Concern (VOCs) 2021.06; 71(1); 19-32

- 1. Reda O, Monde K, Sugata K, Rahman A, Sakhor W, Rajib SA, Tan BJY, Matsuo M, Ono M, Takeuchi H and Satou Y. A new in-vitro model to monitor HIV-1 proviral transcription by timer-fluorescence protein.. Cold Spring Harbor Laboratory Meeting on Retroviruses 2021.05.27 New York, USA
- 2. Prah Isaac, Ayibieke Alafate, Nguyen Thi Thu Huong, Iguchi Atsushi, Mahazu Samiratu, Sato Wakana, Hayashi Takaya, Yamaoka Shoji, Suzuki Toshihiko, Iwanaga Shiroh, Ablordey Anthony, Saito Ryoichi. Virulence Profiles of Diarrheagenic Escherichia coli Isolated from the Western Region of Ghana(和訳中). Japanese Journal of Infectious Diseases 2021.03.01

Immunotherapeutics

Associate Professor: Takao Masuda Assistant Professor: Atsuhiko Hasegawa (Lecturer) Research Assistant: Kuniko Katagiri

(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-a 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 cocept 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 clarkship.

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

(4) Lectures & Courses

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

(5) Clinical 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.

(6) Publications

[Original Articles]

1. Kondo Nobuyo, Nagano Yoshiko, Hasegawa Atsuhiko, Ishizawa Miku, Katagiri Kuniko, Yoneda Takeru, Masuda Takao, Kannagi Mari. Involvement of EZH2 inhibition in lenalidomide and pomalidomide-mediated growth suppression in HTLV-1-infected cells BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 2021.10; 574; 104-109

- 2. Miku Ishizawa, Undrakh Ganbaatar, Atsuhiko Hasegawa, Natsuko Takatsuka, Nobuyo Kondo, Takeru Yoneda, Kuniko Katagiri, Takao Masuda, Atae Utsunomiya, Mari Kannagi. Short-term cultured autologous peripheral blood mononuclear cells as a potential immunogen to activate Tax-specific CTL response in adult T-cell leukemia patients. Cancer Sci. 2021.03; 112(3); 1161-1172
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- 6. Yotaro Tamai, Sayaka Ito, Atsuhiko Hasegawa. Paroxysmal nocturnal haemoglobinuria associated with a novel phosphatidylinositol glycan class A (PIGA) mutation in a patient with Klinefelter syndrome. Ann Hematol. 2021.01;
- 7. Camille Michiko Obayashi, Yoko Shinohara, Takao Masuda, Gota Kawai. Influence of the 5'-terminal sequences on the 5'-UTR structure of HIV-1 genomic RNA. Sci Rep. 2021.05; 11(1); 10920

Cellular and Environmental Biology

Associate Professor Masayuki HARA

(1) Research

Research Subjects

1) Reaction mechanisms of cellular protection systems against environmental oxidation stresses.

2) Modifying mechanisms in higher order structure of chromatin in cellular differentiation.

3) Shifting mechanisms in proteome profiles of cell organelle between pre and post conditions in environment, cell differentiation, disease, or drug exposure.

(2) Education

Living organisms were influenced their life by environment and adapted themselves to it, however, they formed environment and affected it. In other words, the species that cannot fit the changing environment were fallen and replaced by the new species which could adapt itself to. The organisms are as a part of the global environment, so it is thought that the individual structure and working of them are necessary environmental measures for their survival. It may be said that it is excessive suddenness of the change that human activity is environmentally-impacted now.

Main objective of cellular and environmental biology in the graduate course is to provide students opportunity to study the reaction and adaptation of the organisms for the environmental change at cellular level, to consider hazardous property, toxicity, or physiological activity of environmental (or man-made) factor, and to mention the biotechnical action to the environmental problems.

(3) Publications

- Rikako Azuma, Hiroyuki Tsunokuni, Keiichi Matsunami, Masayuki Hara, Shinsuke Katoh, Hiroyuki Iizuka. Efforts for promotion of Use of Radioisotopes (RI) -RI Experimental Protocols for Beginners-. The 94th Annual Meeting of the Japanese Pharmacological Society 2021.03.08
- 1. Chiyomi Matsuoka, Mami Kitaoka, Nobutaka Nakamura, Jun Hatazawa, Keiichi Matsunami,Masayuki Hara,Shinsuke Katoh,Hiroyuki Iizuka. Creating content to connect researchers and RI facilities -Report on the activities of the subcommittee for creating a list of RI facilities nationwide-. Radiation Safety Handling Subcommittee Annual Meeting 2021 2021.10.28
- 2. Chiyomi Matsuoka, Mami Kitaoka, Nobutaka Nakamura, Jun Hatazawa, Keiichi Matsunami,Masayuki Hara,Shinsuke Katoh,Hiroyuki Iizuka. "List of RI facilities nationwide" -For connecting researchers and RI facilities-. The 58th Annual Meeting on Radioisotopes and Radiation Researches 2021.07.07

Biodefense Research

Professor Toshiaki Ohteki Associate Professor Taku Sato Adjunct Lecturer Yasuhiro Murakawa Adjunct Lecturer Nobuyuki Onai Assistant Professor Masashi Kanayama Graduate Student Megumi Akiyama Graduate Student Hajime Sato Graduate Student Hajime Sato Graduate Student Shun Ishikawa Graduate Student Yuta Izumi Graduate Student Mai Nakagawa Graduate Student Eriko Ohashi Research Technician Kisho Shiseki Research Technician Tomiki Hayashi Staff 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 dendritic cells and macrophages

Dendritic cells (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) in response to viral and self-nucleic acids. We have discovered the DC progenitors in the mouse bone marrow, and named common DC progenitors (CDPs) (Immunity 2013; Nat Immunol 2007). Interestingly, we found that 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.

During stress response, monocytes actively influx into various tissues and differentiate into macrophages, which are involved in inflammation, tissue repair, and cancer growth. In addition to CDPs, we recently found human common monocyte progenitors (cMoPs) in human bone marrow and umbilical cord blood (Immunity 2017; Int Immunol 2018). Human cMoP gives rise to only monocytes but not other hematopoietic cells including DCs. Given that monocytes are involved in chronic myelomonocytic leukemia (CMML) and monocyte-derived tumor-associated macrophages (TAMs) promote tumor development, we, in collaboration with a pharmaceutical company, have generated an antibody-drug conjugate (ADC) that selectively targets human cMoP. When this ADC was administered to the CMML PDX model, leukemia cells almost completely disappeared from the bone marrow and peripheral blood. In addition, upon ADC administration into tumor-bearing humanized mice, both peripheral blood monocytes and intratumoral TAMs disappeared, leading to the shrinkage of tumor mass (Front Immunol 2021). Since monocytes are also involved in various inflammatory diseases, the application of human monocyte lineage-specific ADCs to these diseases is also expected (Fig. 1).

2) Impairment of brain function by microglial enhancer in aging and Alzheimer's disease (AD)

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.

Using a novel RIKEN technology that can detect the active enhancer region at single base level, we are trying to identify the enhancers responsible for the microglial transformation during life-stage progression and AD development. To date, we have succeeded to identify 36,320 new microglial enhancers including 937 regions that become different with age, and the analysis of coding regions regulated by the enhancers using Hi-C technology is in progress. As enhancers are activated in a cell-type specific manner, one can expect the development of novel technology that specifically controls the age-related functional alteration of microglia.

- 2. Research on tissue stem cells
- 1) Tissue homeostasis and its breakdown on the basis of immune cell-tissue stem cell interplay

Even under the steady-state, type I interferons (IFNs) are consistently produced, albeit in trace amounts, so called "physiologic type I IFNs". We previously reported that the physiologic 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 achievement, we examined the significance of physiologic type I IFNs in intestinal stem cells (ISCs) and found that it reduces the number and function of ISCs, resulting in the promoted differentiation into secretory progenitors (Nat Cell Biol 2020). Similarly, physiologic type I IFNs impaired the stemness of colonic stem cells (CSCs), leading to the defective colonic regeneration with lethality in a DSS colitis model (Sci Rep 2020).

Although several types of cells are synchronously involved in the damage-induced epithelial regeneration, it remains unclear to what degree each population contributes to the overall epithelial regeneration. Using a combination of genetic lineage tracing, single-cell gene expression profiling, and organoid-formation assays, we characterized the heterogeneity of epithelial stem cells in the radiation-damaged intestine. As a result, we found that the main cell of origin after intestinal injury originated from Lgr5+ cells (Sci Rep 2020).

2) Establishment of human tongue cancer organoid biobank

Squamous cell carcinoma occurs in the oral cavity, esophagus, lungs, and cervix. Tongue cancer accounts for about 60% of oral cancer, and the 5-year survival rate is extremely low for advanced tongue cancer, and the recurrence rate after radical treatment is also high. Similarly, squamous cell carcinoma of the esophagus, which is characteristic of Asian countries including Japan, has a very high recurrence rate after curative treatment. As a multicenter collaborative study, our research group has succeeded in constructing an organoid library specialized for human tongue cancer and human esophageal squamous cell carcinoma, which has never been reported (34 cases of tongue cancer and 18 cases of esophageal cancer, ongoing) (Fig. 2). In addition, we have established cancer organoids that are resistant to anticancer drugs used in clinical treatment (4 cases of tongue cancer and 4 cases of esophageal cancer, ongoing). Using these unique resources, the elucidation of the mechanism for acquiring anticancer drug resistance and the search for drug discovery are in progress.

(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]

- A. Adachi, T. Honda, T. Dainichi, G. Egawa, Y. Yamamoto, T. Nomura, S. Nakajima, A. Otsuka, M. Maekawa, N. Mano, N. Koyanagi, Y. Kawaguchi, T. Ohteki, T. Nagasawa, K. Ikuta, A. Kitoh, K. Kabashima. Prolonged high-intensity exercise induces fluctuating immune responses to herpes simplex virus infection via glucocorticoids. J Allergy Clin Immunol. 2021.05;
- 2. Izumi Y, Kanayama M, Shen Z, Kai M, Kawamura S, Akiyama M, Yamamoto M, Nagao T, Okada K, Kawamata N, Toyota S, Ohteki T. An Antibody-Drug Conjugate That Selectively Targets Human Monocyte Progenitors for Anti-Cancer Therapy. Frontiers in immunology. 2021.02; 12; 618081
- 3. Chikuma S, Yamanaka S, Nakagawa S, Ueda MT, Hayabuchi H, Tokifuji Y, Kanayama M, Okamura T, Arase H, Yoshimura A. TRIM28 Expression on Dendritic Cells Prevents Excessive T Cell Priming by Silencing Endogenous Retrovirus. Journal of immunology (Baltimore, Md. : 1950). 2021.02;

[Misc]

- 1. T. Ohteki, S. Kawamura, N. Onai. Commitment to dendritic cells and monocytes. Int Immunol. 2021.06;
- 2. 佐藤 卓, 樗木 俊聡. 組織再生を担う腸管幹細胞の維持と機能 生化学. 2021; 93(4); 503-511
- 1. Taku Sato, Toshiaki Ohteki. The role of interferon in intestinal stem cells Clinical Immunology & Allergology. 2021.06; 75(6); 759-764

- 1. Yuta Izumi. A Therapeutic Strategy That Selectively Targets Human Monocyte Progenitors for Solid Cancers and Leukemias. The 50th Annual Meeting of the Japanese Society for Immunology 2021.12.10
- 2. Shun Ishikawa. Elucidation of transcriptional regulation mechanism of age-related microglia. . The 27th International Symposium on Molecular Cell Biology of Macrophages. 2021.12.10
- 3. Masashi Kanayama. Myeloid-like B cells boost emergency myelopoiesis during infection.. The 50th Annual Meeting of the Japanese Society for Immunology 2021.12.08
- 4. Shun Ishikawa. Elucidation of transcriptional regulation mechanism of age-related microglia. The 27th International Symposium on Molecular Cell Biology of Macrophages.. The 27th International Symposium on Molecular Cell Biology of Macrophages. 2021.06.16 web
- 5. Taku Sato, Toshiaki Ohteki. Identification of a key dermal immune cell population that disrupt epidermal homeostasis in autoimmune alopecia.. The 27th International Symposium on Molecular Cell Biology of Macrophages 2021.06.15 Web
- 1. Miwako Sase, Taku Sato, Tadahide Noguchi, Yoshiyuki Mori, Toshiaki Ohteki. Establishment of human tongue cancer organoid biobank. The 58th annual meeting of Japanese society of oral oncology 2021.01.28 Nagano

Pathological Cell Biology

Professor : Shigeomi SHIMIZU Associate Professor : Norio SHIMIZU, Satoko ARAKAWA Junior Associate Professor : Satoshi TORII Project Associate Professor : Masatsune TSUJIOKA,Shinya HONDA Assistant Professor : Hirofumi YAMAGUCHI Project Assistant Professor : Michiko MUROHASHI, Hajime SAKURAI, Minkyon SHIN, Youichi NIBE, Saori NOGUCHI, Hazuki ENDO Graduate Student : Toyokazu SEKI, Tomoyo YOSHIDA, Kazuma OHSHIMA,Chinami OGAWA 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 anti- Epstein-Barr virus (EBV).
- 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 development of anti-EBV drugs and 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 development of an exhaustive pathogenic microbial screening system.

(4) Publications

[Original Articles]

1. Shuya Kasai, Xianyu Li, Satoru Torii, Ken-ichi Yasumoto & Kazuhiro Sogawa. Direct protein–protein interaction between Npas4 and IPAS mutually inhibits their critical roles in neuronal cell survival and

death Cell Death Discovery. 2021.10; 7; 300

- Takuto Tokuhiro, Akane Ishikawa, Haruka Sato, Shunya Takita, Ayuri Yoshikawa, Ryoko Anzai, Shinichi Sato, Ryohei Aoyagi, Makoto Arita, Yasuaki Aratani, Shigeomi Shimizu, Masato Tanaka, Satoshi Yotsumoto. Oxidized phospholipids and neutrophil elastase coordinately play critical roles in NET formation Frontiers in Cell and Developmental Biology. 2021.09;
- Yoshimori M, Shibayama H, Imadome KI, Kawano F, Ohashi A, Nishio M, Shimizu N, Kurata M, Fujiwara S, Arai A. Antineoplastic and anti-inflammatory effects of bortezomib on systemic chronic active EBV infection. Blood advances. 2021.04; 5(7); 1805-1815
- 4. Sato S, Noda S, Torii S, Amo T, Ikeda A, Funayama M, Yamaguchi J, Fukuda T, Kondo H, Tada N, Arakawa S, Watanabe M, Uchiyama Y, Shimizu S, Hattori N. Homeostatic p62 levels and inclusion body formation in CHCHD2 knockout mice. Human molecular genetics. 2021.02;
- 5. 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
- 6. 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
- 7. 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. Saori Noguchi, Shigeomi Shimizu. Molecular mechanisms and biological roles of GOMED FEBS Journal. 2021.11;
- 2. Daniel J. Klionsky, et al. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). Autophagy. 2021.02; 17(1); 1-382
- 3. Arakawa S, Honda S, Torii S, Tsujioka M, Shimizu S.. Monitoring of Atg5-independent Mitophagy. Methods in Molecular Biology,"Mitophagy".

Lipid Biology

Professor Takehiko Sasaki Associate Professor Junko Sasaki Assistant Professor Junya Hasegawa Technical Assistant Toshiyoshi Yamamoto JSPS Research Fellow Emi Tokuda JSPS Research Fellow Morioka Shin Graduate student (master) Takumi Ikeda Graduate student (master) Daichi Sato Graduate student (master) Kouichiro Takehashi Graduate research student Yixin Zhang Graduate research student Wang Tian Secretary Kaori Kofuji

(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.

Bio-Environmental Response

 $\cdot\,$ Identification of phospholipids involved in the pathogenesis of inflammatory diseases (pneumonia, colitis, and non-alcoholic steatohepatitis).

- $\cdot\,$ Identification of phospholipids involved in basal ganglia neurodegeneration.
- $\cdot\,$ 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]

- Huang M, Koizumi A, Narita S, Nakanishi H, Sato H, Kashima S, Nara T, Kanda S, Numakura K, Saito M, Satoh S, Nanjo H, Sasaki T, Habuchi T. Altering phosphoinositides in high-fat diet-associated prostate tumor xenograft growth. MedComm. 2021.12; 2(4); 756-764
- 2. Sakihara T, Takiguchi N, Uzawa H, Serizawa R, Kobayashi T. Erylysin A inhibits cytokinesis in Escherichia coli by binding with cardiolipin. Journal of biochemistry. 2021.10; 170(3); 369-377
- 3. Sakihara Tomoko, Takiguchi Naoko, Uzawa Hikari, Serizawa Rika, Kobayashi Tetsuyuki. Erylysin A inhibits cytokinesis in Escherichia coli by binding with cardiolipin(和訳中) The Journal of Biochemistry. 2021.09; 170(3); 369-377
- 4. Daiki Hashimoto, Tsuyoshi Hirashima, Hisao Yamamura, Tomoya Kataoka, Kota Fujimoto, Taiju Hyuga, Atsushi Yoshiki, Kazunori Kimura, Shunsuke Kuroki, Makoto Tachibana, Kentaro Suzuki, Nobuhiko Yamamoto, Shin Morioka, Takehiko Sasaki, Gen Yamada. Dynamic erectile responses of a novel penile organ model utilizing two photon excitation microscopy (TPEM) †. Biology of reproduction. 2021.01;

- 1. Junya Hasegawa, Lois S. Weisman, Junko Sasaki, Takehiko Sasaki. A new insights into the roles of phosphoinositides in lysosomal function. The 44th Annual Meeting of the Molecular Biology Society of Japan 2021.11.03
- 2. 黄 明国, 佐々木 雄彦, 沼倉 一幸, 齋藤 満, 成田 伸太郎, 羽渕 友則. 高脂肪食摂取による前立腺癌増殖とホス ファチジルイノシトールの関連. 日本癌学会総会記事 2021.09.01
- 3. Yixin Zhang, Toshiyoshi Yamamoto, Takehiko Sasaki, Junko Sasaki. Biology of phosphoinositide acyl chains. 次世代を担う若手のためのファーマ・バイオフォーラム 2021.08.28

Pediatrics and Developmental Biology

Professor: Tomohiro MORIO
Associate Professor: Masatoshi TAKAGI
Senior Assistant Professor: Kenichi KASHIMADA, Takeshi ISODA
Assistant Professor:Tomoko MIZUNO, Kei TAKASAWA, Taku ISHII, Tomohiro UDAGAWA,
Noriko MITSUIKI, Yohei YAMAGUCHI, Kazuyuki ITO, Hisae NAKATANI,
Motoi YAMASHITA, Yumie TAMURA
Project Assistant Professor:Fumiko Ozaki
Graduate Students:Akira NISHIMURA, Satoshi MIYAMOTO Kazuaki MATSUMOTO,
Kengo MORIYAMA, Kento INOUE, Haruka HIROKI, Maki GAU, Kei IWATA, Aoi MORISHITA,
Yuko AKUTSU, Takahiro TOMODA,Makito SAKURAI, Mika OKUTSU, Toru KANAMORI,
Eriko ADACHI, Yusuke NOGUCHI, Shuya KANEKO, Shizuka KIRINO, Dan TOMOMASA,
Etsushi TOYOFUKU
Department of Child Health and Development
Professor: Hirokazu KANEGANE
Assistant Professor: Masaki SHIMIZU

Department of Pediatrics, Neonatal and Maternal Medicine Associate Professor: Kohsuke IMAI Project Assistant Professor:Susumu HOSOKAWA, Chikako MORIOKA

Department of Lifecourse Clinical Immunology Professor: Masaaki MORI Project Assistant Professor: Hitoshi IRABU

(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 be dside. Our current main projects are

1. Identification of responsible genes for primary immunodeficiency (PID).

2. Development of the rapeutic approach for PID

3. Development of innovative techniques for ex vivo cell therapy after hematopoietic stem cell transplantation.

4. Multicenter Registry for pediatric Pulmonary arterial hypertension (PAH) (Congenital Heart Disease related PAH (JACPHR) and Idiopathic/heritable PAH (JAPHR))
- 5. Multicenter Registry study on Kawasaki Disease with coronary artery aneurysm
- 6. profile in umbilical cord-derived mesenchymal stem cells due to the intrauterine environment in humans
- 7. profile in stem cells from human exfoliated deciduous teeth of children with cerebral palsy
- 8. Elucidating the molecular mechanisms of gonadal development
- 9. Molecular pathology of congenital adrenal diseases and disorder of sex development
- 10. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
- 11. Study of autoimmunity in Opsoclonus Myoclonus Syndrome
- 12. Development of gene therapy for Ataxia Telangiectasia
- 13. Study of molecular biology in systemic vascular stenosis
- 14. Genetic background of leukemia development
- 15. Study using single cell sequencing analysis in pediatric leukemia
- 16. Development of novel CAR-NK cell therapy for child cancer
- 17. Identifying the molecular pathology of metabolic syndrome in 21 hydroxylase deficiency
- 18. 3D genome structure and molecular mechanism in leukemia
- 19. Mechanistic insight into activation of super-enhancer in T cell commitment
- 20. Genetic analysis and development of therapeutic approach for epilepsy syndrome
- 21. Clarifying immunological profiles of the patients with autoimmune diseases
- 22. Developing a methodology for the diagnosis of cytokine storm syndrome 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
- 25. Research in pathophysiology and prognostic predictor of nephritis /nephrotic syndrome
- 26. Molecular mechanisms and pathology of kidney disease with IEI or hereditary kidney disease

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Sci-ence, 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) Immunology

We have explored inborn error of immunity (IEI) candidate genes using the whole-exome analysis (WES) method using next-generation sequencers and have identified several candidate mutations. Molecular characterization of these candidates has also been conducted parallelly. To date, we have performed WES for 136 cases of IEI and identified candidate genes in 36 cases (27%) (Okano). Imai et al reported novel disease concepts caused by APRIL mutation exhibiting attenuated plasmacyte differentiation. Okano and Morio reported OAS1 (gain-of-function variants) as the new causative gene in IEI associated with pulmonary proteinosis. Yamashita and Morio found another IEI-causing gene, IKZF3, in a family of patients with B cell deficiency and familial lymphoma. Nishimura and Imai reported the summary of 42 IEI cases that underwent hematopoietic stem cell transplantation in our department. Also, we are working with domestic and overseas researchers to analyze the pathogenesis of IEI and to develop therapeutic methods. Imai is conducting a nationwide newborn screening for IEI using the TREC/KREC test. As adoptive immunotherapy to promote immunological reconstitution after transplantation, we have developed virus-specific T cell therapy for refractory viral infections and are pursuing the clinical trial (Kamiya and Morio).

Oncology

In the research for the diseases related to DNA damage response pathways, we have elucidated the usefulness of PARP inhibitors for neuroblastoma by targeting homologous recombination repair and lunched phase I physician-led clinical trials for refractory pediatric solid tumors. We have also developed a simple method to measure genomic copy number aberrations in neuroblastoma using digital PCR to classify the risk. We revealed the existence of a small number of RUNX1-mutant clones at the onset of autoimmune and inflammatory conditions which caused AML-MRC two years later. Thus, our result strongly suggests that a preclinical small number of MDS clone could have induced AIC before the onset of AML-MRC. (Takagi)

- Cardiology Group
- < Basic Research >

We are struggling to elucidate the mechanism of pulmonary arterial hypertension. Our current project is to examine a role of BMP9 in PAH. (Sakurai and Hosokawa)

< Clinical Research >

"Multicenter Registry for pediatric pulmonary arterial hypertension (PAH) (Congenital Heart Disease related PAH (JACPHR) and Idiopathic/heritable PAH (JAPHR))"

"Effectiveness evaluation of live attenuated vaccines for patients using immunosuppresants" (Ishii) "Multicenter Registry study on Kawasaki Disease with coronary artery 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 clarify the cytoprotective effects of astrocytes in oxygen-glucose deprivation condition, we are investigating the role of Nuclear Receptor 4A (NR4A) subfamily and another cytoprotective transcription factor related to hypoxia-induced factor 1 alpha (HIF-1 α). Another study is to establish a rat neonatal white matter injury model. (collaborative project with Hiroshi Sakuma, Tokyo Metropolitan Institute of Medical Science).

< Clnical 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'

"Establishment of quantitative evaluation of pediatric cerebellum-dependent motor learning through prism adaptation and the application to central nervous system diseases"

Endocrinology – Metabolism Group

Molecular mechanisms of gonadal development

To understand the pathophysiology of DSD, our current research is focusing on elucidating the molecular mechanisms of sex determination and gonadal development, especially in the aspect of the transcriptional network of sex determination and gonadal development. Another our 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)

One of our major tasks is supervising the CAH neonatal mass-screening in Tokyo. Currently, large number of CAH patients we treat, and clarifying the clinical details and we are focusing on clarifying the long term prognosis of the disease. In addition to adrenal insufficiency and androgen excess, metabolic syndrome during adulthood is reported to be another major concern of CAH. The precise pathophysiology is not known. We are looking at elucidating the molecular mechanisms of the metabolic syndrome in CAH patients by using mice model.

Identifying novel molecules of congenital endocrinological and congenital metabolic diseases

We aim to identify novel molecules responsible for 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 and metabolic 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 diseases, developing a methodology for the diagnosis of cytokine storm syndrome 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. We aim to identify predictive biomarkers for preterm complications by intrauterine environment using umbilical cord-derived mesenchymal stem cells.

• 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.

• Nephrology Group

Research in pathophysiology and prognostic predictor of nephritis /nephrotic syndrome

A multicentre study with associated hospitals is underway to identify disease pathogenesis and pathogenic factors by analysing patient epidemiological data, peripheral blood cell fraction analysis and serum, urinary protein and miRNA profiling.

Searching for biomarkers associated with the severity, response to treatment and long-term prognosis of idiopathic nephritis and idiopathic nephrotic syndrome, aiming to construct disease models and elucidate the molecular basis of the disease using organoids.

Pathology of hereditary kidney diseases.

Protein and gene expression analyses of human kidney tissue sections, animal models and renal organoids are conducted in collaboration with the Department of Human Pathology to elucidate the molecular mechanisms of pathogenesis in genetic kidney diseases .

Kidney diseases associated with patients with inborn error of immunity

To elucidate the disease pathogenesis with regard to renal disease associated with IEI.

(3) Education

Block Lecture

The systematic lecture was performed for M4 students. One third of lectures "were performed using an active-learning" style. Eighteen frames of the active-learning and two frames of team -based learning (TBL) were provided. Although one frame of active-learning alone cannot cover the whole area of pediatrics, we believe that the active learning is very useful because it can promote students' independent study.

Project semester

This provides the opportunities of basic research for the 4th grade students for half a year. Every year, a few students are 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) for 5th-year medical students in pediatrics was shortened from 1 month (4 weeks) to 2 weeks due to the pandemic of COVID-19. Each student spent two weeks in one of the two groups (hematology, immunology, cardiology, neurology, Endocrinology-metabolism, nephrology, Rheumatology, neonatology).

Lectures were given to all students six times in two weeks selected from a lot of topics such as diagnostics, congenital heart disease, neonates, infusion, EEG, endocrinology, leukemia, immunodeficiency infections, and the role of the Child Life Specialist in pediatrics, and student conferences were held every Friday for further understanding of the clinical practice program.

During the period when ward practice was interrupted due to COVID-19, miniCEX based problem-solving lectures were performed to each assigned medical group every day using web conferencing tools to promote their self-study, and two to three lectures were given to all students per week.

Two 6th-year medical students accepted for clinical training in pediatrics, and they joined a practice for two weeks in a medical group of their choice as an advanced program.

In terms of post-graduate education, at least one month of basic clinical education was provided to the first and second year of clinical residents at on-campus. For the second semester clinical residents at the university, we provided a wide range of more specialized clinical education to prepare them to become pediatric specialists.

(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 raked 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 FY2020, we performed HCT for 10 (10 allo-HCT). For IEI (7 cases), 1 related bone marrow cell transplantation, 1 unrelated bone marrow transplantations, and 5 HLA haplo-matched transplantations were performed.

For malignancies (3 cases), 3 HLA haplo-matched transplantations were performed.

For a relapsed Ph+ALL case, CAR-T cas performed.

Our experience of HCT exceeds 230 cases including more than 100 cases with primary immunod eficiency diseases, so far.

Clinical trial

Clinical trials led by the pediatric department of Tokyo Medical and Dental University are ongoing.

" Phase 2 study of the efficacy and safety of sirolumus in patients with primary immunodeficiency '

"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 83, which consisted of 47 congenital heart disease, 14 pulmonary hypertension, 5 Kawasaki Disease, 9 arrhythmia, 2 cardiomyopathy and 6 others. Cardiac catheterizations were performed in 44 patients and cardiac surgery was performed in 15 patients (14 open-heart surgery), which consisted of 7 VSDs, 5 ASDs, 1 TOF, 1 DORV, 1 AVSD, 1 severeTR.. The number of outpatients was 1,841, echocardiogram was performed in 591, Treadmill exercise-induced electrocardiogram was perform in 84, and Holter 24hr electrocardiogram was performed in 88 patients.

• Neurology Group

We provide medical care in a wide range of pediatric nerologic 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 provide nucleic acid drug and gene therapy for patients with spinal muscular atrophy. We focus on diagnosis, genetic analysis and treatment for rare neurologic diseases.

• Endocrinology- Metabolism Group

We provide comprehensive diagnostic and treatment services for children with disorders of endocrinology and metabolism, including 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. Percutaneous needle renal biopsy under general anaesthesia is performed in patients with nephritis and nephrotic syndrome in infancy, in collaboration with anaesthetists. Last year, seven percutaneous needle renal biopsies under general anaesthesia were performed. No major complications occurred and the procedure was performed safely.

We performed peritoneal dialysis for infants and provided acute hemodialysis for children who developed acute kidney injury. Also patients with tubulointerstitial nephritis and renal disease complicated by uveitis are treated.

• Rheumatology group

We treat children with rheumatic diseases, undiagnosed cases such as fever of unknown origin, and autoinflammatory syndrome represented by periodic fever. The emphasis is on the issues and challenges of transitional care in adulthood for pediatric rheumatic diseases.

• 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 babys 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 incractable epilepsy, cerebellar ataxia, immune-mediated neurological disease, spinal muscular atrophy, involuntary movement, perinatal brain damage, infection of nervous system, acute encephalopathy/encephalitis, neurodegenerative disease.

• Endocrinology- Metabolism Group

The leader of our endocrinology group is a supervisor of congenital adrenal hyperplasia (CAH) newborn screening in Tokyo. We treat substantial number of 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 organizing a Type 1 DM patients' association (Wakamatsu-kai) and have the summer camp for diabetic children every year.

• Nephrology Group

We treat various pediatric kidney diseases, such as congenital nephrotic syndrome, refractory nephrotic syndrome, IgA nephropathy, Henoch-Scho[¨] nlein purpura nephritis and tubulointerstitial nephritis with or without uveitis, etc. Chronic kidney disease management and dialysis treatment for children with acute renal failure. Acute hemodialysis and plasma exchange therapy for acute renal failure associated with hematological disease and collagen diseases, as well as autoimmune encephalitis, are also provided. Needle kidney biopsy performed to more than 30 patients for infants and over children. We cooperate in school urinalysis to prevent exacerbations of renal disease, we

• Rheumatology group

Clinically, our target is not only pediatric rheumatic disease, but also inflammatory diseases such as periodic fever, fever of 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.

• 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 sever persistent asthma patients.

(7) Publications

[Original Articles]

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[Misc]

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- 2. Motoi Yamashita, Tomohiro Morio. Inborn errors of IKAROS and AIOLOS Curr Opin Immunol. 2021.07; 72; 239-248
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- 1. Kento Inoue, Hirokazu Kanegane. Defects in innate immunity : vulnerability to virus and bacterial infections 2021.02; (53); 777-82
- 2. Hirokazu Kanegane, Kay Tanita. Primary immunodeficiencies predisposing to Epstein-Barr virus including X-linked lymphoproliferative 2021.02; (53); 749-57

[Conference Activities & Talks]

- Hirokazu Kanegane. Updates in Primary antibody deficiencies. 16th Congress of Asian Society for Pediatric Research (ASPR 2021) 2021.12.11 Web 開催
- 2. Matsusaka Taiji, Udagawa Tomohiro, Osafune Kenji, Araoka Toshikazu. Podocyte Damage in Chimeric Kidney Organoids. American Society of Nephrology kidney week 2021 2021.11.02 San Diego, USA
- 3. Yohei Yamaguchi, Susumu Hosokawa, Satoshi Nagahara, Ayako Nagashima-Otsuki, Taku Ishii, Tomoyuki Umemoto, Shozaburo Doi. How should we manage women with Kawasaki disease with giant coronary aneurysms who want a child? case reports . The 13th International Kawasaki Disease Symposium 2021.10.29 Web
- 4. Masatoshi Takagi, Chitose Ogawa, Tomoko Iehara, Yuki Aoki-Nogami, Eri Isibashi, Minoru Imai, Toshimi Kimura, Masashi Nagata, Masato Yasuhara, Mitsuko Masutani, Kenichi Yoshimura, Daisuke Tomizawa, Atsushi Ogawa, Kan Yonemori, Tetsuro Kihara, Kiyoshi Nobori, Kazuhisa Hasebe, Shuki Mizutani, Tomohiro Morio, Hajime Hosoi, Ryuji Koike. First In Children Phase I Clinical Study Of Oral Olaparib In Pediatric Patients With Refractory Solid Tumors. SIOP2021 2021.10.24 Honolulu (Web)
- 5. Ryuichi Nakagawa, Hideya Kawaji, Yasuhiro Murakawa, Shuji Takada, Satoshi Narumi, Maki Fukami, Josephine Bowles, Andrew Sinclair, Peter Koopman, Kenichi Kashimada. Two ovarian enhancer candidates, identified by time series enhancer RNA analyses, harbored rare SNVs identified in ovarian insufficiency. First Virtual International Symposium on Vertebrate Sex Determination 2021.10.04 Web
- 6. Hirokazu Kanegane. Tips of hematopoietic cell transplantation for inborn errors of immunity. Chinese PID Summer School 2021 2021.09.25 Web 開催

- 7. Imai K.. Newly reported primary antibody deficiencies (PADs). Chinese PID Summer School 2021.09.24 Shenzhen/Web
- Yohei Yamaguchi, Susumu Hosokawa, Yusuke Kajikawa, Yasuhiro Maejima, Mitsuaki Isobe, Tetsushi Furukawa, Shozaburo Doi. Pathophysiological Role of Dexmedetomidine for Monocrotaline-induced Pulmonary Arterial Hypertension in Rats.. The 8th Congress of the Asia-Pacific Pediatric Cardiac Society - APPCS 2021 2021.07.15
- 9. Imai K.. Severe Combined Immunodeficiency (SCID). APSID Summer Webinar 2021 2021.06.16 web
- 10. Hirokazu Kanegane. Revisiting X-linked agammaglobulinemia. 12th International Congress of Immunodeficiency Diseases(ICID) 2021.04.27 Web 開催
- 1. Endeavor toward constant supply of human raw materials for industrial use in Japan. 2021.12.10
- 2. Successful TCRABCD 19-depleted hematopoietic cell transplantation for a patient with Artemis deficiency. 2021.11.25
- 3. Epstein-Barr Virus-negative granulomatous disease due to SAP deficiency; a case report. 2021.11.25
- 4. Characteristics of Li-Fraumeni Syndrome in Japan; a review study by the Japanese Society for Hereditary Tumors. 2021.11.25
- 5. Utlization and prospects of single-cell RNA sequencing -Aiming to elucidate heterogeneity of cancer cells-. 2021.11.25
- 6. A case with RAS-associated lymphoproliferative disease developing acute myeloid leukemia during follow up. 2021.11.25
- 7. First in children phase I clinical study of oral olaparib in pediatric patients with refractory solid tumors. 2021.11.25
- 8. Characteristics of Li-Fraumeni Syndrome in Japan; A Review Study by the Japanese Society for Hereditary Tumors.. 2021.10.16
- 9. Characteristics of Li-Fraumeni Syndrome in Japan; A Review Study by the Special Committee of the JSHT. 2021.10.02
- 10. Rare Diseases and Regenerative Medicine. 2021.03.12
- 11. A study of adenosine deaminase 2 deficiency by multi-omics analysis. 2021.02.07
- 12. Discriminant analysis of primary immunodeficiency using Recognizing Textual Entailment AI. 2021.02.07
- 13. Delayed recovery of chimeric status after non-myeloablative cord blood transplantation in a patient with DNA ligase IV deficiency. 2021.02.06
- 14. Diagnosis and Treatment for LOCID(Late onset combined immunodeficiency) . 2021.02.06
- 15. Inborn Errors of Immunity : Lessons learnt from outliers. 2021.01.26

[Awards & Honors]

1. 8th JSI Human Immunology Research Award Winner, 2021.12

Rheumatology

Professor	Shinsuke YASUDA
	Masaaki MORI(1)
	Koike Ryuji(2)
	Kazuki TAKADA (3)
Junior Associate Profes	sor
	Hisanori HASEGAWA
	Tadashi HOSOYA
	Naoki KIMURA(2)
	Hideyuki IWAI
Assistant Professor	Tetsuya SAITO, Natsuka UMEZAWA,
	Natsuka UMEZAWA, Mari KAMIYA,
	Hirokazu SASAKI(2),
	Youji KOMIYA, Yasuhiro TAGAWA,
	Seiji NODA
Visiting Lecturer	Kimito KAWAHATA, Hiroyuki HAGIYAMA,
	Kenji NAGASAKA, Akito TAKAMURA,
	Makoto SOEJIMA, Yusuke MATSUO,
	Kaori WATANABE, Yasuo HIRANO,
	Mari KIHARA, Toshihiro MATSUI,
	Tokishige MIYABE, Shoko KASAI
Affiliated Hospital	Fumiaki KONDO, Wakako KAWSAKI,
	Akiou YAMAMOTO, Masami TOKURA,
	Riku YOSHITUKA, Yasuo YAMAGUCHI,
	Tomoko NIWANO, Yuriko YAGYU,
	Takahiro NAKAHARA
Resident	Daisuke KAWADA, Takuji ITAKURA,
	Motohiko SATO, Takuna TSUBATA,
	Yoshinori AIZEKI
Graduate Student	Fumiaki KONDO, Nao TANAKA,
	Marina TSUCHIDA, Hiroyuki BABA
	Seiya OBA
Office Administrator	Yukako NAKAMURA, Kasumi KUBO,
	Tomoko TAKAHASHI (1)
Technical Staff	Kazuko YAMAZAKI, Naoko FUJITA

Department of Lifetime Clinical Immunology, (2) Medical Innovation Promotion Center,
Instutute 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 the rapeutics 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. Yusuke Ota, Natsune Hongou, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Evaluation of polymerase chain reaction-based open reading frame typing method for the clonality investigation of Clostridioides difficile isolates. Anaerobe. 2021.12; 72; 102462
- 2. Hiromu Tanaka, Ho Lee, Atsuho Morita, Ho Namkoong, Shotaro Chubachi, Hiroki Kabata, Hirofumi Kamata, Makoto Ishii, Naoki Hasegawa, Norihiro Harada, Tetsuya Ueda, Soichiro Ueda, Takashi Ishiguro, Ken Arimura, Fukuki Saito, Takashi Yoshiyama, Yasushi Nakano, Yoshikazu Mutoh, Yusuke Suzuki, Koji Murakami, Yukinori Okada, Ryuji Koike, Yuko Kitagawa, Katsushi Tokunaga, Akinori Kimura, Seiya Imoto, Satoru Miyano, Seishi Ogawa, Takanori Kanai, Koichi Fukunaga, The Japan COVID-19 Task Force. Clinical Characteristics of Patients with Coronavirus Disease (COVID-19): Preliminary Baseline Report of Japan COVID-19 Task Force, a Nationwide Consortium to Investigate Host Genetics of COVID-19. Int J Infect Dis. 2021.12; 113; 74-81
- 3. Noda S, Honda S, Hirota Y, Ito T, Hasegawa H, Kimura N, Matsuo Y, Iwai H, Kohsaka H, Yasuda S. Azathioprine Monotherapy for the Cases of Immunoglobulin G4-Related Disease With Contraindications to Glucocorticoids. Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases. 2021.12; 27(8S); S327-S330
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- 5. Sei Muraoka, Zento Yamada, Mai Kawazoe, Wataru Hirose, Hajime Kono, Shinsuke Yasuda, Yukiko Komano, Hiroshi Kawano, Toshihiko Hidaka, Shusaku Nakashima, Tsuyoshi Kasama, Tamio Teramoto, Toshihiro Nanki, . Abatacept is Efficacious in the Treatment of Older Patients with csDMARD-Refractory Rheumatoid Arthritis: A Prospective, Multicenter, Observational Study. Rheumatol Ther. 2021.12; 8(4); 1585-1601
- 6. Hosoya T, Saito T, Baba H, Tanaka N, Noda S, Komiya Y, Tagawa Y, Yamamoto A, Mizoguchi F, Kawahata K, Miyasaka N, Kohsaka H, Yasuda S. Chondroprotective effects of CDK4/6 inhibition via enhanced ubiquitin-dependent degradation of JUN in synovial fibroblasts. Rheumatology (Oxford, England). 2021.11;
- Hosoya T, Oda G, Nakagawa T, Onishi I, Hosoya T, Ishiguro M, Ishikawa T, Uetake H. Plasma Levels of Decorin Increased in Patients during the Progression of Breast Cancer. Journal of clinical medicine. 2021.11; 10(23);

- 8. Sugihara T, Nakaoka Y, Uchida HA, Yoshifuji H, Maejima Y, Watanabe Y, Amiya E, Tanemoto K, Miyata T, Umezawa N, Manabe Y, Ishizaki J, Shirai T, Nagafuchi H, Hasegawa H, Miyamae T, Niiro H, Ito S, Ishii T, Isobe M, Harigai M. Establishing Clinical Remission Criteria and the Framework of a Treat-To-Target Algorithm for Takayasu arteritis: Results of a Delphi Exercise Carried out by an Expert Panel of the Japan Research Committee of the Ministry of Health, Labour, and Welfare for intractable vasculitis. Modern rheumatology. 2021.11;
- Tadashi Hosoya, Tetsuya Saito, Hiroyuki Baba, Nao Tanaka, Seiji Noda, Youji Komiya, Yasuhiro Tagawa, Akio Yamamoto, Fumitaka Mizoguchi, Kimito Kawahata, Nobuyuki Miyasaka, Hitoshi Kohsaka, Shinsuke Yasuda. Chondroprotective effects of CDK4/6 inhibition via enhanced ubiquitin-dependent degradation of JUN in synovial fibroblasts. Rheumatology (Oxford). 2021.11;
- 10. Takagi M., Ogawa C., Iehara T., Aoki-Nogami Y., Isibashi E., Imai M., Kimura T., Nagata M., Yasuhara M., Masutani M., Yoshimura K., Tomizawa D., Ogawa A., Yonemori K., Kihara T., Nobori K., Hasebe K., Mizutani S., Morio T., Hosoi H., Koike R.. First in Children Phase I Clinical Study of Oral Olaparib in Pediatric Patients with Refractory Solid Tumors PEDIATRIC BLOOD & CANCER. 2021.11; 68; S85-S86
- 11. Ishiguro Nobuhisa, Ito Yoichi M., Iwasaki Sumio, Nagao Miki, Kawamura Hideki, Kanai Shinichiro, Nukui Yoko, Tokuda Koichi, Miyara Takayuki, Igari Hidetoshi, Yamada Koichi, Chikumi Hiroki, Sano Chiaki, Koike Ryuji, Yagi Tetsuya, Murakami Nobuo. Three-day regimen of oseltamivir for post-exposure prophylaxis of influenza in hospital wards: a study protocol for a prospective, multi-center, single-arm trial BMC INFECTIOUS DISEASES. 2021.08; 21(1); 887
- 12. Yuichiro Fujieda, Tetsuya Horita, Naoki Nishimoto, Kazuhide Tanimura, Yoshiharu Amasaki, Hideki Kasahara, Shin Furukawa, Tsuyoshi Takeda, Shinji Fukaya, Kazuo Matsui, Akito Tsutsumi, Akira Furusaki, Akira Sagawa, Kou Katayama, Kaoru Takeuchi, Kazuaki Katsumata, Takashi Kurita, Peter Shane, Masaru Kato, Kenji Oku, Shinsuke Yasuda, Masahiko Takahata, Norimasa Iwasaki, Tatsuya Atsumi. Efficacy and safety of sodium RISedronate for glucocorticoid-induced OsTeoporosis with rheumaTOid arthritis (RISOTTO study): A multicentre, double-blind, randomized, placebo-controlled trial. Mod Rheumatol. 2021.05; 31(3); 593-599
- 13. Mori M, Watabe S, Taguchi T, Hasegawa H, Ishige M, Tanuma N, Hirakawa A, Koike R, Kusuda S. Study protocol: a multicenter, uncontrolled, open-label study of palivizumab in neonates, infants, and preschool children at high risk of severe respiratory syncytial virus infection. BMC pediatrics. 2021.03; 21(1); 106
- 14. Noda S, Honda S, Hirota Y, Ito T, Hasegawa H, Kimura N, Matsuo Y, Iwai H, Kohsaka H, Yasuda S. Azathioprine Monotherapy for the Cases of Immunoglobulin G4-Related Disease With Contraindications to Glucocorticoids. Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases. 2021.02;
- 15. Yoshiya Tanaka, Hideto Kameda, Kazuyoshi Saito, Yuko Kaneko, Eiichi Tanaka, Shinsuke Yasuda, Naoto Tamura, Keishi Fujio, Takao Fujii, Toshihisa Kojima, Tatsuhiko Anzai, Chikuma Hamada, Yoshihisa Fujino, Shinya Matsuda, Hitoshi Kohsaka. Response to tocilizumab and work productivity in patients with rheumatoid arthritis: 2-year follow-up of FIRST ACT-SC study. Mod Rheumatol. 2021.01; 31(1); 42-52
- 16. Yoshiya Tanaka, Masataka Kuwana, Takao Fujii, Hideto Kameda, Yoshinao Muro, Keishi Fujio, Yasuhiko Itoh, Hidekata Yasuoka, Shusaku Fukaya, Konomi Ashihara, Daisuke Hirano, Koichiro Ohmura, Yuya Tabuchi, Hisanori Hasegawa, Ryo Matsumiya, Yuichiro Shirai, Takehisa Ogura, Yumi Tsuchida, Mariko Ogawa-Momohara, Hidehiko Narazaki, Yoshino Inoue, Ippei Miyagawa, Kazuhisa Nakano, Shintaro Hirata, Masaaki Mori. 2019 Diagnostic criteria for mixed connective tissue disease (MCTD): From the Japan research committee of the ministry of health, labor, and welfare for systemic autoimmune diseases. Mod Rheumatol. 2021.01; 31(1); 29-33
- 17. Sugihara T, Ishizaki T, Onoguchi W, Baba H, Matsumoto T, Iga S, Kubo K, Kamiya M, Hirano F, Hosoya T, Miyasaka N, Harigai M. Effectiveness and safety of treat-to-target strategy in elderly-onset rheumatoid arthritis: a 3-year prospective observational study. Rheumatology (Oxford, England). 2021.01;
- 18. Tanaka Yoshiya, Kuwana Masataka, Fujii Takao, Kameda Hideto, Muro Yoshinao, Fujio Keishi, Itoh Yasuhiko, Yasuoka Hidekata, Fukaya Shusaku, Ashihara Konomi, Hirano Daisuke, Ohmura Koichiro, Tabuchi Yuya, Hasegawa Hisanori, Matsumiya Ryo, Shirai Yuichiro, Ogura Takehisa, Tsuchida Yumi, Ogawa-Momohara Mariko, Narazaki Hidehiko, Inoue Yoshino, Miyagawa Ippei, Nakano Kazuhisa, Hirata

Shintaro, Mori Masaaki, the Japan research committee of the ministry of health, labor, and welfare for systemic autoimmune diseases. 2019 Diagnostic criteria for mixed connective tissue disease(MCTD): From the Japan research committee of the ministry of health, labor, and welfare for systemic autoimmune diseases(和訳中) Modern Rheumatology. 2021.01; 31(1); 29-33

- 19. Shunsuke Furuta, Daiki Nakagomi, Yoshihisa Kobayashi, Masaki Hiraguri, Takao Sugiyama, Koichi Amano, Takeshi Umibe, Hajime Kono, Kazuhiro Kurasawa, Yasuhiko Kita, Ryutaro Matsumura, Yuko Kaneko, Keita Ninagawa, Keiju Hiromura, Shin-Ichiro Kagami, Yosuke Inaba, Hideki Hanaoka, Kei Ikeda, Hiroshi Nakajima, . Effect of Reduced-Dose vs High-Dose Glucocorticoids Added to Rituximab on Remission Induction in ANCA-Associated Vasculitis: A Randomized Clinical Trial. JAMA. 2021.01; 325(21); 2178-2187
- 20. Natsuki Aokia , Taro Fujikawaa , Natsuka Umezawab , Yoshiyuki Kawashimaa , Taku Itoa , Keiji Hondaa , and Takeshi Tsutsumia. 3Tesla magnetic resonance imaging reveals vasculitis-caused otitis media in a patient with giant cell arteritis ACTA OTO-LARYNGOLOGICA CASE REPORTS. 2021; 6; 6-10
- 21. Hosoya T, Cordelia D, Michael BD, Miyabe C, Nagai J, Murooka TT, Miyabe Y. Editorial: Targeting the Chemoattractant System in Inflammation. Frontiers in pharmacology. 2021; 12; 744290
- 22. Hosoya T., Sugihara T., Miyasaka N., Yasuda S.. Novel treatment strategy of polymyalgia rheumatica targeting drug-free remission CLINICAL AND EXPERIMENTAL RHEUMATOLOGY. 2021; 39(3); 701-702
- 23. Saito T, Sako Y, Sato-Kaneko F, Hosoya T, Yao S, Lao FS, Shpigelman J, Messer K, Pu M, Shukla NM, Chan M, Chu PJ, Cottam HB, Hayashi T, Carson DA, Corr M. Small Molecule Potentiator of Adjuvant Activity Enhancing Survival to Influenza Viral Challenge. Frontiers in immunology. 2021; 12; 701445
- 24. Oba S, Hosoya T, Amamiya M, Mitsumura T, Kawata D, Sasaki H, Kamiya M, Yamamoto A, Ando T, Shimada S, Shirai T, Okamoto T, Tateishi T, Endo A, Aiboshi J, Nosaka N, Yamanouchi H, Ugawa T, Nagaoka E, Oi K, Tao S, Maejima Y, Tanaka Y, Tanimoto K, Takeuchi H, Tohda S, Hirakawa A, Sasano T, Arai H, Otomo Y, Miyazaki Y, Yasuda S. Arterial and Venous Thrombosis Complicated in COVID-19: A Retrospective Single Center Analysis in Japan. Frontiers in cardiovascular medicine. 2021; 8; 767074

[Conference Activities & Talks]

- Masatoshi Takagi, Chitose Ogawa, Tomoko Iehara, Yuki Aoki-Nogami, Eri Isibashi, Minoru Imai, Toshimi Kimura, Masashi Nagata, Masato Yasuhara, Mitsuko Masutani, Kenichi Yoshimura, Daisuke Tomizawa, Atsushi Ogawa, Kan Yonemori, Tetsuro Kihara, Kiyoshi Nobori, Kazuhisa Hasebe, Shuki Mizutani, Tomohiro Morio, Hajime Hosoi, Ryuji Koike. First In Children Phase I Clinical Study Of Oral Olaparib In Pediatric Patients With Refractory Solid Tumors. SIOP2021 2021.10.24 Honolulu (Web)
- 2. Seiji Noda, Yoji Komiya, Yasuhiro Tagawa, Shinsuke Yasuda, Yasuhiro Takahara, Kazutaka Sugimoto, Fumitaka Mizoguchi. . CD34+ synovial fibroblast subset has high osteogenic and chondrogenic potentials in vitro. . The 65th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology. 2021.04
- 3. Mari Kamiya, Shinsuke Yasuda. Targeting necroptosis in muscle fibers ameliorates experimental inflammatory myopathies. The 50 th Annual Meeting of the Japanese Society for Immunology 2021.12.09 Nara, Japan
- 4. Mari Kamiya, Fumitaka Mizoguchi, Hirokazu Sasaki, Natsuka Umezawa, and Shinsuke Yasuda. Glucagon-like Peptide-1 Receptor Agonist Suppresses Muscle Fiber Necroptosis and Muscle Inflammation and Ameliorates Muscle Weakness in Experimental Polymyositis. ACR Convergence 2021 2021.11.07
- 5. Mari Kamiya, Shinsuke Yasuda, Fumitaka Mizoguchi. HMGB1 is highly expressed in injured muscle fibers and accelerates inflammation and muscle injury in inflammatory myopathies. 65th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2021.04.27

Dermatology

Professor: Hiroo YOKOZEKI Associate Professor: Takeshi NAMIKI Junior Associate Professor: Tsukasa UGAJIN, Takichi MUNETSUGU Project Associate Professor: Kaoru TAKAYAMA Project Junior Associate Professor: Makiko NISHIDA Assistant Professor: Shown TOKORO, Kohei KATO, Tadatsune IIDA Senior Resident: Masahiro KATAGIRI, Rina Otake, Shogo WADA Resident: Masato FUNAZUMI, Misaki KITAHARA Doctoral Student: Minako INAZAWA, Aiko FURUI, Michiko NAKAMURA, Kohei NOJIMA, Kohei KATO, Sally ESHIBA, 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 mochanisms' 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 theories (STAT6 decoy ODN) for

severe atopic dermatitis in the clinic.

(4) **Publications**

[Original Articles]

- Iida T, Nakamura M, Inazawa M, Munetsugu T, Nishida M, Fujimoto T, Sasaki Y, Ohshima Y, Nakazato Y, Namiki T, Yokozeki H. Prognosis after steroid pulse therapy and seasonal effect in acquired idiopathic generalized anhidrosis. The Journal of Dermatology. 2021.03; 48(3); 271-278
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NCCHD Child Health and Development

Collaborative Professor	Akutsu, Hidenori
Collaborative Professor	Onodera, Masashi
Collaborative Professor	Fukami, Maki
Collaborative Professor	Hata, Kenichiro
Collaborative Professor	Takada, Shuji
Collaborative Professor	Matsumoto, Kenji

(1) Research

1) Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells Application studies for reproductive medicine and regenerative medicine

(Akutsu, Hidenori; Center for Regenerative Medicine, National Institute for Child Health and Development)

Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells. Application studies for reproductive medicine and regenerative medicine.

2) Studying for cellular model in human severe disease by advancing flow cytometry (Onodera, Masashi; Dept. of Human Genetics, National Institute for Child Health and Development)

We aim to identify causative genes for child intractable hereditary diseases and analyze their functions to develop new gene-based therapeutic options. We also establish iPS cells from peripheral blood or skin fibroblasts obtained from patients with intractable hereditary diseases such as primary immunodeficiencies and congenital metabolic disorders.

3) Elucidation of genetic abnormality in congenital severe metabolic diseases using advanced genetic analysis

(Fukami, Maki; Dept. of Molecular Endocrinology, National Institute for Child Health and Development)

Our objective is to clarify the molecular basis of congenital endocrine-related disorders and apply our findings to new innovations in clinical medicine. We investigate the molecular basis of single gene disorders, epigenetic/inprinting disorders, and multifanctorial 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 underlysing 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, allogenic 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.

(2) Education

The goal of this course is to learn the developmental process of human life from the viewpoints of latest molecular biology and genetics. Medical science for child health and

development is the study to comprehensively grasp various health problems related to "human life cycle" to begin with the fertilization and to continue to the next generation through generation and development. Students of this course are required to understand a role and a function of medical care for child health and development, to acquire ability to handle such health problems and support relevant person with specialized theory and technique.

(3) Publications

[Original Articles]

- Sasaki K, Inoue M, Machida M, Kawasaki T, Tsuruta S, Uchida H, Sakamoto S, Kasahara M, Umezawa A, Akutsu H*. Human Pluripotent Stem Cell-Derived Organoids as a Model of Intestinal Xenobiotic Metabolism. Stemjournal. 2021; 3(1): 1-10.
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Kimura AP: A testis-specific long noncoding RNA, Start, is a regulator of steroidogenesis in mouse Leydig cells. Frontiers in Endocrinology (Lausanne), 12:665874 (2021).

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[Review Articles]

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- 4. Fukami M, Ogata T. Congenital disorders of estrogen biosynthesis and action. Best Pract Res Clin Endocrinol Metab. 36(1):101580, 2021
- 5. Akiba K, Katoh-Fukui Y, Yoshida K, Narumi S, Miyado M, Hasegawa Y, Fukami M. Role of liquid-liquid separation in endocrine and living cells. J Endocr Soc. 5(10):bvab126, 2021.

Human Pathology

Professor: Kenichi OHASHI Assistant Professor: Daisuke KOBAYASHI,Takashi ITO,Kurara YAMAMOTO Technician: Asuka FURUKAWA Graduate Students: (Doctoral Program) Yuki KATO, Kazuhiro TAMURA, Chiina HATA (Master's Program) Momoka SAKAI, Minami MIYAUCHI Secretary: Miho IWAMITSU

(1) Outline

Pathology is the studies in which one theorizes and understands disease, as the language implies disease (pathos hardship) + theory (logus logic). Later, as research subjects that caused diseases were subdivided and research methods advanced, bacteriology (microbiology), parasitology (medical zoology), immunology, and molecular biology became independent from the category of pathology. In recent years, academic fields have been restructured beyond the framework of conventional academic fields, and there is a tendency for them to be further subdivided according to purposes, research subjects, and research methods. At present, pathology, based on morphology, is the study of understanding and organizing the causes of diseases (etiology), the formation of lesions (histogenesis), and disease status (pathogenesis). In the recent pathology, the fields of experimental pathology, in which hypotheses are experimentally proven using laboratory animals and cultured cells, and the fields of surgical pathology and diagnostic pathology, which are closely related to the clinical medicine, tend to be separated, and the number of pathologists engaged in the latter, which deals with human tissues, is increasing.

In the field of Human Pathology of TMDU, we aim to train pathologists who can accurately make pathological diagnosis of various human diseases, and at the same time, to develop pathologists who have a research mind capable of carrying out research that leads to improvement of pathological diagnosis, with the aim of elucidating the etiology, histogenesis and mechanism of human diseases.

(2) Research

About human cancer:

There are three main purposes.

(1) Carcinogenesis and histogenesis of cancers: For the understanging of G-I tract cancers, such as esophageal cancers, gastric cancers, colorectal cancers, and colitic cancers, and lung cancers, premalignant lesions will be clarified by histopathological analyses, clinicopathological analyses, and genetic analyses, and the process and molecular basis of carcinogenesis from premalignant lesions will be clarified.

(2) Objective diagnosis of pathological diagnosis related to cancer: Cancer originating from any organ is difficult to differentiate from benign tumors originating from that organ, and there are also borderline tumors of benign and malignant tumors. In addition, many of the pathological findings with clinical significance are based on subjective judgment, and the objectivity, reproducibility, and agreement rate among observers of the findings are problematic. In pathological diagnosis, it is important to apply computer, Ai, and image analysis technology, and establishment of new pathological diagnosis which integrates genome information and various marker expression information of which the advance is remarkable recently is required.

(3) Malignant tumor progression and mechanism of metastasis: In human esophageal cancer, gastric cancer, colorectal cancer, and lung cancer, early cancer is often found, and reduced operations and treatments such as endoscopic resection are often performed. However, there are some high-grade cases showing metastasis from the early stage, and it is necessary to diagnose them in the early stage and select an appropriate therapy. In the process of invasion of early cancers, it is important to clarify the pathological findings related to metastasis and recurrence and to clarify the molecular basis closely related to them. By establishing markers that can be applied to pathological diagnosis, more accurate pathological diagnosis will become possible. About chronic inflammatory diseases:

To clarify the etiology and origin of a chronic inflammatory disease of unknown origin by thoroughly analyzing the lesion site from a pathological standpoint. In addition, markers useful for diagnosis will be developed and applied to actual pathological diagnosis.

1) The possibility that intracellular latent infection in the deep organ of Propionibacterium acnes and rapid activation of autophagy and induction of Th1 immune response with the endogenous activation are causes of granuloma formation is studied on the sarcoidosis from the immunopathology viewpoint. Acne infection has been reported to be associated with diseases other than sarcoidosis, and its relationship to other diseases is also being studied.

2) Regarding the pathogenetic mechanism of chronic gastritis caused by infection of Helicobacter pylori on the surface of gastric mucosa, we found that Helicobacter pylori invades the lamina propria and translocates to regional lymph nodes of the stomach due to injury of the surface epithelium of the mucosa. Therefore, we investigated the possibility that Helicobacter pylori contributes to chronic inflammation of the gastric mucosa by directly stimulating immunocompetent cells in the mucosa and chronically stimulates the immune system in the paracortical region after influx to the lymph nodes. It is also known that the risk of developing gastric cancer varies depending on the structure of Helicobacter pylori. We are also developing test kits that can clarify the relationship between the structure of H. pylori and the risk of carcinogenesis and evaluate the risk of carcinogenesis by H. pylori.

3) Characteristic pathological findings observed in inflammatory colitis such as ulcerative colitis and Crohn's disease are analyzed, and their occurrence mechanism and significance are verified. In addition, evaluation of the activity of inflammation using biopsy materials and expression of molecular markers are studied.

4) Diagnosis of the type of systemic amyloidosis is very important for deciding the treatment plan of patients, but useful antibodies for diagnosis are not sufficiently available. Research is being conducted on the development and application of diagnostic antibodies that can improve the accuracy of pathological diagnosis.

(3) Education

In the graduate school doctoral program, the acquisition of the pathology medical specialist qualification is also made to be a goal with the doctor degree acquisition. First of all, training in autopsy, biopsy tissue diagnosis, rapid tissue diagnosis, tissue diagnosis of surgical specimens, etc., will be conducted, and training in the department of Diagnostic Pathology, TMDU hospital, as well as in the department of pathological diagnosis of the related hospitals will be conducted, with the aim of forming the basis for a "pathologist". During the training, participants will participate in various conferences or meetings in joint with clinical departments to announce pathological diagnoses, identify current problems in each clinical field, and discuss or collaborate with clinicians. While forming a basis as a pathologist, we will conduct research using clinicopathological, immunohistologic, and molecular pathological methods on issues directly related to the causes, diagnosis, and treatment of human diseases. The results will be published in academic meetings and academic journals in Japan and overseas.

(4) Lectures & Courses

What society calls for in medical care is proper diagnosis and treatment. Therefore, in the field of Human Pathology, the aim is to study the etiology, histogenesis, diagnosis, and treatment of human diseases with a strong awareness of problems and deep thought, while focusing on the study of clinical pathology, including histopathological diagnosis of autopsy, biopsy and surgically resected specimens. The results of the research

should not only deepen the understanding of diseases, but also be useful for medical care and pathological diagnosis.

(5) Clinical Services & Other Works

As a general rule, all graduate students with a medical doctor's license are concurrently engaged in the Diagnostic Pathology department, TMDU hospital, where they are trained in pathological diagnosis and autopsy, with the aim of acquiring a qualification as a pathology specialist. In addition, staff and graduate students are working as part-time physicians at affiliated hospitals of TMDU in Tokyo, Kanagawa, Saitama, Chiba, and Ibaraki prefectures, which play a central role in supporting local medical care, to support pathological diagnosis and conduct joint research. In the field of Human Pathology, we hope to contribute to community medicine and society by improving the accuracy of pathological diagnosis. We are also actively cooperating in various academic activities, such as lecture presentations and conference participation in local hospitals. We also actively participate in and cooperate with the activities of various academic societies, including the Japanese Society of Pathology. In particular, we are involved in the management of the Japanese Society of Pathology and play a core role. Staff members also participate in and cooperate with various committees of ministries and agencies, including the Ministry of Health, Labour and Welfare.

(6) 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 the apeutic 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.

(7) Publications

[Original Articles]

- 1. Suzuki T, Katsuki N, Tsutsumi R, Uchida K, Ohashi K, Eishi Y, Kinoshita S. Reconsidering the pathogenesis of chalazion. The ocular surface. 2021.12; 24; 31-33
- 2. Sawamura M, Sawa N, Yamanouchi M, Ikuma D, Sekine A, Mizuno H, Kawada M, Hiramatsu R, Hayami N, Hasegawa E, Suwabe T, Hoshino J, Kono K, Kinowaki K, Ohashi K, Yamaguchi Y, Ubara Y. Use of biologic agents and methotrexate improves renal manifestation and outcome in patients with rheumatoid arthritis: a retrospective analysis. Clinical and experimental nephrology. 2021.11;
- 3. Chiba Keitaro, Sugawara Takashi, Kobayashi Daisuke, Sato Akihito, Murota Yasuhiro, Maehara Taketoshi. Atypical Histological Features as Risk Factors for Recurrence in Newly Diagnosed WHO Grade I Meningioma Neurologia medico-chirurgica. 2021.11; 61(11); 647-651
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- 6. Hatano M, Kitajima I, Nakamura M, Isawa K, Suwabe T, Hoshino J, Kinowaki K, Ohashi K, Sawa N, Yamamoto S, Ubara Y. Long-Term Use of Glucocorticoid Exacerbates Bone Lesions in Postmenopausal Women With Rheumatoid Arthritis. Modern rheumatology case reports. 2021.09;
- 7. Isshiki T, Homma S, Eishi Y, Yabe M, Koyama K, Nishioka Y, Yamaguchi T, Uchida K, Yamamoto K, Ohashi K, Arakawa A, Shibuya K, Sakamoto S, Kishi K. Immunohistochemical Detection of Propionibacterium acnes in Granulomas for Differentiating Sarcoidosis from Other Granulomatous Diseases Utilizing an Automated System with a Commercially Available PAB Antibody. Microorganisms. 2021.08; 9(8);
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- 9. Yudai Kawamura, Kenro Kawada, Takashi Ito, Katsumasa Saito, Naoto Fujiwara, Takuya Okada, Akihiro Hoshino, Yutaka Tokairin, Yasuaki Nakajima, Tatsuyuki Kawano, Masanori Tokunaga, Yusuke Kinugasa. Histological changes in the human esophagus following triamcinolone injection to prevent esophageal stricture after endoscopic submucosal dissection. Esophagus. 2021.07; 18(3); 594-603
- 10. Watanabe S, Sawa N, Mizuno H, Yamanouchi M, Suwabe T, Hoshino J, Kinowaki K, Ohashi K, Fujii T, Yamaguchi Y, Ubara Y. Development of osmotic vacuolization of proximal tubular epithelial cells following treatment with sodium-glucose transport protein 2 inhibitors in type II diabetes mellitus patients-3 case reports. CEN case reports. 2021.05; 10(4); 563-569
- Koga-Kobori Sayako, Sawa Naoki, Kido Ryo, Sekine Akinari, Mizuno Hiroki, Yamanouchi Masayuki, Hayami Noriko, Suwabe Tatsuya, Hoshino Junichi, Kinowaki Keiichi, Ohashi Kenichi, Fujii Takeshi, Ubara Yoshifumi. Fabry Disease on Peritoneal Dialysis with Cardiac Involvement Internal Medicine. 2021.05; 60(10); 1561-1565
- 12. Sawamura Masato, Sawa Naoki, Yamanouchi Masayuki, Ikuma Daisuke, Sekine Akinari, Mizuno Hiroki, Suwabe Tatsuya, Hoshino Junichi, Kono Kei, Kinowaki Keiichi, Ohashi Kenichi, Nagashima Yoji, Ubara Yoshifumi. Renal epithelial and stromal tumor with a multiple cystic lesion localized in the upper portion of the right kidney CEN Case Reports. 2021.05; 10(2); 230-235
- 13. Sato Keisuke, Matsumura Mai, Anzai Yoko, Arai Hiromasa, Sekiya Motoki, Sugiyama Misaki, Kataoka Toshiaki, Koike Chihiro, Ohashi Kenichi, Okudela Koji. A lung tumor with features of salivary duct carcinoma Pathology International. 2021.04; 71(4); 284-286
- 14. Terakawa Kanako, Sawa Naoki, Mizuno Hiroki, Sekine Akinari, Hayami Noriko, Ikuma Daisuke, Kawada Masahiro, Hiramatsu Rikako, Sumida Keiichi, Yamanouchi Masayuki, Hasegawa Eiko, Suwabe Tatsuya, Hoshino Junichi, Kinowaki Keiichi, Ohashi Kenichi, Fujii Takeshi, Ubara Yoshifumi. Renal Squamous Cell Carcinoma-related Polymyositis in a Patient with Autosomal Dominant Polycystic Kidney Disease Internal Medicine. 2021.04; 60(8); 1237-1242
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- 17. Oba Y, Sawa N, Mizuno H, Hoshino J, Kinowaki K, Ohashi K, Morisada N, Iijima K, Yamaguchi Y, Ubara Y. Autosomal Dominant Tubulointerstitial Kidney Disease HNF1B With Maturity-Onset Diabetes of the Young: A Case Report With Kidney Biopsy. Kidney medicine. 2021.03; 3(2); 278-281
- Yamaguchi T, Costabel U, McDowell A, Guzman J, Uchida K, Ohashi K, Eishi Y. Immunohistochemical Detection of Potential Microbial Antigens in Granulomas in the Diagnosis of Sarcoidosis. Journal of clinical medicine. 2021.03; 10(5);

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[Conference Activities & Talks]

- 1. Uehara Sho, Matsuoka YoH, Yamamoto Kurara, Toide Masahiro, Uchida Masahiro, Fukuda Shohei, Fukushima Hiroshi, Yasuda Yousuke, Tanaka Hajime, Yoshida Soichiro, Yokoyama Minato, Ohashi Kenichi, Fujii Yasuhisa. Usefulness of MRI-targeted biopsy in detecting cribriform carcinoma and intraductal carcinoma of the prostate. The Japanese Urological Association 2021.12.01
- 2. Watanabe Shun, Sawa Naoki, Mizuno Hiroki, Yamanouchi Masayuki, Suwabe Tatsuya, Hoshino Junichi, Kinowaki Keiichi, Ohashi Kenichi, Fujii Takeshi, Yamaguchi Yutaka, Ubara Yoshifumi. Development of osmotic vacuolization of proximal tubular epithelial cells following treatment with sodium-glucose transport protein 2 inhibitors in type II diabetes mellitus patients-3 case reports. CEN Case Reports 2021.11.01
- 3. Koga-Kobori Sayako, Sawa Naoki, Kido Ryo, Sekine Akinari, Mizuno Hiroki, Yamanouchi Masayuki, Hayami Noriko, Suwabe Tatsuya, Hoshino Junichi, Kinowaki Keiichi, Ohashi Kenichi, Fujii Takeshi, Ubara Yoshifumi. Fabry Disease on Peritoneal Dialysis with Cardiac Involvement. Internal Medicine 2021.05.01
- 4. Terakawa Kanako, Sawa Naoki, Mizuno Hiroki, Sekine Akinari, Hayami Noriko, Ikuma Daisuke, Kawada Masahiro, Hiramatsu Rikako, Sumida Keiichi, Yamanouchi Masayuki, Hasegawa Eiko, Suwabe Tatsuya, Hoshino Junichi, Kinowaki Keiichi, Ohashi Kenichi, Fujii Takeshi, Ubara Yoshifumi. Renal Squamous Cell Carcinoma-related Polymyositis in a Patient with Autosomal Dominant Polycystic Kidney Disease. Internal Medicine 2021.04.01

Physiology and Cell Biology

Professor: Yoshikazu Isomura Associate professor: Riichiro Hira Assistant professor: Alain Rios Assistant professor: Masanori Kawabata

(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, Two-photon imaging of neural activity, 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-linc 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.

5. Two-photon imaging of neural activity

We are constructing a two-photon microscope with the world's largest field-of-view. Using this microscope, we will record more than 100,000 neuronal activities from the brain during task execution and clarify the mechanism by which neurons cooperatively express brain functions.

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) Lectures & Courses

We respect each one's independence and positive attitude, and foster a sense of social cooperation and responsibility.

(5) **Publications**

[Original Articles]

- CH Yu, JN Stirman, Y Yu, R Hira, SL Smith. Diesel2p mesoscope with dual independent scan engines for flexible capture of dynamics in distributed neural circuitry Nature Communications. 2021.11; 12(1); 6639
- 2. Motoki Kajiwara, Ritsuki Nomura, Felix Goetze, Masanori Kawabata, Yoshikazu Isomura, Tatsuya Akutsu, Masanori Shimono. Inhibitory neurons exhibit high controlling ability in the cortical microconnectome. PLoS Comput Biol. 2021.04; 17(4); e1008846
- 3. Shun Hamada, Masashi Nagase, Tomohiko Yoshizawa, Akari Hagiwara, Yoshikazu Isomura, Ayako M Watabe, Toshihisa Ohtsuka. An engineered channelrhodopsin optimized for axon terminal activation and circuit mapping. Commun Biol. 2021.04; 4(1); 461

[Conference Activities & Talks]

- 1. Mitani K, Kawabata M, Isomura Y, Sakai Y. Automatic and parallel spike collision test for efficient identification of interareal spike signals. The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo) 2021.07.31
- 2. Hamada S, Nagase M, Yoshizawa T, Hagiwara A, Isomura Y, Watabe AM, Ohtsuka T. An engineered channelrhodopsin optimized for axon terminal activation and circuit mapping. The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo) 2021.07.31
- 3. Riichiro Hira, Shinichiro Tsutsumi. Holism in neuroscience: Large-scale recording and simulation. the 44th Annual Meeting of the Japan Neuroscience Society/the 1st CJK International Meeting 2021.07.30 Kobe
- 4. Riichiro Hira, Spencer L Smith. Large-scale imaging reveals concordance between mesoscale functional and anatomical input correlations. the 44th Annual Meeting of the Japan Neuroscience Society/the 1st CJK International Meeting 2021.07.30 Kobe
- 5. Nonomura S, Rios A, Kato S, Sakai Y, Nambu A, Takada M, Kobayashi K, Isomura Y, Kimura M. Predictive coding for action selection by indirect pathway neurons in the rat dorsolateral striatum. The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo) 2021.07.29
- 6. Kawabata M, Rios AA, Sakairi T, Sakai Y, Isomura Y. Mapping of sensory/motor related neuronal activities in the rodent cerebral cortices by using Phase-Scaling analysis. Neuroscience 2021, The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo) 2021.07.29 Kobe
- 7. Ikezoe K, Hidaka N, Manita S, Murakami M, Tsutsumi S, Isomura Y, Kano M, Kitamura K. Encoding model analysis of complex spikes of Purkinje cells in mice cerebellum during a voluntary lever-pull task. The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo) 2021.07.28
- 8. Sugisaki E, Fukushima Y, Isomura Y, Aihara T. Acetylcholine effects on spike timing-dependent plasticity in functionally differentiated CA3 pyramidal neurons. The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo) 2021.07.28
- 1. Yoshikazu Isomura. The cortico-basal ganglia circuit for behavioral expression. 2021.06.26
- 2. Large-scale imaging. 2021.03.20

[Social Contribution]

- 1. Plenary lecture: Discovering, reinforcing and refining actions (by Prof. Rui Costa), The Japan Neuroscience Society, The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo), 2021.07.28
- 2. Luncheon seminar:Paradigm Shift of Animal Behavioral Training for Neuroscience, The Japan Neuroscience Society, The 44th Annual Meeting of the Japan Neuroscience Society (Virtual: Kobe International Conference Center, Kobe, Hyogo), 2021.07.29

Molecular Cellular Cardiology

Professor	Tetsushi Furukawa
Associate professor	Jun Takeuchi
Assistant professor	Kensuke Ihara
Post-doc (PD)	Yoshitake Higashijima
Post-doc	Masahiro Yamazoe
Post-doc	Hiroko Kushige
D3	Xiaoki Yang
D3(Department of Pediatrics)	Yohei Yamaguchi
D2(Department of Dental Anesthetics)	Keiko Abe
D1	Sun Yihan
D1	Nodoka Yanagi
M1	Sae Kakeno
M1	Hiroaki Komuro
Technician	Reiko Kimura
Secretary	Yukiko Takakura
Secretary	Akemi Oshikiri

(1) Outline

This laboratory focuses on understanding pathogenesis of intractable and common cardiovascular diseases using multidisciplinary approach (patch-clamp, cell biology, optical recording, genetic analysis, and computational analysis). Our ultimate goal is to improve diagnosis and management of intractable and common cardiovascular diseases.

(2) Research

1. Highlight: Electrophysiological Assessment of Murine heart with High-Resolution Optical Mapping

Conventional optical mapping of murine heart, especially of its atria, has some critical problems due to its small size. To overcome them, we developed the novel electrophysiological assessment method for elucidating the underlying mechanism of arrhythmogenesis using murine heart by combining high spatial and temporal resolution optical mapping system and precise electrophysiological study (J. Vis. Exp 2018). This novel method will contribute to assessing the onset and maintenance mechanism of arrhythmias precisely in various mouse models.

2. Biological pacemaker utilizing in vivo genome editing

In the current clinical medicine, the only therapy for bradycardia is the electrical pacemaker, which has many serious problems such as battery longevity, device infection. As an alternative, biological pacemaker has been studied for decades. Previous attempts to make biological pacemaker by gene delivery had a limitation that the effect was transient. Application of genome editing by CRISPR/Cas9 is expected to generate permanent gene knockout. We found that in vivo genome editing can generate pacemaker activity, and are now optimizing this technique for better efficacy.

3. Systemic inflammation accompanied with atrial fibrillation

Various inflammatory markers and mediators such as c-reactive protein (CRP) and pro-inflammatory cytokines have been reported to be linked with the presence and outcome of atrial fibrillation (AF). These systemic inflammatory responses could cause and worsen not only AF related systemic dysfunctions including coagulation activity and endothelial dysfunctions, but also AF pathogenesis through atrial electrical and structural remodeling. However, the underling mechanism why AF is accompanied with systemic inflammation remains to be elucidated.

We focused the nucleic acid circulating in blood as potential contributor for systemic inflammation accompanied with AF. First, we found that AF patients had higher nucleic acid levels in plasma compared with non-AF subjects. We also confirmed this finding in AF mimicking models; rapid tachycardia stimulation for cultured atrial cardiomyocytes, and murine right atrium. Second, we observed that nucleic acid promoted IL-1 β and IL-6 expression in macrophages and clarified its signal pathway. Additionally, we identified the essential characters of nucleic acids in inducing pro-inflammatory cytokines in macrophages. Taken together, we revealed the potential contributor for systemic inflammation accompanied with AF, suggesting the circulating nucleic acid might be the novel biomarker for AF occurrence and development.

4. Understanding the mechanisms of heart induction and its compartment

The mammalian heart has systematic four-chamber structures including the left-right/atria-ventricular with functional differences. These complicated morphologies in mammals create difficult questions in addressing the mechanisms of human heart diseases. To answer these questions, many scientists initially generated knockout mice, before establishing the methods for in vitro CM induction from embryonic stem cells (ESCs) or induced pluripotency stem cells (iPSCs). However, the general methods for cardiac cell induction are insufficient to completely produce the chamber-like heart structures with regional identities like the embryonic heart. Furthermore, no information has been reported about the differences of the heart structures, physiological functions and transcriptional regulations between in human and in mice. To address these questions, we performed two projects; 1. the cardiac induction and 2. the heart chamber formation.

5. Epigenetic transcription regulation of inflammation-related genes in vascular endothelial cells The spatial organization of the genome is functionally linked to gene expression programs. Pro-inflammatory stimuli elicit rapid transcriptional responses via transduced signals to master transcription factors, but it is largely unknown how the genome and epigenome spatially control gene expression during early inflammation. Here, we performed Hi-C in combination with chromatin interaction analysis by paired-end tag sequencing (ChIA-PET) using anti-active RNA polymerase II antibody and found that inflammatory gene expression in human endothelial cells (ECs) is controlled by newly formed chromatin interactions between tumor necrosis factor alpha (TNF- α)-induced super-enhancers (SEs). Importantly, these SE-SE loops (approximately 200 to 500 kb length) are formed within 1 hour after TNF- α -treatment although megabase-size toplogically associating domains (long interactions) are unchanged. We also found that lysine demthylase 7A (KDM7A) and 6A (UTX) are rapidly mobilized to TNF- α -induced SEs where nuclear factor kappa-B are highly occupied, and demethylate their H3K9me2 and H3K27me3 marks, respectively, and are responsible for rapid formation of SE-SE loops. Collectively, these findings suggest that erasing of repressive histone marks by KDM7A and UTX within NF κ B-related elements might functionally associate with formation of SE-SE loops and could be a cue signal during inflammatory responses in human endothelial cells.

(3) Education

School of Medicine
2nd grade Introduction to Neurophysiology (2 units)
2nd grade Physiology (6 units)
3rd grade Cardiology (1 unit)
4th grade Project semester
School of Dentistry
3rd grade Pharmacology III(2 units)
3rd grade Practice for Pathophysiological Sciences (2 units)
School of Health Care Medicine
3rd/4th grade Cardiac physiology (8 units)

(4) Publications

[Original Articles]

 Yamazoe M, Sasano T, Ihara K, Takahashi K, Nakamura W, Takahashi N, Komuro H, Hamada S, Furukawa T. Sparsely methylated mitochondrial cell free DNA released from cardiomyocytes contributes to systemic inflammatory response accompanied by atrial fibrillation. Scientific reports. 2021.03; 11(1); 5837

- Yohei Yamaguchi, Susumu Hosokawa, Yusuke Kajikawa, Yasuhiro Maejima, Mitsuaki Isobe, Tetsushi Furukawa, Shozaburo Doi. Pathophysiological Role of Dexmedetomidine for Monocrotaline-induced Pulmonary Arterial Hypertension in Rats.. The 8th Congress of the Asia-Pacific Pediatric Cardiac Society - APPCS 2021 2021.07.15
- 2. Furukawa T, Okata S, Yuasa S, Suzuki T, Makita N, Kurokawa J, Egashira T, Yamakawa H, Seki T, Aizawa T, Hashimoto H, Kuroda Y, Tanaka A, Yae K, Murata M, Aiba T, Shimizu W, Horie M, Kodama I, Ogawa S, Fukuda K. Disease modeling using iPS cells. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
- 3. Sato Y, Satoh A, Nitta J, Honda Y, Kuroda S, Sekigawa M, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Impact of SNP on IL6R (rs7514452) for age at onset of atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
- 4. Sekigawa M, Satoh A, Nitta J, Sato Y, Honda Y, Kuroda S, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Effect of SNP on 9q22 (rs6479562) on the progression from paroxysmal atrial fibrillation to persistent atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

Stem Cell Regulation

Professor Tetsuya TAGA Junior Associate Professor Kouichi TABU Assistant Professor Yoshitaka MUROTA Administrative Assistant Maya MAKINO Technical Assistant Taketo MATSUMARU

(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) Development of bio-functional polymers and their applications for cancer stem cell regulation

(3) Education

Our education has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. The projects have been performed, for instance by elucidation of stem cell characteristics, analysis of transcriptional regulatory signaling pathways, and identification of niche signals.

(4) Lectures & Courses

Under our education program, students will learn the molecular basis of stem cell regulation in view of cell-extrinsic signals and cell intrinsic-programs during tissue development, maintenance, and regeneration from molecular to whole-body levels. Students will receive exposure to cutting edge concepts and research technologies, and study regulatory mechanisms in neural, hematopoietic, and cancer stem cells. With emphasis also on physiological and pathological conditions surrounding the stem cells, we aims to improve student's understanding of stem cells from multiple viewpoints.

(5) **Publications**

[Original Articles]

1. Suzuki I, Yoshida S, Tabu K, Kusunoki S, Matsumura Y, Izumi H, Asanoma K, Yagi H, Onoyama I, Sonoda K, Kohno K, Taga T, Takeda S, Kato K. YBX2 and cancer testis antigen 45 contribute to stemness, chemoresistance and a high degree of malignancy in human endometrial cancer Scientific Reports. 2021.02; 11(1); 4220

- 1. Kouichi Tabu and Tetsuya Taga. Cancer stem cell niche-mimicking polymer-based exploration of the factors responsible for glioma recurrence. The 80th Annual Meeting of the Japanese Cancer Association 2021.10.01
- 2. Gerel Melig, Ikuo Nobuhisa, Kiyoka Saito, Ryota Tsukahara, Ayumi Itabashi, Yoshiakira Kanai, Masami Kanai, Tetsuya Taga. Involvement of Rasip1 in the maintenance of hematopoietic ability of intra-aortic hematopoietic cell clusters in midgestation mouse embryos. The 42nd Annual Meeting of the Japanese Society of Inflammation and Regeneration 2021.07.07
- 3. Kouichi Tabu, Tetsuya Taga. Polymer-based elucidation of molecular basis underlying cancer stem cell-mediated niche reconstruction and glioma recurrence. The 18th Stem Cell Research Symposium 2021.05.21
- 4. Mariko Nagane, Kouichi Tabu, Yoshitaka Murota, Shinji Tanaka, Tetsuya Taga. Niche-mimicking polymer-based characterization of human pancreatic cancer stem cells (pCSCs). The 18th Stem Cell Research Symposium 2021.05.21

Respiratory Medicine

Professor: Yasunari Miyazaki Junior Associate Professor: Tomoya Tateishi Assistant Professor: Furusawa Haruhiko, Tuyoshi Shirai, Takayuki Honda, Sho Shibata, Masahiro Ishizuka (Research leave) Project Assistant Professor: Takahiro Mitsumura, Rie Sakakibara, Yuki Iijima, Sho Shimada, Takashi Yamana Clinical Fellow: Satoshi Endo, Soichi Maruyama, Takashi Kumagai, Shota Kitagawa, Yasutaka Hata Resident: Kazuaki Sato Ph.D. student; Shinji Katayanagi, Masaru Ejima, Takafumi Suzuki, Yuri Tasaka, Hidetaka Majima, Rei Sagawa, Seiko Takazawa, Hikaru Aoki, Shohei Yamashita, Takahiro Ando, Shun Endo, Jun Sugihara, Akifumi Mochizuki, Takashi Shimamura, Masaru Ito Professor, Department of Respiratory and Nervous System Science: Yuki Sumi Professor, Health Administration Center: Ryushi Tazawa Assistant Professor, Health Administration Center: Keiko Komatsuzaki Associate Professor, Department of Respiratory Physiology and Sleep Medicine: Meiyo Tamaoka Associate Professor, Department of Pulmonary Immunotherapeutics: Tsukasa Okamoto Specially-appointed Professor: Yasuhiro Setoguchi

(1) **Outline**

The lungs are in contact with the outside environment for breathing and are susceptible to external factors such as bacterial / viral infections, smoking, and dust exposure. Therefore, respiratory diseases include tumors, infectious diseases, allergic diseases, other inflammations, and congenital anomalies. In this field, we will foster researchers who are able to understand the pathophysiology of a wide range of respiratory diseases and to conduct research that approaches the mechanism of disease development having a scientific perspective.

(2) Research

- 1. Pathophysiology of hypersensitivity pneumonitis, identification of causative antigens in the environment
- 2. Pathophysiology in lung fibrosis
- 3. Pathophysiology of acute exacerbations in interstitial pneumonia
- 4. Pathophysiology of pulmonary fibrosis and emphysematous changes
- 5. Tumor immunity in mesothelioma
- 6. Examination of oral allergy syndrome and asthma desensitization
- 2. Airway remodeling mechanism in asthma model
- 6. Pathophysiology of sleep apnea
- 7. Development of treatment for antibacterial drug-resistant 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 lug diseases in Japan are referred to our clinic.

(7) Publications

[Original Articles]

- 1. [: OKAMOTO Tsukasa] Yamana T, Okamoto T, Ishizuka M, Hanzawa S, Ejima M, Shibata S, Miyazaki Y. Correction: IL-17A-Secreting Memory $\gamma \delta$ T Cells Play a Pivotal Role in Sensitization and Development of Hypersensitivity Pneumonitis. Journal of immunology (Baltimore, Md. : 1950). 2021.12; 207(11); 2892
- 2. [Respiratory Medicine : MIYAZAKI Yasunari] Shimada S, Nakai R, Aoki K, Kudoh S, Imura S, Shimoeda N, Ohno G, Watanabe K, Miyazaki Y, Ishii Y, Tateda K. Characterization of the First Cultured Psychrotolerant Representative of < i> Legionella< /i> from Antarctica Reveals Its Unique Genome Structure. Microbiology spectrum. 2021.10; 9(2); e0042421
- 3. [Respiratory Medicine : MIYAZAKI Yasunari] Arai Teppei, Umeyama Takashi, Majima Hidetaka, Inukai Tatsuya, Watanabe Akira, Miyazaki Yoshitsugu, Kamei Katsuhiko. Hmg1 mutations in Aspergillus fumigatus and their contribution to triazole susceptibility MEDICAL MYCOLOGY. 2021.10; 59(10); 980-984
- 4. [Respiratory Medicine : MIYAZAKI Yasunari] Majima Hidetaka, Arai Teppei, Kusuya Yoko, Takahashi Hiroki, Watanabe Akira, Miyazaki Yasunari, Kamei Katsuhiko. Genetic differences between Japan and other countries in cyp51A polymorphisms of Aspergillus fumigatus MYCOSES. 2021.09; 64(11); 1354-1365
- 5. [Respiratory Medicine : MIYAZAKI Yasunari] Shindo Y, Kondoh Y, Kada A, Doi Y, Tomii K, Mukae H, Murata N, Imai R, Okamoto M, Yamano Y, Miyazaki Y, Shinoda M, Aso H, Izumi S, Ishii H, Ito R, Saito AM, Saito TI, Hasegawa Y. Phase II Clinical Trial of Combination Therapy with Favipiravir and Methylprednisolone for COVID-19 with Non-Critical Respiratory Failure. Infectious diseases and therapy. 2021.08;
- 6. [Pulmonary Medicine : HONDA Takayuki] Mitsumura T, Kumaki Y, Takahashi K, Matsudera S, Sakakibara R, Honda T, Ishizuka M, Iijima Y, Shirai T, Okamoto T, Tateishi T, Sakashita H, Miyake S, Ikeda S, Miyazaki Y. Treatment of advanced lung cancer based on genomic profiling using liquid biopsy (plasma): A review of three cases. Thoracic cancer. 2021.08;

- 7. [Respiratory Medicine : MIYAZAKI Yasunari] Katayanagi S, Setoguchi Y, Kitagawa S, Okamoto T, Miyazaki Y. Alternative gene expression by TOLLIP variant is associated with lung function in chronic hypersensitivity pneumonitis. Chest. 2021.08; 161(2); 458-469
- 8. [Department of Biostatistics : ANZAI Tatsuhiko] Masaru Ejima, Tsukasa Okamoto, Takafumi Suzuki, Tatsuhiko Anzai, Kunihiko Takahashi, Yasunari Miyazaki. Efficacy of treatment with corticosteroids for fibrotic hypersensitivity pneumonitis: a propensity score-matched cohort analysis. BMC Pulm Med. 2021.07; 21(1); 243
- 9. [Respiratory Medicine : MIYAZAKI Yasunari] Komatsu M, Yamamoto H, Matsui S, Terasaki Y, Hebisawa A, Iwasawa T, Johkoh T, Baba T, Miyamoto A, Handa T, Tomii K, Waseda Y, Bando M, Ishii H, Miyazaki Y, Yoshizawa A, Takemura T, Kawabata Y, Ogura T. Clinical characteristics of immunoglobulin G< sub> 4< /sub> -positive interstitial pneumonia. ERJ open research. 2021.07; 7(3);
- 10. [Department of Biostatistics : TAKAHASHI Kunihiko] Takahiro Mitsumura, Tsukasa Okamoto, Tsuyoshi Shirai, Yuki Iijima, Rie Sakakibara, Takayuki Honda, Masahiro Ishizuka, Junichi Aiboshi, Tomoya Tateishi, Meiyo Tamaoka, Hidenobu Shigemitsu, Hirokuni Arai, Yasuhiro Otomo, Shuji Tohda, Tatsuhiko Anzai, Kunihiko Takahashi, Shinsuke Yasuda, Yasunari Miyazaki. Predictors associated with clinical improvement of SARS-CoV-2 pneumonia. J Infect Chemother. 2021.06; 27(6); 857-863
- 11. [Pulmonary Medicine : ISHIZUKA Masahiro] Mitsumura Takahiro, Okamoto Tsukasa, Shirai Tsuyoshi, Iijima Yuki, Sakakibara Rie, Honda Takayuki, Ishizuka Masahiro, Aiboshi Junichi, Tateishi Tomoya, Tamaoka Meiyo, Shigemitsu Hidenobu, Arai Hirokuni, Otomo Yasuhiro, Tohda Shuji, Anzai Tatsuhiko, Takahashi Kunihiko, Yasuda Shinsuke, Miyazaki Yasunari. Predictors associated with clinical improvement of SARS-CoV-2 pneumonia(和訳中) Journal of Infection and Chemotherapy. 2021.06; 27(6); 857-863
- 12. [Respiratory Medicine : MIYAZAKI Yasunari] Ikeda S, Misumi T, Izumi S, Sakamoto K, Nishimura N, Ro S, Fukunaga K, Okamori S, Tachikawa N, Miyata N, Shinkai M, Shinoda M, Miyazaki Y, Iijima Y, Izumo T, Inomata M, Okamoto M, Yamaguchi T, Iwabuchi K, Masuda M, Takoi H, Oyamada Y, Fujitani S, Mineshita M, Ishii H, Nakagawa A, Yamaguchi N, Hibino M, Tsushima K, Nagai T, Ishikawa S, Ishikawa N, Kondoh Y, Yamazaki Y, Gocho K, Nishizawa T, Tsuzuku A, Yagi K, Shindo Y, Takeda Y, Yamanaka T, Ogura T. Corticosteroids for hospitalized patients with mild to critically-ill COVID-19: a multicenter, retrospective, propensity score-matched study. Scientific reports. 2021.05; 11(1); 10727
- 13. [Trauma and Acute Critical Care Medical Center : MORISHITA Koji] Hideto Shiraki, Koji Morishita, Mitsuhiro Kishino, Keita Nakatsutsumi, Koichiro Kimura, Tsuyoshi Shirai, Masahiro Ishizuka, Yasunari Miyazaki, Junichi Aiboshi, Yasuhiro Otomo. An Experience of Multiple Hematomas in a Coronavirus Disease-19 Patient Administered with ART-123 and Heparin. Open Access Emerg Med.. 2021.05; 13; 207-211
- 14. [Pulmonary Medicine : HONDA Takayuki] Murakami Naoya, Asami Yuka, Yoshida Hiroshi, Takayanagi Daisuke, Hirose Sou, Kuno Ikumi, Takahashi Kazuaki, Matsuda Maiko, Shimada Yoko, Yamano Shotaro, Sunami Kuniko, Honda Takayuki, Nakahara Tomomi, Watanabe Tomoko, Okuma Kae, Kuroda Takafumi, Kohno Takashi, Kato Tomoyasu, Shiraishi Kouya, Itami Jun. Distribution of genetic alterations in high-risk early-stage cervical cancer patients treated with postoperative radiation therapy SCIENTIFIC REPORTS. 2021.05; 11(1); 10567
- 15. [Pulmonary Medicine : SHIRAI Tsuyoshi] Sato H, Shirai T, Fujii H, Ishii T, Harigae H. Cyclophosphamide-associated enteritis presenting with severe protein-losing enteropathy in granulomatosis with polyangiitis: A case report. World journal of gastroenterology. 2021.05; 27(20); 2657-2663
- 16. [: OKAMOTO Tsukasa] Tateishi T., Okamoto T., Takasawa S., Aoki H., Miyazaki Y.. Angiopoietin-1 Has a Protective Role in Acute Exacerbation of Interstitial Pneumonia AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2021.05; 203(9);
- [Pulmonary Medicine : TATEISHI Tomoya] Tateishi T., Okamoto T., Takasawa S., Aoki H., Miyazaki Y.. Angiopoietin-1 Has a Protective Role in Acute Exacerbation of Interstitial Pneumonia AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2021.05; 203(9);
- 18. [Respiratory Medicine : MIYAZAKI Yasunari] Nawa Nobutoshi, Kuramochi Jin, Sonoda Shiro, Yamaoka Yui, Nukui Yoko, Miyazaki Yasunari, Fujiwara Takeo. Seroprevalence of SARS-CoV-2 in Utsunomiya City,

Greater Tokyo, after the first pandemic in 2020(和訳中) Journal of General and Family Medicine. 2021.05; 22(3); 160-162

- 19. [Medical Education Research and Development : NAWA NOBUTOSHI] Nawa N, Yamaoka Y, Koyama Y, Nishimura H, Sonoda S, Kuramochi J, Miyazaki Y, Fujiwara T. Association between Social Integration and Face Mask Use Behavior during the SARS-CoV-2 Pandemic in Japan: Results from U-CORONA Study. International journal of environmental research and public health. 2021.04; 18(9);
- 20. [Respiratory Medicine : MIYAZAKI Yasunari] Nawa N, Yamaoka Y, Koyama Y, Nishimura H, Sonoda S, Kuramochi J, Miyazaki Y, Fujiwara T. Association between Social Integration and Face Mask Use Behavior during the SARS-CoV-2 Pandemic in Japan: Results from U-CORONA Study. International journal of environmental research and public health. 2021.04; 18(9);
- 21. [Respiratory Medicine : MIYAZAKI Yasunari] Okazaki T, Yokoyama K, Tsuchiya J, Honda T, Ishikawa Y, Kirimura S, Miyazaki Y, Tateishi U. SMARCA4-deficient thoracic tumor detected by [< sup> 18< /sup> F] FDG PET/CT. European journal of hybrid imaging. 2021.04; 5(1); 8
- 22. [Pulmonary Medicine : SHIRAI Tsuyoshi] Akiyama C, Shirai T, Sato H, Fujii H, Ishii T, Harigae H. Association of various myositis-specific autoantibodies with dermatomyositis and polymyositis triggered by pregnancy. Rheumatology international. 2021.04;
- 23. [Respiratory Medicine : SETOGUCHI Yasuhiro] Kawagoe Junichiro, Kono Yuta, Togashi Yuki, Ishiwari Mayuko, Toriyama Kazutoshi, Yajima Chika, Nakayama Hideaki, Kasagi Satoshi, Abe Shinji, Setoguchi Yasuhiro. Serum Neutrophil Gelatinase-associated Lipocalin (NGAL) Is Elevated in Patients with Asthma and Airway Obstruction CURRENT MEDICAL SCIENCE. 2021.04; 41(2); 323-328
- 24. [Pulmonary Medicine : SHIRAI Tsuyoshi] Shirai Tsuyoshi, Tanino Yoshinori, Nikaido Takefumi, Takaku Yotaro, Hashimoto Seishu, Taguchi Yoshio, Baba Tomohisa, Ogura Takashi, Kataoka Kensuke, Nakayama Masayuki, Yamada Yoshihito, Matsushima Sayomi, Nakayama Satoshi, Miyazaki Yasunari. Screening and diagnosis of acute and chronic bird-related hypersensitivity pneumonitis by serum IgG and IgA antibodies to bird antigens with ImmunoCAP(和訳中) Allergology International. 2021.04; 70(2); 208-214
- 25. [Medical Education Research and Development : NAWA NOBUTOSHI] Koyama Y, Nawa N, Yamaoka Y, Nishimura H, Sonoda S, Kuramochi J, Miyazaki Y, Fujiwara T. Interplay between social isolation and loneliness and chronic systemic inflammation during the COVID-19 pandemic in Japan: Results from U-CORONA Study. Brain, behavior, and immunity. 2021.03;
- 26. [Temporomandibular Disorders Clinic : ISHIYAMA Hiroyuki] Hiroyuki Ishiyama, Masayuki Hideshima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki. Evaluation of Respiratory Resistance as a Predictor for Oral Appliance Treatment Response in Obstructive Sleep Apnea: A Pilot Study. Journal of Clinical Medicine. 2021.03; 10(6); 1255-1268
- 27. [: OKAMOTO Tsukasa] Tasaka Y, Honda T, Nishiyama N, Tsutsui T, Saito H, Watabe H, Shimaya K, Mochizuki A, Tsuyuki S, Kawahara T, Sakakibara R, Mitsumura T, Okamoto T, Kobayashi M, Chiaki T, Yamashita T, Tsukada Y, Taki R, Jin Y, Sakashita H, Natsume I, Saitou K, Miyashita Y, Miyazaki Y. Non-inferior clinical outcomes of immune checkpoint inhibitors in non-small cell lung cancer patients with interstitial lung disease. Lung Cancer (Amsterdam, Netherlands). 2021.03; 155; 120-126
- 28. [Pulmonary Medicine : SHIRAI Tsuyoshi] Shirai T, Kakuta Y, Fujii H. Distinct autoantibodies against endothelial protein C receptor in ulcerative colitis. Gastroenterology. 2021.03;
- 29. [Department of Biostatistics : ANZAI Tatsuhiko] Yuki Iijima, Tsukasa Okamoto, Tsuyoshi Shirai, Takahiro Mitsumura, Rie Sakakibara, Takayuki Honda, Masahiro Ishizuka, Tomoya Tateishi, Meiyo Tamaoka, Junichi Aiboshi, Yasuhiro Otomo, Tatsuhiko Anzai, Kunihiko Takahashi, Yasunari Miyazaki. MuLBSTA score is a useful tool for predicting COVID-19 disease behavior. J Infect Chemother. 2021.02; 27(2); 284-290
- 30. [Global Health Promotion : FUJIWARA Takeo] Sonoda S*, Kuramochi J, Matsuyama Y, Miyazaki Y, Fujiwara T.. Validity of Clinical Symptoms Score to Discriminate Patients with COVID-19 from Common Cold Out-Patients in General Practitioner Clinics in Japan. J Clin Med. 2021.02; 10(4); 854

- 31. [Pulmonary Medicine : ISHIZUKA Masahiro] Iijima Yuki, Okamoto Tsukasa, Shirai Tsuyoshi, Mitsumura Takahiro, Sakakibara Rie, Honda Takayuki, Ishizuka Masahiro, Tateishi Tomoya, Tamaoka Meiyo, Aiboshi Junichi, Otomo Yasuhiro, Anzai Tatsuhiko, Takahashi Kunihiko, Miyazaki Yasunari. MuLBSTA score is a useful tool for predicting COVID-19 disease behavior(和訳中) Journal of Infection and Chemotherapy. 2021.02; 27(2); 284-290
- 32. [Respiratory Medicine : MIYAZAKI Yasunari] Shimada S, Nakai R, Aoki K, Shimoeda N, Ohno G, Kudoh S, Imura S, Watanabe K, Miyazaki Y, Ishii Y, Tateda K. Chasing waterborne pathogens in Antarctic human-made and natural environments with special reference to Legionella spp. Applied and Environmental Microbiology. 2021.01; 48(7); e02247-20
- 33. [Gerodontology and Oral Rehabilitation : KOMAGAMINE Yuriko] Doke M, Komagamine Y, Kanazawa M, Iwaki M, Suzuki H, Miyazaki Y, Mizuno T, Okayasu K, Minakuchi S. Effect of dental intervention on improvements in metabolic syndrome patients: a randomized controlled clinical trial. BMC oral health. 2021.01; 21(1); 4
- 34. [Pulmonary Medicine : TATEISHI Tomoya] Nishiyama Naoki, Masuo Masahiro, Nukui Yoshihisa, Tateishi Tomoya, Kishino Mitsuhiro, Tateishi Ukihide, Morota Kaori, Ohbo Kazuyuki, Miyazaki Yasunari. Human epididymis protein 4 is a new biomarker to predict the prognosis of progressive fibrosing interstitial lung disease(和訳中) Respiratory Investigation. 2021.01; 59(1); 90-98
- 35. [Respiratory Medicine : MIYAZAKI Yasunari] Sugihara J, Shibata S, Doi M, Shimmura T, Inoue S, Matsumoto O, Suzuki H, Makino A, Miyazaki Y. Atypical lymphocytes in the peripheral blood of COVID-19 patients: A prognostic factor for the clinical course of COVID-19. PloS one. 2021; 16(11); e0259910
- 36. [Intensive Care Medicine : NOSAKA Nobuyuki] Oba S, Hosoya T, Amamiya M, Mitsumura T, Kawata D, Sasaki H, Kamiya M, Yamamoto A, Ando T, Shimada S, Shirai T, Okamoto T, Tateishi T, Endo A, Aiboshi J, Nosaka N, Yamanouchi H, Ugawa T, Nagaoka E, Oi K, Tao S, Maejima Y, Tanaka Y, Tanimoto K, Takeuchi H, Tohda S, Hirakawa A, Sasano T, Arai H, Otomo Y, Miyazaki Y, Yasuda S. Arterial and Venous Thrombosis Complicated in COVID-19: A Retrospective Single Center Analysis in Japan. Frontiers in cardiovascular medicine. 2021; 8; 767074
- 37. [Respiratory Medicine : MIYAZAKI Yasunari] Oba S, Hosoya T, Amamiya M, Mitsumura T, Kawata D, Sasaki H, Kamiya M, Yamamoto A, Ando T, Shimada S, Shirai T, Okamoto T, Tateishi T, Endo A, Aiboshi J, Nosaka N, Yamanouchi H, Ugawa T, Nagaoka E, Oi K, Tao S, Maejima Y, Tanaka Y, Tanimoto K, Takeuchi H, Tohda S, Hirakawa A, Sasano T, Arai H, Otomo Y, Miyazaki Y, Yasuda S. Arterial and Venous Thrombosis Complicated in COVID-19: A Retrospective Single Center Analysis in Japan. Frontiers in cardiovascular medicine. 2021; 8; 767074

- 1. [Respiratory Medicine : MIYAZAKI Yasunari] Setoguchi Yasuhiro, Miyazaki Yasunari, Nakayama Yoshiki, Matsuyama Len, Ando Mari, Matsuba Seiji, Uchida Masaki. Development of image processing-based smartphone App(Application Software) for self-management of inhaled medicines for patients with asthma or COPD(和訳中). 日本呼吸器学会誌 2021.04.01
- 2. [Respiratory Medicine : MIYAZAKI Yasunari] Setoguchi Yasuhiro, Miyazaki Yasunari, Nakayama Yoshiki, Matsuyama Len, Ando Mari, Matsuba Seiji, Uchida Masaki. 喘息または COPD 患者の吸 入薬の自己管理のための画像処理を用いたスマホアプリ (ソフトウエア)の開発 (Development of image processing-based smartphone App(Application Software) for self-management of inhaled medicines for patients with asthma or COPD). 日本呼吸器学会誌 2021.04.01

Cardiovascular Surgery

Professor: Hirokuni ARAI Associate Professor: Tomohiro MIZUNO Junior Associate Professor: Keiji OI, Eiki NAGAOKA Assistant Professor: Masafumi YASHIMA, Tatsuki FUJIWARA, Kiyotoshi OISHI, Masashi TAKESHITA Graduate Student: Dai TASAKI, Kenji SAKAI, Ryoji KINOSHITA, Kiyotoshi OISHI, Kenji YOKOYAMA Masashi TAKESHITA, Hironobu SAKURAI, Haruna SEKI, Tomoki TAHARA Hospital Staff: 3

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 regargitation. 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. Yoshihiko Sano, Toyomu Ugawa, Ayato Takeda, Toru Hyakutake, Takashi Nakazawa, Shinichiro Yanase, Hidenobu Shigemitsu, Hirokuni Arai. Hydrodynamic Approach for Revealing Venous Anastomotic Stenosis Formation Within a Dialysis Arteriovenous Graft. ASAIO J. 2021.12; 67(12); 1269-1276
- 2. Mario Gaudino, Sigrid Sandner, Gabriele Di Giammarco, Antonino Di Franco, Hirokuni Arai, Tohru Asai, Faisal Bakaeen, Torsten Doenst, Stephen E Fremes, David Glineur, Teresa M Kieser, Jennifer S Lawton, Roberto Lorusso, Nirav Patel, John D Puskas, James Tatoulis, David P Taggart, Michael Vallely, Marc Ruel. The Use of Intraoperative Transit Time Flow Measurement for Coronary Artery Bypass Surgery: Systematic Review of the Evidence and Expert Opinion Statements. Circulation. 2021.10; 144(14); 1160-1171
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[Conference Activities & Talks]

- 1. Arai H.. Coronary Masterclass: OPCABG on the Lateral Wallonline. 7th Annual International Coronary Congress 2021.12.06 Virtual (New York, USA)
- 2. Arai H.. How to Run a Successful CABG program/Building a Successful CABG Program in the Most Competitive Asian Market. 7th Annual International Coronary Congress 2021.12.06 Virtual (New York, USA)
- 3. Arai H.. CABG in Patients with Low EF /Associated Procedures: MR, AF, etc. 7th Annual International Coronary Congress 2021.12.04 Virtual (New York, USA)
- 4. Oishi K, Arai.H, Mizuno.T, Oi.K, Nagaoka.E, Yashima.M, Fujiwara.T, Takeshita.M, Nabeshima.J, Tahara.T. Surgical strategy for isolated coronary ostial stenosis in Takayasu disease: coronary ostial patch angioplasty using femoral artery.. 7th Annual International Coronary Congress 2021.12.03 Vurtual
- 5. Fujiwara T, Sakurai H, Ohuchi K, Hijikata W, Tanaka Y, Hatakenaka K, Inoue Y, Takewa Y, Maruyama O, Mizuno T, Arai H. Verification of an acute animal experimental model for comparison of antithrombotic properties of different extracorporeal circulation circuits. 16th European mechanical circulatory support summit International society for mechanical circulatory support (EUMS-ISMCS) 2021.12.01 Virtual
- 6. Arai H.. Pathophysiologic changes and repair strategy in secondary mitral regurgitation. Annual Congress of the Association of Thoracic and Cardiovascular Surgeons of Asia 2021.11.06 Web
- 7. Oi K.. Mitral Valve Repair with Bilateral Papillary Muscle Relocation in the Direction of the Anterior Mitral Annulus Improves the Long Term Outcomes for Functional Mitral Regurgitation. MITRAPLUS Kick-off meeting 2021.10.23 Virtual
- 8. Arai H., Repair of secondary MR: where are we?. 35th EACTS ANNUAL MEETING 2021.10.16 Hybrid (Barcelona, Spain)
- 9. Takeshita M, Arai H, Mizuno T, Oi K, Fujiwara T, Oishi K. Surgical results of subvalvular procedures for tricuspid regurgitation patients with leaflet tethering. 35th EACTS Annual Meeting 2021.10.15 Virtual
- 10. Oishi K, Arai H, Mizuno T, Oi K, Nagaoka E, Yashima M, Fujiwara T, Takeshita M.. Implications for valve-sparing aortic root replacement. 35th EACTS Annual Meeting 2021.10.15 Virtual
- 11. Eiki Nagaoka. MIS mitral surgery, the Japanese way. 6th Singapore Valve 2021 2021.08.15 SINGAPORE
- 12. Arai H.. (Moderator)Cardiac Abstract Session 3 Revascularization.. 21 ISMICS Re-imagined 2021.06.20 Web
- 13. Eiki Nagaoka, Hirokuni Arai, Tomohiro Mizuno, Keiji Oi, Tatsuki Fujiwara, Kiyotoshi Oishi. . A 13-year Experience Of Tentacles. 21 ISMICS Re-imagined 2021.06.20 Poland, Warshaw
- 14. Sakurai H, Fujiwara T, Ohuchi K, Hijikata W, Inoue Y, Mizuno T, Arai H. Real-time Visualization Of Thrombus Formation In An Extracorporeal Membrane Oxygenator Using Indocyanine Green Fluorescence. 66th Annual Conference of the American Society for Artificial Organs (the 2021 ASAIO Meeting) 2021.06.10 Washington DC (& virtual)
- 15. Arai H.. When and How I use the Gastroepiploic Artery. ASCVTS 2021 Online Conference 2021.06.05 Web
- 16. Arai H. (Moderator) Ischemic Heart Disease. ASCVTS 2021 Online Conference 2021.06.05 Web
- 17. Arai H.. Perfused Beating Heart has its Role. AATS 2021 101st Annual Meeting 2021.05.02 Web
- E Nagaoka, T Mizuno, K Oi, M Yashima, T Fujiwara, K Oishi, M Takeshita, T Tahara, Y Sai, H Arai. Utility and Limitation of Pericardial Patch for Mitral Valve Repair. The 51st Annual Meeting of the Japanese Society for Cardiovascular Surgery 2021.02.19

[Patents]

1. OSTEOSYNTHESIS MEMBER, Patent Number : CN201610307896.7

Nephrology

Professor: Shinichi UCHIDA Tatemitsu RAI (Dept. of Nephrology and Regional Medicine (Ibaraki)) Associate Professor: Eisei SOHARA Shotaro NAITO (Dept. of Blood Purification) Junior Associate Professor: Soichiro IIMORI Assistant Professor: Koichiro SUSA Takayasu MORI (Dept. of Blood Purification) Fumiaki ANDO Shintaro MANDAI (Dept. of Blood Purification) Project Assistant Professor Tamami FUJIKI, Yuichiro AKAGI, Taku GENMA Graduate Student: Azuma NANAMATSU Yu HARA, Soichiro SUZUKI, Tomoki YANAGI, Takaaki KOIDE Hisazumi MATSUKI, Ryosuke KAWAMOTO, Yuta NAKANO, Hideki YANAGAWA Takefumi SUZUKI Hospital Staff: Akira TOYAMA, Yurie MATSUNAGA Rieko HIGASHIDE, Haruto MAKIGUCHI, Savumi KOYAMA 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). Since 2020, we have continued to deal with the spread of COVID-19 infection, but some conferences have returned to being held locally, and we feel that we are gradually returning to the activities of the past.

In FY2021, Professor Shinichi Uchida (Hospital Director) received the Japan Kidney Foundation Award for Academic Achievement, which is given to those who have achieved research achievements in nephrology that have been recognized by many people academically and are expected to continue to develop in the future. At the Annual Meeting of the Japanese Society of Nephrology, Dr. Hitoshi Endo, Dr. Tatsuo Shiigai, Dr. Yasuhiko Iino, and Dr. Kimio Tomita, all alumni of our department, received the Ueda Award from the Japanese Society of Nephrology, which is given to honorary members of the society who have made notable contributions to the development of the society, such as academic and social contributions and fostering the next generation. Of the six winners, four were from our laboratory, it was a remarkable accomplishment. Dr. Shintaro Mandai's presentation entitled "Burden of Kidney Disease on Discrepancy between Reasons for Admission and Death: A Nationwide Cohort Study of Japanese Adults" and Dr. Naohiro Takahashi's presentation entitled "Alox15 knock-out mice improve renal injury and fibrosis in CKD via increasing PGD2 in kidney" received Best Presentation Awards. Dr. Mandai's presentation also received the Best Abstract Award, which is given to the best presentation. In addition, Dr. Katsuhito Ihara received the YIA (Young Investigator Award), which is given to a young researcher of the Society of Nephrology who is expected to develop further in the future. In addition, at the 670th Kanto Regional Meeting of the Japanese Society of Internal Medicine, Dr. Katsuo Mori, a resident, received the Encouragement Award for his presentation "A case of Edwadsiella tarda bacteremia in exacerbation of chronic heart failure". Assistant Professor Takayasu Mori received the Medical Advisor Award, and in a competition for collaboration within Tokyo Medical and Dental University, Dr. Koichiro Susa's "Proposal for the construction of a system for mutual use of laboratory equipment across disciplines" won a prize, and many other awards were received.

Original papers were published in Hypertension (Nanamatsu et al. IF: 9.9), Kidney International Report (Fujimaru et al. IF: 6.2), Clinical Experimental Nephrology (Takahashi N et al. IF: 2.6), 18 papers were reported in English-language journals, and two press releases were issued.

Also, comprehensive genetic diagnosis using next-generation sequencers and clinical research related to genome information are on track, contributing to the diagnosis of as many as 200 patients per year.

(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 so that the students will be able to study independently and bi-directionally. Due to the corona disaster in FY2021, as in the previous year, all the lectures were conducted in remote form.

(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 ectures and eight weeks of small-class lectures), which are more practical and interactive than the previous lectures held in the classroom. This year, all lectures were conducted in remote form. 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. Although limitations were set for the frequency and time of actual access to the ward, the students were assigned to be in charge of one new inpatient each week and make a presentation about their patient at the regular ward conference. They 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. In FY2021, although there was some increase in the number of inpatient dialysis patients during the period of settled down of infection, the number of treatment patients increased only about 10% compared to FY2020. In order to increase the number of peritoneal dialysis patients in accordance with the revision of medical fees in FY2021, preparations are underway for outpatient treatment for renal replacement therapy options. We are also actively engaged in the treatment of intractable diseases. Furthermore, using the latest molecular biology, we are the first in Japan to conduct genetic analysis of inherited renal diseases such as renal enuresis, Liddle syndrome, pseudohyperaldosteronism type II, polycystic kidney disease, Alport syndrome and thin basement membrane disease, and are receiving requests for analysis from all over Japan. Recently, we have been performing comprehensive genetic diagnosis using next-generation sequencing technology, which enables us to diagnose rare inherited renal diseases.

(5) Publications

[Original Articles]

- 1. Sakurasawa Takatoshi, Ohkubo Atsushi, Hoshikawa Yuki, Yamauchi Daisuke, Yamamoto Hiroko, Seshima Hiroshi, Kurashima Naoki, Iimori Soichiro, Rai Tatemitsu, Uchida Shinichi, Naito Shotaro. 治療的アフェ レーシスの除去率計算におけるヘマトクリット値による調整 (Adjustment by hematocrit level in calculation of removal rate in therapeutic apheresis) Therapeutic Apheresis and Dialysis. 2021.08; 25(4); 425-431
- Fujii Shinya, Kikuchi Eriko, Suzuyama Honoka, Watanabe Yuko, Ishigami-Yuasa Mari, Masuno Hiroyuki, Mori Takayasu, Isobe Kiyoshi, Uchida Shinichi, Kagechika Hiroyuki. Structural Development of Salicylanilide-Based SPAK Inhibitors as Candidate Antihypertensive Agents CHEMMEDCHEM. 2021.07;
- 3. Kumagai A, Takeda S, Sohara E, Uchida S, Iijima H, Itakura A, Koya D, Kanasaki K. Dietary Magnesium Insufficiency Induces Salt-Sensitive Hypertension in Mice Associated With Reduced Kidney Catechol-O-Methyl Transferase Activity. Hypertension (Dallas, Tex. : 1979). 2021.07; 78(1); 138-150
- 4. Shimohata H, Miyake Y, Yoshida Y, Usui J, Mori T, Sohara E, Uchida S, Hirayama K, Kobayashi M. LMX1B-associated nephropathy that showed myelin figures on electron microscopy. CEN case reports. 2021.06;
- 5. Kandhaya-Pillai Renuka, Hou Deyin, Zhang Jiaming, Yang Xiaomeng, Compoginis Goli, Mori Takayasu, Tchkonia Tamara, Martin George M., Hisama Fuki M., Kirkland James L., Oshima Junko. SMAD4 mutations and cross-talk between TGF-beta/IFN gamma signaling accelerate rates of DNA damage and cellular senescence, resulting in a segmental progeroid syndrome-the Myhre syndrome GEROSCIENCE. 2021.06; 43(3); 1481-1496
- 6. Takuya Fujimaru, Kunio Kawanishi, Takayasu Mori, Eikan Mishima, Akinari Sekine, Motoko Chiga, Masayuki Mizui, Noriaki Sato, Motoko Yanagita, Yuki Ooki, Kiyotaka Nagahama, Yuko Ohnuki, Naoto Hamano, Saki Watanabe, Toshio Mochizuki, Katsushi Nagatsuji, Kenichi Tanaka, Tatsuo Tsukamoto, Hideo Tsushima, Mamiko Shimamoto, Takahiro Tsuji, Tamaki Kuyama, Shinya Kawamoto, Kenji Maki, Ai Katsuma, Mariko Oishi, Kouhei Yamamoto, Shintaro Mandai, Hiroaki Kikuchi, Fumiaki Ando, Yutaro Mori, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Tatemitsu Rai, Junichi Hoshino, Yoshifumi Ubara, Mariko Miyazaki, Michio Nagata, Shinichi Uchida, Eisei Sohara. Genetic Background and Clinicopathologic Features of Adult-onset Nephronophthisis. Kidney Int Rep. 2021.05; 6(5); 1346-1354
- 7. Takahashi Naohiro, Kikuchi Hiroaki, Usui Ayaka, Furusho Taisuke, Fujimaru Takuya, Fujiki Tamami, Yanagi Tomoki, Matsuura Yoshiaki, Asano Kenichi, Yamamoto Kouhei, Ando Fumiaki, Susa Koichiro, Mandai Shintaro, Mori Takayasu, Rai Tatemitsu, Uchida Shinichi, Arita Makoto, Sohara Eisei. Deletion

of Alox15 improves kidney dysfunction and inhibits fibrosis by increased PGD2 in the kidney Clinical and Experimental Nephrology. 2021.05; 25(5); 445-455

- Takedani K, Notsu M, Koike S, Yamauchi M, Mori T, Sohara E, Yamauchi A, Yoshikane K, Ito T, Kanasaki K. Osteomalacia caused by atypical renal tubular acidosis with vitamin D deficiency: a case report. CEN case reports. 2021.05; 10(2); 294-300
- 9. Takatoshi Sakurasawa, Atsushi Ohkubo, Yuki Hoshikawa, Daisuke Yamauchi, Hiroko Yamamoto, Hiroshi Seshima, Naoki Kurashima, Soichiro Iimori, Tatemitsu Rai, Shinichi Uchida, Shotaro Naito. Adjustment by hematocrit level in calculation of removal rate in therapeutic apheresis. Ther Apher Dial. 2021.04;
- Nanamatsu A, Mori T, Ando F, Furusho T, Mandai S, Susa K, Sohara E, Rai T, Uchida S. Vasopressin Induces Urinary Uromodulin Secretion By Activating PKA (Protein Kinase A). Hypertension (Dallas, Tex. : 1979). 2021.04; HYPERTENSIONAHA12117127
- 11. Oe Y, Mishima E, Mori T, Okamoto K, Honkura Y, Nagasawa T, Yoshida M, Sato H, Suzuki J, Ikeda R, Sohara E, Uchida S, Katori Y, Miyazaki M. A Novel Mutation in LMX1B (p.Pro219Ala) Causes Focal Segmental Glomerulosclerosis with Alport Syndrome-like Phenotype. Internal medicine (Tokyo, Japan). 2021.04;
- 12. Tao K, Awazu M, Honda M, Shibata H, Mori T, Uchida S, Hasegawa T, Ishii T. An infant with congenital nephrogenic diabetes insipidus presenting with hypercalcemia and hyperphosphatemia. Endocrinology, diabetes & metabolism case reports. 2021.04; 2021;
- 13. Takahashi N, Kikuchi H, Usui A, Furusho T, Fujimaru T, Fujiki T, Yanagi T, Matsuura Y, Asano K, Yamamoto K, Ando F, Susa K, Mandai S, Mori T, Rai T, Uchida S, Arita M, Sohara E. Deletion of Alox15 improves kidney dysfunction and inhibits fibrosis by increased PGD< sub> 2< /sub> in the kidney. Clinical and experimental nephrology. 2021.02;
- 14. Ihara K, Rai T, Nishida H, Sasaki S, Uchida S. Minimal change disease concurrent with acute interstitial nephritis after long-term use of sorafenib in a patient with renal cell carcinoma. CEN case reports. 2021.01;
- 15. Onoe Tamehito, Hara Satoshi, Yamada Kazunori, Zoshima Takeshi, Mizushima Ichiro, Ito Kiyoaki, Mori Takayasu, Daimon Shoichiro, Muramoto Hiroaki, Shimizu Maki, Iguchi Akira, Kuma Akihiro, Ubara Yoshifumi, Mitobe Michihiro, Tsuruta Hiroaki, Kishimoto Nao, Imura Junko, Konoshita Tadashi, Kawano Mitsuhiro. Significance of kidney biopsy in autosomal dominant tubulointerstitial kidney disease-UMOD: is kidney biopsy truly nonspecific? BMC NEPHROLOGY. 2021.01; 22(1); 1
- 16. Mandai S, Ando F, Mori T, Susa K, Iimori S, Naito S, Sohara E, Uchida S, Fushimi K, Rai T. Burden of kidney disease on the discrepancy between reasons for hospital admission and death: An observational cohort study. PloS one. 2021; 16(11); e0258846
- 17. Mandai S, Yamada T, Uchihara T, Iida T, Ito T, Sato H, Sato K, Chida Y, Hirokawa K, Noda Y. Severe Dialysis-Related Amyloidosis Spared the Brain: An Autopsy Case of a Patient Receiving Hemodialysis for 41 Years. Journal of neuropathology and experimental neurology. 2021.03;
- Hashimoto Hiroko, Shikuma Satomi, Mandai Shintaro*, Adachi Susumu, Uchida Shinichi. Calcium-based phosphate binder use is associated with lower risk of osteoporosis in hemodialysis patients SCIENTIFIC REPORTS. 2021.01; 11(1); 1648

[Misc]

- 1. Ando F*. Activation of AQP2 water channels by protein kinase A: the rapeutic strategies for congenital nephrogenic diabetes insipidus Clin Exp Nephrol. 2021.10; 25(10); 1051-1056
- 2. Yoshihide Ota, Tadahide Noguchi, Masahiko Miura et al.. General rules for clinical and pathological studies on oral cancer (2nd edition): a synopsis. Int J Clin Oncol. 2021.04; 26(4); 623-635

- 1. Mandai Shintaro, Ando Fumiaki, Mori Takayasu, Susa Koichiro, Iimori Soichiro, Naito Shotaro, Sohara Eisei, Uchida Shinichi, Fushimi Kiyohide, Rai Tatemitsu. 腎臓病に関する入院理由と死因の不一致がもた らす負荷 日本人成人に関する全国調査 (Burden of Kidney Disease on Discrepancy between Reasons for Admission and Death: A Nationwide Cohort Study of Japanese Adults). 第 64 回日本腎臓学会学術総会 2021.06
- 2. 高橋直宏, 蘇原映誠, 有田誠, 菊池寛昭, 安藤史顕, 須佐紘一郎, 萬代新太郎, 森崇寧, 頼建光, 内田信一. Alox15 knock-out マウスは、腎臓における PGD2 の増加を介して CKD の腎障害及び線維化を改善する. 第 64 回日 本腎臓学会学術総会 2021.06

Comprehensive Reproductive Medicine

2022.3.1

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,Takafumi TSUKADA, Haruko OHNO,Reiko NAKAMURA,Asuka HIROSE Project Assistant Professor : Takashi NAKASUJI,Kazuki SAITO,Tamami ODAI HospitalStaff : Kotoi TSURANE,Ayako FUDONO,Rinko IBI,Eiko USHIKI,Hisae KAMO,Chihiro MANO Graduate Student : Misako IWATA,Nobuyuki KIDERA,Ayako FUDONO,Kotoi TSURANE, Atsushi FUSEGI, Shiho HIDAKA,Hiroshi YOMOGITA,Yuan FANG,Junitiro MITSUI,Akiyo TORIUMI

(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 clump)
- 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]

- Shotaro Matsudera, Yoshihito Kano, Yasuko Aoyagi, Kohki Tohyama, Kenta Takahashi, Yuichi Kumaki, Takahiro Mitsumura, Koichiro Kimura, Iichiro Onishi, Akira Takemoto, Daisuke Ban, Hiroaki Ono, Atsushi Kudo, Noriko Oshima, Kei Ogino, Shun Watanabe, Yukiko Tani, Takeshi Yamaguchi, Masanobu Nakajima, Shinji Morita, Satoru Yamaguchi, Masatoshi Takagi, Toshiaki Ishikawa, Tsuyoshi Nakagawa, Kentaro Okamoto, Hiroyuki Uetake, Minoru Tanabe, Satoshi Miyake, Takashi Tsuchioka, Kazuyuki Kojima, Sadakatsu Ikeda. A Pilot Study Analyzing the Clinical Utility of Comprehensive Genomic Profiling Using Plasma Cell-Free DNA for Solid Tumor Patients in Japan (PROFILE Study). Ann Surg Oncol. 2021.12; 28(13); 8497-8505
- 2. Sato N, Fudono A, Imai C, Takimoto H, Tarui I, Aoyama T, Yago S, Okamitsu M, Mizutani S, and Miyasaka N. Placenta mediates the effect of maternal hypertension polygenic score on offspring birth weight: a study of birth cohort with fetal growth velocity data BMC Medicine. 2021.11; 19(1); 260
- 3. Fudono A, Imai C, Takimoto H, Tarui I, Aoyama T, Yago S, Okamitsu M, Muramatsu M, Sato N, Miyasaka N.. Trimester-specific associations between extracellular vesicle microRNAs and fetal growth. J Matern Fetal Neonatal Med. 2021.11; 1-7
- 4. Makiko Tomida, Rei Otsuka, Chikako Tange, Yukiko Nishita, Tomomi Kimura, Matthias Stoelzel, Keiko Tanaka-Amino, Hiroshi Shimokata, Masakazu Terauchi. Vasomotor symptoms, sleep problems, and depressive symptoms in community-dwelling Japanese women. J Obstet Gynaecol Res. 2021.10; 47(10); 3677-3690
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Urology

Professor and Chairman: Yasuhisa Fujii
Associate Professor: Yoh Matsuoka
Junior Associate Professor: Minato Yokoyama (Department of Insured Medical Care Management), Soichiro Yoshida, Hajime Tanaka
Assistant Professor: Yosuke Yasuda, Sho Uehara, Hiroshi Fukushima, Shohei Fukuda
Hospital Staff: Masahiro Toide, Yusuke Uchida, Yuki Nakamura, Madoka Kataoka, Yoshitomo Yamaguchi, Wataru Shimada
Graduate Student: Bo Fan

(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-weighed 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. Clampless 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

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Gastrointestinal Surgery

Professor Yusuke KINUGASA
Associate Professor Masanori TOKUNAGA
Junior Associate Professor Kenro KAWADA, Takuya OKADA
Assistant Professor Akihiro HOSHINO, Naoto FUJIWARA, Katsumasa SAITO
Yuya SATO, Chiharu TOMII, Shinichi YAMAUCHI Taiki MASUDA, Noriko IWATA, Marie HANAOKA
Graduate Student (Hospital Staff) Hajime SHINOHARA, Hiroyuki SHIOBARA, Miyako TAZAWA, Masako MIZOGUCHI, Takafumi SHIGENO, Ryuta KAKUTA, Naoya ISHIBASHI Rumi Shimano, Fumio TSUKAMOTO, Kyoko RYU, Shiho MATSUNAGA Shunsaku NAKAGAWA

(1) Research

- 1) Development of esophageal surgery.
- 2) Development of gastric surgery.
- 3) Development of colorectal surgery.

(2) Education

The history of the department started as both the Department of Esophageal and General Surgery and the Department of Surgical Oncology of TMDU, and many surgeons and researchers in various specialties have gathered and have been keeping a high level of activities. Our main purposes of education are to make the post-graduate physicians grown up to excellent surgeons and to contribute in development of medical/surgical sciences. Surgeons with high-level medical knowledge and techniques are expected to grow up in this department. Moreover, making surgeons with matured humanity is one of the purposes. The department has a peaceful atmosphere and stands for active work in solving difficult problems.

(3) Clinical Performances

Main clinical services are diagnosis and treatment for esophageal, gastric and colorectal diseases. Post-graduate students learn and study general surgery and sub-specialty, e.g. esophageal surgery, gastric surgery and colorectal surgery. The territory of clinics is wide and the department provides a full spectrum of standard and special technologies such as minimally invasive surgery and extended radical surgery for malignancies.

(4) **Publications**

[Original Articles]

- 1. Imai Kenichiro, Hotta Kinichi, Ito Sayo, Yamaguchi Yuichiro, Kishida Yoshihiro, Yamaoka Yusuke, Manabe Shoichi, Hino Hitoshi, Kagawa Hiroyasu, Yamaguchi Tomohiro, Shiomi Akio, Kinugasa Yusuke, Mori Keita, Ono Hiroyuki. Small-Dose Endoscopic Tattooing Using a Novel Needle for Localization Prior to Laparoscopic Surgery of Colorectal Cancer DIGESTIVE DISEASES AND SCIENCES. 2021.12; 66(12); 4448-4456
- 2. Yukihide Kanemitsu, Yasuhiro Shimizu, Junki Mizusawa, Yoshitaka Inaba, Tetsuya Hamaguchi, Dai Shida, Masayuki Ohue, Koji Komori, Akio Shiomi, Manabu Shiozawa, Jun Watanabe, Takeshi Suto, Yusuke Kinugasa, Yasumasa Takii, Hiroyuki Bando, Takaya Kobatake, Masafumi Inomata, Yasuhiro Shimada, Hiroshi Katayama, Haruhiko Fukuda, JCOG Colorectal Cancer Study Group. Hepatectomy Followed by mFOLFOX6 Versus Hepatectomy Alone for Liver-Only Metastatic Colorectal Cancer (JCOG0603): A Phase II or III Randomized Controlled Trial Journal of clinical oncology. 2021.12; 39(34); 3789-3799
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- 8. Okuno Keisuke, Tokunaga Masanori, Yamashita Yamato, Umebayashi Yuya, Saito Toshifumi, Fukuyo Ryosuke, Sato Yuya, Saito Katsumasa, Fujiwara Naoto, Hoshino Akihiro, Kawada Kenro, Matsuyama Takatoshi, Kinugasa Yusuke. Impact of Preoperative Time Interval on Survival in Patients With Gastric Cancer WORLD JOURNAL OF SURGERY. 2021.09; 45(9); 2860-2867
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- 10. Shunsuke Kasai, Akio Shimoi, Hiroyasu Kagawa, Hitoshi Hino, Shoichi Manabe, Yusuke Yamaoka, Kai Chen, Kenji Nanishi, Yusuke Kinugasa. The effectiveness of machine learning in predicting lateral lymph node metastasis from lower rectal cancer: A single center development and validation study Annals of Gastroenterological Surgery. 2021.09; 6(1); 92-100
- 11. Shuji Saito, Tomonori Akagi, Hiroshi Katayama, Masashi Wakabayashi, Masafumi Inomata, Seiichiro Yamamoto, Masaaki Ito, Yusuke Kinugasa, Hiroyuki Egi, Yasuhiro Munakata, Yukihito, Kokuba, Hiroyuki Bando, Masayoshi Yasui, Masataka Ikeda, Kentaro Nakajima, Dai Shida, Yukihide Kanemitsu, Seigo

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- 13. Yudai Kawamura, Kenro Kawada, Takashi Ito, Katsumasa Saito, Naoto Fujiwara, Takuya Okada, Akihiro Hoshino, Yutaka Tokairin, Yasuaki Nakajima, Tatsuyuki Kawano, Masanori Tokunaga, Yusuke Kinugasa. Histological changes in the human esophagus following triamcinolone injection to prevent esophageal stricture after endoscopic submucosal dissection Esophagus. 2021.07; 18(3); 594-603
- 14. Katayama Hiroshi, Inomata Masafumi, Mizusawa Junki, Nakamura Kenichi, Watanabe Masahiko, Akagi Tomonori, Yamamoto Seiichiro, Ito Masaaki, Kinugasa Yusuke, Okajima Masazumi, Takemasa Ichiro, Okuda Junji, Shida Dai, Kanemitsu Yukihide, Kitano Seigo. Institutional variation in survival and morbidity in laparoscopic surgery for colon cancer: From the data of a randomized controlled trial comparing open and laparoscopic surgery (JCOG0404) ANNALS OF GASTROENTEROLOGICAL SURGERY. 2021.07; 5(6); 823-831
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- 16. Kentaro Ochiai, Kazushige Kawai, Hiroaki Nozawa, Kazuhito Sasaki, Manabu Kaneko, Koji Murono, Shigenobu Emoto, Hiroaki Ishii, Hirofumi Sonoda, Shinichi Yamauchi, Kenichi Sugihara, Soichiro Ishihara. Prognostic Impact and Clinicopathological Features of Multiple Colorectal Cancers and Extracolorectal Malignancies: A Nationwide Retrospective Study Digestion. 2021.07; 102(6); 911-920
- 17. Hiroaki Inoue, Kazuhito Sasaki, Hiroaki Nozawa, Kazushige Kawai, Koji Murono, Shigenobu Emoto, Yuuki Iida, Hiroaki Ishii, Yuichiro Yokoyama, Hiroyuki Anzai, Hirofumi Sonoda, Kousuke Ozaki, Shinichi Yamauchi, Kenichi Sugihara, Soichiro Ishihara. Therapeutic significance of D3 dissection for low rectal cancer: a comparison of dissections between the lateral pelvic lymph nodes and the lymph nodes along the root of the inferior mesenteric artery in a multicenter retrospective cohort study International journal of colorectal disease. 2021.06; 36(6); 1263-1270
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- 25. Akihiro Hoshino, Masanori Tokunaga, Yusuke Kinugasa. Totally Laparoscopic Transhiatal Middle and Lower Mediastinal Lymphadenectomy for Esophageal Cancer Surgical laparoscopy, endoscopy & percutaneous techniques. 2021.06; 31(6); 808-811
- 26. Yutaka Tokairin, Kagami Nagai, Yudai Kawamura, Yasuaki Nakajima, Kenro Kawada, Akihiro Hoshino, Takuya Okada, Satoru Muro, Keiichi Akita, Yusuke Kinugasa. Correction to: Histological study of the thin membranous dense connective tissue around the middle and lower thoracic esophagus, caudal to the bifurcation of the trachea. Gen Thorac Cardiovasc Surg. 2021.05; 69(5); 910
- 27. Yuka Ahiko, Dai Shida, Yozo Kudose, Yuya Nakamura, Konosuke Moritani, Shinichi Yamauchi, Kenichi Sugihara, Yukihide Kanemitsu, Japanese Study Group for Postoperative Follow-up of Colorectal Cancer. Recurrence hazard of rectal cancer compared with colon cancer by adjuvant chemotherapy status: a nationwide study in Japan Journal of gastroenterology. 2021.04; 56(4); 371-381
- 28. Shin-Ei Kudo, Katsuro Ichimasa, Benjamin Villard, Yuichi Mori, Masashi Misawa, Shoichi Saito, Kinichi Hotta, Yutaka Saito, Takahisa Matsuda, Kazutaka Yamada, Toshifumi Mitani, Kazuo Ohtsuka, Akiko Chino, Daisuke Ide, Kenichiro Imai, Yoshihiro Kishida, Keiko Nakamura, Yasumitsu Saiki, Masafumi Tanaka, Shu Hoteya, Satoshi Yamashita, Yusuke Kinugasa, Masayoshi Fukuda, Toyoki Kudo, Hideyuki Miyachi, Fumio Ishida, Hayato Itoh, Masahiro Oda, Kensaku Mori. Artificial Intelligence System to Determine Risk of T1 Colorectal Cancer Metastasis to Lymph Node Gastroenterology. 2021.03; 160(4); 1075-1084
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- 30. Kawada Kenro, Matsui Toshihiro, Yamaguchi Kazuya, Shinohara Gen, Hoshino Akihiro, Tokairin Yutaka, Ohno Kazuchika, Kawabe Hiroaki, Sugimoto Taro, Tokunaga Masanori, Nakajima Yasuaki, Kinugasa Yuusuke, Asakage Takahiro. ELPS combined with ESD for treating superficial neoplasm of the pharyngoesophageal junction(和訳中) 日本内視鏡外科学会雑誌. 2021.03; 25(7); DP70-6
- 31. Yamaoka Yusuke, Kagawa Hiroyasu, Shiomi Akio, Yamakawa Yushi, Hino Hitoshi, Manabe Shoichi, Kinugasa Yusuke. Robotic-assisted surgery may be a useful approach to protect urinary function in the modern era of diverse surgical approaches for rectal cancer SURGICAL ENDOSCOPY AND OTHER INTERVENTIONAL TECHNIQUES. 2021.03; 35(3); 1317-1323
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- 33. Masanori Tokunaga, Yukinori Kurokawa, Ryunosuke Machida, Yuya Sato, Shuji Takiguchi, Yuichiro Doki, Hiroshi Yabusaki, Masaya Watanabe, Shinji Hato, Mikihito Nakamori, Seiji Ito, Takaki Yoshikawa, Masanori Terashima . Impact of postoperative complications on survival outcomes in patients with gastric cancer: exploratory analysis of a randomized controlled JCOG1001 trial Gastric Cancer. 2021.01; 24(1); 214-223

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- 35. Shoko Ono, Kenro Kawada, Osamu Dohi, Shinji Kitamura, Tomoyuki Koike, Shinichiro Hori, Hiromitsu Kanzaki, Takahisa Murao, Nobuaki Yagi, Fumisato Sasaki, Keiichi Hashiguchi, Shiro Oka, Kazuhiro Katada, Ryo Shimoda, Kazuhiro Mizukami, Mitsuhiko Suehiro, Toshihisa Takeuchi, Shinichi Katsuki, Momoko Tsuda, Yuji Naito, Tatsuyuki Kawano, Ken Haruma, Hideki Ishikawa, Keita Mori, Mototsugu Kato . Linked Color Imaging Focused on Neoplasm Detection in the Upper Gastrointestinal Tract : A Randomized Trial Annals of internal medicine. 2021.01; 17(1); 18-24
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- 37. Shunsuke Kasai, Hiroyasu Kagawa, Akio Shiomi, Hitoshi Hino, Shoichi Manabe, Yusuke Yamaoka, Shunichiro Kato, Marie Hanaoka, Yusuke Kinugasa . Advantages of robotic abdominoperineal resection compared with laparoscopic surgery: a single-center retrospective study Surgery today. 2021; Online ahead of print;
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- 1. Yasuaki Nakajima, Kazuo Ogiya, Sadao Takahashi, Katsumasa Saito, Naoto Fujiwara, Takuya Okada, Akihiro Hoshino, Kenro Kawada. Larynx-preserving cervical esophagectomy using the "larynx rotation method". 第75回日本食道学会学術集会 2021.09.23 Tokyo
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- 7. Yutaka Tokairin, Akihiro Hoshino, Kagami Nagai, Yusuke Kinugasa. The usefulness of mediastinoscopic esophagectomy under pneumomediastinum for high-risk patients. The 33rd Annual Meeting of the Japanese Society for Endoscopic Surgery 2021.03.12 WEB

- 8. Yuriko Matsumiya, Akifumi Kikuchi, Yasuko Aoyagi, Yudai Yamamoto, Ayumi Takaoka, Hironobu Baba, Shinichi Yamauchi, Takatoshi Matsuyama, Masanori Tokunaga, Yusuke Kinugasa. The safety robotic-assisted laparoscopic surgery for rectal cancer in elderly patients. The 33rd Annual Meeting of the Japanese Society for Endoscopic Surgery 2021.03.10 WEB
- 9. Yudai Yamamoto, Shinichi Yamauchi, Yasuko Aoyagi, Ayumi Takaoka, Yuriko Matsumiya, Hironobu Baba, Akihiro Kikuchi, Takatoshi Matsuyama, Masanori Tokunaga, Yusuke Kinugasa. Short term outcomes of robotic-assisted abdominoperineal resection in our hospital. The 33rd Annual Meeting of the Japanese Society for Endoscopic Surgery 2021.03.10 WEB
- 10. Hajime Shinohara, Akihiro Hoshino, Kazuya Yamaguchi, Takahiro Matsui, Yutaka Tokairin, Kenro Kawada, Takatoshi Matsuyama, Masanori Tokunaga, Yasuaki Nakajima, Yusuke Kinugasa. A case of Behcet's disease manifested and treated after robot-assisted subtotal esophagectomy. The 33rd Annual Meeting of the Japanese Society for Endoscopic Surgery 2021.03.10 WEB
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- 12. Akihoro Hoshino, Kazuya Yamaguchi, Toshihiro Matsui, Yutaka Tokairin, Takatoshi Matsuyama, Kenro Kawada, Masanori Tokunaga, Yasuaki Nakajima, Yusuke Kinugasa. The clinical pathway to initiate early oral ingestion in thoracoscopic esophagectomy. 2021.03.10 WEB
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- 14. Masanori Tokunaga. Diffuse Type Gastric Cancer. The CCMW Global Outreach Initiative: SSAT Clinical Case Management Webinar 2021.02.19 WEB
- 15. Yusuke Kinugasa. Laparoscopic right-sided hemicolectomy with D3 lymph node dissection. Russian Society of Colorectal Surgeons 2021.02.12 WEB
- 16. 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 Hospital assistant professor Ryo Wakejima Hospital assistant professor Katsutoshi Seto Hospital assistant professor Syunichi Baba Graduate Student Akiko Sugawara Graduate Student Ayaka Asakawa Graduate Student Yuya Ishikawa Graduate Student Mariko Hanafusa Graduate Student Yasuyuki Kurihara Graduate Student Yusuke Sugita Graduate Student Hirotomo Takahara

(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
- \cdot Surgery for metastatic lung tumors
- \cdot 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, 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. Shunichi Baba, Takumi Akashi, Kou Kayamori, Tomoyuki Ohuchi, Ikuko Ogawa, Nobuhisa Kubota, Keisuke Nakano, Hitoshi Nagatsuka, Hiromasa Hasegawa, Kenichi Matsuzaka, Shohei Tomii, Keisuke Uchida, Noriko Katsuta, Takahiro Sekiya, Noboru Ando, Keiko Miura, Hironori Ishibashi, Yousuke Ariizumi, Takahiro Asakage, Yasuyuki Michi, Hiroyuki Harada, Kei Sakamoto, Yoshinobu Eishi, Kenichi Okubo, Tohru Ikeda. Homeobox transcription factor engrailed homeobox 1 is a possible diagnostic marker for adenoid cystic carcinoma and polymorphous adenocarcinoma Pathology International. 2021.02; 71(2); 113-123
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- Mariko Hanafusa, Jin Kuramochi, Katsutoshi Ishihara, Makiko Honda, Nobutoshi Nawa, Takeo Fujiwara. Clinical Characteristics of Patients with SARS-CoV-2 N501Y Variants in General Practitioner Clinic in Japan Journal of Clinical Medicine [Accepted: 8 December 2021]. 2021.12;

[Others]

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- 2. A rare case of thymoma with entire-tumor calcification, 2021.04 Journal of Surgical Case Reports. Vol.2021(4):1-3.April 2021.Ayaka Asakawa, Hironori Ishibashi, Masashi Kobayashi, Toshizumi Shirai and Kenichi Okubo
- 3. Successful excision of a giant subcarinal bronchogenic cyst by video assisted thoracoscopic surgery, 2021.10 General Thoracic and Cardiovascular Surgery. Accepted:22 October 2021. Hironori Ishibashi, Airi Kato, Yusuke Sugita, Yasuhiro Nakashima, Katsutoshi Seto, Ryo Wakejima, Kenichi Okubo

Igakuken Disease-oriented Molecular Biology

Visiting Professor Takahiko Hara Visiting Professor Makoto Arai Visiting Professor Masato Hasegawa Associate Visiting Professor Takashi Shichita Associate Visiting Professor Yuichiro Mitaoka Graduate Student Mai Asakura, Akari Nakamura, Satoko Takagi, Kyoka Iino, Daiki Kondo, Ittetsu Nakajima, Risa Saito (April~), Minako Shingai (April~), Shiho Sasaki (April~), Terumi Ono (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.
- [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, stroke, and genetic disorders. 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]

- R. Iwase, N. Naruse, M. Nakagawa, R. Saito, A. Shigenaga, A. Otaka, T. Hara*, and K. Tanegashima*. Identification of functional domains of CXCL14 involved in high-affinity binding and intracellular transport of CpG DNA. *J. Immunol.*, 207: 459-469, 2021. *Co-corresponding author.
- T. Suzuki, E. Katada, Y. Mizuoka, S. Takagi, Y. Kazuki, M. Oshimura, M. Shindo, and T. Hara. A novel all-in-one conditional knockout system uncovered an essential role of DDX1 in ribosomal RNA processing. *Nucl. Acid Res.*, 49: e40, 2021.
- 3. C. Yoshida, T. Higashi, Y. Hachiro, Y. Fujita, T. Yagi, A. Takechi, C. Nakata, K. Miyashita, N. Kitada, R. Saito, R. Obata, T. Hirano, T. Hara, and S. A. Maki. Synthesis of polyenylpyrrole derivatives with selective growth inhibitory activity against T-cell acute lymphoblastic leukemia cells. *Bioorg. Med. Chem. Lett.*, 30: 127837, 2021.
- 4. K. Iino, K. Toriumi, R. Agarie, M. Miyashita, K. Suzuki, Y. Horiuchi, K. Niizato, K. Oshima, A. Imai, Y. Nagase, I. Kushima, S. Koike, T. Ikegame, S. Jinde, E. Nagata, S.

Washizuka, T. Miyata, S. Takizawa, R. Hashimoto, K. Kasai, N. Ozaki, M. Itokawa, and M. Arai. AKR1A1 Variant Associated With Schizophrenia Causes Exon Skipping, Leading to Loss of Enzymatic Activity. *Front Genet.*, 12: 762999, 2021.

- 5. S. Hirai, H. Miwa, T. Tanaka, K. Toriumi, Y. Kunii, H. Shimbo, T. Sakamoto, M. Hino, R. I. Nohara, A. Nagaoka, H. Yabe, T. Nakamachi, S. Shioda, T. Dan, T. Miyata, Y. Nishito, K. Suzuki, M. Miyashita, T. Tomoda, T. Hikida, J. Horiuchi, M. Itokawa, M. Arai, and H. Okado. High-sucrose diets contribute to brain angiopathy with impaired glucose uptake and psychosis-related higher brain dysfunctions in mice. *Sci. Adv.*, 7: eabl6077, 2021.
- 6. M. Miyashita, S. Yamasaki, S. Ando, K. Suzuki, K. Toriumi, Y. Horiuchi, A. Yoshikawa, A. Imai, Y. Nagase, Y. Miyano, T. Inoue, K. Endo, Y. Morimoto, M. Morita, T. Kiyono, S. Usami, Y. Okazaki, A. Furukawa, M. Hiraiwa-Hasegawa, M. Itokawa, K. Kasai, A. Nishida, and M. Arai. Fingertip advanced glycation end products and psychotic symptoms among adolescents. *NPJ Schizophr.*, 7: 37, 2021.
- K. Toriumi, S. Berto, S. Koike, N. Usui, T. Dan, K. Suzuki, M. Miyashita, Y. Horiuchi, A. Yoshikawa, M. Asakura, K. Nagahama, HC. Lin, Y. Sugaya, T. Watanabe, M. Kano, Y. Ogasawara, T. Miyata, M. Itokawa, G. Konopka, and M. Arai. Combined glyoxalase 1 dysfunction and vitamin B6 deficiency in a schizophrenia model system causes mitochondrial dysfunction in the prefrontal cortex. *Redox Biol.*, 45: 102057, 2021.
- 8. R. Saiga, M. Uesugi, A. Takeuchi, K. Uesugi, Y. Suzuki, S. Takekoshi, C. Inomoto, N. Nakamura, Y. Torii, I. Kushima, S. Iritani, N. Ozaki, K. Oshima, M. Itokawa, M. Arai, and R. Mizutani. Brain capillary structures of schizophrenia cases and controls show a correlation with their neuron structures. *Sci. Rep.*, 11: 11768, 2021.
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- A. Kobori, M. Miyashita, Y. Miyano, K. Suzuki, K. Toriumi, K. Niizato, K. Oshima, A. Imai, Y. Nagase, A. Yoshikawa, Y. Horiuchi, S. Yamasaki, A. Nishida, S. Usami, S. Takizawa, M. Itokawa, H. Arai, and M. Arai. Advanced glycation end products and cognitive impairment in schizophrenia. *PLoS ONE*, 16: e0251283, 2021.
- K. Toriumi, M. Miyashita, K. Suzuki, N. Yamasaki, M. Yasumura, Y. Horiuchi, A. Yoshikawa, M. Asakura, N. Usui, M. Itokawa, and M. Arai. Vitamin B6 deficiency hyperactivates the noradrenergic system, leading to social deficits and cognitive impairment. *Transl. Psychiatry*, 11: 262, 2021.

- R. Mizutani, R. Saiga, Y. Yamamoto, M. Uesugi, A. Takeuchi, K. Uesugi, Y. Terada, Y. Suzuki, V. De Andrade, F. De Carlo, S. Takekoshi, C. Inomoto, N. Nakamura, Y. Torii, I. Kushima, S. Iritani, N. Ozaki, K. Oshima, M. Itokawa, and M. Arai. Structural diverseness of neurons between brain areas and between cases. *Transl. Psychiatry*, 11: 49, 2021.
- Y. Shi, W. Zhang, Y. Yang, A. Murzin, B. Falcon, A. Kotecha, M. van Beers, A. Tarutani, F. Kametani, H. Garringer, R. Vidal, G. Hallinan, T. Lashley, Y. Saito, S. Murayama, M. Yoshida, H. Tanaka, A. Kakita, T. Ikeuchi, A. Robinson, D. Mann, G. Kovacs, T. Revesz, B. Ghetti, M. Hasegawa, M. Goedert, and S. Scheres. Structure-based classification of tauopathies, *Nature*, 598: 359-363, 2021.
- 14. A. Tarutani, H. Miyata, T. Nonaka, K. Hasegawa, M. Yoshida, Y. Saito, S. Murayama, A.C. Robinson, D.M.A. Mann, T. Tomita, and M. Hasegawa. Human tauopathy-derived tau strains determine the substrates recruited for templated amplification. *Brain*, awab091, 2021.
- K. Nakamura, S. Sakai, J. Tsuyama, A. Nakamura, K. Otani, K. Kurabayashi, Y. Yogiashi, H. Masai, and T. Shichita. Extracellular DJ-1 induces sterile inflammation in the ischemic brain. *PLoS Biol.*, 19: e3000939, 2021.
- C. Nakahashi-Oda, S. Fujiyama, Y. Nakazawa, K. Kanemaru, Y. Wang, W. Lyu, T. Shichita, J. Kitaura, F. Abe, and A. Shibuya A. CD300a blockade enhances efferocytosis by infiltrating myeloid cells and ameliorates neuronal deficit after ischemic stroke. *Sci. Immunol.*, 6: eabe7915, 2021.
- A. M. Fenix*, Y. <u>Miyaoka</u>*, A. Bertero, S. M. Blue, M. J. Spindler, K. K. B. Tan, J. A. Perez-Bermejo, A. H. Chan, S. J. Mayerl, T. D. Nguyen, C. R. Russell, P. P. Lizarraga, A. Truong, P. L. So, A. Kulkarni, K. Chetal, S. Sathe, N. J. Sniadecki, G. W. Yeo, C. E. Murry, B. R. Conklin, and N. Salomonis. Gain-of-function cardiomyopathic mutations in RBM20 rewire splicing regulation and re-distribute ribonucleoprotein granules within processing bodies. *Nat. Commun.*, 12: 6324, 2021. *Co-first authors.

[Review Articles]

[Books]

[Conference Activities & Talks]

1. M Arai. Schizophrenia and Glycation. 14th Triennial Conference of the International Millard Reaction Society, 2021.9.23, On line.

Clinical Anatomy

Professor : Keiichi AKITA Professor : Akimoto NIMURA (Department of Functional Joint Anatomy) Junior Associate Professor : Kumiko YAMAGUCHI (Institute of Education Curricular Management Division) Junior Associate Professor : Kouji FUJITA(Department of Functional Joint Anatomy) Junior Associate Professor (Career Track) : Masayo HARADA Assistant Professor : Satoru MURO Assistant Professor : Takuya IBARA (Department of Functional Joint Anatomy) (April \sim) Research Technician : Rintaro YAMAMOTO (April \sim) Staff Assistant : Kaoru SUZUKI (\sim March), Mayuri IKEDA (April \sim) Parttime Lecturer : Kenji IBUKURO, Itsuko OKUDA, Sachiyuki TSUKADA, Masataka NAKAZAWA, Kaoru KITSUKAWA, Tomoyuki YANO, Kenro CHIKAZAWA, Shirou SUZUKI, Masahiro TSUTSUMI Graduate Student : Eiichirou KAGAWA (~ March), Kohtaro EGUCHI (~ March), Saya HORIUCHI (\sim March), Yusuke UEDA (\sim March), Souichi HATTORI (\sim March), Koh MIWA (\sim March), Haruka EISHI (\sim March), Wachirawit SIRIRAT (\sim March), Syuusaku HOSONO, Shouko MOUE, Ming Yan HE, Areeva JIAMJUNYASIRI, Atsuhiro FUKAI, Tharnmanularp SUTHASINEE, Ryo KARAKAWA, Hidehiko YOSHIMATSU, Georgina Isabella DJAMEH (October \sim) Research student : Tong LIU (April \sim), Tomo SUGIMOTO (April \sim)

(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. Itsuko Okuda, Minoru Yamada, Yoshitake Yamada, Yoichi Yokoyama, Natnicha Kampan, Keiichi Akita, Masahiro Jinzaki. Anatomic and diagnostic considerations of facial mobility for understanding the effectiveness of facial massage: A pilot study. Skin Res Technol. 2021.11; 27(6); 1057-1063
- 2. Masahiro Tsutsumi, Akimoto Nimura, Hajime Utsunomiya, Keiichi Akita. Dynamic changes of the joint capsule in relation to the zona orbicularis: An anatomical study with possible implications for hip stability mechanism. Clin Anat. 2021.11; 34(8); 1157-1164
- 3. Kenro Chikazawa, Satoru Muro, Keiichi Akita, Ken Imai, Tomoyuki Kuwata, Ryo Konno. En bloc pelvic lymphadenectomy with the vesicohypogastric fascia serving as a medial border: An approach with ten standardized steps. Eur J Obstet Gynecol Reprod Biol. 2021.11; 266; 7-8
- 4. Takafumi Koyama, Koji Fujita, Hirotaka Iijima, Mio Norose, Takuya Ibara, Toru Sasaki, Toshitaka Yoshii, Akimoto Nimura, Masaki Takahashi, Atsushi Okawa. Analysis of Spastic Gait in Patients With Cervical Myelopathy Using the Timed Up and Go Test With a Laser Range Sensor. Spine (Phila Pa 1976). 2021.11;
- 5. Masahiro Tsutsumi, Akimoto Nimura, Hajime Utsunomiya, Shintarou Kudo, Keiichi Akita. Spatial distribution of loose connective tissues on the anterior hip joint capsule: a combination of cadaveric and in-vivo study. Sci Rep. 2021.11; 11(1); 22813
- 6. Sukwoo Hong, Toshikazu Kimura, Tomoyuki Yano, Hirotaka Hasegawa, Shunsuke Ichi. Totally Endoscopic Resection of Recurrent Convexity Meningioma Following Multiple Surgeries: Oblique Trajectory to Avoid Manipulation of a Vascularized Free Flap: A Technical Note. World Neurosurg. 2021.11; 158; 152-155
- 7. Yuma Fuse, Hidehiko Yoshimatsu, Ryo Karakawa, Tomoyuki Yano. Pedicled anterolateral thigh flap transfer for the reconstruction of a large gluteal defect assisted by preoperative computed tomographic angiography and intraoperative indocyanine green angiography: A case report. Microsurgery. 2021.11; 41(8); 777-781

- 8. Tomoyuki Yano, Ryo Karakawa, Tomoyoshi Shibata, Yuma Fuse, Akiyo Suzuki, Yukiko Kuramoto, Nobuko Suesada, Hiroki Miyashita, Hidehiko Yoshimatsu. Ideal esthetic and functional full-thickness lower eyelid "like with like" reconstruction using a combined Hughes flap and swing skin flap technique. J Plast Reconstr Aesthet Surg. 2021.11; 74(11); 3015-3021
- Hidehiko Yoshimatsu, Ryo Karakawa, Yuma Fuse, Akira Okada, Akitatsu Hayashi, Tomoyuki Yano. Use of Preoperative High-Resolution Ultrasound System to Facilitate Elevation of the Superficial Circumflex Iliac Artery Perforator Flap. J Reconstr Microsurg. 2021.11; 37(9); 735-743
- 10. Masahiro Tsutsumi, Akimoto Nimura, Keiichi Akita. Clinical anatomy of the musculoskeletal system in the hip region. Anat Sci Int. 2021.10; 97(2); 157-164
- Yuki Tsuruta, Tomoyuki Yano, Yukiko Kuramoto, Nobuko Suesada, Yuma Fuse, Ryo Karakawa, Hidehiko Yoshimatsu, Kenta Tanakura, Hiroki Miyashita. Breast Shape Evaluation After Free Flap Breast Reconstruction After More Than 10 Years Follow-up Using 3-Dimensional Imaging Device. Ann Plast Surg. 2021.10;
- Ryo Karakawa, Tomoyuki Yano, Hidehiko Yoshimatsu, Mayu Koto, Atsushi Nakao, Shunsuke Ichi. Use of Ultra-high-frequency Ultrasound for Aplasia Cutis Congenita of the Scalp. Plast Reconstr Surg Glob Open. 2021.10; 9(10); e3876
- 13. Ryo Karakawa, Tomoyuki Yano, Hidehiko Yoshimatsu. Use of the wearable smart glasses for intraoperative indocyanine green (ICG) lymphography of a lymphatic surgery. Microsurgery. 2021.10; 41(7); 697-698
- 14. Airi Kugisaki, Toshikazu Kimura, Tomoyuki Yano, Shunsuke Ichi. Reconstruction of the temporal line for sinking skin flap syndrome using split rib grafts: a technical note. Br J Neurosurg. 2021.09; 1-3
- 15. Chihena H Banda, Mitsunaga Narushima, Kohei Mitsui, Kanako Danno, Minami Fujita, Megumi Furuya, Ryo Karakawa, Shinya Ogishima, Ryohei Ishiura. Donor site morbidity of postauricular free flaps and full thickness skin grafts. J Plast Reconstr Aesthet Surg. 2021.09; 74(9); 2392-2442
- 16. Hidehiko Yoshimatsu, Ryo Karakawa, Mario F Scaglioni, Yuma Fuse, Kenta Tanakura, Tomoyuki Yano. Application of intraoperative indocyanine green angiography for detecting flap congestion in the use of free deep inferior epigastric perforator flaps for breast reconstruction. Microsurgery. 2021.09; 41(6); 522-526
- Kohtaro Eguchi, Kenya Kobayashi, Tomonari Takano, Akiko Ito, Azusa Sakai, Atsuo Ikeda, Yoshifumi Matsumoto, Go Omura, Fumihiko Matsumoto, Seiichi Yoshimoto. Carotid artery ligation via sternotomy as a palliative surgery: Case report of advanced intramediastinal malignant soft tissue tumor. Clin Case Rep. 2021.08; 9(8);
- Satoru Muro, Janyaruk Suriyut, Keiichi Akita. Anatomy of Cowper's gland in humans suggesting a secretion and emission mechanism facilitated by cooperation of striated and smooth muscles. Sci Rep. 2021.08; 11(1); 16705
- Yuma Fuse, Hidehiko Yoshimatsu, Ryo Karakawa, Tomoyuki Yano. Novel Classification of the Branching Patterns of the Superficial Branch and the Deep Branch of the Superficial Circumflex Iliac Artery and the Superficial Inferior Epigastric Artery on Computed Tomographic Angiography. J Reconstr Microsurg. 2021.08;
- 20. Natsumi Saka, Akimoto Nimura, Masahiro Tsutsumi, Taiki Nozaki, Yoshinobu Watanabe, Keiichi Akita. Anatomic study of fibrous structures attached to the volar ulnar corner of the radius: implications in the volar rim fracture. J Hand Surg Eur Vol. 2021.07; 46(6); 637-646
- 21. Keiko Fukino, Masahiro Tsutsumi, Akimoto Nimura, Koh Miwa, Takashi Ono, Keiichi Akita. Reply to "Palatopharyngeus muscle in pharyngoplasty surgery for OSAS: cut or not to cut?" Eur Arch Otorhinolaryngol. 2021.07; 278(7); 2659-2660
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- 23. Eiichiro Kagawa, Akimoto Nimura, Hisayo Nasu, Ryuichi Kato, Keiichi Akita. Fibrous Connection Between Cervical Nerve and Zygapophysial Joint and Implication of the Cervical Spondylotic Radiculopathy: An Anatomic Cadaveric Study. Spine (Phila Pa 1976). 2021.07; 46(13); E704-E709

- 24. Tokairin Y, Nagai K, Kawamura Y, Nakajima Y, Kawada K, Hoshino A, Okada T, Muro S, Akita K, Kinugasa Y. Histological study of the thin membranous dense connective tissue around the middle and lower thoracic esophagus, caudal to the bifurcation of the trachea. General thoracic and cardiovascular surgery. 2021.06; 69(6); 983-992
- 25. Satoru Muro, Wachirawit Sirirat, Daisuke Ban, Yuichi Nagakawa, Keiichi Akita. What comprises the plate-like structure between the pancreatic head and the celiac trunk and superior mesenteric artery? A proposal for the term "P-A ligament" based on anatomical findings. Anat Sci Int. 2021.06; 96(3); 370-377
- 26. Ibara T, Takahashi M, Shinkoda K, Kawashima M, Anan M. Hip Sway in Patients With Hip Osteoarthritis During One-Leg Standing With a Focus on Time Series Data. Motor control. 2021.06; 25(3); 502-518
- 27. Rintaro Yamamoto, Mizuki Izumida, Tohma Sakuraya, Kenji Emura, Takamitsu Arakawa. The ulnar nerve is surrounded by the tendon expansion of the flexor carpi ulnaris muscle at the wrist: an anatomical study of Guyon's canal. Anat Sci Int. 2021.06; 96(3); 422-426
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- 29. Atsuhiro Tano, Akimoto Nimura, Masahiro Tsutsumi, Reiko Yamaguchi, Atsushi Okawa, Keiichi Akita. Anatomical Study of the Interosseous Ligament of the Tibiofibular Syndesmosis: An Analysis of Osseous Morphology and Attaching Interposing Structures. J Bone Joint Surg Am. 2021.05; 103(10); 905-912
- 30. Yutaka Tokairin, Kagami Nagai, Yudai Kawamura, Yasuaki Nakajima, Kenro Kawada, Akihiro Hoshino, Takuya Okada, Satoru Muro, Keiichi Akita, Yusuke Kinugasa. Correction to: Histological study of the thin membranous dense connective tissue around the middle and lower thoracic esophagus, caudal to the bifurcation of the trachea. Gen Thorac Cardiovasc Surg. 2021.05; 69(5); 910
- 31. Kamo M, Nozaki T, Horiuchi S, Muraishi N, Yamamura J, Akita K. There are no three physiological narrowings in the upper urinary tract: a new concept of the retroperitoneal anatomy around the ureter. Japanese journal of radiology. 2021.05; 39(5); 407-413
- 32. Yasuhito Iwao, Daisuke Ban, Satoru Muro, Atsushi Kudo, Shinji Tanaka, Krishna Menon, Minoru Tanabe. Extraordinary first jejunal arterial variation associated with annular pancreas undergoing pancreaticoduodenectomy for pancreatic cancer: a case report. Surg Radiol Anat. 2021.05; 43(5); 805-810
- 33. Tomoyuki Yano, Hidehiko Yoshimatsu, Ryo Karakawa, Yuma Fuse, Yukiko Kuramoto, Tomoyoshi Shibata, Nobuko Suesada, Hiroki Miyashita. Use of a combined SIEA and SCIP based double pedicled abdominal flap for breast reconstruction. Microsurgery. 2021.05; 41(4); 319-326
- 34. Sasin Sritara, Masahiro Tsutsumi, Keiko Fukino, Yoshiro Matsumoto, Takashi Ono, Keiichi Akita. Evaluating the morphological features of the lateral pterygoid insertion into the medial surface of the condylar process. Clinical and Experimental Dental Research. 2021.04; 7(2); 219-225
- 35. Keiko Fukino, Masahiro Tsutsumi, Akimoto Nimura, Koh Miwa, Takashi Ono, Keiichi Akita. Anatomy of inferior end of palatopharyngeus: its contribution to upper esophageal sphincter opening. Eur Arch Otorhinolaryngol. 2021.03; 278(3); 749-754
- 36. Muro S, Tsukada Y, Ito M, Akita K. The series of smooth muscle structures in the pelvic floors of men: Dynamic coordination of smooth and skeletal muscles. Clinical anatomy (New York, N.Y.). 2021.03; 34(2); 272-282
- 37. Hidehiko Yoshimatsu, Ryo Karakawa, Yuma Fuse, Kenta Tanakura, Takumi Yamamoto, Akira Okada, Bassem W Daniel, Tomoyuki Yano. Use of the superficial circumflex iliac artery perforator flap for reconstruction after sarcoma resection. J Surg Oncol. 2021.03; 123(4); 1067-1080
- 38. Kenro Chikazawa, Ken Imai, Takaki Ito, Shigenori Hayashi, Tomoyuki Kuwata, Ryo Konno. Delayed Ureteral Leak Related to Use of Suspension Tapes during Laparoscopic Radical Hysterectomy. J Minim Invasive Gynecol. 2021.02; 28(2); 164-165
- Okuda I, Akita K, Komemushi T, Irimoto M, Nakajima Y. Basic Consideration for Facial Aging: Analyses of the Superficial Musculoaponeurotic System Based on Anatomy. Aesthetic surgery journal. 2021.02; 41(3); NP113-NP123

- 40. Miho Saiga, Yuko Hosoya, Hiroki Utsunomiya, Yukiko Kuramoto, Satoko Watanabe, Koichi Tomita, Yukiko Aihara, Mayu Muto, Makoto Hikosaka, Takashi Kawaguchi, Tempei Miyaji, Takuhiro Yamaguchi, Sadamoto Zenda, Aya Goto, Minoru Sakuraba, Taro Kusano, Kenta Miyabe, Tomoaki Kuroki, Tomoyuki Yano, Mifue Taminato, Mitsuru Sekido, Yui Tsunoda, Toshihiko Satake, Hiroyoshi Doihara, Yoshihiro Kimata. Protocol for a multicentre, prospective, cohort study to investigate patient satisfaction and quality of life after immediate breast reconstruction in Japan: the SAQLA study. BMJ Open. 2021.02; 11(2); e042099
- 41. Ryo Karakawa, Hidehiko Yoshimatsu, Kenta Tanakura, Tomohiro Imai, Tomoyuki Yano, Masayuki Sawaizumi. Triple-lobe combined latissimus dorsi and scapular flap for reconstruction of a large defect after sarcoma resection. Microsurgery. 2021.01; 41(1); 26-33
- 42. Hiromitsu Hiruma, Kaoru Kitsukawa, Yukihisa Ogawa, Hidefumi Mimura. Venous malformation of the foot: Spontaneous regression postpartum on MRI. Radiol Case Rep. 2021.01; 16(1); 62-65
- 43. Yusuke Ueda, Akimoto Nimura, Keisuke Matsuki, Kumiko Yamaguchi, Hiroyuki Sugaya, Keiichi Akita. Morphology of the Undersurface of the Anterolateral Acromion and Its Relationship to Surrounding Structures. Orthop J Sports Med. 2021.01; 9(1); 2325967120977485
- 44. Ken Imai, Kenro Chikazawa, Takaki Ito, Azusa Kimura, Hiroyoshi Ko, Yokota Miho, Tomoyuki Kuwata, Ryo Konno. Assessing the Effectiveness of a Weight Reduction Program in Hospitalized Obese Patients Undergoing Laparoscopic Surgery. Gynecol Minim Invasive Ther. 2021.01; 10(1); 44-46

[Misc]

1. Ochi J, Nozaki T, Nimura A, Yamaguchi T, Kitamura N. Subchondral insufficiency fracture of the knee: review of current concepts and radiological differential diagnoses. Jpn J Radiol. 2021.11;

[Conference Activities & Talks]

- 1. Ryo Karakawa. Free flap reconstruction for a large defect after sarcoma resection on the posterior trunk. 5th congress of Asian Pacific Federation of Societies for Reconstructive Microsurgery 2021.12.02 Web
- 2. Ryo Karakawa. Functional reconstruction using immediate tendon transfer for a dorsal forearm sarcoma. 5th congress of Asian Pacific Federation of Societies for Reconstructive Microsurgery 2021.12.02 Web
- 3. Kenro Chikazawa. Dissection for douglas pouch closure , mainly by blunt dissection. EDGE EXPERITISE, Complex Endometriosis 2021.11.18 Web
- 4. Suthasinee Tharnmanularp, Akimoto Nimura, Masahiro Tsutsumi, Keiichi Akita. An Anatomical Study Regarding the Medial Patellofemoral Ligament in Terms of Bone Morphology and Attaching Aponeurotic Structures. 16th Congress of the European Association of Clinical Anatomy (EACA) and XII Meeting of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2021.09.16 Web
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- 6. Masahiro Tsutsumi, Akimoto Nimura, Hajime Utsunomiya, Keiichi Akita. Morphological changes of the joint capsule during hip movement in relation to the zona orbicularis. 16th Congress of the European Association of Clinical Anatomy (EACA) and XII Meeting of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2021.09.15 Web
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- 8. Satoru Muro, Janyaruk Suriyut, Keiichi Akita. Anatomical study of striated and smooth muscles surrounding the Cowper's gland. 16th Congress of the European Association of Clinical Anatomy (EACA) and XII Meeting of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2021.09.14 Web

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- 11. Ryo Karakawa. Tips and expanded application of ultra-high frequency US. 3rd Ultrasound Reconstructive Microsurgery 2021.09.11 Web
- 12. Tomoyuki Yano. Our strategy and surgical tips of using the DIEP, PAP and SaS flap for breast reconstruction. The Annual Scientific Meeting Indonesian Association of Plastic Reconstructive and Aesthetic Surgeons 2021.07.04 Web
- Tomoyuki Yano. Surgical tricks and challenges for difficult head and neck reconstruction. The Annual Scientific Meeting Indonesian Association of Plastic Reconstructive and Aesthetic Surgeons 2021.07.04 Web
- 14. Satoru Muro, Sachiyuki Tsukada, Keiichi Akita. Tibial Attachment of Anterior Cruciate Ligament and Relationship with Lateral Meniscus. American Association Clinical Anatomists 38th annual meeting 2021.06.28 Web
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- 16. Tomoyuki Yano. An idea of combined SIEA and SCIA (SaS) double pedicle flap for breast reconstruction. Chinese national oncoplastic surgery course 2021.06.05 Web
- 17. Akimoto Nimura, Saya Horiuchi, Masahiro Tsutsumi, Keiichi Akita. Anatomical study regarding radioulnar ligament attachment to the styloid process of the ulna. 19th ESSKA(European Society of Sports Traumatology, Knee Surgery and Arthroscopy)CONGRESS VIRTUAL 2021.05.11 Web
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- 19. Hirotaka Ishikawa, Mizuki Izumida, Rintaro Yamamoto, Tohma Sakuraya, Kenji Emura, Takamitsu Arakawa. Composition for lower part of thoracolumbar fascia. the 126th Annual Meeting of The Japanese Association of Anatomists and the 98th Annual Meeting of The Physiological Society of Japan 2021.03.30 Web
- 20. Masayo Harada, Keiichi Akita. Mouse Fgf9N143T leads to cartilage widening, resulting in widened long bones. the 126th Annual Meeting of The Japanese Association of Anatomists and the Annual Meeting of The Physiological Society of Japan 2021.03.30 Web
- 21. Satoru Muro, Keiichi Akita. Anatomical study of striated and smooth muscles surrounding the Cowper's gland. the 126th Annual Meeting of The Japanese Association of Anatomists and the 98th Annual Meeting of The Physiological Society of Japan 2021.03.28 Web
- 22. Mingyan He, Satoru Muro, Keiichi Akita. Positional relationship between the lateral border of the Denonvilliers' fascia and pelvic plexus. the 126th Annual Meeting of The Japanese Association of Anatomists and the 98th Annual Meeting of The Physiological Society of Japan 2021.03.28 Web
- 23. Kenro Chikazawa. Nine Steps of En-bloc Pelvic Lymphadenectomy. APGET WEBINAR 2021.03.07 Web
- 24. Tomoyuki Yano. Breast surgery trends in Japan -trends of breast reconstruction-. Global trends in breast surgery 2021.02.24 Web
- 25. Tomoyuki Yano. Asymmetry of breast reconstruction : How to select implant and the essentials of breast reduction on the contralateral breast. Best of SABCS(San Antonio Breast Cancer Symposium) Shenzhen 2021 2021.01.17 Web

Systems BioMedicine

Professor Hiroshi ASAHARA Junior Associate Professor Ryouta KURIMOTO Assistant Professor Tomoki CHIBA, Takahide MATSUSHIMA, Yuta Fujii Postdoctoral fellow Yutaro UCHIDA Graduate Students Hiroki TSUTSUMI, Maiko INOTSUME, Lin LIU, Takayuki MIYAZAKI, Kaho TAKADA, Risa YAGASAKI, Sun Shiwei, Suzu CHIDA, Mari MATSUNAGA, Mayu KOIKE, Risa SANADA, Nao WATANABE

(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.

In research education for undergraduate students, as part of the research practice program, a new research training system was established as the "Meister Training Course," covering basic and applied research from molecular biology to experiments using individual mice, in order to enhance their basic research skills.

(3) Publications

[Original Articles]

- 1. Yoshiaki Ito, Tokio Matsuzaki, Fumiaki Ayabe, Sho Mokuda, Ryota Kurimoto, Takahide Matsushima, Yusuke Tabata, Maiko Inotsume, Hiroki Tsutsumi, Lin Liu, Masahiro Shinohara, Yoko Tanaka, Ryo Nakamichi, Keiichiro Nishida, Martin K Lotz, Hiroshi Asahara. Both microRNA-455-5p and -3p repress hypoxia-inducible factor-2 α expression and coordinately regulate cartilage homeostasis. Nat Commun. 2021.07; 12(1); 4148
- 2. Takayuki Miyazaki, Ryota Kurimoto, Tomoki Chiba, Takahide Matsushima, Ryo Nakamichi, Hiroki Tsutsumi, Kaho Takada, Lisa Yagasaki, Tomomi Kato, Kana Shishido, Yukiho Kobayashi, Tsutomu Matsumoto, Keiji Moriyama, Hiroshi Asahara. Mkx regulates the orthodontic tooth movement via osteoclast induction. J Bone Miner Metab. 2021.05; 39(5); 780-786
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- 5. Keiko Itano, Koji Ochiai, Takahide Matsushima, Hiroshi Asahara and Koichi Takahashi. Automation of Foci-Cell-State Judgement with Regression Models Transactions of the Institute of Systems, Control and Information Engineers. 2021; 34(3); 69-80

[Conference Activities & Talks]

- 1. Lin Liu, Tomoki Chiba, Ryota Kurimoto, Hiroki Tsutsumi, Yuta Fujii, Hiroshi Asahara. Single-cell transcriptome profiles in mouse limb buds . 第7回日本筋学会学術集会 2021.12.11
- 2. Endogenous protein analysis using genome editing technology and HiBiT system. Discover Glo 2021 2021.09.14
- 3. Hiroshi Asahara. Muscle to tendon for physical performance. the 9th Seoul Symposium on Bone Health & the 33rd Spring Scientific Congress of the Korean Society for Bone and Mineral Research (SSBH 2021) 2021.06.04
- 4. Hiroshi Asahara. Tenocytes: gatekeepers of tendon homeostasis. EULAR 2021 2021.06.03
- 5. Yutaro Uchida, Takahide Matsushima, Ryota Kurimoto, Tomoki Chiba, Yuki lnutani, Hiroshi Asahara.. HiBiT tagging system for high throughput chemical screening for chemotherapy. AACR 2021 2021.04.11
- 6. Ryota Kurimoto, Hiroki Tsutsumi, Saki lkeuchi, Hiroshi Asahara. Tumor suppression potential of tRNA modification enzyme TruBs via let-7. AACR 2021 2021.04.10

Comprehensive Pathology

Professor Masanobu KITAGAWA Junior associate Professor Morito KURATA Assistant Professor Kouhei YAMAMOTO, Yuko Kinowaki Lecturer (part-time) Towako TAGUCHI Laboratory Technician Miori INOUE Technical Assistant Sachiko ISHIBASHI, Masumi IKEDA, Graduate Students Ryoko KATO, Keisuke Sugita, Jyunko KUNIEDA, Genji KAWADE, Yuki WATARI, Jyunichiro SATO, Masahiro KAWADA, Noriaki FUKUHARA, Tomohiro YOKOUCHI, Shigeo TODA, Jyunnosuke HAYASAKA, Jyunpei KAWAMURA, Azusa TERAO

(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

In vivo and in vitro using mice as experimental models, immunohistological, virological, biochemical and molecular biological analyzes 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) Clinical Services & Other Works

I the university hospital, surgical materials, biopsy materials, and various organs obtained by pathological dissection are subjected to immunohistological technic in addition to the usual morphological methods.

(6) Clinical Performances

To improve diagnostic accuracy, the methods of molecular pathology are also applied.

(7) Publications

[Original Articles]

 Shotaro Matsudera, Yoshihito Kano, Yasuko Aoyagi, Kohki Tohyama, Kenta Takahashi, Yuichi Kumaki, Takahiro Mitsumura, Koichiro Kimura, Iichiro Onishi, Akira Takemoto, Daisuke Ban, Hiroaki Ono, Atsushi Kudo, Noriko Oshima, Kei Ogino, Shun Watanabe, Yukiko Tani, Takeshi Yamaguchi, Masanobu Nakajima, Shinji Morita, Satoru Yamaguchi, Masatoshi Takagi, Toshiaki Ishikawa, Tsuyoshi Nakagawa, Kentaro Okamoto, Hiroyuki Uetake, Minoru Tanabe, Satoshi Miyake, Takashi Tsuchioka, Kazuyuki Kojima, Sadakatsu Ikeda. A Pilot Study Analyzing the Clinical Utility of Comprehensive Genomic Profiling Using Plasma Cell-Free DNA for Solid Tumor Patients in Japan (PROFILE Study). Ann Surg Oncol. 2021.12; 28(13); 8497-8505

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- 4. Mori M, Kubota K, Fujioka T, Katsuta L, Yashima Y, Nomura K, Yamaga E, Tsuchiya J, Hosoya T, Oda G, Nakagawa T, Onishi I, Tateishi U. Virtual Navigator Real-Time Ultrasound Fusion Imaging with Positron Emission Tomography/Computed Tomography for Preoperative Breast Cancer. Medicina (Kaunas, Lithuania). 2021.11; 57(12);
- 5. Oda Goshi, Nakagawa Tsuyoshi, Uemura Noriko, Mori Hiroki, Mori Mio, Fujioka Tomoyuki, Onishi Iichiroh, Uetake Hiroyuki. Immediate breast reconstruction is oncologically safe for node-positive patients: Comparison using propensity score matching. Medicine (Baltimore). 2021.09; 100(36); e27184
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- 13. Ikeda Sadakatsu, Kudo Ryo, Yamashita Yamato, Noji Rika, Yokobori Jyunko, Ohki Mika, Takamine Eriko, Kobayashi Yumi, Egawa Makiko, Ebana Yusuke, Kimura Koichiro, Yokoyama Kohta, Onishi Iichiro, Takemoto Akira, Kirimura Susumu, Kinowaki Yuko, Tanimoto Kosuke, Miya Fuyuki, Kano Yoshihito, Yoshida Masayuki, Miyake Satoshi. Clinical utility of multi-disciplinary expert panel discussion in precision cancer medicine ANNALS OF ONCOLOGY. 2021.07; 32; S287
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- 18. Maekawa A, Kudo A, Kishino M, Murase Y, Watanabe S, Ishikawa Y, Ueda H, Akahoshi K, Ogawa K, Ono H, Tanaka S, Kinowaki Y, Tanabe M. Hormonal tumor mapping for liver metastases of gastroenteropancreatic neuroendocrine neoplasms: a novel therapeutic strategy. Journal of Cancer Research and Clinical Oncology. 2021.04; published online;
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- 20. Maekawa Aya, Kudo Atsushi, Kishino Mitsuhiro, Murase Yoshiki, Watanabe Shuichi, Ishikawa Yoshiya, Ueda Hiroki, Akahoshi Keiichi, Ogawa Kosuke, Ono Hiroaki, Tanaka Shinji, Kinowaki Yuko, Tanabe Minoru. Hormonal tumor mapping for liver metastases of gastroenteropancreatic neuroendocrine neoplasms: a novel therapeutic strategy JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY. 2021.04; 148(3); 697-706
- 21. Yuki Fukawa, Kei Sakamoto, Takuma Kugimoto, Yasuyuki Michi, Hiroyuki Harada, Masahide Yamamoto, Masanobu Kitagawa, Tohru Ikeda, Kouhei Yamamoto. Nodular lymphocyte-predominant Hodgkin lymphoma involving the hard palate. Pathol Int. 2021.03; 71(3); 213-215
- 22. Oda G, Nakagawa T, Uemura N, Mori H, Mori M, Fujioka T, Onishi I, Uetake H. Axillary lymph node recurrence in patients with breast cancer who underwent breast reconstruction using a latissimus dorsi flap after mastectomy. Molecular and clinical oncology. 2021.03; 14(3); 49
- 23. Takahashi N, Kikuchi H, Usui A, Furusho T, Fujimaru T, Fujiki T, Yanagi T, Matsuura Y, Asano K, Yamamoto K, Ando F, Susa K, Mandai S, Mori T, Rai T, Uchida S, Arita M, Sohara E. Deletion of Alox15 improves kidney dysfunction and inhibits fibrosis by increased PGD< sub> 2< /sub> in the kidney. Clinical and experimental nephrology. 2021.02;
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- 28. Tomoyuki Fujioka, Mio Mori, Yuka Yashima, Emi Yamaga, Jun Oyama, Kota Yokoyama, Kazunori Kubota, Goshi Oda, Tsuyoshi Nakagawa, Iichiroh Onishi, Ukihide Tateishi. A useful case of ultrasound-guided axillary lymph node aspiration in a breast cancer patient with improved needle visibility. Radiol Case Rep. 2021.11; 16(11); 3295-3299
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[Misc]

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[Conference Activities & Talks]

- 1. Takeda Takamori, Ito Taku, Onishi Iichiroh, Yokomura Masaru, Kawashima Yoshiyuki, Fujikawa Taro, Tsutsumi Takeshi. Denosumab-induced osteonecrosis of external auditory canal(和訳中). Auris· Nasus-Larynx 2021.12.01
- 2. Morito Kurata, JP-AID. Establishing the database to utilize pooled whole slide images Japan Pathology Artificial Intelligence Diagnostics Project (JP-AID)". The 12th Asia Pacific International Academy of Pathology Congress 2021.11.12 Okayama, Japan
- 3. 田中 陽典, 倉田 盛人, 上林 秀孝, 山本 亜希子, 山本 浩平, 大西 威一郎, 北川 昌伸. CRISPR activation library を用いた MYC の発現調節因子の探求. 日本癌学会総会記事 2021.09.01
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- 5. 渡部 紫織, 山本 浩平, 倉田 盛人, 大西 威一郎, 川出 玄二, 北川 昌伸. 肝細胞癌における 4-hydroxynonenal 蓄積の臨床病理学的および分子生物学的研究. 日本癌学会総会記事 2021.09.01
- 6. 川出 玄二, 山本 浩平, 福田 翔, 大西 威一郎, 倉田 盛人, 北川 昌伸. 肺扁平上皮癌における GPX4、FSP1 発 現と 4HNE 蓄積の臨床病理学的検討. 日本癌学会総会記事 2021.09.01
- 7. 大西 威一郎, 倉田 盛人, 村岡 香琳, 小柳 杏莉, 木村 剛, 岸田 晶夫, 山本 浩平, 北川 昌伸. 脱細胞化骨を用いた、ヒト骨髄微小環境構築の試み. 日本癌学会総会記事 2021.09.01
- 8. 山本 浩平, 川出 玄二, 松木 裕子, 福田 翔, 倉田 盛人, 大西 威一郎, 北川 昌伸. Diffuse large B-cell lymphoma における 4-HNE の蓄積の臨床病理学的・分子生物学的意義.日本癌学会総会記事 2021.09.01
- 9. 田中 陽典, 倉田 盛人, 上林 秀孝, 山本 亜希子, 山本 浩平, 大西 威一郎, 北川 昌伸. CRISPR activation library を用いた MYC の発現調節因子の探求. 日本癌学会総会記事 2021.09.01
- 10. 杉田 佳祐, 倉田 盛人, 成田 莉菜, 大西 威一郎, 山本 浩平, 北川 昌伸. CRISPR KO Library を用いた細胞間 相互作用により誘導される薬剤耐性機序の解明を目指して. 日本癌学会総会記事 2021.09.01
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- 12. 友利 愛奈, 原田 拓実, 坂東 夏菜, 石田 信也, 山本 晃, 大西 威一郎, 熊谷 二朗. Spontaneous complete remission of grade3a follicular lymphoma with high-tumor-burden(和訳中). 日本血液学会学術集会 2021.09.01
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- 14. 川出 玄二, 山本 浩平, 福田 翔, 大西 威一郎, 倉田 盛人, 北川 昌伸. 肺扁平上皮癌における GPX4、FSP1 発 現と 4HNE 蓄積の臨床病理学的検討. 日本癌学会総会記事 2021.09.01
- 15. 大西 威一郎, 倉田 盛人, 村岡 香琳, 小柳 杏莉, 木村 剛, 岸田 晶夫, 山本 浩平, 北川 昌伸. 脱細胞化骨を用いた、ヒト骨髄微小環境構築の試み. 日本癌学会総会記事 2021.09.01
- 16. Largaespada David A., Kurata Morito, Pope Emily A., Beckmann Pauli J., Larson Jon D., Shu Jingmin, Temiz Nuri A., Sarver Aaron L., Seshagiri Somasekar. RNA sequencing により、transposon mutagenesis に誘発されるマウス腫瘍の"molecular pathology"が明らかになる (RNA sequencing reveals the "molecular pathology" of mouse tumors induced by transposon mutagenesis). 日本病理学会会誌 2021.03.01

[Social Contribution]

- 1. Journal of Cancer Research and Clinical Oncology, Springer Nature, Journal of Cancer Research and Clinical Oncology, 2017.04.01 Now
- 2. Guest editor, International Journal of Molecular Sciences, 2021.08 Now

Molecular Oncology

Professor: Shinji TANAKA Associate Professor: Yoshimitsu AKIYAMA Assistant Professor: Shu SHIMADA Assistant Professor: Ayano NIIBE Laboratory Technician: Hiromi NAGASAKI Graduate Student: Kouya YASUKAWA Graduate Student: Ayumi KONO

(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. Murase Y, Ono H, Ogawa K, Yoshioka R, Ishikawa Y, Ueda H, Akahoshi K, Ban D, Kudo A, Tanaka S, Tanabe M. Inhibitor library screening identifies ispinesib as a new potential chemotherapeutic agent for

pancreatic cancers. Cancer Science. 2021.11; 112(11); 4641-4654

- 2. Aramaki O, Takayama T, Moriguchi M, Sakamoto H, Yodono H, Kokudo N, Yamanaka N, Kawasaki S, Sasaki Y, Kubota K, Otsuji E, Tanaka S, Matsuyama Y, Fujii M.. Arterial chemoembolisation with cisplatin versus epirubicin for hepatocellular carcinoma (ACE 500 study): A multicentre, randomised controlled phase 2/3 trial. European Journal of Cancer. 2021.09; 157; 373-382
- 3. Taniai T, Shirai Y, Shimada Y, Hamura R, Yanagaki M, Takada N, Horiuchi T, Haruki K, Furukawa K, Uwagawa T, Tsuboi K, Okamoto Y, Shimada S, Tanaka S, Ohashi T, Ikegami T.. Inhibition of acid ceramidase elicits mitochondrial dysfunction and oxidative stress in pancreatic cancer cells. Cancer Science. 2021.09; 112(11); 4570-4579
- 4. Zhang M, Sugita I, Komura D, Katoh H, Shimada S, Inazawa J, Tanaka S, Ishikawa S. Genomic landscape of a mouse model of diffuse-type gastric adenocarcinoma. Gastric cancer : official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association. 2021.08;
- 5. Akasu M, Shimada S, Kabashima A, Akiyama Y, Shimokawa M, Akahoshi K, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Intrinsic activation of β -catenin signaling by CRISPR/Cas9-mediated exon skipping contributes to immune evasion in hepatocellular carcinoma. Scientific Reports. 2021.08; 11(1);
- Matsui S, Ono H, Asano D, Ishikawa Y, Ueda H, Akahoshi K, Ogawa K, Kudo A, Tanaka S, Tanabe M. Pancreatic metastasis from renal cell carcinoma presenting as gastrointestinal hemorrhage: a case report. Jornal of Surgical Case Reports. 2021.08; 2021(8);
- Kato T, Ono H, Fujii M, Akahoshi K, Ogura T, Ogawa K, Ban D, Kudo A, Tanaka S, Tanabe M. Cytoplasmic RRM1 activation as an acute response to gemcitabine treatment is involved in drug resistance of pancreatic cancer cells. PLoS One. 2021.06; 16(6);
- 8. Iwao Y, Ban D, Muro S, Kudo A, Tanaka S, Menon K, Tanabe M. Extraordinary first jejunal arterial variation associated with annular pancreas undergoing pancreaticoduodenectomy for pancreatic cancer: a case report. Surgical and Radiologic Anatomy. 2021.05; 43(5); 805-810
- Ishida H, Ishikawa Y, Akahoshi K, Ueda H, Morimoto K, Yamashita H, Ogawa K, Ono H, Kudo A, Tanaka S, Tanabe M. Laparoscopic distal pancreatectomy in a patient with aberrant splenic artery originating from the superior mesenteric artery: A case report. Medicine (Baltimore). 2021.05; 100(18);
- 10. Ono H, Kato T, Murase Y, Nakamura Y, Ishikawa Y, Watanabe S, Akahoshi K, Ogura T, Ogawa K, Ban D, Kudo A, Akiyama Y, Tanaka S, Ito H, Tanabe M. C646 inhibits G2/M cell cycle-related proteins and potentiates anti-tumor effects in pancreatic cancer. Scientific Reports. 2021.05; 11(1);
- 11. Kato Tomotaka, Kudo Atsushi, Kinowaki Yuko, Ishikawa Yoshiya, Watanabe Shuichi, Akahoshi Keiichi, Ogawa Kosuke, Ono Hiroaki, Ban Daisuke, Tanaka Shinji, Tanabe Minoru. A novel classification of portal venous tumor invasion to predict residual tumor status after surgery in patients with pancreatic neuroendocrine neoplasms. Journal of Cancer Research and Clinical Oncology . 2021.05;
- 12. Tatsuya Fukuda, Ryotaro Bouchi, Takato Takeuchi, Kikuko Amo-Shiinoki, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe, Takumi Akashi, Kazuhiro Hirayama, Toshitaka Odamaki, Miki Igarashi, Ikuo Kimura, Katsuya Tanabe, Yukio Tanizawa, Tetsuya Yamada, Yoshihiro Ogawa. Importance of Intestinal Environment and Cellular Plasticity of Islets in the Development of Postpancreatectomy Diabetes. Diabetes Care. 2021.04; 44(4); 1002-1011
- Sugawara T, Ban D, Nishino J, Watanabe S, Maekawa A, Ishikawa Y, Akahoshi K, Ogawa K, Ono H, Kudo A, Tanaka S, Tanabe M. Prediction of early recurrence of pancreatic ductal adenocarcinoma after resection. PLoS One. 2021.04; 16(4);
- 14. Maekawa A, Kudo A, Kishino M, Murase Y, Watanabe S, Ishikawa Y, Ueda H, Akahoshi K, Ogawa K, Ono H, Tanaka S, Kinowaki Y, Tanabe M. Hormonal tumor mapping for liver metastases of gastroenteropancreatic neuroendocrine neoplasms: a novel therapeutic strategy. Journal of Cancer Research and Clinical Oncology. 2021.04; published online;
- 15. Fukuda T, Bouchi R, Takeuchi T, Amo-Shiinoki K, Kudo A, Tanaka S, Tanabe M, Akashi T, Hirayama K, Odamaki T, Igarashi M, Kimura I, Tanabe K, Tanizawa Y, Yamada T, Ogawa Y. Importance of Intestinal Environment and Cellular Plasticity of Islets in the Development of Postpancreatectomy Diabetes. Diabetes Care. 2021.04; 44(4); 1002-1011

- 16. Murase Y, Kudo A, Akahoshi K, Maekawa A, Ishikawa Y, Ueda H, Ogawa K, Ono H, Tanaka S, Tanabe M. Surgery after sunitinib administration to improve survival of patients with advanced pancreatic neuroendocrine neoplasms. Annals of Gastroenterological Surgery. 2021.03; 0(0); 1-9
- 17. Amo-Shiinoki K, Tanabe K, Hoshii Y, Matsui H, Harano R, Fukuda T, Takeuchi T, Bouchi R, Takagi T, Hatanaka M, Takeda K, Okuya S, Nishimura W, Kudo A, Tanaka S, Tanabe M, Akashi T, Yamada T, Ogawa Y, Ikeda E, Nagano H, Tanizawa Y. Islet cell dedifferentiation is a pathologic mechanism of long-standing progression of type 2 diabetes. JCI insight. 2021.01; 6(1);
- Kabashima Ayano, Shimada Shu, Shimokawa Masahiro, Akiyama Yoshimitsu, Tanabe Minoru, Tanaka Shinji. Molecular and immunological paradigms of hepatocellular carcinoma: Special reference to therapeutic approaches Journal of Hepato-Biliary-Pancreatic Sciences . 2021.01; 28(1); 62-75

[Conference Activities & Talks]

- 1. Shinji Tanaka. Invited Lecture; Stemness and heterogeneity of liver cancer. JSH International Liver Conference 2021 2021.10.02 Hakata International Exhibition Hall & Conference Center, Fukuoka (on-line)
- 2. Kohei Yagi, Hiroki Ueda, Koichiro Morimoto, Hironari Yamashita, Yoshiki Murase, Aya Maekawa, Takeshi Ishii, Toshitaka Sugawara, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akashoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, SHinji Tanaka, Minoru Tanabe. A review of resected cases of primary duodenal cancer in our hospital. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 3. Yoshiki Murase, Hiroaki Ono, Risa Yoshioka, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Kosuke Ogawa, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. High Eg5 expression predicts poor prognosis in pancreatic cancer. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 4. Aya Maekawa, Keiichi Akahoshi, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Validation of the international consensus guideline 2017 for intraductal papillary mucinous neoplasms. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 5. Keiichi Akahoshi, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Conversion surgery after lenvatinib treatment for advanced hepatocellular carcinoma. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 6. Hiroyuki Ishida, Hiroki Ueda, Keiichi Akahoshi, Yoshiya Ishikawa, Hironari Yamashita, Koichiro Morimoto, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Early recurrence after curative hepatectomy for colorectal liver metastases. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 7. Yoshiya Ishikawa, Hiroyuki Ishida, Koichiro Morimoto, Hironari Yamashita, Hiroki Ueda, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Laparoscopic distal pancreatectomy for pancreatic ductal adenocarcinoma using supracolic anterior approach to the superior mesenteric artery. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 8. Takeshi Ishii, Atsushi Kudo, Yoshiki Murase, Aya Maekawa, Toshitaka Sugawara, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Kousuke Ogawa, Hiroaki Ono, Shinji Tanaka, Minoru Tanabe. The management of GEP-NET with MEN type 1 in our department. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 9. Koichiro Morimoto, Keiichi Akahoshi, Hironari Yamashita, Hiroyuki Ishida, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Takeshi Ishii, Toshitaka Sugawara, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Granulomatous Langerhans isletitis followed by nivolumab-induced type 1 diabetes mellitus in a distal pancreatectomy: case report. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 10. Hiroki Ueda, Koichiro Morimoto, Hironari Yamashita, Hiroyuki Ishida, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Toshitaka Sugawara, Takeshi Ishii, Yoshiya Ishikawa, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Perioperative outcomes in elderly

patients over 75-years-old undergoing distal pancreatectomy. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka

- 11. Hiroaki Ono, Atsushi Kudo, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Kosuke Ogawa, Shinji Tanaka, Minoru Tanabe. Combination of Weekly Streptozocin and Oral S-1 Treatment is effective treatment for unresectable or metastatic pancreatic NET-G1 and NET-G2 patients. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 12. Hironari Yamashita, Keiichi Akahoshi, Koichirou Morimoto, Hiroyuki Ishida, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Takeshi Ishii, Toshitaka Sugawara, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Effect of neoadjuvant chemotherapy on short-term outcome in patients undergoing pancreaticoduodenectomy for borderline resectable pancreatic cancer with elevated serum tumor markers. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 13. Tomotaka Kato, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Comparison of open and laparoscopic hepatectomy for obese patients with HCC. The 33rd Annual Meeting of the Japan Society for Endoscopic Surgery 2021.03.10 Yokohama
- 14. Takeshi Ishii, Keiichi Akahoshi, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Toshitaka Sugawara, Masafumi Akasu, Tomotaka, Kato, Yoshiya Ishikawa, Shuichi Watanabe, Kousuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical Analysis of 23 Cases of total pancreatectomy in Tokyo Medical and Dental University. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 15. Kohei Yagi, Atsushi Kudo, Aya Maekawa, Yoshiki Murase, Takeshi Ishii, Tomotaka Kato, Masafumi Akasu, Toshitaka Sugawara, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Ogawa Kosuke, Hiroaki Ono, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. Evaluation of laparoscopic distal pancreatectomy for pancreatic neuroendocrine tumors. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 16. Keiichi Akahoshi, Kohei Yagi, Yoshiki Murase, Takeshi Ishii, Toshitaka Sugawara, Yoshiya Ishikawa, Shuichi Watanabe, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Non-viral hepatocellular carcinoma and, diabetes and obesity as its risk factorslar carcinoma and, diabetes and obesity as its risk factors. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 17. Keiichi Akahoshi, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Liver resection after systemic chemotherapy improved overallsurvival of metastatic neuroendocrine neoplasms. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 18. Hiroaki Ono, Tomotaka Kato, Aya Maekawa, Kouhei Yagi, Yoshiya Ishikawa, SHuichi Watanabe, Keiichi Akahoshi, Kousuke Ogawa, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Cytoplasmic RRM1 activation in acute phase of gemcitabine treatment is involved in acquired resistance of pancreatic cancer. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 19. Shuichi Watanabe, Shu Shimada, Jo NIshino, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Toshitaka Sugawara, Takeshi Ishii, Tomotaka Kato, Masafumi Akasu, Yoshiya Ishikawa, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Estimation of the type of HCC metastasis based on the multicellular colonization model. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 1. Shinji Tanaka. JCA-Mauverney Award Session Invited Lecture; Surgical oncology to develop novel targeted and immunotherapies for hepato-biliary-pancreatic cancer. 80th Annual Meeting of Japanese Cancer Association 2021.10.02 Yokohama
- 2. Shu Shimada, Shinji Tanaka.. Establishment of molecular-immunological subtypes and development of specific models for therapeutic application in hepatocellular carcinoma.. The 80th Annual Meeting of the Japanese Cancer Association. 2021.09.30 Yokohama

[Patents]

- 1. Dominant negative mutants of IRS-1 and uses there of (Tanaka S, Wands JR), Patent Number : United States Patent 6,528,479
- 2. Compositions and methods for detection and treatment of hepatocellular carcinoma (Tanaka S, MacDonald G), Application Number : US 61/811,360

Surgical Pathology

Associate Professor: Takumi AKASHI Assistant Professor: Onishi Iichiro,Susumu KIRIMURA,Shohei TOMII,Hiroshi Shintaku Project Assistant Professor: Keiko MIURA Secretary: Ayako UENO

(1) Outline

Missons 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-subspecilized 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. 宮本 秀明, 三浦 圭子. 【脂腺の病気】腰部の脂腺母斑 基底細胞癌とほかの 2 種の腫瘍が生じた 皮膚病診 療. 2021.12;
- 2. 内田 千恵, 壷井 聡史, 大山 希理子, 加藤 恒平, 沢田 泰之, 三浦 圭子. 【潰瘍をきたす疾患】HIV 感染患者に 合併した陰部基底細胞癌 皮膚病診療. 2021.11;
- ティーラウォン・チャンヤーヌット,坂本 啓,布川 裕規,土谷 麻衣子,栢森 高,明石 巧,濱垣 美和子,富岡 博文, 黒嶋 雄志,森田 圭一,原田 浩之,池田 通. 舌癌症例にみられるヒトパピローマウイルス (HPV) 感染と無関係な p16 免疫染色陽性反応 (Immunohistochemical Positivity for p16 Unrelated to Human Papillomavirus(HPV) Infection in Lingual Squamous Cell Carcinomas) 口腔病学会雑誌. 2021.11; 88(2-3); 115-126
- 4. Keisuke Uchida, Asuka Furukawa, Akiko Yoneyama, Haruhiko Furusawa, Daisuke Kobayashi, Takashi Ito, Kurara Yamamoto, Masaki Sekine, Keiko Miura, Takumi Akashi, Yoshinobu Eishi, Kenichi Ohashi. Propionibacterium acnes-Derived Circulating Immune Complexes in Sarcoidosis Patients Microorganisms. 2021.10; 9(11);
- 5. Sekine Y, Yamamoto K, Kurata M, Honda A, Onishi I, Kinowaki Y, Kawade G, Watabe S, Nomura S, Fukuda S, Ishibashi S, Ikeda M, Yamamoto M, Kitagawa M. HADHB, a fatty acid beta-oxidation enzyme, is a potential prognostic predictor in malignant lymphoma. Pathology. 2021.09;
- 6. Kinowaki Yuko, Abe Shiho, Abe Shinya, Tomii Shohei, Yukimori Akane, Akashi Takumi, Tokunaga Masanori, Kitagawa Masanobu. 胃原発滑膜肉腫 症例報告とシステマティックレビュー (Synovial sarcoma of the stomach: a case report and a systematic review of literature) Clinical Journal of Gastroenterology. 2021.08; 14(4); 1020-1026
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[Misc]

1. Kinowaki Y, Taguchi T, Onishi I, Kirimura S, Kitagawa M, Yamamoto K. Overview of Ferroptosis and Synthetic Lethality Strategies. International journal of molecular sciences. 2021.08; 22(17);

[Conference Activities & Talks]

1. Shintaku Hiroshi, et al.. Two cases of insulitis associated with immune checkpoint inhibitors. 2021.04.22

[Social Contribution]

- 1. The Japanese Society of Diagnostic Dermatopathology, Department of Pathology, Fukuoka University, 2005.04.17 Now
- 2. Ochanomizu Study Meeting of Dermatopathology, 2009.04 Now

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**

[Original Articles]

1. Tometsuka C, Funato N, Mizuno K, Taga Y. Long-term intake of ginger protease-degraded collagen hydrolysate reduces blood lipid levels and adipocyte size in mice. Current research in food science. 2021.03; 4; 175-181

[Books etc]

1. Extracellular matrix experimental method:From basic research on collagen to application to regenerative medicine. 2021.12 (ISBN : 978-4621306857)

[Others]

- Grants-in-Aid for Scientific Research (C), 2021.04 "Elucidation of new transcription target of DiGeorge syndrome disease gene product TBX1 and its molecular mechanism" Noriko Funato
- $2.\ 2021.12$

PR TIMES https://prtimes.jp/main/html/rd/p/00000001.000083625.html

Hematology

Professor Takehiko Mori

Junior Associate Professor Masahide Yamamoto

Assistant Professor Toshikage Nagao, Yoshihiro Umezawa, Keigo Okada, Kota Yoshifuji

Project Assistant Professor. Chizuko Sakashita

Assistant Professor (Department of Clinical Laboratory) Ayako Nogami

Senior Resident Yuuki Osada, Makiko Saito, Hiroki Fujiwara, Satoshi Koi, Kana Bando, Keisuke Tanaka

Graduate Student Satoru Aoyama, Yotarou Motomura

(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

Our laboratory has been engaged in various research activities, focusing on elucidation of "crosstalk among intracellular signaling pathways, involved in cell proliferation or tumorigenesis of hematopoietic malignancies" as well as "comprehensive mechanisms by which chemotherapeutic agents induce apoptosis in hematopoietic tumors". Based on those accomplishments, we are energetically pursuing new insights, supported by recent drastic advances in molecular biological and genetic analysis methods.

1) New molecular targets in refractory B-cell malignancies and the potential for therapeutic application.

2) Elucidation of the molecular mechanisms involved in formation of drug resistance in acute leukemias with specific oncogenic mutations.

3) Development of novel Chimeric Antigen Receptor (CAR) T cell technologies.

4) Analyses on pathogenesis-related genetic aberrations and their implication to clinical presentation in primary vitreoretinal lymphoma.

5) Analyses on pathogenesis of myeloproliferative neoplasms, mechanisms of drug resistance, and development of effective therapeutic methodologies.

6) Establishment, characterization of novel cell lines derived from hematopoietic tumors and their application in basic research,

7) Development of novel diagnostic methods and management of infectious complications immunocompromised

patients.

(3) Education

Department of hematology is responsible for teaching basic and clinical hematology to the 3rd-year medical students in Hematology/Oncology block course. We are also responsible for the 5th-year students in clinical clerkship to obtain basic knowledge and problem-solving abilities in hematology as well as general internal medicine. In the clerkship, we focus on the participation in the team, which would be helpful to proceed to the post-graduate training.

Even under the restriction due to COVID-19 pandemic, lectures based on case study and group work are provided.

In the resident training course, we provide training to acquire the basic skills of total health care including communications, diagnosis and treatment of various hematological disorders. Our training is based on the essential issues and skills to obtain the certificate of Hematology Specialist.

We always guide the young doctors, including Ph.D. students, to search for the solutions of their own questions by planning and performing basic and/or clinical studies. Our goal is to raise researchers with an excellent research mind.

(4) Lectures & Courses

As described in 3, our goal is to raise experts with ability to solve problems and provide total health care through learning clinical and basic hematology.

(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, hematopoietic cell transplantation, and CAR-T cell therapy.

(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. Kamiya T, Sakurai M, Kikuchi T, Okayama M, Mizuno K, Tanigawa T, Koda Y, Kato J, Mori T.. Efficacy of ondansetron against emesis induced by a multiple-day cisplatin-based chemotherapy regimen for malignant lymphoma. Hematology. 2021 Dec;26(1):945-949. 2021.12; 26(1); 945-949
- 2. Takayoshi Tachibana, Junya Kanda, Takuma Ishizaki, Yuho Najima, Masatsugu Tanaka, Noriko Doki, Shin-Ichiro Fujiwara, Shun-Ichi Kimura, Makoto Onizuka, Satoshi Takahashi, Takeshi Saito, Takehiko Mori, Shin Fujisawa, Emiko Sakaida, Takuya Miyazaki, Nobuyuki Aotsuka, Moritaka Gotoh, Reiko Watanabe, Katsuhiro Shono, Heiwa Kanamori, Yoshinobu Kanda, Shinichiro Okamoto, . Pre-conditioning intervention in patients with relapsed or refractory acute lymphoblastic leukemia who underwent allogeneic hematopoietic cell transplantation: a KSGCT multicenter retrospective analysis Ann Hematol. 2021.11; 100(11); 2763-2771
- 3. Shunichiro Yasuda, Satoru Aoyama, Ryoto Yoshimoto, Huixin Li, Daisuke Watanabe, Hiroki Akiyama, Kouhei Yamamoto, Takeo Fujiwara, Yuho Najima, Noriko Doki, Emiko Sakaida, Yoko Edahiro, Misa Imai, Marito Araki, Norio Komatsu, Osamu Miura, Norihiko Kawamata. MPL overexpression induces a high level of mutant-CALR/MPL complex: a novel mechanism of ruxolitinib resistance in myeloproliferative neoplasms with CALR mutations. Int J Hematol. 2021.10; 114(4); 424-440

- 4. Hideki Nakasone, Shinichi Kako, Takayoshi Tachibana, Masatsugu Tanaka, Makoto Onizuka, Satoshi Takahashi, Akira Yokota, Shin-Ichiro Fujiwara, Toru Sakura, Emiko Sakaida, Shin Fujisawa, Rie Yamazaki, Moritaka Gotoh, Maki Hagihara, Nobuyuki Aotsuka, Nobuhiro Tsukada, Yoshihiro Hatta, Hiroaki Shimizu, Kensuke Usuki, Reiko Watanabe, Takehiko Mori, Shingo Yano, Heiwa Kanamori, Yoshinobu Kanda. Novel Indicators of Transplant Outcomes for PhALL: Current Molecular-Relapse-Free Survival. Transplant Cell Ther. 2021.09; 27(9); 800.e1-800.e8
- 5. Yuji Sekine, Kouhei Yamamoto, Morito Kurata, Ayaka Honda, Iichiroh Onishi, Yuko Kinowaki, Genji Kawade, Shiori Watabe, Serina Nomura, Sho Fukuda, Sachiko Ishibashi, Masumi Ikeda, Masahide Yamamoto, Masanobu Kitagawa. HADHB, a fatty acid beta-oxidation enzyme, is a potential prognostic predictor in malignant lymphoma. Pathology. 2021.09; (21); 435-439
- 6. Shunichiro Yasuda, Yuho Najima, Tatsuya Konishi, Yuta Yamada, Akihito Nagata, Toshiaki Takezaki, Satoshi Kaito, Shuhei Kurosawa, Masahiro Sakaguchi, Kaito Harada, Naoki Shingai, Kosuke Yoshioka, Kyoko Inamoto, Junichi Mukae, Takashi Toya, Aiko Igarashi, Hiroaki Shimizu, Takeshi Kobayashi, Kazuhiko Kakihana, Hisashi Sakamaki, Norihiko Kawamata, Kazuteru Ohashi, Noriko Doki. Outcome of allogeneic hematopoietic stem cell transplantation for T-cell lymphoblastic leukemia/lymphoma: A single-center study. Leuk Res. 2021.09; 108; 106627
- 7. Ikuko Hirai, Takeru Funakoshi, Hajime Kamijuku, Keitaro Fukuda, Mariko Mori, Masatoshi Sakurai, Yuya Koda, Jun Kato, Takehiko Mori, Naohide Watanabe, Shinobu Noji, Tomonori Yaguchi, Takashi Iwata, Shigeki Ohta, Tomonobu Fujita, Ryuji Tanosaki, Makoto Handa, Shinichiro Okamoto, Masayuki Amagai, Yutaka Kawakami. Adoptive cell therapy using tumor-infiltrating lymphocytes for melanoma refractory to immune-checkpoint inhibitors. Cancer Sci. 2021.08; 112(8); 3163-3172
- 8. Saiko Kurosawa, Takuhiro Yamaguchi, Ayako Mori, Tomoko Matsuura, Takehiko Mori, Masatsugu Tanaka, Tadakazu Kondo, Yukari Umemoto, Hideki Goto, Satoshi Yoshioka, Shinichiro Machida, Takahiko Sato, Yuta Katayama, Seiko Kato, Katsuhiro Shono, Ishikazu Mizuno, Shin-Ichiro Fujiwara, Akio Kohno, Miyako Takahashi, Takahiro Fukuda. Resignation and return to work in patients receiving allogeneic hematopoietic cell transplantation close up. J Cancer Surviv. 2021.08;
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- Masayuki Nagasawa, Noriko Mitsuiki, Masakatsu Yanagimachi, Masahide Yamamoto, Tetsuya Fukuda, Osamu Miura, Ryutaro Oba, Akira Igarashi, Kinya Nagata, Tomohiro Morio. Utility of novel T-cell-specific extracellular vesicles in monitoring and evaluation of acute GVHD. Int J Hematol. 2021.06; 113(6); 910-920
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- 12. Uno S, Takano Y, Iketani O, Abiko T, Miwa T, Nanki K, Kurihara T, Tamura Y, Ara M, Uwamino Y, Shinjoh M, Mori T, Hasegawa N. Digestive Decolonization of Colorectal Carriage of Vancomycin-resistant Enterococcus faecium in a Japanese Adult: A Case Report. Internal medicine . 2021.06; 61(2); 249-252
- 13. Sakurai M, Mori T, Kato K, Kanaya M, Mizuno S, Shiratori S, Wakayama T, Uchida N, Kobayashi H, Kubo K, Amano I, Ohta T, Miyazaki Y, Kanda J, Fukuda T, Atsuta Y, Kondo E, Adult Lymphoma Working Group of the Japan Society for Hematopoietic Cell Transplantation (JSHCT).. Outcome of allogeneic hematopoietic stem cell transplantation for follicular lymphoma relapsing after autologous transplantation: analysis of the Japan Society for Hematopoietic Cell Transplantation. Bone marrow transplantation. 2021.06; 56(6); 1462-1466
- 14. Mori T, Kikuchi T, Yamazaki R, Koda Y, Saburi M, Sakurai M, Shigematsu N, Okamoto S, Kato J. Phase 1 study of plerixafor in combination with total body irradiation-based myeloablative conditioning
for allogeneic hematopoietic stem cell transplantation. International journal of hematology. 2021.06; 113(6); 877-883

- 15. Nakasone H, Kako S, Mori T, Takahashi S, Onizuka M, Fujiwara SI, Sakura T, Sakaida E, Yokota A, Aotsuka N, Hagihara M, Tsukada N, Hatta Y, Usuki K, Watanabe R, Gotoh M, Fujisawa S, Yano S, Kanamori H, Okamoto S, Kanda Y. Stopping tyrosine kinase inhibitors started after allogeneic HCT in patients with Philadelphia chromosome-positive leukemia. Bone marrow transplantation. 2021.06; 56(6); 1402-1412
- 16. Amikura T, Kikuchi T, Kato J, Koda Y, Sakurai M, Yamazaki R, Mikita K, Saburi M, Nakazato T, Mori T. Toxoplasmosis after allogeneic hematopoietic stem cell transplantation: Impact of serostatus-based management. Transplant infectious disease : an official journal of the Transplantation Society. 2021.06; 23(3); e13506
- 17. Kota Yoshifuji, Takashi Toya, Noriyo Yanagawa, Fumikazu Sakai, Akihito Nagata, Noritaka Sekiya, Kazuteru Ohashi, Noriko Doki. CT classification of acute myeloid leukemia with pulmonary infiltration Japanese Journal of Radiology. 2021.06; 39(11); 1049-1058
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- 19. Kaori Uchino, Lam Vu Quang, Shohei Mizuno, Tomohiro Horio, Hidesuke Yamamoto, Ichiro Hanamura, Yoshihisa Kodera, J Luis Espinoza, Makoto Onizuka, Koichi Kashiwase, Yasuo Morishima, Takahiro Fukuda, Noriko Doki, Koichi Miyamura, Takehiko Mori, Eriko Morishita, Shinji Nakao, Akiyoshi Takami. Donor UNC-93 Homolog B1 genetic polymorphism predicts survival outcomes after unrelated bone marrow transplantation. Genes Immun. 2021.05; 22(1); 35-43
- 20. Keigo Okada, Hiroki Fujiwara, Tomoyuki Arimatsu, Yotaro Motomura, Tsuyoshi Kato, Naoki Takezako, Takashi Kumagai. Efficacy and Safety of Balloon Kyphoplasty for Pathological Vertebral Fractures in Patients with Hematological Malignancies in Our Institution. Intern Med. 2021.04; 60(8); 1169-1174
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[Conference Activities & Talks]

 Chikashi Yoshida, Hiroki Yamaguchi, Noriko Doki, Kazunori Murai, Masaki Iino, Yoshihiro Hatta, Makoto Onizuka, Norio Yokose, Katsumichi Fujimaki, Masao Hagihara, Gaku Oshikawa, Kayoko Murayama, Takashi Kumagai, Shinya Kimura, Hideharu Muto, Kensuke Usuki, Kenji Yokoyama, Koh Yamamoto, Nobuyuki Aotsuka, Kenichi Ishizawa, Naoki Takezako, Takuto Miyagishima, Tadao Ishida, Atsushi Shinagawa, Kentaro Wakasa, Tsuyoshi Nakamaki, Naoto Tomita, Katsutoshi Ozaki, Takayoshi Itoh, Shugo Kowata, Kenji Tajika, Takayuki Fujio, Masahiro Onozawa, Masahide Yamamoto, Takeshi Kondo, Yuho Najima, Noriyoshi Iriyama, Ikuyo Tsutsumi, Koji Oba, Hiroshi Kojima, Hisashi Sakamaki, Koiti Inokuchi. Importance of the Duration of TKI Treatment in Treatment-Free Remission of Chronic Phase Chronic Myeloid Leukemia: Results of D-Free Trial . 63rd ASH annual meeting and exposition 2021.12.13

- 2. Ayako Arai, Masahide Yamamoto, Maho Sato, Yasushi Onishi, Yoji Sasahara, Hideki Sano, Masayoshi Masuko, Hirohisa Nakamae, Ken-Ichi Matsuoka, Takahide Ara, Kana Washio, Makoto Onizuka, Kenichiro Watanabe, Tsuneaki Hirakawa, Miwako Nishio, Chizuko Sakashita, Tohru Kobayashi, Akihisa Sawada, Tatsuo Ichinohe, Takahiro Fukuda, Yoshiko Hashii, Yoshiko Atsuta. The Outcomes of Systemic Chronic Active EBV Infection Treatment By Allogeneic Hematopoietic Stem Cell Transplantation: An Analysis of Japanese Registry Data. 63rd ASH annual meeting and exposition 2021.12.13
- 3. Noriharu Nakagawa, Ken Ishiyama, Kensuke Usuki, Satoru Takada, Tatsuki Tomikawa, Hiroshi Handa, Yuna Katsuoka, Daiki Hirano, Nobuo Sezaki, Masahiko Sumi, Shin Fujisawa, Yasuhiro Taniguchi, Takuro Yoshimura, Eiichi Ohtsuka, Ken Takase, Youko Suehiro, Shuichi Ota, Tomohiro Kajiguchi, Tomoya Maeda, Masahide Yamamoto, Shigeki Ohtake, Akira Katsumi, Hitoshi Kiyoi, Itaru Matsumura, Yasushi Miyazaki. Outcomes of Transplant-Eligible Patients with Myelodysplastic Syndrome-Refractory Anemia with Excess Blasts Registered in a Prospective Observational Study: The JALSG-CS11-MDS-SCT . 63rd ASH annual meeting and exposition 2021.12.13
- 4. Kentaro Yamaguchi, Junji Koya, Kota Yoshifuji, Yuta Ito, Mitsuhiro Yuasa, Yuki Saito, Makiko Tabata, Sumito Shingaki, Yasuhiro Kogure, Kazutaka Nakashima, Koichi Oshima, Keisuke Kataoka . High-throughput screening to elucidate in vivo oncogenicity of lymphoma-related genetic alterations. The 83rd annual meeting of Japanese society of hematology 2021.09.24
- 5. Satoru Aoyama, Shunichiro Yasuda, Huixin Li, Daisuke Watanabe, Hiroki Akiyama, Keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Osamu Miura, Norihiko Kawamata. Protease mediated Regulatory Chimeric Antigen Receptor (CAR) Improves Target Specificity.. The 83rd Annual Meeting of the Japanese Society of Hematology 2021.09.24
- 6. Y. Minami, I. Matsumura, N. Takahashi, S. Ohtake, Y. Atsuta, M. Kurata, S. Yano, N. Iriyama, Y. Ueda, Y. Ozawa, E. Sakaida, A. Mori, M. Yamamoto, T. Ono, K. Fujimaki, C. Nakaseko, T. Miyamoto, N. Asou, H. Kiyoi, Y. Miyazaki. TREATMENT-FREE REMISSION IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA IN CHRONIC PHASE FOLLOWING FRONTLINE DASATINIB: RESULTS FROM JALSG D-STOP216. EHA 2021 congress virtual 2021.06.09
- 7. Naoto Takahashi, Itaru Matsumura, Yosuke Minami, Takaaki Ono, Tomoko Hata, Shigeki Ohtake, Yoshiko Atsuta, Mio Kurata, Katsumichi Fujimaki, Toshikage Nagao, Chiaki Nakaseko, Noriyoshi Iriyama, Toshihiro Miyamoto, Norio Asou, Hitoshi Kiyoi, Yasushi Miyazaki. Treatment-Free Remission in patients with Chronic Myeloid Leukemia in Chronic Phase following frontline Nilotinib: results from JALSG N-STOP216. EHA 2021 congress virtual 2021.06.09 2021.06.09
- 1. Kota Yoshifuji, Yotaro Motomura, Ayako Nogami, Keigo Okada, Takehiko Mori, Toshikage Nagao. Involvement of TPL2/p105/STAT3 axis in tumorigenesis of ABC-DLBCL. 2021.09.24
- 2. Inhibition of USP14 induces apoptosis in FLT3-ITD-positive AML cells through upregulation of Nrf-2. 2021.09.23
- 3. Keisuke Tanaka,Masahide Yamamoto,Atsushi Takahata,Satoshi Koi,Fumihiko Ouchi,Naoko Nakamaki,Naoya Nakamura,Shigeo Toyoda. Outcome of initial treatment for untreated Waldenstrom macroglobulinemia. 2021.09.23
- 4. Atsushi Takahata,Kesisuke Tanak,Yoshihiro Umezawa,Toshikage Nagao,Shigeo Toyoda,Masahide Yamamoto. Bendamustine plus rituximab/obinutuzumab in previously untreated follicular lymphoma. The 83rd annual meeting of Japanese society of hematology 2021.09.23
- 5. Naoto Takahashi, Itaru Matsumura, Yosuke Minami, Takaaki Ono, Tomoko Hata, Shigeki Ohtake, Yoshiko Atsuta, Mio Kurata, Katsumichi Fujimaki, Toshikage Nagao, Chiaki Nakaseko, Noriyoshi Iriyama, Toshihiro Miyamoto, Norio Asou, Hitoshi Kiyoi, Yasushi Miyazaki. Treatment-free remission in patients with CML-CP following frontline nilotinib: JALSG N-STOP 216. 2021.09.23
- 6. Moyu KIMURA,Yu NISHIYAMA,Hiroki UEDA,Tomoyuki ARIMATSU,Mai KUBOKI,Atsushi TAKAHATA,Makiko SAITO,Shuji TOHDA,Ayako NOGAMI. Perioperative management of a PNH patient treated with ravulizumab: in case of gallstone disease. The 83rd Annual Meeting of the Japanese Society of Hematology 2021.09.23 Sendai
- 7. Kentaro Yamaguchi, Junji Koya, Kota Yoshifuji, Yuta Ito, Mitsuhiro Yuasa, Yuki Saito, Makiko Tabata, Sumito Shingaki, Yasuhiro Kogure, Koichi Oshima, Keisuke Kataoka . High-throughput screening to elucidate in vivo oncogenicity of lymphoma-related genetic alterations. 2021.09.01

Molecular Endocrinology and Metabolism

Professor: Tetsuya Yamada Associate Professor: Kenji Ikeda Assistant Professor: Chikara Komiya, Kazutaka Tsujimoto, Kumiko Shiba, Masanori Murakami Clinical Fellow: Satoru Uchida, Jun Aoki, Rei Okazaki, Daisuke Hamada, Ryo Kaneda Resident: Emi Kiuchi, Akiko Hirano Project Assistant Professor: Mitsuyuki Numasawa Graduate Students (Doctor's course): Yoshihiro Niitsu, Akira Takeuchi, Kazunari Hara, Masato Horino

(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]

- Takahiro Fukaishi, Yuko Nakagawa, Ayako Fukunaka, Takashi Sato, Akemi Hara, Keiko Nakao, Michiko Saito, Kenji Kohno, Takeshi Miyatsuka, Motoyuki Tamaki, Munehide Matsuhisa, Taka-Aki Matsuoka, Tetsuya Yamada, Hirotaka Watada, Yoshio Fujitani. Characterisation of Ppy-lineage cells clarifies the functional heterogeneity of pancreatic beta cells in mice. Diabetologia. 2021.12; 64(12); 2803-2816
- 2. Saito K, Kurihara I, Itoh H, Ichijo T, Katabami T, Tsuiki M, Wada N, Yoneda T, Sone M, Oki K, Yamada T, Kobayashi H, Tamura K, Ogawa Y, Kawashima J, Inagaki N, Yamamoto K, Yamada M, Kamemura

K, Fujii Y, Suzuki T, Yasoda A, Tanabe A, Naruse M, Japan Primary Aldosteronism Study/Japan Rare Intractable Adrenal Diseases Study Group.. Subtype-specific trends in the clinical picture of primary aldosteronism over a 13-year period. Journal of hypertension. 2021.11; 39(11); 2325-2332

- 3. Yuko Adachi, Kazuki Ota, Isao Minami, Tetsuya Yamada, Takayuki Watanabe. Lower insulin secretion is associated with hippocampal and parahippocampal gyrus atrophy in elderly patients with type 2 diabetes mellitus. J Diabetes Investig. 2021.10; 12(10); 1908-1913
- 4. Hiroko Beppu, Tatsuya Fukuda, Tomoko Kawanishi, Fumihiko Yasui, Minami Toda, Hitomi Kimura, Yuki Nakamura, Yuka Nakamura, Kaori Kojima, Hina Ogawa, Ayumi Ishiwatari, Yuiko Kamei, Toshie Ogawa, Yasutomo Abe, Mariko Endo, Tomohide Hanawa, Rie Mizobuchi, Chise Sugita, Koh Okamoto, Shuji Hatakeyama, Tetsusya Yamada, Michinori Kohara, Sachiko Wakai. Hemodialysis patients with coronavirus disease 2019: reduced antibody response. Clin Exp Nephrol. 2021.09; 26(2); 170-177
- Numasawa M, Nawa N, Funakoshi Y, Noritake K, Tsuruta J, Kawakami C, Nakagawa M, Yamaguchi K, Akita K. A mixed methods study on the readiness of dental, medical, and nursing students for interprofessional learning. PloS one. 2021.07; 16(7); e0255086
- 6. Masanori Murakami, Na Sun, Christian Greunke, Annette Feuchtinger, Stefan Kircher, Timo Deutschbein, Thomas Papathomas, Nicole Bechmann, Paal William Wallace, Mirko Peitzsch, Esther Korpershoek, Juliane Friemel, Anne-Paule Gimenez-Roqueplo, Mercedes Robledo, Henri J L M Timmers, Letizia Canu, Achim Weber, Ronald R de Krijger, Martin Fassnacht, Thomas Knösel, Thomas Kirchner, Martin Reincke, Axel Karl Walch, Matthias Kroiss, Felix Beuschlein. Mass spectrometry imaging identifies metabolic patterns associated with malignant potential in pheochromocytoma and paraganglioma. European Journal of Endocrinology. 2021.06; 185(1); 179-191
- 7. Ryo Nakamaru, Koichi Yamamoto, Hiroshi Akasaka, Hiromi Rakugi, Isao Kurihara, Takashi Yoneda, Takamasa Ichijo, Takuyuki Katabami, Mika Tsuiki, Norio Wada, Tetsuya Yamada, Hiroki Kobayashi, Kouichi Tamura, Yoshihiro Ogawa, Junji Kawashima, Nobuya Inagaki, Megumi Fujita, Minemori Watanabe, Kohei Kamemura, Shintaro Okamura, Akiyo Tanabe, Mitsuhide Naruse, . Age-stratified comparison of clinical outcomes between medical and surgical treatments in patients with unilateral primary aldosteronism. Scientific Reports. 2021.05; 11(1); 6925
- 8. Takeshi Yoneshiro, Naoya Kataoka, Jacquelyn M Walejko, Kenji Ikeda, Zachary Brown, Momoko Yoneshiro, Scott B Crown, Tsuyoshi Osawa, Juro Sakai, Robert W McGarrah, Phillip J White, Kazuhiro Nakamura, Shingo Kajimura. Metabolic flexibility via mitochondrial BCAA carrier SLC25A44 is required for optimal fever. Elife. 2021.05; 10;
- 9. Tatsuya Fukuda, Ryotaro Bouchi, Takato Takeuchi, Kikuko Amo-Shiinoki, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe, Takumi Akashi, Kazuhiro Hirayama, Toshitaka Odamaki, Miki Igarashi, Ikuo Kimura, Katsuya Tanabe, Yukio Tanizawa, Tetsuya Yamada, Yoshihiro Ogawa. Importance of Intestinal Environment and Cellular Plasticity of Islets in the Development of Postpancreatectomy Diabetes. Diabetes Care. 2021.04; 44(4); 1002-1011
- Ryotaro Bouchi, Noriyuki Sonoda, Jun Itoh, Yasuhiro Ono, Tatsuya Fukuda, Takato Takeuchi, Junji Kishimoto, Tetsuya Yamada, Yoshihiro Ogawa. Effects of intensive exercise combined with dapagliflozin on body composition in patients with type 2 diabetes: a randomized controlled trial. Endocrine Journal. 2021.03; 68(3); 329-343
- 11. Martin Reincke, Adriana Albani, Guillaume Assie, Irina Bancos, Thierry Brue, Michael Buchfelder, Olivier Chabre, Filippo Ceccato, Andrea Daniele, Mario Detomas, Guido Di Dalmazi, Atanaska Elenkova, James Findling, Ashley B Grossman, Celso E Gomez-Sanchez, Anthony P Heaney, Juergen Honegger, Niki Karavitaki, Andre Lacroix, Edward R Laws, Marco Losa, Masanori Murakami, John Newell-Price, Francesca Pecori Giraldi, Luis G Pérez-Rivas, Rosario Pivonello, William E Rainey, Silviu Sbiera, Jochen Schopohl, Constantine A Stratakis, Marily Theodoropoulou, Elisabeth F C van Rossum, Elena Valassi, Sabina Zacharieva, German Rubinstein, Katrin Ritzel. Corticotroph tumor progression after bilateral adrenalectomy (Nelson's syndrome): systematic review and expert consensus recommendations. European Journal of Endocrinology. 2021.03; 184(3); P1-P16
- 12. Ryo Nakamaru, Koichi Yamamoto, Hiroshi Akasaka, Hiromi Rakugi, Isao Kurihara, Takashi Yoneda, Takamasa Ichijo, Takuyuki Katabami, Mika Tsuiki, Norio Wada, Tetsuya Yamada, Hiroki Kobayashi, Kouichi Tamura, Yoshihiro Ogawa, Junji Kawashima, Nobuya Inagaki, Megumi Fujita, Kenji Oki, Kohei

Kamemura, Akiyo Tanabe, Mitsuhide Naruse, . Sex Differences in Renal Outcomes After Medical Treatment for Bilateral Primary Aldosteronism. Hypertension. 2021.02; 77(2); 537-545

- 13. Crystal S Conn, Haojun Yang, Harrison J Tom, Kenji Ikeda, Juan A Oses-Prieto, Hieu Vu, Yasuo Oguri, Supna Nair, Ryan M Gill, Shingo Kajimura, Ralph J DeBerardinis, Alma L Burlingame, Davide Ruggero. The major cap-binding protein eIF4E regulates lipid homeostasis and diet-induced obesity. Nat Metab. 2021.02; 3(2); 244-257
- 14. Kikuko Amo-Shiinoki, Katsuya Tanabe, Yoshinobu Hoshii, Hiroto Matsui, Risa Harano, Tatsuya Fukuda, Takato Takeuchi, Ryotaro Bouchi, Tokiyo Takagi, Masayuki Hatanaka, Komei Takeda, Shigeru Okuya, Wataru Nishimura, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe, Takumi Akashi, Tetsuya Yamada, Yoshihiro Ogawa, Eiji Ikeda, Hiroaki Nagano, Yukio Tanizawa. Islet cell dedifferentiation is a pathologic mechanism of long-standing progression of type 2 diabetes. JCI Insight. 2021.01; 6(1);

[Conference Activities & Talks]

- 1. Mitsuyuki Numasawa, Nobutoshi Nawa, Yu Funakoshi, Kumiko Yamaguchi, Chiharu Kawakami, Mina Nakagawa. Comparison of the readiness of medical, dental, and nursing students for interprofessional learning. AMEE 2021 2021.08.27 The Virtual Conference
- 2. Kumiko Yamaguchi, Nobutoshi Nawa, Mitsuyuki Numasawa, Yu Funakoshi, Keiichi Akita. Evaluation of the effectiveness of multiple terminology test and e-learning materials in a human anatomy course. AMEE 2021 2021.08.27 The Virtual Conference
- 3. Yu Funakoshi, Nobutoshi Nawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Takeo Fujiwara, Keiichi Akita. The association between social capital and succeeding academic performance A multilevel analysis. AMEE 2021 2021.08.27 The Virtual Conference
- 4. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Yu Funakoshi, Janelle Moross, Jun Tsuruta. Remote interprofessional learning for students from health professions during COVID-19 pandemic. AMEE 2021 2021.08.27 The Virtual Conference
- 1. Development of Excel macro to automatically output files showing questionnaire data graphically. The 53rd Annual Meeting of the Japan Society for Medical Education 2021.07.30
- 2. The effectiveness of multiple terminology tests and e-learning materials in a human anatomy course. The 53rd Annual Meeting of the Japan Society for Medical Education 2021.07.30
- 3. The association between social capital and succeeding academic performance: A multilevel analysis. The 53rd Annual Meeting of the Japan Society for Medical Education 2021.07.30
- 4. Remote interprofessional learning for students from health professions during COVID-19 pandemic. The 53rd Annual Meeting of the Japan Society for Medical Education 2021.07.30
- 5. Analysis of the effect of interprofessional education by community medical practice in students. The 53rd Annual Meeting of the Japan Society for Medical Education 2021.07.30
- 6. Theory and Practice of Educational Program Evaluation: From the perspective of organizational projects on Institutional Research. The 53rd Annual Meeting of the Japan Society for Medical Education 2021.07.30

[Works]

1. Excel VBA macros for building adjacency matrix, Software, GitHub, 2021.08 - Now

Hepatobiliary and Pancreatic Surgery

Director & Professor Minoru Tanabe MD, PhD Associate Professor Atsushi Kudo MD, PhD Lecturer Keiichi Akahoshi MD, PhD(from November) Hiroaki Ono MD, PhD(from November) Assistant Professor Hiroki Ueda MD, PhD Yoshiya Ishikawa MD, PhD Shuichi Watanabe MD, PhD (from October) Daisuke Asano MD, PhD (from April) Graduate School Students Toshitaka Sugawara MD (until September) Takeshi Ishii MD Yoshiki Murase MD (until March) Aya Maekawa MD (until March) Kohei Yagi MD Hironari Yamashita MD Hiroyuki Ishida MD (until March) Koichiro Morimoto MD Munetaka Kimura MD (from April) Akira Ito MD (from April) Shotaro Gan MD (from April) Atsushi Nara 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:

- \cdot Biomolecular mechanisms of carcinogenesis, cancer growth, invasion and metastasis
- \cdot Molecular target the rapy for malignant diseases
- \cdot Cancer stem cell
- · Extended indication for hepatectomy
- \cdot The system of liver microcirculation

- \cdot Laparoscopic surgery for hepatobiliary and pancreatic cancers
- \cdot Liver transplantation and organ preservation
- \cdot Treatments for neuroendocrine tumor
- \cdot Innovation of imaging modality for hepatobiliary and pancreatic cancers
- \cdot 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

In 2021, the influence of surgery restrictions by COVID-19 was strong, and the total number of surgeries was 177 (255 in 2019), 44 hepatectomy and 67 pancreatic resection. It is one of the top-class high volume facilities in Japan and covers a wide variety of surgical procedures from characteristic minimally invasive surgery to extended surgery.

Laparoscopic surgery accounts for more than half of all cases, and laparoscopic surgery is about half for both hepatectomy and pancreatic resection, and the number of cases is increasing year by year. We expanded robotic pancreatectomy, which started in 2020, to include a new indication for pancreaticoduodenectomy: 4 robotic

pancreaticoduodenectomies and 1 pancreaticoduodenectomy were successfully performed.

The treatment of neuroendocrine tumors, which is a feature of our department, spans surgery, drug therapy, and radiotherapy, and we aim to improve results by performing multidisciplinary treatment. Last year, the cumulative number of first-visit patients exceeded 800, the largest number in Japan.

(7) **Publications**

[Original Articles]

- 1. Shotaro Matsudera, Yoshihito Kano, Yasuko Aoyagi, Kohki Tohyama, Kenta Takahashi, Yuichi Kumaki, Takahiro Mitsumura, Koichiro Kimura, Iichiro Onishi, Akira Takemoto, Daisuke Ban, Hiroaki Ono, Atsushi Kudo, Noriko Oshima, Kei Ogino, Shun Watanabe, Yukiko Tani, Takeshi Yamaguchi, Masanobu Nakajima, Shinji Morita, Satoru Yamaguchi, Masatoshi Takagi, Toshiaki Ishikawa, Tsuyoshi Nakagawa, Kentaro Okamoto, Hiroyuki Uetake, Minoru Tanabe, Satoshi Miyake, Takashi Tsuchioka, Kazuyuki Kojima, Sadakatsu Ikeda. A Pilot Study Analyzing the Clinical Utility of Comprehensive Genomic Profiling Using Plasma Cell-Free DNA for Solid Tumor Patients in Japan (PROFILE Study). Ann Surg Oncol. 2021.12; 28(13); 8497-8505
- 2. Ban D, Tanabe M, Kumamaru H, Nitta H, Otsuka Y, Miyata H, Kakeji Y, Kitagawa Y, Kaneko H, Wakabayashi G, Yamaue H, Yamamoto M. Safe Dissemination of Laparoscopic Liver Resection in 27,146 Cases Between 2011 and 2017 From the National Clinical Database of Japan. Ann Surg. 2021.12; 274(6); 1043-1050
- 3. Morimoto M, Monden K, Wakabayashi T, Gotohda N, Abe Y, Honda G, Abu Hilal M, Aoki T, Asbun HJ, Berardi G, Chan ACY, Chanwat R, Chen KH, Chen Y, Cherqui D, Cheung TT, Ciria R, Fuks D, Geller DA, Han HS, Hasegawa K, Hatano E, Itano O, Iwashita Y, Kaneko H, Kato Y, Kim JH, Liu R, López-Ben S, Rotellar F, Sakamoto Y, Sugioka A, Yoshizumi T, Akahoshi K, Alconchel F, Ariizumi S, Benedetti Cacciaguerra A, Durán M, García Vázquez A, Golse N, Miyasaka Y, Mori Y, Ogiso S, Shirata C, Tomassini F, Urade T, Nishino H, Kunzler F, Kozono S, Osakabe H, Takishita C, Ban D, Hibi T, Kokudo N, Ohtsuka M, Nagakawa Y, Ohtsuka T, Tanabe M, Nakamura M, Yamamoto M, Tsuchida A, Wakabayashi G. Minimally invasive anatomic liver resection: Results of a survey of world experts. J Hepatobiliary Pancreat Sci. 2021.12; 29(1); 33-40
- 4. Wakabayashi G, Cherqui D, Geller DA, Abu Hilal M, Berardi G, Ciria R, Abe Y, Aoki T, Asbun HJ, Chan ACY, Chanwat R, Chen KH, Chen Y, Cheung TT, Fuks D, Gotohda N, Han HS, Hasegawa K, Hatano E, Honda G, Itano O, Iwashita Y, Kaneko H, Kato Y, Kim JH, Liu R, López-Ben S, Morimoto M, Monden K, Rotellar F, Sakamoto Y, Sugioka A, Yoshiizumi T, Akahoshi K, Alconchel F, Ariizumi S, Benedetti Cacciaquerra A, Durán M, Garcia Vazquez A, Golse N, Miyasaka Y, Mori Y, Ogiso S, Shirata C, Tomassini F, Urade T, Wakabayashi T, Nishino H, Hibi T, Kokudo N, Ohtsuka M, Ban D, Nagakawa Y, Ohtsuka T, Tanabe M, Nakamura M, Tsuchida A, Yamamoto M. The Tokyo 2020 terminology of liver anatomy and resections: Updates of the Brisbane 2000 system. J Hepatobiliary Pancreat Sci. 2021.12; 29(1); 6-15
- 5. Kudo A, Tateishi U, Yoshimura R, Tsuchiya J, Yokoyama K, Takano S, Kobayashi N, Utunomiya D, Hata M, Ichikawa Y, Tanabe M, Hosono M, Kinuya S. Safety and Response after Peptide Receptor Radionuclide Therapy with 177 Lu-DOTATATE for Neuroendocrine Tumors in Phase 1/2 Prospective Japanese Trial. J Hepatobiliary Pancreat Sci. 2021.12;
- 6. Murase Y, Ono H, Ogawa K, Yoshioka R, Ishikawa Y, Ueda H, Akahoshi K, Ban D, Kudo A, Tanaka S, Tanabe M. Inhibitor library screening identifies ispinesib as a new potential chemotherapeutic agent for pancreatic cancers. Cancer Science. 2021.11; 112(11); 4641-4654
- 7. Gotohda N, Cherqui D, Geller DA, Abu Hilal M, Berardi G, Ciria R, Abe Y, Aoki T, Asbun HJ, Chan ACY, Chanwat R, Chen KH, Chen Y, Cheung TT, Fuks D, Han HS, Hasegawa K, Hatano E, Honda G, Itano O, Iwashita Y, Kaneko H, Kato Y, Kim JH, Liu R, López-Ben S, Morimoto M, Monden K, Rotellar F, Sakamoto Y, Sugioka A, Yoshiizumi T, Akahoshi K, Alconchel F, Ariizumi S, Benedetti Cacciaguerra A, Durán M, Garcia Vazquez A, Golse N, Miyasaka Y, Mori Y, Ogiso S, Shirata C, Tomassini F, Urade T, Wakabayashi T, Nishino H, Hibi T, Kokudo N, Ohtsuka M, Ban D, Nagakawa Y, Ohtsuka T, Tanabe M, Nakamura M, Yamamoto M, Tsuchida A, Wakabayashi G. Expert Consensus Guidelines: How to safely perform minimally invasive anatomic liver resection. J Hepatobiliary Pancreat Sci. 2021.11; 29(1); 16-32

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- 10. Nagakawa Y, Nakata K, Nishino H, Ohtsuka T, Ban D, Asbun HJ, Boggi U, He J, Kendrick ML, Palanivelu C, Liu R, Wang SE, Tang CN, Takaori K, Abu Hilal M, Goh BKP, Honda G, Jang JY, Kang CM, Kooby DA, Nakamura Y, Shrikhande SV, Wolfgang CL, Yiengpruksawan A, Yoon YS, Watanabe Y, Kozono S, Ciria R, Berardi G, Garbarino GM, Higuchi R, Ikenaga N, Ishikawa Y, Maekawa A, Murase Y, Zimmitti G, Kunzler F, Wang ZZ, Sakuma L, Takishita C, Osakabe H, Endo I, Tanaka M, Yamaue H, Tanabe M, Wakabayashi G, Tsuchida A, Nakamura M. International expert consensus on precision anatomy for minimally invasive pancreatoduodenectomy: PAM-HBP surgery project. J Hepatobiliary Pancreat Sci. 2021.11; 29(1); 124-135
- 11. Ito T, Fujimori N, Honma Y, Kudo A, Hijioka S, Katsushima S, Kimura Y, Fukutomi A, Hisamatsu S, Nakajima A, Shimatsu A. Long-term safety and efficacy of lanceotide autogel in Japanese patients with neuroendocrine tumors: Final results of a phase II open-label extension study. Asia Pacific J Clinical Oncology. 2021.10; 17(5); e153-e161
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- 13. Ito R, Kobayashi M, Ohtsuka K, Tanabe M, Okamoto R. A rare case of hepatocellular carcinoma with bile duct invasion diagnosed by peroral cholangioscopy. VideoGIE : an official video journal of the American Society for Gastrointestinal Endoscopy. 2021.08; 6(8); 354-357
- 14. Akasu M, Shimada S, Kabashima A, Akiyama Y, Shimokawa M, Akahoshi K, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Intrinsic activation of β -catenin signaling by CRISPR/Cas9-mediated exon skipping contributes to immune evasion in hepatocellular carcinoma. Scientific Reports. 2021.08; 11(1);
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- 25. Fukuda T, Bouchi R, Takeuchi T, Amo-Shiinoki K, Kudo A, Tanaka S, Tanabe M, Akashi T, Hirayama K, Odamaki T, Igarashi M, Kimura I, Tanabe K, Tanizawa Y, Yamada T, Ogawa Y. Importance of Intestinal Environment and Cellular Plasticity of Islets in the Development of Postpancreatectomy Diabetes. Diabetes Care. 2021.04; 44(4); 1002-1011
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- 29. Amo-Shiinoki K, Tanabe K, Hoshii Y, Matsui H, Harano R, Fukuda T, Takeuchi T, Bouchi R, Takagi T, Hatanaka M, Takeda K, Okuya S, Nishimura W, Kudo A, Tanaka S, Tanabe M, Akashi T, Yamada T, Ogawa Y, Ikeda E, Nagano H, Tanizawa Y. Islet cell dedifferentiation is a pathologic mechanism of long-standing progression of type 2 diabetes. JCI insight. 2021.01; 6(1);
- 30. Iwasaki T, Nara S, Nishimura Y, Ueda H, Kishi Y, Esaki M, Shimada K, Hiraoka N. Postoperative acute multiple organ failure after hepatectomy in a Nigerian male with sickle cell trait: a case report. Surg Case Rep. 2021.01; 7(1); 19
- 31. Kabashima Ayano, Shimada Shu, Shimokawa Masahiro, Akiyama Yoshimitsu, Tanabe Minoru, Tanaka Shinji. Molecular and immunological paradigms of hepatocellular carcinoma: Special reference to therapeutic approaches Journal of Hepato-Biliary-Pancreatic Sciences . 2021.01; 28(1); 62-75

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[Conference Activities & Talks]

- 1. Minoru Tanabe. Japanese Society of Gastroenterological Surgery. XX Semana Brasileria do Aparelho Digestivo 2021.11.26 Brasil (Web)
- 2. Minoru Tanabe. The Novel Treatment Strategies for Hepatocellular Carcinoma. The 32nd World Congress of International Association of Surgeons, Gastroenterologists and Oncologists 2021.11.21 Taiwan (Web)
- 3. Keiichi Akahoshi, Takeshi Ishii, Yoshiya Ishikawa, Kosuke Ogawa, Minoru Tanabe. Preliminary experience of surgical resection after lenvatinib therapy for advanced hepatocellular carcinoma. IASGO-CME Advanced Post-Graduate Course in Nagasaki 2021 2021.10.09 Web
- 4. Akira Ito, Keiichi Akahoshi, Daisuke Asano, Hiroki Ueda, Minoru Tanabe. A Case of Dissection Abscess Complicated by Hepatis Resection after Pancreaticoduodenectomy. IASGO-CME Advanced Post-Graduate Course in Nagasaki 2021 2021.10.09 Web
- 5. Minoru Tanabe. Knacks for laparoscopic Whipple operation based on a better understanding of anatomy around SMA and SMV. TAES Summer Meeting 2021.07.24 Taiwan (Web)
- 6. Minoru Tanabe. Registry Data and Clinical Trials Update. ILLS(INTERNATIONAL LAPAROSCOPIC LIVER SOCIETY) 3rd World Congress 2021.06.13 New York (Web)
- 7. Kohei Yagi, Hiroki Ueda, Koichiro Morimoto, Hironari Yamashita, Yoshiki Murase, Aya Maekawa, Takeshi Ishii, Toshitaka Sugawara, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akashoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, SHinji Tanaka, Minoru Tanabe. A review of resected cases of primary duodenal cancer in our hospital. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 8. Yoshiki Murase, Hiroaki Ono, Risa Yoshioka, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Kosuke Ogawa, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. High Eg5 expression predicts poor prognosis in pancreatic cancer. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 9. Aya Maekawa, Keiichi Akahoshi, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Validation of the international consensus guideline 2017 for intraductal papillary mucinous neoplasms. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 10. Keiichi Akahoshi, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Conversion surgery after lenvatinib treatment for advanced hepatocellular carcinoma. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 11. Keiichi Akahoshi. Surgical resection after lenvatinib therapy for HCC. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 12. Hiroyuki Ishida, Hiroki Ueda, Keiichi Akahoshi, Yoshiya Ishikawa, Hironari Yamashita, Koichiro Morimoto, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Early recurrence after curative hepatectomy for colorectal liver metastases. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 13. Yoshiya Ishikawa, Hiroyuki Ishida, Koichiro Morimoto, Hironari Yamashita, Hiroki Ueda, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Laparoscopic distal pancreatectomy for pancreatic ductal adenocarcinoma using supracolic anterior approach to the superior mesenteric artery. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka

- 14. Takeshi Ishii, Atsushi Kudo, Yoshiki Murase, Aya Maekawa, Toshitaka Sugawara, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Kousuke Ogawa, Hiroaki Ono, Shinji Tanaka, Minoru Tanabe. The management of GEP-NET with MEN type 1 in our department. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 15. Koichiro Morimoto, Keiichi Akahoshi, Hironari Yamashita, Hiroyuki Ishida, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Takeshi Ishii, Toshitaka Sugawara, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Granulomatous Langerhans isletitis followed by nivolumab-induced type 1 diabetes mellitus in a distal pancreatectomy: case report. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 16. Hiroki Ueda, Koichiro Morimoto, Hironari Yamashita, Hiroyuki Ishida, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Toshitaka Sugawara, Takeshi Ishii, Yoshiya Ishikawa, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Perioperative outcomes in elderly patients over 75-years-old undergoing distal pancreatectomy. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 17. Hiroaki Ono, Atsushi Kudo, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Kosuke Ogawa, Shinji Tanaka, Minoru Tanabe. Combination of Weekly Streptozocin and Oral S-1 Treatment is effective treatment for unresectable or metastatic pancreatic NET-G1 and NET-G2 patients. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 18. Kosuke Ogawa, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Minoru Tanabe. Analysis of completion rate of Gemcitabine/Nabpaclitaxel combination therapy for pancreatic cancer before and after pancreatectomy. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 19. Hironari Yamashita, Keiichi Akahoshi, Koichirou Morimoto, Hiroyuki Ishida, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Takeshi Ishii, Toshitaka Sugawara, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Effect of neoadjuvant chemotherapy on short-term outcome in patients undergoing pancreaticoduodenectomy for borderline resectable pancreatic cancer and resectable pancreatic cancer with elevated serum tumor markers. The 33rd Meeting of Japanese Society of Hepato-Billiary-Pancreatic Surgery 2021.06.02 Osaka
- 20. Minoru Tanabe. How to prevent bile duct injuries. ISDS webinar series 2021.05.08 Web
- 21. Kohei Yagi, Yoshiya Ishikawa, Daisuke Ban, Shuichi Watanabe Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Minoru Tanabe. Stomach retraction methods in laparoscopic distal pancreatectomy. The 33rd Annual Meeting of the Japan Society for Endoscopic Surgery 2021.03.12 Yokohama
- 22. Yoshiya Ishikawa, Daisuke Ban, Shuichi Watanabe, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Minoru Tanabe. Benefits of performing No.8 dissection from the left side of patient during LDP.. The 33rd Annual Meeting of the Japan Society for Endoscopic Surgery 2021.03.12 Yokohama
- 23. Daisuke Ban, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Kohei Ogawa, Hiroaki Ono, Atsushi Kudo, Ishikawa, Shuichi Watanabe, Hiroki Ueda, Kohei Ogawa, Hiroaki Ono, Atsushi Kudo, Minoru TanabeMinoru Tanabe. Hepatic vein approach is useful in advanced laparoscopic liver resection. The 33rd Annual Meeting of the Japan Society for Endoscopic Surgery 2021.03.11 Yokohama
- 24. Tomotaka Kato, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Comparison of open and laparoscopic hepatectomy for obese patients with HCC. The 33rd Annual Meeting of the Japan Society for Endoscopic Surgery 2021.03.10 Yokohama
- 25. Daisuke Ban, Minoru Tanabe. Reconsideration of the evaluation of difficulty score in laparoscopic liver resection. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.24 Yokohama
- 26. Minoru Tanabe. Pancreaticoduodenectomy "That's my technique" Future prospects . The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.24 Web
- 27. Daisuke Ban. Strategies to improve safety and peace for laparoscopic advanced liver resection. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.24 Web

- 28. Takeshi Ishii, Keiichi Akahoshi, Kohei Yagi, Aya Maekawa, Yoshiki Murase, Toshitaka Sugawara, Masafumi Akasu, Tomotaka, Kato, Yoshiya Ishikawa, Shuichi Watanabe, Kousuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical Analysis of 23 Cases of total pancreatectomy in Tokyo Medical and Dental University. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 29. Yasuhito Iwao, Minoru Tanabe, Nigel D Heaton. A review of the role of the retroportal artery in the blood supply of the biliary tree: Implications for hepato-pancreato-biliary and liver transplant surgeons. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 30. Yoshiki Murase, Hiroaki Ono, Kohei Yagi, Aya Maekawa, Takeshi Ishii, Tomotaka Kato, Masafumi Akasu, Toshitaka Sugawara, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Ogawa Kosuke, Daisuke Ban, Atsushi Kudo, Minoru Tanabe. Comparison of super-elderly and non-elderly patients in laparoscopic hepatectomy. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 31. Kohei Yagi, Atsushi Kudo, Aya Maekawa, Yoshiki Murase, Takeshi Ishii, Tomotaka Kato, Masafumi Akasu, Toshitaka Sugawara, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Ogawa Kosuke, Hiroaki Ono, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. Evaluation of laparoscopic distal pancreatectomy for pancreatic neuroendocrine tumors. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 32. Keiichi Akahoshi, Kohei Yagi, Yoshiki Murase, Takeshi Ishii, Toshitaka Sugawara, Yoshiya Ishikawa, Shuichi Watanabe, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Non-viral hepatocellular carcinoma and, diabetes and obesity as its risk factorslar carcinoma and, diabetes and obesity as its risk factors. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 33. Keiichi Akahoshi, Yoshiya Ishikawa, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Liver resection after systemic chemotherapy improved overallsurvival of metastatic neuroendocrine neoplasms. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 34. Hiroaki Ono, Tomotaka Kato, Aya Maekawa, Kouhei Yagi, Yoshiya Ishikawa, SHuichi Watanabe, Keiichi Akahoshi, Kousuke Ogawa, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Cytoplasmic RRM1 activation in acute phase of gemcitabine treatment is involved in acquired resistance of pancreatic cancer. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 35. Minoru Tanabe. "EmprintTM": Liver Cancer Ablation by Surgeon. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 36. Yoshiya Ishikawa, Daisuke Ban, Shuichi Watanabe, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Minoru Tanabe. Accidental dissection of left gastric artery during LDP, lessons learned from the case. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
- 37. Kosuke Ogawa, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Minoru Tanabe. Therapeutic Strategy of advanced Hepatocellular Carcinoma Analysis of advanced HCC operated cases who died of primary disease within one year after operation-. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web
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- 39. Toshiro Ogura, Akihumi Kimura, Amane Takahashi, Katsumi Amikura, Daisuke Ban, Minoru Tanabe, Hirohiko Sakamoto. Hepatic vein first approach; To set the goal first increases the quality of liver transection. The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2021.02.23 Web

1. Moyu KIMURA,Yu NISHIYAMA,Hiroki UEDA,Tomoyuki ARIMATSU,Mai KUBOKI,Atsushi TAKAHATA,Makiko SAITO,Shuji TOHDA,Ayako NOGAMI. Perioperative management of a PNH patient treated with ravulizumab: in case of gallstone disease. The 83rd Annual Meeting of the Japanese Society of Hematology 2021.09.23 Sendai

[Others]

1. 2021.02

Tanabe M, Moderator, Project study organized by JSHBPS, The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery, 20210223, Web

2. 2021.02

Tanabe M, Moderator, Special Session2 Advanced HBP surgery-New surgical device, Robotic surgery-, The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery, 20210223, Web

3. 2021.02

Tanabe M, Moderator, Luncheon Seminar
8 Open the new era of robotic-assisted pancreatectomy -safe introduction and future prospects-, The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery, 20210224, Web

4. 2021.02

Kudo A, Moderator, Workshop1 Surgical management for pancreatic neuroendocrine tumor, The 32nd Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery, 20210223, Web

5. 2021.06

Tanabe M, Moderator, Plenary session, The 33rd Meeting of Japanese society of Hepato-Biliary-Pancreatic Surgery, 20210603, Osaka

6. 2021.10

Minoru Tanabe, Chair, Poster Discussion A Liver2, IASGO-CME Advanced Post-Graduate Course in Nagasaki 2021, 20211009, Web Meeting

Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa Associate Professor: Toshitaka Yoshii Junior Associate Professor: Takashi Hirai Assistant Professor: Yuko Segawa, Hidetoshi Kaburagi, Yu Matsukura, Yuki Funauchi, Ryohei Takada Specially Appointed Assistant Professor: Naoto Watanabe, Yutaka Kobayashi, Jae-Sung An

□Department of Orthopaedic and Trauma Research」 Associate Professor: Hiroyuki Inose Junior Associate Professor: Yoto Oh Assistant Professor: Satoru Egawa

「Joint Research Department of Advanced Technology in Medicine」 Joint Research Professor: Shigenori Kawabata Visiting Professor∶ Kensuke Sekihara Junior Associate Professor: Yuko Hoshino

☐ Joint Research Department of Functional Joint Anatomy」 Joint Research Professor: Akimoto Nimura Junior Associate Professor: Koji Fujita Assistant Professor: Takuya Ibara

「Joint Research Department of Nano-Bioscience」 Joint Research Professor: Yoshinori Asou Joint Research Professor: Kunikazu Tsuji Assistant Professor: Hailati Aini

(1) Outline

The Department of Orthopaedic Surgery is in charge of "Orthopedic Surgery" in collaboration with the Department of Orthopaedic Joint Surgery, and is engaged in medical treatment, education, and research. The Department of Orthopedic Surgery deals with the skeletal system including bones, cartilage, joints, tendons, ligaments, and muscles, and the nervous system including spinal cord and peripheral nerves, and treats a wide variety of injuries and diseases including trauma, degeneration, tumors, and systemic bone diseases.

The Department also conducts a wide range of basic research and operations, including reconstruction of motor function of the spine and joints, clinical application of regenerative medicine methods, development of artificial materials and joint prostheses, biomechanical approaches, and pain control. In addition to conducting research by each specialty group, we actively collaborate other research facilities in order to elucidate the pathophysiology of intractable diseases and to develop state-of-the-art diagnostic testing methods.

(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

(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 methodoloy 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 in all Japan who are members of a nation-wide research organization for spinal ligament ossification.

(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 ossification of spinal ligaments, adult spinal deformity, and tumor of the spine are our other interest.

(7) Publications

[Original Articles]

- Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Toshitaka Yoshii, Shigenori Kawabata, Atsushi Okawa. Does surgical body position influence the risk for neurovascular injury in total hip arthroplasty? A magnetic resonance imaging study. Orthop Traumatol Surg Res. 2021.12; 102817
- 2. Satoshi Maki, Takeo Furuya, Toshitaka Yoshii, Satoru Egawa, Kenichiro Sakai, Kazuo Kusano, Yukihiro Nakagawa, Takashi Hirai, Kanichiro Wada, Keiichi Katsumi, Kengo Fujii, Atsushi Kimura, Narihito Nagoshi, Tsukasa Kanchiku, Yukitaka Nagamoto, Yasushi Oshima, Kei Ando, Masahiko Takahata, Kanji Mori, Hideaki Nakajima, Kazuma Murata, Shunji Matsunaga, Takashi Kaito, Kei Yamada, Sho Kobayashi,

Satoshi Kato, Tetsuro Ohba, Satoshi Inami, Shunsuke Fujibayashi, Hiroyuki Katoh, Haruo Kanno, Shiro Imagama, Masao Koda, Yoshiharu Kawaguchi, Katsushi Takeshita, Morio Matsumoto, Seiji Ohtori, Masashi Yamazaki, Atsushi Okawa. Machine Learning Approach in Predicting Clinically Significant Improvements After Surgery in Patients with Cervical Ossification of the Posterior Longitudinal Ligament. Spine (Phila Pa 1976). 2021.12; 46(24); 1683-1689

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- 4. Toshitaka Yoshii, Satoru Egawa, Kenichiro Sakai, Kazuo Kusano, Yukihiro Nakagawa, Takashi Hirai, Kanichiro Wada, Keiichi Katsumi, Kengo Fujii, Atsushi Kimura, Takeo Furuya, Narihito Nagoshi, Tsukasa Kanchiku, Yukitaka Nagamoto, Yasushi Oshima, Kei Ando, Masahiko Takahata, Kanji Mori, Hideaki Nakajima, Kazuma Murata, Shunji Matsunaga, Takashi Kaito, Kei Yamada, Sho Kobayashi, Satoshi Kato, Tetsuro Ohba, Satoshi Inami, Shunsuke Fujibayashi, Hiroyuki Katoh, Haruo Kanno, Shiro Imagama, Masao Koda, Yoshiharu Kawaguchi, Katsushi Takeshita, Morio Matsumoto, Masashi Yamazaki, Atsushi Okawa. Perioperative Complications in Posterior Surgeries for Cervical Ossification of the Posterior Longitudinal Ligament: A Prospective Nationwide Investigation. Clin Spine Surg. 2021.12; 34(10); E594-E600
- 5. Satoru Egawa, Toshitaka Yoshii, Kenichiro Sakai, Kazuo Kusano, Yukihiro Nakagawa, Takashi Hirai, Atsushi Kimura, Takeo Furuya, Tsukasa Kanchiku, Yukitaka Nagamoto, Masahiko Takahata, Kanji Mori, Hiroyuki Katoh, Narihito Nagoshi, Shiro Imagama, Masao Koda, Yoshiharu Kawaguchi, Katsushi Takeshita, Morio Matsumoto, Masashi Yamazaki, Atsushi Okawa. Prospective Investigation of Postoperative Complications in Anterior Decompression with Fusion for Severe Cervical Ossification of the Posterior Longitudinal Ligament: A Multi-institutional Study. Spine (Phila Pa 1976). 2021.12; 46(23); 1621-1629
- 6. Shimizu Masaki, Shimbo Asami, Yamazaki Susumu, Segawa Yuko, Mori Masaaki. Septic arthritis of the pubic symphysis in a patient with SLE PEDIATRICS INTERNATIONAL. 2021.12;
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- 9. Atsushi Okawa. Near future image of orthopedics after COVID-19 pandemic. J Orthop Sci. 2021.12;
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- 15. Kazuyoshi Kobayashi, Eijiro Okada, Toshitaka Yoshii, Mikito Tsushima, Tsuyoshi Yamada, Kei Watanabe, Keiichi Katsumi, Akihiko Hiyama, Hiroyuki Katoh, Masahiko Watanabe, Yukihiro Nakagawa, Motohiro Okada, Teruaki Endo, Yasuyuki Shiraishi, Kazuhiro Takeuchi, Shunji Matsunaga, Keishi Maruo, Kenichiro Sakai, Sho Kobayashi, Tetsuro Ohba, Kanichiro Wada, Junichi Ohya, Kanji Mori, Hirosuke Nishimura, Takashi Tsuji, Kota Watanabe, Atsushi Okawa, Morio Matsumoto, Shiro Imagama. Risk factors for delayed diagnosis of spinal fracture associated with diffuse idiopathic skeletal hyperostosis: A nationwide multiinstitution survey. J Orthop Sci. 2021.11; 26(6); 968-973
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- 21. Motoyoshi Takayuki, Hirai Takashi, Yoshii Toshitaka, Inose Hiroyuki, Matsukura Yu, Egawa Satoru, Kobayashi Yutaka, Utagawa Kurando, Hashimoto Jun, Kawabata Atsuyuki, Takahashi Takuya, Tanaka Tomoyuki, Okawa Atsushi. Association between diffuse idiopathic skeletal hyperostosis and thoracic kyphosis in patients with cervical myelopathy: a retrospective observational study. BMC Musculoskelet Disord. 2021.11; 22(1); 964
- 22. Hiroyuki Inose, Toshitaka Yoshii, Atsushi Okawa. Surgery with or without Fusion for Lumbar Spondylolisthesis. N Engl J Med. 2021.11; 385(19); 1823
- 23. Naoki Yamamoto, Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Kazuyoshi Yagishita, Atsushi Okawa. Wear rate and osteolysis in two types of second-generation annealed highly cross-linked polyethylene in total hip arthroplasty: A retrospective comparative study with a minimum of five years. Orthop Traumatol Surg Res. 2021.11; 103147

- 24. Hirotaka Chikuda, Yurie Koyama, Yoshitaka Matsubayashi, Toru Ogata, Hiroshi Ohtsu, Shurei Sugita, Masahiko Sumitani, Yuho Kadono, Toshiki Miura, Sakae Tanaka, Toru Akiyama, Kei Ando, Masato Anno, Seiichi Azuma, Kenji Endo, Toru Endo, Takayuki Fujiyoshi, Takeo Furuya, Hiroyuki Hayashi, Akiro Higashikawa, Akihiko Hiyama, Chiaki Horii, Seiji Iimoto, Yoichi Iizuka, Hisanori Ikuma, Shiro Imagama, Koichi Inokuchi, Hirokazu Inoue, Tomoo Inoue, Keisuke Ishii, Masayoshi Ishii, Takui Ito, Akira Itoi, Kohei Iwamoto, Motoki Iwasaki, Takashi Kaito, Tsuyoshi Kato, Hiroyuki Katoh, Yoshiharu Kawaguchi, Osamu Kawano, Atsushi Kimura, Kazuyoshi Kobayashi, Masao Koda, Miki Komatsu, Gentaro Kumagai, Takeshi Maeda, Takahiro Makino, Chikato Mannoji, Kazuhiro Masuda, Keisuke Masuda, Koji Matsumoto, Morio Matsumoto, Shunji Matsunaga, Yukihiro Matsuyama, Tokue Mieda, Kota Miyoshi, Joji Mochida, Hiroshi Moridaira, Hiroyuki Motegi, Yukihiro Nakagawa, Yutaka Nohara, Kazunori Oae, Shinji Ogawa, Rentaro Okazaki, Akinori Okuda, Eijiro Onishi, Atsushi Ono, Masashi Oshima, Yusuke Oshita, Kazuo Saita, Yutaka Sasao, Kimiaki Sato, Kimihiko Sawakami, Atsushi Seichi, Shoji Seki, Hideki Shigematsu, Kota Suda, Yasutaka Takagi, Masahito Takahashi, Ryosuke Takahashi, Eiji Takasawa, Shota Takenaka, Katsushi Takeshita, Yujiro Takeshita, Takamitsu Tokioka, Yasuaki Tokuhashi, Juichi Tonosu, Hiroshi Uei, Kanichiro Wada, Masahiko Watanabe, Tadashi Yahata, Kei Yamada, Taketoshi Yasuda, Keigo Yasui, Toshitaka Yoshii. Effect of Early vs Delayed Surgical Treatment on Motor Recovery in Incomplete Cervical Spinal Cord Injury With Preexisting Cervical Stenosis: A Randomized Clinical Trial. JAMA Netw Open. 2021.11; 4(11); e2133604
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[Misc]

1. Ochi J, Nozaki T, Nimura A, Yamaguchi T, Kitamura N. Subchondral insufficiency fracture of the knee: review of current concepts and radiological differential diagnoses. Jpn J Radiol. 2021.11;

[Conference Activities & Talks]

- 1. Toshitaka Yoshii. ANTERIOR APPROACH 「Avoidance of Dysphagia」. CSRS Asia Pacific 2nd Virtual Instructional Course 2021.12.11 WEB
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- 4. Takahisa Ogawa. Home visitng care for vulnerable patient with COVID-19 "KISA2TAI" ∼ Combining the skills of visiting physicians and digital technology to maximize health care resources as a system and strengthen resilience ∼. G1 global summit 2021.11.03
- 5. Suthasinee Tharnmanularp, Akimoto Nimura, Masahiro Tsutsumi, Keiichi Akita. An Anatomical Study Regarding the Medial Patellofemoral Ligament in Terms of Bone Morphology and Attaching Aponeurotic Structures. 16th Congress of the European Association of Clinical Anatomy (EACA) and XII Meeting of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2021.09.16 Web
- 6. Rintaro Yamamoto, Mizuki Izumida, Tohma Sakuraya, Kenji Emura, Takamitsu Arakawa, Akimoto Nimura, Keiichi Akita. The fibrous arrangement of flexor carpi ulnaris tendon at Guyon's canal. 16th Congress of the European Association of Clinical Anatomy (EACA) and XII Meeting of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2021.09.15 Web

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- 12. Yuko Segawa, Reiko Yamaguchi, Kazumasa Miyatake, Atsushi Okawa. Four-years experience with new screening system on developmental dysplasia of the hip. 13th Combined Meeting of Asia Pacific Spine Society & Asia Pacific Paediatric Orthopaedic Society 2021.06.09 online
- 13. Yasuhiro Oikawa, Jun Kakizaki, Rei Abe, Takuto Takeda, Akiko Yamamoto, Yuko Segawa, Takashi Saisu, Makoto Kamegaya, Seiji Ohtori. Arthroscopic treatment for septic arthritis in children. 13th Combined Meeting of Asia Pacific Spine Society & Asia Pacific Paediatric Orthopaedic Society 2021.06.09 online
- 14. Takahisa Ogawa, Tetsuya Jinno, Atsushi Okawa. Association between Hospital Surgical Volume and Complications after Total Hip Arthroplasty in Femoral Neck Fracture: a Propensity Score-matched Cohort Study. 94th Annual Meeting of the Japanese Orthopaedic Association 2021.05.20 Tokyo Japan
- 15. Toshitaka Yoshii. Cervical ossification of the posterior longitudinal ligament: Epidemiology, treatment. 94th Annual Meeting of the Japanese Orthopaedic Association 2021.05.20 Tokyo Japan
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[Patents]

- 1. BIOMAGNETISM MEASUREMENT DEVICE , Patent Number : US10952631
- 2. MAGNETIC MEASURING DEVICE, Patent Number : US10918293
- 3. BIOMAGNETISM MEASURING DEVICE, Patent Number : EP3494879
- 4. BIOLOGICAL INFORMATION MEASURING APPARATUS, Patent Number : US11076790
- 5. BIOLOGICAL INFORMATION MEASURING APPARATUS, Patent Number : US11076790
- 6. NERVE STIMULATION APPARATUS AND BIOMAGNETIC FIELD MEASUREMENT SYSTEM, Patent Number : ZL201680068325.0
- 7. DIAGNOSTIC SUPPORT SYSTEM AND DIAGNOSTIC SUPPORT METHOD, Patent Number: US11138746

Diagnostic Radiology and Nuclear Medicine

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(1) Outline

While diagnostic radiology and nuclear medicine demand high-level capabilities and therefore extensive training to acquire those capabilities, keeping a watch on developments in medical knowledge and maintaining those skills is also an issue for these disciplines. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Contributing to the community is a basic responsibility of diagnostic radiology so it remains the university's mission to unflinchingly fulfill its responsibility to provide high-level, advanced medical care, working toward resolution of community problems through education, research and medical activities, as well as to develop the diagnostic radiology professionals who will bear the responsibility for providing community medical care, and to develop professionals who have a global outlook and can flourish in this age of globalization. More than ever, advancing the fundamental medical concepts of "patient-oriented medical care" and "thorough medical safety management" are core principles in the field of diagnostic radiology and nuclear medicine, so continuing to maintain capabilities from this perspective is essential in daily practice. Under the new radiologist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiologist examination (sixth year after graduation). After passing that examination, it is then possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

Diagnostic radiology and nuclear medicine was divided off the specialist field responsible for diagnostic 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 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 18F-FDG (glucose metabolism), 11C-choline (lipid metabolism), 11C-acetate (lipid metabolism), 18F-FAZA (hypoxia), 18F-FACBC (amino acid metabolism), 62/64Cu-ATSM (redox), 18F-FLT (DNA synthesis), 18F-NaF (bone metabolism), 68Ga-DOTATATE (somatostatin receptor), and 18F-Fluorobetapir (Amyloid), 18F-Flutemetamol (Amyloid). The usefulness of multiple tracers in the discipline of oncology has been observed in numerous carcinomas. 177Lu-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

 \cdot CT: A total of three CT scanners are involved in diagnostic radiology: five in the radiology department and one in the ER center.

 \cdot MRI: A total of four MRI scanners are involved in diagnostic radiology: one 1.5-tesla scanners and four 3-tesla scanners. This has allowed for an increase in examinations.

 \cdot 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.

 \cdot 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.

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 Non-FDG tracers (C-11 acetate, F-18 FLT, F-18 FAZA, F-18 PSMA1007) for malignancies were introduced.

(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]

- Shotaro Matsudera, Yoshihito Kano, Yasuko Aoyagi, Kohki Tohyama, Kenta Takahashi, Yuichi Kumaki, Takahiro Mitsumura, Koichiro Kimura, Iichiro Onishi, Akira Takemoto, Daisuke Ban, Hiroaki Ono, Atsushi Kudo, Noriko Oshima, Kei Ogino, Shun Watanabe, Yukiko Tani, Takeshi Yamaguchi, Masanobu Nakajima, Shinji Morita, Satoru Yamaguchi, Masatoshi Takagi, Toshiaki Ishikawa, Tsuyoshi Nakagawa, Kentaro Okamoto, Hiroyuki Uetake, Minoru Tanabe, Satoshi Miyake, Takashi Tsuchioka, Kazuyuki Kojima, Sadakatsu Ikeda. A Pilot Study Analyzing the Clinical Utility of Comprehensive Genomic Profiling Using Plasma Cell-Free DNA for Solid Tumor Patients in Japan (PROFILE Study). Ann Surg Oncol. 2021.12; 28(13); 8497-8505
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- Toshiki Terao, Youichi Machida, Kentaro Narita, Ayumi Kuzume, Rikako Tabata, Takafumi Tsushima, Daisuke Miura, Masami Takeuchi, Ukihide Tateishi, Kosei Matsue. Total diffusion volume in MRI vs. total lesion glycolysis in PET/CT for tumor volume evaluation of multiple myeloma. Eur Radiol. 2021.08; 31(8); 6136-6144
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[Books etc]

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Genomic Function and Diversity

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MATSUZAWA Ayumi Graduate Student KATOU Daiki Student LIU Yuhan Student ZHUANG Zhaohui INAMO JUN

(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. To further seek disease susceptible loci for rheumatoid arthritis and systemic lupus erythematosus, we are performing GWAS meta-analysis in world-wide collaboration.

3. Using polygenic risk score (PRS), we established a statistical model to predict radiographic progression in rheumatoid arthritis.

4. Using long-read sequencing technology, we unraveled disease-associated structural and repetitive variants.

(3) Education

We lectured how to understand the etiology of complex traits through big data such as GWAS and eQTL/sQTL for undergraduate students and postgraduate students.

(4) Lectures & Courses

With the advent of research methods and technologies such as GWAS and next-generation sequencers, we can easily access to disease big-data in public databases. We will bring up young researchers to have skills to understand the fundamental of disease etiology by data-driven approaches.

(5) Publications

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- Mitsuhashi Satomi, Nakagawa So, Sasaki-Honda Mitsuru, Sakurai Hidetoshi, Frith Martin C., Mitsuhashi Hiroaki. Nanopore direct RNA sequencing detects DUX4-activated repeats and isoforms in human muscle cells HUMAN MOLECULAR GENETICS. 2021.04; 30(7); 552-563
- 12. Inamo J, Kochi Y, Takeuchi T. Is type 2 diabetes mellitus an inverse risk factor for the development of rheumatoid arthritis? Journal of human genetics. 2021.02; 66(2); 219-223
- 13. Watanabe K, Katagiri S, Takahashi H, Sasaki N, Maekawa S, Komazaki R, Hatasa M, Kitajima Y, Maruyama Y, Shiba T, Komatsu K, Ohsugi Y, Tanaka K, Matsuzawa A, Hirota T, Tohara H, Eguchi Y, Anzai K, Hattori A, Iwata T. Porphyromonas gingivalis impairs glucose uptake in skeletal muscle associated with altering gut microbiota FASEB JOURNAL. 2021.02; 35(2); e21171
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- 15. Inamo Jun, Kochi Yuta, Takeuchi Tsutomu. 2型糖尿病は関節リウマチ発症の逆危険因子であるか (Is type 2 diabetes mellitus an inverse risk factor for the development of rheumatoid arthritis?) Journal of Human Genetics. 2021.02; 66(2); 219-223
- 16. Mitsuhashi S, Frith MC, Matsumoto N. Genome-wide survey of tandem repeats by nanopore sequencing shows that disease-associated repeats are more polymorphic in the general population. BMC medical genomics. 2021.01; 14(1); 17
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- Frith MC, Mitsuhashi S, Katoh K. lamassemble: Multiple Alignment and Consensus Sequence of Long Reads. Methods in molecular biology (Clifton, N.J.). 2021; 2231; 135-145
- 19. Hirabayashi A, Yahara K, Mitsuhashi S, Nakagawa S, Imanishi T, Ha VTT, Nguyen AV, Nguyen ST, Shibayama K, Suzuki M. Plasmid analysis of NDM metallo- β -lactamase-producing Enterobacterales isolated in Vietnam. PloS one. 2021; 16(7); e0231119

Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka

(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

- Sagawa Y, Ogawa T, Matsuyama Y, Nakagawa Kang J, Yoshizawa Araki M, Unnai Yasuda Y, Tumurkhuu T, Ganburged G, Bazar A, Tanaka T, Fujiwara T, Moriyama K. Association between Smoking during Pregnancy and Short Root Anomaly in Offspring. International Journal of Environmental Research and Public Health. 2021.11; 18(21); 11662
- 2. Inagaki Y, Ogawa T, Tabata MJ, Nagata Y, Watanabe R, Kawamoto T, Moriyama K, Tanaka T. Identification of OPN3 as associated with non-syndromic oligodontia in a Japanese population. Journal of human genetics. 2021.02;

Applied Regenerative Medicine

Professor:Ichiro SEKIYA Assistant Professor: Hisako KATANO, Nobutake OZEKI Project Assistant Professor:Mitsuru MIZUNO, Kentaro ENDO, Yuji KOHNO Specially Appointed Researcher : Keiichiro KOMORI,Kimiko TAKANASHI Graduate Student:Yoshihisa KUSHIDA, So SUZUKI, Akinobu HYODO, Hayato AOKI Kiyotaka HORIUCHI, Rei KUBOTA, Shunichi FUJII, Yugo MIURA Hideto FURUOKA, Takahiro TANIMOTO, Seiya MATSUTA Misaki YAGI, Miku KOMURA Assistant Clerk:Harumi ANDO

(1) Outline

Stem cell medicine and regenerative medicine have been developing remarkably in recent years, and the competition for the advancement of regenerative medicine products to obtain a global market has been growing. We conduct basic research in the field of stem cell medicine and regenerative medicine from the viewpoint of practical application of regenerative medicine that shows high efficacy against existing therapies, and perform translational researcesh. In addition, we apply the results of our studies clinically and eventually aim at industrialization.

(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

We are working on basic, translational, and clinical researches with the aim of establishing a new treatment for knee osteoarthritis. Since 2000, we have discovered that mesenchymal stem cells derived from synovium (synovial MSCs) can highly differentiate into cartilage and meniscus, and that transplantation of these cells promotes the natural healing process. After these basic and translational studies using medium-sized animals, we started a physician-led clinical trial of autologous synovial stem cells for meniscus injury in August 2017. We made a patent license agreement with a company in March 2019, and are preparing for a corporate clinical trial, which will be a validation study, based on the results of the clinical trial completed in June 2019. In addition, we began a clinical study "Intra-articular injection of synovial MSCs for osteoarthritis of the knee" in December 2017 under the financial support of AMED Research for Practical Application of Regenerative Medicine (Principal Investigator: Ichiro Sekiya) to develop a treatment method using a new route of administration of synovial MSCs, and completed the observation period for all research subjects in March 2020. Currently, we are planning to conduct a comparative study as a physician-led clinical trial. In addition, we developed MRI 3D analysis software that can automatically display cartilage and meniscus in knee joints in collaboration with a company.

This software has been installed in a volume analyzer that is being commercialized in 2019 and is now widely used in orthopedic practice in Japan.

(4) **Publications**

- 1. Katsuaki Yanagisawa, Toshifumi Watanabe, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta, Tetsuya Jinno. Do the distal femur and the proximal tibia have narrower aspect ratios in smaller knees? : A morphological analysis of osteoarthritic knees in the Japanese population using computed tomography. Knee. 2021.12; 33; 84-92
- 2. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Yuji Kohno, Ichiro Sekiya. Surgical Repair of Symptomatic Wrisberg Variant Discoid Lateral Mensicus with Pull-Out Repair and Capsulodesis. Arthrosc Tech. 2021.12; 11(1); e61-e68
- 3. Mitsuru Mizuno, Kentaro Endo, Hisako Katano, Naoki Amano, Masaki Nomura, Yoshinori Hasegawa, Nobutake Ozeki, Hideyuki Koga, Naoko Takasu, Osamu Ohara, Tomohiro Morio, Ichiro Sekiya. Transplantation of human autologous synovial mesenchymal stem cells with trisomy 7 into the knee joint and 5 years of follow-up. Stem Cells Transl Med. 2021.11; 10(11); 1530-1543
- 4. Kentaro Endo, Kiyotaka Horiuchi, Hisako Katano, Nobutake Ozeki, Yuriko Sakamaki, Hideyuki Koga, Ichiro Sekiya. Intra-articular Injection of PDGF-BB Explored in a Novel in Vitro Model Mobilizes Mesenchymal Stem Cells From the Synovium Into Synovial Fluid in Rats. Stem Cell Rev Rep. 2021.10; 17(5); 1768-1779
- Hisako Katano, Nobutake Ozeki, Yuji Kohno, Yusuke Nakagawa, Hideyuki Koga, Toshifumi Watanabe, Tetsuya Jinno, Ichiro Sekiya. Trends in arthroplasty in Japan by a complete survey, 2014-2017. J Orthop Sci. 2021.09; 26(5); 812-822
- 6. Misaki Yagi, Mitsuru Mizuno, Ryota Fujisawa, Hisako Katano, Kentaro Endo, Nobutake Ozeki, Yuriko Sakamaki, Hideyuki Koga, Ichiro Sekiya. Optimal Pore Size of Honeycomb Polylactic Acid Films for In Vitro Cartilage Formation by Synovial Mesenchymal Stem Cells. Stem Cells Int. 2021.08; eCollection; 2021:9239728
- 7. Takashi Hoshino, Toshifumi Watanabe, Yusuke Nakagawa, Hiroki Katagiri, Nobutake Ozeki, Toshiyuki Ohara, Mikio Shioda, Yuji Kono, Ichiro Sekiya, Hideyuki Koga. Clinical outcomes of two-stage revision total knee arthroplasty in infected cases with antibiotic-loaded cement spacers produced using a handmade silicone mold. Knee Surg Relat Res. 2021.08; 33(1); 27
- Toshifumi Watanabe, Kazuyoshi Gamada, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta, Tetsuya Jinno. Consistent femoral external rotation during weight-bearing knee flexion is associated with better patient-reported pain and mediolateral balance after total knee arthroplasty. Clin Biomech (Bristol, Avon). 2021.08; 88; 105438
- Hiroko Ueki, Hiroki Katagiri, Kunikazu Tsuji, Kazumasa Miyatake, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Effect of transplanted mesenchymal stem cell number on the prevention of cartilage degeneration and pain reduction in a posttraumatic osteoarthritis rat model. J Orthop Sci. 2021.07; 26(4); 690-697
- 10. Hiroki Katagiri, Kaori Nakamura, Takeshi Muneta, Toshifumi Watanabe, Kazumasa Miyatake, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. Inflammatory and healing environment in synovial fluid after anterior cruciate ligament reconstruction: Granulocytes and endogenous opioids as new targets of postoperative pain. Biochem Biophys Rep. 2021.07; 26; 100981
- 11. Ichiro Sekiya, Hisako Katano, Mitsuru Mizuno, Hideyuki Koga, Jun Masumoto, Makoto Tomita, Nobutake Ozeki. Alterations in cartilage quantification before and after injections of mesenchymal stem cells into osteoarthritic knees. Sci Rep. 2021.07; 11(1); 13832
- 12. Kazumasa Kawata, Hideyuki Koga, Kunikazu Tsuji, Kazumasa Miyatake, Yusuke Nakagawa, Takanori Yokota, Ichiro Sekiya, Hiroki Katagiri. Extracellular vesicles derived from mesenchymal stromal cells mediate endogenous cell growth and migration via the CXCL5 and CXCL6/CXCR2 axes and repair menisci. Stem Cell Res Ther. 2021.07; 12(1); 414

- Nobutake Ozeki, Yusuke Nakagawa, Mitsuru Mizuno, Yuji Kohno, Hisako Katano, Hideyuki Koga, Ichiro Sekiya. Ultrasound-Guided Harvesting of Synovium for Regenerative Medicine of Cartilage and Meniscus Using Synovial Mesenchymal Stem Cells. Arthrosc Tech. 2021.07; 10(7); e1723-e1727
- 14. Ichiro Sekiya, Yuji Kohno, Akinobu Hyodo, Hisako Katano, Keiichiro Komori, Hideyuki Koga, Makoto Tomita, Kenji Suzuki, Jun Masumoto, Nobutake Ozeki. Interscan measurement error of knee cartilage thickness and projected cartilage area ratio at 9 regions and 45 subregions by fully automatic three-dimensional MRI analysis. Eur J Radiol. 2021.06; 139; 109700
- 15. Kiyotaka Horiuchi, Nobutake Ozeki, Kentaro Endo, Mitsuru Mizuno, Hisako Katano, Masako Akiyama, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Thawed cryopreserved synovial mesenchymal stem cells show comparable effects to cultured cells in the inhibition of osteoarthritis progression in rats. Sci Rep. 2021.05; 11(1); 9683
- 16. Kiyotaka Horiuchi, Mitsuru Mizuno, Hisako Katano, Kentaro Endo, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Optimal initial cell density that yields the highest number of primary synovial mesenchymal stem cells in a clinical setting. J Med Dent Sci. 2021.04; 68; 17-26
- 17. J-S An, K Tsuji, H Onuma, N Araya, M Isono, T Hoshino, K Inomata, J Hino, M Miyazato, H Hosoda, K Kangawa, Y Nakagawa, H Katagiri, K Miyatake, I Sekiya, T Muneta, H Koga. Inhibition of fibrotic changes in infrapatellar fat pad alleviates persistent pain and articular cartilage degeneration in monoiodoacetic acid-induced rat arthritis model. Osteoarthritis Cartilage. 2021.03; 29(3); 380-388
- Ichiro Sekiya, Hisako Katano, Nobutake Ozeki. Characteristics of MSCs in Synovial Fluid and Mode of Action of Intra-Articular Injections of Synovial MSCs in Knee Osteoarthritis. Int J Mol Sci. 2021.03; 22(6); 2838
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- 21. Weiding Cui, Yusuke Nakagawa, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Takashi Hoshino, Aritoshi Yoshihara, Ichiro Sekiya, Hideyuki Koga. Knee laxity, lateral meniscus tear and distal femur morphology influence pivot shift test grade in ACL injury patients. Knee Surg Sports Traumatol Arthrosc. 2021.02; 29(2); 633-640
- 22. Nobutake Ozeki, Yuji Kohno, Yoshihisa Kushida, Naoto Watanabe, Mitsuru Mizuno, Hisako Katano, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Synovial mesenchymal stem cells promote the meniscus repair in a novel pig meniscus injury model. J. Orthop. Res. 2021.01; 39(1); 177-183
- 23. Nobutake Ozeki, Romain Seil, Aaron J Krych, Hideyuki Koga. Surgical treatment of complex meniscus tear and disease: state of the art. J ISAKOS. 2021.01; 6(1); 35-45

- 1. Ichiro Sekiya. Intraarticular injections of mesenchymal stem cells in knee osteoarthritis.. Osteoarthritis Research Society International 2021 2021.04.29 WEB
- 2. Nobutake Ozeki, Hiroki Katagiri, Yusuke Nakagawa , Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga.. Ramp lesions in anterior cruciate ligament deficient knees.. 2nd International Knee Day 2021.03.18 WEB
- 3. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Yuji Kohno, Hisako Katano, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya.. 3D MRI Analysis For Cartilage In Anterior Cruciate Ligament Deficient Knees Using Radially Projected Images.. Orthopaedic Research Society 2021 Annual Meeting 2021.02.12 California, USA
- 4. Yugo Miura, Nobutake Ozeki, Yuji Kohno, Hisako Katano, Hayato Aoki, Noriya Okanouchi, Makoto Tomita, Kenji Suzuki, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya.. Difference In The Joint Space Of The Medial Knee Compartment Between Full Extension And Rosenberg Weight-bearing Radiographs.. Orthopaedic Research Society 2021 Annual Meeting 2021.02.12 California,USA

Frontier Biomaterials

Tsuyoshi KIMURA

(1) Research

1) Specific capture of Treg cells

In order to remove Treg cells, which induce immunotolerance, a device of capturing of Treg cells is developed. 2) Decellularization of native tissue for regenerative medicine

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

3) Inducing molecular aggregation using ultra-high pressurization

The basic and applied science on molecular aggregation triggered by hydrogen bonding at over 6,000 atm is studied. This technique is being applied for hybridization of DNA with polymer for drug delivery system. 4) Bio-interface

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

(2) Education

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

(3) Publications

[Original Articles]

- 1. Tsuyoshi Kimura, Rino Tokunaga, Yoshihide Hashimoto, Naoko Nakamura, Akio Kishida. Tumor growth suppression by implantation of an anti-CD25 antibody-immobilized material near the tumor via regulatory T cell capture Science and Technology of Advanced Materials. 2021.08; 22(1); 607-615
- 2. Mako Kobayashi, Masako Ohara, Yoshihide Hashimoto, Naoko Nakamura, Toshiya Fujisato, Tsuyoshi Kimura, Akio Kishida. Effect of luminal surface structure of decellularized aorta on thrombus formation and cell behavior PLoS One. 2021.05; 16(5); e0246221

[Conference Activities & Talks]

1. Mika Suzuki, Yuta Nakano, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Noko Nakamura, Tsuyoshi Kimura, Akio Kishida. Recellularization of partially mineralized membranous decellularized tissue for locomotor regeneration. MRM2021 2021.12.13 Kanagawa, Japan

- 2. Tsuyohi Kimura, Rino Tokunaga, Yoshihide Hashimoto, Naoko Nakamura, Akio Kishida. Tumor growth suppression by releasing cancer immune suppression using an anti-CD25 antibody-immobilized material. MRM2021 2021.12.13 Kanagawa, Japan
- 3. Mika Suzuki, Yuta Nakano, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Naoko Nakamura, Tsuyoshi Kimura, Akio Kishida . Preparation of a mineralized decellularized pericardium by alternate soaking for enhancing bone affinity. ISBE2021 2021.12.02 Web
- 4. Tsuyoshi Kimura, Eri Yasuda, Yoshihide Hashimoto, Ikuro Suzuki, Naoko Nakamura, Akio Kishida. Classification of HHP and SDS decellularized tissue histology images using artificial intelligence. ISBE2021 2021.12.02 Web
- 5. Yoshihide Hashimoto, Akitatsu Yamashita, Jun Negishi, Tsuyoshi Kimura, Seiichi Funamoto, Akio Kishida. Four-arm PEG-functionalized decellularized pericardium as an effective post-operative pericardial adhesion barrier. ISBE2021 2021.12.02 Web
- 6. Tsuyoshi Kimura, Mika Suzuki, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Naoko Nakamura, Akio Kishida. In vitro tissue reconstruction using decellularized pericardium cultured with cells for ligament regeneration. 2021 6th TERMIS-WC 2021.11.15 Web
- 7. Mako Kobayashi, Naoki Ishida, Yoshihide Hashimoto, Jun Negishi, Hideki Saga, Yoshihiro Sasaki, Kazunari Akiyoshi, Tsuyoshi Kimura, Akio Kishida. Extraction of matrix-bound nanovesicles (MBVs) from high-hydrostatic pressure decellularized tissue and evaluation on vascular endothelial cells. 2021 6th TERMIS-WC 2021.11.15 Web
- 8. Shota Toda, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Preparation of macrophage adhering particles for immunological evaluation of biomaterials . 2021 6th TERMIS-WC 2021.11.15 Web

[Patents]

- 1. HYBRID GEL CONTAINING PARTICULATE DECELLULARIZED TISSUE, Patent Number: CA2911592
- 2. METHOD FOR PRODUCING PARTICULATE DECELLULARIZED TISSUE, Patent Number: KR2240373
- 3. HYBRID GEL CONTAINING PARTICULATE DECELLULARIZED TISSUE, Patent Number: KR2339700
- 4. ANTI-ADHESION MATERIAL AND ARTIFICIAL BIOLOGICAL MEMBRANE EACH COMPRISING DECELLULARIZED TISSUE, Patent Number : US11033661
- 5. ANTI-ADHESION MATERIAL AND SUBSTITUTE BIOMEMBRANE USING DECELLULARIZED TISSUE, Patent Number : BR112017018772-8
- 6. METHOD FOR PRODUCING PARTICULATE DECELLULARIZED TISSUE, Patent Number: EP3556406

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, Ayumi Fujimoto, Hironobu Sugita, Saho Matsui Hisamichi Tanaka, Nana Kamakura

(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, including functional RNAs and Histone variants (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 the molecular background and pathological significance of chromosomal instability of cancer cells, and to explore strategies to target chromosomal instability (Hirota)

(3) Publications

[Original Articles]

 Kunieda J, Yamashita K, Togashi Y, Baba S, Sakata S, Inamura K, Ae K, Matsumoto S, Machinami R, Kitagawa M, Takeuchi K. High prevalence of TERT aberrations in myxoid liposarcoma: TERT reactivation may play a crucial role in tumorigenesis. Cancer Sci. 2021.

- Kure S, Chiba T, Ebina A, Toda K, Jikuzono T, Motoda N, Mitani H, Sugitani I, Takeuchi K, Ohashi R. Correlation between low expression of protein disulfide isomerase A3 and lymph node metastasis in papillary thyroid carcinoma and poor prognosis: a clinicopathological study of 1,139 cases with long-term follow-up. *Endocr* J. 2021.
- Hoshino M, Inoue K, Kaneda T, Nishimura M, Kusama K, Sakashita H, Sato Y, Takeuchi K, Nagao T, Kikuchi K. A Case of Buccal Clear Cell Carcinoma Caused by Rare Fusion Gene: EWSR1-CREM. *Case Rep Dent*. 2021;2021:5557247.
- 4. Kogure Y, Kameda T, Koya J, Yoshimitsu M, Nosaka K, Yasunaga JI, Imaizumi Y, Watanabe M, Saito Y, Ito Y, McClure MB, Tabata M, Shingaki S, Yoshifuji K, Chiba K, Okada A, Kakiuchi N, Nannya Y, Kamiunten A, Tahira Y, Akizuki K, Sekine M, Shide K, Hidaka T, Kubuki Y, Kitanaka A, Hidaka M, Nakano N, Utsunomiya A, Sica RA, Acuna-Villaorduna A, Janakiram M, Shah UA, Ramos JC, Shibata T, Takeuchi K, Takaori-Kondo A, Miyazaki Y, Matsuoka M, Ishitsuka K, Shiraishi Y, Miyano S, Ogawa S, Ye BH, Shimoda K, Kataoka K. Whole-genome landscape of adult T-cell leukemia/lymphoma. *Blood*. 2021.
- Yamashita K, Funauchi Y, Hayakawa K, Ae K, Matsumoto S, Ikuta K, Nishida Y, Ueno T, Shimoyama Y, Hiruta N, Machinami R, Kawachi H, Takeuchi K. S100-negative epithelioid malignant peripheral nerve sheath tumor with possible perineurial differentiation. *Virchows Arch*. 2021.
- Okumura S, Konishi Y, Narukawa M, Sugiura Y, Yoshimoto S, Arai Y, Sato S, Yoshida Y, Tsuji S, Uemura K, Wakita M, Matsudaira T, Matsumoto T, Kawamoto S, Takahashi A, Itatani Y, Miki H, Takamatsu M, Obama K, Takeuchi K, Suematsu M, Ohtani N, Fukunaga Y, Ueno M, Sakai Y, Nagayama S, Hara E. Gut bacteria identified in colorectal cancer patients promote tumourigenesis via butyrate secretion. *Nat Commun*. 2021;12:5674.
- Yu YT, Takeuchi K, Baba S, Chang KC. Morphologically Suspected Burkitt-like Lymphoma With 11q Aberrations Confirmed by Fluorescence In Situ Hybridization. *Am J Surg Pathol*. 2021.
- Osako T, Kurisaki-Arakawa A, Dobashi A, Togashi Y, Baba S, Shiozawa S, Ishigame H, Ishige H, Ohno S, Ishikawa Y, Takeuchi K. Distinct Clinicopathologic Features and Possible Pathogenesis of Localized ALK-positive Histiocytosis of the Breast. Am J Surg Pathol. 2021.
- 9. Sugiura Y, Machinami R, Matsumoto S, Kanda H, Ae K, Takazawa Y, Takeuchi K. Prognostic value of CD34 expression status in patients with myxofibrosarcomas and

undifferentiated pleomorphic sarcomas. Sci Rep. 2021;11:15494.

- 10. Nishimura Y, Fajgenbaum DC, Pierson SK, Iwaki N, Nishikori A, Kawano M, Nakamura N, Izutsu K, Takeuchi K, Nishimura MF, Maeda Y, Otsuka F, Yoshizaki K, Oksenhendler E, van Rhee F, Sato Y. Validated international definition of the thrombocytopenia, anasarca, fever, reticulin fibrosis, renal insufficiency, and organomegaly clinical subtype (TAFRO) of idiopathic multicentric Castleman disease. *Am J Hematol.* 2021;96:1241-1252.
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- Akiya M, Osako T, Morizono H, Furuta N, Kikuchi M, Ueno T, Ohno S, Takeuchi K. Myofibroblastoma of the breast showing rare palisaded morphology and uncommon desmin- and CD34-negative immunophenotype: A case report. *Pathol Int.* 2021;71:548-555.
- 13. Yoshizawa T, Uchibori K, Araki M, Matsumoto S, Ma B, Kanada R, Seto Y, Oh-Hara T, Koike S, Ariyasu R, Kitazono S, Ninomiya H, Takeuchi K, Yanagitani N, Takagi S, Kishi K, Fujita N, Okuno Y, Nishio M, Katayama R. Microsecond-timescale MD simulation of EGFR minor mutation predicts the structural flexibility of EGFR kinase core that reflects EGFR inhibitor sensitivity. *NPJ Precis Oncol.* 2021;5:32.
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[Review Articles]

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- Toru Hirota "The robust control of metaphase-to-anaphase transition preventing chromosome missegregation" 11th Salk Institute Cell Cycle Meeting. June 23-26, 2021. Invited.
- 2. Toru Hirota "How karyotypic evolution is controlled in cancer stem cells" Seminar at the Okinawa Institute of Science and Technology, March 24, 2021.
- <u>3.</u> Takuro Nakamura Targeting the gene regulatory network in cancer: Modeling leukemia and sarcoma. The 39th Sapporo International Cancer Symposium, July 5, 2021.

Organogenesis and Neogenesis

Takanori Takebe, MD, PhD, Professor Yosuke Yoneyama, PhD, Assistant Professor Shogo Nagata, DVM, PhD, Assistant Professor Norikazu Saiki, PhD, Project Assistant Professor Daisuke Hishikawa, PhD, Project Assistant Professor Shunsuke Mori, PhD, Project Assistant Professor Rie Ouchi-Koike, PhD, Project Researcher Ichiro Fukunaga, PhD, Project Researcher Ryo Okabe, Part-time Lecturer Yoshihiro Shimada, Part-time Lecturer Fumiya Moribe, Part-time Lecturer Mari Maezawa, Research Assistant Kanae Ohtsu, Research Assistant Naoko Sekinami, Technical Assistant Michiko Mori, Administrative Assistant Noriko Yokota, Administrative Assistant Xu Zeyu, Graduate Student Zhang Jianchun, Graduate Student Hitomi Yamaguchi, Graduate Student Shuntaro Kawamura, Graduate Student Asei Hirai, Graduate Student

(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

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- 2. Takebe T. Human organoids in precision toxicology. 2021 KSOT/KEMS conference inKorea 2021.11.01
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- 6. Takebe T. Engineering Organoids and Organs. Cell Symposia 2021.04.26
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Department of Integrated Analytics

Specialy Appointed ProfessorMIYNO SatoruAssociate ProfessorHASEGAWA TakanoriAssistant ProfessorITO SatoshiSpecially Appointed Assistant ProfessorKAKUTA MasanoriSpecially Apointed Assistant ProfessorOGAWA MihoProject ResearcherTANAKA HirokoGuest ProfessorOKAMOTO SeishiGuest ProfessorMARUHASHI Koji

(1) **Outline**

We will develop new mathematical analysis methods using bioinformatics and artificial intelligence technologies for integrated analysis of multidimensional and ultra-heterogeneous big data in the medical field such as medicine and dentistry.

By using advanced information processing technologies such as supercomputers and artificial intelligence, we aim to elucidate biological and biological systems, discover drugs, and build the foundation for new treatment strategies.

Research Topics

- 1. Knowledge discovery from big data using supercomputers and artificial intelligence technology
- 2. Elucidation of origin and diversity of cancer by large-scale data analysis and mathematical modeling
- 3. Multi-omics large-scale data analysis research
- 4. Research on system modeling and simulation of pathological conditions

(2) Research

Development and application of mathematical analysis methods for biological big data

The pathophysiology of the disease is a situation in which control abnormalities affect each other in a complex manner due to the influence of multiple genes and the environment including the intestine and skin, and in particular, cancer is a state that deviates from integrated control as a system. In the field of integrated data science, we will integrate ultra-multidimensional and ultra-heterogeneous biological big data such as genome and other omics data, pathological conditions, and environmental data by making full use of cutting-edge computational science strategies and information processing technologies such as supercomputers. Study mathematical methodologies to analyze and their applications. By doing so, we will clarify the mechanism of the breakdown of the biological and biological systems called pathological conditions, and develop the results into drug discovery and therapeutic method development.

Adopted by the Ministry of Education, Culture, Sports, Science and Technology "FUGAKU" result creation acceleration program, and conducted research on "elucidation of the origin and diversity of cancer by large-scale data analysis and artificial intelligence technology" (jointly with the field of AI technology development).

Construction of integrated analysis platform for M & D data and promotion of cooperation system

Medical dentistry and medical research are entering a new era in terms of both quality and quantity of information. In the analysis of health status and diseases, it is common to acquire and use a large amount of biological information through genomic information analysis and single cell analysis, and by analyzing such information in an integrated manner, new findings and new findings can be obtained. It has become possible to create treatment strategies for diseases. Based on this situation, in the field of integrated analysis, we will practice integrated analysis of medical big data of our university by organically collaborating with existing organizations. Then we promote information education and the construction of information infrastructure necessary for integrated analysis.

In particular, we developed the activities of the "Medical Data Society Return WG" established at Tokyo Medical and Dental University. In addition, a new 1PB storage server was introduced to build a system that connects the hospital DWH and the disease bio-resource center. A new data science infrastructure was built at Tokyo Medical and Dental University.

(3) Education

We joined the following activities:

- [Undergraduate School]
- Introduction to Medical Care and AI / Big Data
- Mathematical/DS/AI Education Literacy Level WG
- Basic Research Physician Program
- Public Health Education Course
- Consortium for Strengthening Mathematical and Data Science Education
- Support for the "TMDU Mathematics Club"
- Hosted the "National Medical and AI Contest" for undergraduate students
- Respond to inquiries about data science from undergraduate students

[Graduate School]

- Introduction to Medical Data Science (Master Course)
- Data Science Special Lecture II (English version) (hosted by Professor Kunihiko Takahashi)
- Data Science Special Lecture 1 (English version) (hosted by Professor Kunihiko Takahashi)
- Support for research/career inquiries from graduate students

(4) Lectures & Courses

Our education policy is to enable students in clinical/basic research to independently perform data science. Not just for data analysis support, we foster world top-level biomedical data scientists at Tokyo Medical and Dental University.

(5) Clinical Services & Other Works

1. To support COVID-19, Tokyo Medical and Dental University, Keio University School of Medicine, Department of Oncology, Graduate School of Medicine, Kyoto University, Department of Genetic Statistics, Graduate School of Medicine, Osaka University, Human Genome Analysis Center, Institute of Medical Science, University of Tokyo Became the main founder and created a network-type research organization called " the Coronavirus Task Force". About 120 hospitals from all over the country participated, and currently, about 6,000 samples had been collected. Host whole-genome analysis and RNA sequence analysis are performed on more than 1,200 of these samples to search for aggravating factors.

2. Through this task force, we are participating in the International COVID-19 Consortium.

3. We actively conducted cancer genomics research with a group such as Professor Seishi Ogawa of Kyoto

(6) Publications

- 1. COVID-19 Host Genetics Initiative. Mapping the human genetic architecture of COVID-19. Nature. 2021.12; 600(7889); 472-477
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- 10. Mapping the human genetic architecture of COVID-19 Nature. 2021.07;
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[Works]

1. Virtual Grid Engine, Software, IEEE BIBM2018, 2018.12 - Now

Department of Biostatistics

Professor TAKAHASHI Kunihiko Junior Associate Professor ANZAI Tatsuhiko Assistant Professor ITO Tsubasa

(1) Outline

Biostatistics has a central role in medical research. We aim to develop methodologies for data analysis focused on medical, dental and healthcare applications, and will collaborate on practical research.

(2) Research

1) Methodology development for data analysis in M&D field

We are developing biostatistical methodologies for data analysis in the field of M&D. Our focus includes methodologies and applications for spatial epidemiological research with geographic and temporal data, disease surveillance and monitoring, real-world data (RWD) analysis, meta-analysis, dynamic modeling, and their implementation in software.

2) Practical research on M&D field

Another focus is joint research in the field of M&D with medical, dental, and healthcare professionals. Some of our contributions include the design and analysis of any types of medical/clinical, health related studies.

(3) Education

Data Science I, Biostatistics I, Clinical Biostatistics and Statistical Genetics.

(4) Lectures & Courses

The objective of this course is to master methodologies in biostatistics, and will be able to interpret the results of data analysis in medical research.

(5) Publications

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- 2. Ayumi Fujimoto, Tatsuhiko Anzai, Takahiro Fukuda, Naoyuki Uchida, Takanori Ohta, Takehiko Mori, Masashi Sawa, Satoshi Yoshioka, Toshihiro Miyamoto, Hitoji Uchiyama, Yuta Katayama, Ken-ichi Matsuoka, Souichi Shiratori, Hideyuki Nakazawa, Junya Kanda, Tatsuo Ichinohe, Yoshiko Atsuta, Eisei Kondo, Ritsuro Suzuki.. Impact of Event-Free Survival Status after Stem Cell Transplantation on Subsequent Survivalin Lymphoma Patients.. The 2021 Transplantation & Cellular Therapy Meetings 2021.02

Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi Junior Associate Professor: Takahiro Arakawa (~2021.9, Lecturer (part-time): 2021.10~) Assistant Professor: Koji Toma (~2021.10, Junior Associate Professor: 2021.11~) Project Assistant Professor: Kenta Iitani Lecturer (part-time): Kazuyoshi Yano Lecturer (part-time): Yasuhiko Iwasaki Lecturer (part-time): Naoya Takeda Lecturer (part-time): Ming Ye Lecturer (part-time): Tomoko Gessei

(1) Outline

Our research is based on a broad range of areas such as electrochemistry, mechanical engineering, electrical engineering, material science and biochemistry. The group aims to pursue interdisciplinary research in bio-MEMS, bio-optics, bio-electronics or bioinformatics by combining biotechnology and information technology.

(2) Research

1. Detachable "Cavitas sensors" as bioinformation monitoring systems in body cavities "Cavitas sensors" such as a soft contact-lens biosensor and a mouth guard biosensor have been developed for novel biomonitoring methods by using advanced polymer microelectromechanical systems (MEMS) techniques.

2. Biochemical gas sensor "Bio-sniffers" and spatiotemporal gas visualization system "Sniff-camera" for volatile organic compounds from human body

Highly selective gas sensors "Bio-sniffers" and gas visualization systems "Sniff-camera" for acquiring spatiotemporal information of distribution of volatile chemicals have been developed by exploiting metabolizing enzymes in human liver. Potential applications of these gas sensors include halitosis analysis, breath alcohol and aldehyde measurement, medical screening or dental health, etc.

3. Immunosensors for medical treatment and environmental medicine

Development of optical or surface acoustic wave immunosensors have been pursued for semi-continuos (rapid and repeated) measurement of antigens in body and airborne allergens in living environment.

4. "Organic engine" and "Air bio-battery" based on chemo-mechanical energy conversion

Novel chemo-mechanical energy conversion systems (Organic engine and Air bio-battery) that utilize enzyme reactions and active transport of chemicals has been constructed. Biomedical applications (chemical pumps, drug release systems, etc.) are also investigated.

(3) Education

In advanced medicine, technologies enabling to accurately measure biological information are highly demanded. The development of "human-friendly" non-invasive measurement methods could release patients from the pain and the risks of sampling. The students will learn the basic knowledge and skills of biological information measurement through the lectures (e.g., "Biomedical Engineering", "Biomedical Device Science and Engineering", "Wearable & IoT Devices and Applications", "Advanced Biomedical Devices", "Integrative Biomedical Sciences for Preemptive Medicine", and "Advanced Medical Device and System"), seminars and practical training. Especially research including biochemical measurement, the development of biosensing devices and their applications to medicine will be carried out based on "sensor and biomedical engineering.

(4) Lectures & Courses

The students will learn the basic technology related to advanced medicine and biological information measurement. Through practical training, they will also engage in research activities for biochemical measurement, the development of biosensing devices and their applications to medicine based on "sensor and biomedical engineering". The objective of this course is to help the students be able to think about and conduct a research by themselves throughout the activities with academic researches.

(5) **Publications**

[Original Articles]

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- 2. Arakawa T, Mizukoshi N, Iitani K, Toma K, Mitsubayashi K. A Bio-Fluorometric Acetone Gas Imaging System for the Dynamic Analysis of Lipid Metabolism in Human Breath Chemosensors. 2021.09; 9(9); 258
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- 4. Toma K, Suzuki S, Arakawa T, Iwasaki Y, Mitsubayashi K. External ears for non-invasive and stable monitoring of volatile organic compounds in human blood. Scientific reports. 2021.06; 11(1); 10415
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- 1. Mitsubayashi K. Non-Contact Vital Signs Monitoring. 2021.05 (ISBN : 978-4-7813-1606-2)
- 2. Toma K, Arakawa T, Mitsubayashi K. Panoramic View of the Life Science and Clinical Research Field (2021). JST-CRDS, 2021.03
- 3. Toma K, Arakawa T, Mitsubayashi K. Panoramic View of the Life Science and Clinical Research Field (2021). JST-CRDS, 2021.03

[Misc]

- 1. 三林 浩二. 医療・健康科学のための無拘束&連続バイオ計測 精密工学会誌. 2021.12; 87(12); 907-911
- 2. Iitani K, Ramamurthy SS, Ge X, Rao G. Transdermal sensing: in-situ non-invasive techniques for monitoring of human biochemical status Current Opinion in Biotechnology. 2021.10; 71; 198-205
- 3. 荒川 貴博, 三林 浩二. 生体ガス計測用バイオスニファとイメージングシステム ガステックニュース. 2021.07; 116; 1-2
- 4. 飯谷 健太、當麻 浩司、荒川 貴博、三林 浩二. 非侵襲生体計測のための気相用バイオセンサシステム Chemical Sensors. 2021.01; 37(1); 2-10

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- 2. Toma K, Oishi K, Arakawa T, Mitsubayashi K. Surface plasmon-enhanced fluorescence biosensor for semi-continuous monitoring of cardiac marker: troponin I. EUROPT(R)ODE2021 2021.11.28 online
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- 4. Mitsubayashi K. Biofluorometric gas sensing and imaging of volatile chemicals in exhaled breath and skin gas. 10th International Workshop on Surface Modification for Chemical and Biochemical Sensing (SMCBS-2021) 2021.11.05 online
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- 6. Mitsubayashi K. Biofluorometric Sensing and Imaging of Body Volatile Chemicals. The 4th International Workshop by the 174 Committee on Coexistence of Biology and Nanodevices 2021.11.04 online
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- 8. Arakawa T, Aota T, Toma K, Mitsubayashi K. Skin gas monitoring device with ethanol biochemical gas sensor and gas concentrator. 31st Anniversary World Congress of Biosensors 2021.07.26 online
- 9. Toma K, Seshima F, Arakawa T, Mitsubayashi K. Enzyme O2 charger-boosted air bio-battery as a dual energy approach of glucose. 31st Anniversary World Congress of Biosensors 2021.07.26 online
- 10. Iitani K, Toma K, Arakawa T, Mitsubayashi K. 2D bio-fluorometric gas-imaging system (sniff-cam) for transdermal ethanol vapor based on enzymatic recognition. 31st Anniversary World Congress of Biosensors 2021.07.26 online
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- 13. Mitsubayashi K. Bio-Sniffers & Sniff-Cam: Biofluorometirc Gas Sensor and Imaging System for Human Volatile Chemicals. 18th International Meeting on Chemical Sensors 2021.06.03 online
- 14. Mitsubayashi K. Cavitas Sensors: Non-Invasive Bio/Chemical Sensing in Human Body Cavities for Medical and Healthcare. 18th International Meeting on Chemical Sensors 2021.06.03 online
- 15. Iitani K, Mizukoshi N, Toma K, Arakawa T, Takeda N, Mitsubayashi K. Biofluorometric real-time image sensing of transcutaneously emitted ethanol vapor by enzyme-immobilized mesh sheet. 18th International Meeting on Chemical Sensors 2021.06.01 online

- 16. Arakawa T, Ye M, Iitani K, Toma K, Mitsubayashi K. Acetone Bio-Sniffer (Gas-Phase Biosensor) for Monitoring of Human Volatile Using Enzymatic Reaction of Secondary Alcohol Dehydrogenase. 8th International Symposium on Sensor Science 2021.05.17 online
- 17. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Gas-Phase Chemical Imaging System by Biofluorometry for Human VOCs Measurement. 8th International Symposium on Sensor Science 2021.05.17 online
- 18. Toma K, Arakawa T, Mitsubayashi K. Self-Detachable Body Cavity Sensors with Biocompatible Materials for Medical and Healthcare. 8th International Symposium on Sensor Science 2021.05.17 online
- 19. Arakawa T, Suzuki T, Iitani K, Toma K, Mitsubayashi K. Monitoring of skin volatiles using gas-phase biosensor for the non-invasive evalution of volatile blood compounds. OPTICS & PHOTONICS International Congress 2021 2021.04.22 online
- 20. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Bio-optic gas visualization system (Sniff-cam) for human volatiles. OPTICS & PHOTONICS International Congress 2021 2021.04.22 online
- 21. Toma K, Oishi K, Arakawa T, Mitsubayashi K. Surface Plasmon-Enhanced Fluorescence Biosensor for Repeated Measurement of Cardiac Marker. OPTICS & PHOTONICS International Congress 2021 2021.04.21 online

[Social Contribution]

1. A clean environment that evaluates transcutaneous gas measuring devices constructed in Tokyo Medical and Dental University through a NEDO project, Japan Science and Technology Agency, 2021.06.24
Bioelectronics

Staff

Yuji Miyahara (Professor) Akira Matsumoto (Associate Professor) Miyuki Tabata (tenure track Assistant Professor) Yukichi Horiguchi (Assistant Professor) KHAN Thahomina Tareque (Project Assistant Professor) Michiko Ito (Collaborative Researcher) Takuya Miyazaki (Collaborative Researcher) Hiroko Matsumoto (Technical Assistant) Yuki Morooka (Technical Assistant) Chiharu Mizoi (Technical Assistant) Sayo Kotaki (Technical Assistant) Sayaka Kanai (Technical Assistant) Kiyoshi Ikehara (Technical Assistant) Barthelmes (Technical Assistant) Kevin Xinyue Liu (Technical Assistant) Ririko Kobayashi (Technical Assistant) Ulala Minamibata (Staff Assistant)

Graduate student Hideki Fujisaki,Kyouka Susawa

(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

- 1. Miyuki Tabata, Chindanai Ratanaporncharoen, Noboru Ishihara, Kazuya Masu, Mana Sriyudthsak, Yuichi Kitasako, Masaomi Ikeda, Junji Tagami, Yuji Miyahara. Surface analysis of dental caries using a wireless pH sensor and Raman spectroscopy for chairside diagnosis Talanta. 2021.12; 235; 122718
- Miyazaki T, Khan T, Tachihara Y, Itoh M, Miyazawa T, Suganami T, Miyahara Y, Cabral H, Matsumoto A. Boronic Acid Ligands Can Target Multiple Subpopulations of Pancreatic Cancer Stem Cells via pH-Dependent Glycan-Terminal Sialic Acid Recognition. ACS applied bio materials. 2021.09; 4(9); 6647-6651
- Horiguchi Yukichi, Barthelmes Kevin, Miyahara Yuji, Matsumoto Akira. pH-responsive Adsorption and Dissociation of Sialic Acid Expressed Protein on Boronic Acid Immobilized Surface CHEMISTRY LETTERS. 2021.08; 50(8); 1467-1469
- 4. Hong T, Miyazaki T, Matsumoto A, Koji K, Miyahara Y, Anraku Y, Cabral H. Phosphorylcholine-Installed Nanocarriers Target Pancreatic Cancer Cells through the Phospholipid Transfer Protein. ACS biomaterials science & engineering. 2021.08; 7(9); 4439-4445
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- 6. Tabata Miyuki, Kataoka-Hamai Chiho, Nogami Kozue, Tsuya Daiju, Goda Tatsuro, Matsumoto Akira, Miyahara Yuji. Organic and inorganic mixed phase modification of a silver surface for functionalization with biomolecules and stabilization of electromotive force RSC ADVANCES. 2021.07; 11(40); 24958-24967
- 7. Rophukdeekul S, Tabata M, Ratanaporncharoen C, Takeuchi Y, Somboon P, Boonlue W, Miyahara Y, Sriyudthsak M. Quantitative assessment of periodontal bacteria using a cell-based immunoassay with functionalized QCM Chemosensors. 2021.06; 9(7); 159

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- 11. Takuya Miyazaki, Thahomina Khan, Yoshihiro Tachihara, Michiko Itoh, Taiki Miyazawa, Takayoshi Suganami, Yuji Miyahara, Horacio Cabral, Akira Matsumoto. Boronic acid ligands can target multiple subpopulations of pancreatic cancer stem cells via pH-dependent glycan-terminal sialic acid recognition ACS Applied Bio Materials. 2021;
- 12. Wenqian Yang, Takuya Miyazaki, Pengwen Chen, Taehun Hong, Mitsuru Naito, Yuji Miyahara, Akira Matsumoto, Kazunori Kataoka, Kanjiro Miyata, Horacio Cabral. Block Catiomer with Flexible Cationic Segment Enhances Complexation with siRNA and the Delivery Performance in Vitro Science and Technology of Advanced Materials. 2021;

[Misc]

1. 松元亮*、宮崎拓也、伊藤美智子、菅波孝祥、宮原裕二. ボロン酸ゲルを用いた糖尿病治療デバイスの社会実装 バイオマテリアル. 2021.10; 39(4); 253-257

[Patents]

- 1. DRUG DELIVERY DEVICE, Patent Number : US11141486
- 2. DRUG DELIVERY DEVICE, Patent Number : US11141486

Material-Based Medical Engineering

Prof. Akio Kishida Assoc. Prof. Tsuyoshi Kimura Assist. Prof. Yoshihide Hashimoto Researcher Mako Kobayashi Secretary Naomi Hiwatari Lecturer(part-time) Hisatoshi Kobayashi Lecturer(part-time) Seiichi Funamoto Lecturer(part-time) Akitatsu Yamashita Lecturer(part-time) Masaki Tabuchi Lecturer(part-time) Jun Negishi Lecturer(part-time) Naoko Nakamura Lecturer(part-time) Yongwei Zhang

Doctor Course Student Takuya Konishi Kohei Yabuuchi Shota Toda Say Sreypich

(1) **Outline**

Our laboratory has dealt with 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) Development of processing and high-performance technology for biological materials

This research focuses on developing functional materials with novel functions by processing biological materials. Specifically, we are conducting research on processing into powders, fibers, and hydrogels, and hybrid technology with functional molecules.

(3) Development of inflammatory evaluation method for biomaterials

Macrophages are polarized into an inflammatory type (M1 type) that contributes to inflammation and an anti-inflammatory type (M2 type) that contributes to healing. We are developing an inflammatory evaluation method for biomaterials using macrophage polarization in vitro.

(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. Tsuyoshi Kimura, Rino Tokunaga, Yoshihide Hashimoto, Naoko Nakamura, Akio Kishida. Tumor growth suppression by implantation of an anti-CD25 antibody-immobilized material near the tumor via regulatory T cell capture Science and Technology of Advanced Materials. 2021.08; 22(1); 607-615
- 2. Shunji Kurokawa, Yoshihide Hashimoto, Seiichi Funamoto, Kozue Murata, Akitatsu Yamashita, Kazuhiro Yamazaki, Tadashi Ikeda, Kenji Minatoya, Akio Kishida, Hidetoshi Masumoto . In vivo recellularization of xenogeneic vascular grafts decellularized with high hydrostatic pressure method in a porcine carotid arterial interpose model PLoS One. 2021.07; 16(7); e0254160
- Mako Kobayashi, Masako Ohara, Yoshihide Hashimoto, Naoko Nakamura, Toshiya Fujisato, Tsuyoshi Kimura, Akio Kishida. Effect of luminal surface structure of decellularized aorta on thrombus formation and cell behavior PLoS One. 2021.05; 16(5); e0246221

- 1. Mika Suzuki, Yuta Nakano, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Noko Nakamura, Tsuyoshi Kimura, Akio Kishida. Recellularization of partially mineralized membranous decellularized tissue for locomotor regeneration. MRM2021 2021.12.13 Kanagawa, Japan
- 2. Tsuyohi Kimura, Rino Tokunaga, Yoshihide Hashimoto, Naoko Nakamura, Akio Kishida. Tumor growth suppression by releasing cancer immune suppression using an anti-CD25 antibody-immobilized material. MRM2021 2021.12.13 Kanagawa, Japan
- 3. Mika Suzuki, Yuta Nakano, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Naoko Nakamura, Tsuyoshi Kimura, Akio Kishida . Preparation of a mineralized decellularized pericardium by alternate soaking for enhancing bone affinity. ISBE2021 2021.12.02 Web
- 4. Tsuyoshi Kimura, Eri Yasuda, Yoshihide Hashimoto, Ikuro Suzuki, Naoko Nakamura, Akio Kishida. Classification of HHP and SDS decellularized tissue histology images using artificial intelligence. ISBE2021 2021.12.02 Web
- 5. Yoshihide Hashimoto, Akitatsu Yamashita, Jun Negishi, Tsuyoshi Kimura, Seiichi Funamoto, Akio Kishida. Four-arm PEG-functionalized decellularized pericardium as an effective post-operative pericardial adhesion barrier. ISBE2021 2021.12.02 Web
- 6. Tsuyoshi Kimura, Mika Suzuki, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Naoko Nakamura, Akio Kishida. In vitro tissue reconstruction using decellularized pericardium cultured with cells for ligament regeneration. 2021 6th TERMIS-WC 2021.11.15 Web

- 7. Mako Kobayashi, Naoki Ishida, Yoshihide Hashimoto, Jun Negishi, Hideki Saga, Yoshihiro Sasaki, Kazunari Akiyoshi, Tsuyoshi Kimura, Akio Kishida. Extraction of matrix-bound nanovesicles (MBVs) from high-hydrostatic pressure decellularized tissue and evaluation on vascular endothelial cells. 2021 6th TERMIS-WC 2021.11.15 Web
- 8. Shota Toda, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Preparation of macrophage adhering particles for immunological evaluation of biomaterials . 2021 6th TERMIS-WC 2021.11.15 Web

[Patents]

- 1. HYBRID GEL CONTAINING PARTICULATE DECELLULARIZED TISSUE, Patent Number: CA2911592
- 2. HYBRID GEL CONTAINING PARTICULATE DECELLULARIZED TISSUE, Patent Number : CA2911592
- 3. METHOD FOR PRODUCING PARTICULATE DECELLULARIZED TISSUE, Patent Number: KR2240373
- 4. METHOD FOR PRODUCING PARTICULATE DECELLULARIZED TISSUE, Patent Number : KR2240373
- 5. HYBRID GEL CONTAINING PARTICULATE DECELLULARIZED TISSUE, Patent Number: KR2339700
- 6. HYBRID GEL CONTAINING PARTICULATE DECELLULARIZED TISSUE, Patent Number: KR2339700
- 7. ANTI-ADHESION MATERIAL AND ARTIFICIAL BIOLOGICAL MEMBRANE EACH COMPRISING DECELLULARIZED TISSUE, Patent Number : US11033661
- 8. ANTI-ADHESION MATERIAL AND ARTIFICIAL BIOLOGICAL MEMBRANE EACH COMPRISING DECELLULARIZED TISSUE, Patent Number : US11033661
- 9. ANTI-ADHESION MATERIAL AND SUBSTITUTE BIOMEMBRANE USING DECELLULARIZED TISSUE, Patent Number : BR112017018772-8
- 10. ANTI-ADHESION MATERIAL AND SUBSTITUTE BIOMEMBRANE USING DECELLULARIZED TISSUE, Patent Number : BR112017018772-8
- 11. ANTI-ADHESION MATERIAL AND ARTIFICIAL BIOLOGICAL MEMBRANE EACH COMPRISING DECELLULARIZED TISSUE, Patent Number : TWI715560
- 12. METHOD FOR PRODUCING PARTICULATE DECELLULARIZED TISSUE, Patent Number: EP3556406
- 13. METHOD FOR PRODUCING PARTICULATE DECELLULARIZED TISSUE, Patent Number: EP3556406

Organic and Medicinal Chemistry

Professor Hiroyuki KAGECHIKA Associate Professor Shinya Fujii Assistant Professor Mari YUASA Assistant Professor Ryosuke ISHIDA Eng. Official Hiroyuki Masuno

Graduate Student Yu Miyajima Kotaro Ochiai Nao Namba Chai Xikun Saki Haraoka Yuga Yamamoto Mana Nomiya Zeng Xi Saki Hatsuzawa Yoshihiro Tada Zhang Huize

(1) Outline

1) Medicinal Chemistry of Retinoids

Retinoids regulates various significant biological phenomena, such as cell differentiation, proliferation, morphogenesis, metabolism and homeostasis. We have developed novel synthetic retinoid, Am80 (tamibarotene) as drug for acute promyelocytic leukemia. Novel synthetic retinoids have been developed foe clinical use in the field of autoimmune diseases, neurodegenerative diseases, metabolic syndromes.

2) Medicinal Chemistry of Nuclear Receptors

Small hydrophobic molecules such as steroid hormones and activated vitamins A/D control various biological phenomena, including growth, development, metabolism, and homeostasis, by binding to and activating specific nuclear receptors. Nuclear receptors have become one of the most significant molecular targets for drug discovery in the fields of cancer, metabolic syndrome, autoimmune diseases, and so on. In this project, novel ligands of various nuclear receptors have been developed.

3) Development of Novel Functional Fluorescent Molecules for Elucidation of Intracellular Signal Transduction Pathways

Functional fluorescent molecules useful in many fields of scientific research, including analytical chemistry or cell biology have been developed.

4) Aromatic Architecture Based on the Steric Properties of N-Methylated Amides

The amide bond structure of amide derivatives often plays a key role in functions such as molecular recognition events or biological activities. In contrast to the extended trans structures of most secondary amides, the corresponding N-methylated compounds exist in cis form in the crystals and predominantly in cis form in various solvents. The cis conformational preference is useful as a building block to construct aromatic molecules with unique crystal or solution structures.

(2) Lectures & Courses

Organic and Medicinal Chemistry covers several aspects of organic chemistry, medicinal chemistry and chemical biology. Through this course, students are expected to understand the fundamental knowledge, recent topics, and experimental techniques related to these fields.

(3) Publications

- Takayanagi, S.; Watanabe, K.; Maruyama, T.; Ogawa, M.; Morishita, K.; Soga, M.; Hatta, T.; Natsume, T.; Hirano, T.; Kagechika, H.; Hattori, K.; Naguro, I.; Ichijo, H.. ASKA technology-based pull-down method reveals a suppressive effect of ASK1 on the inflammatory NOD-RIPK2 pathway in brown adipocytes Sci. Rep.. 2021.10; 11; 22009
- Fujii, S.; Kikuchi, E.; Suzuyama, H.; Watanabe, Y.; Ishigami-Yuasa, M.; Masuno, H.; Mori, T.; Isobe, K.; Uchida, S.; Kagechika, H.. Structural Development of Salicylanilide-Based SPAK Inhibitors as Candidate Antihypertensive Agents ChemMedChem. 2021.09; 16(18); 2817-2822
- Lin Liu, Hiroyuki Koike, Takehito Ono, Shinichiro Hayashi, Fujimi Kudo, Atsushi Kaneda, Hiroyuki Kagechika, Ichiro Manabe, Tomoki Nakashima, Yumiko Oishi. Identification of a KLF5-dependent program and drug development for skeletal muscle atrophy. Proc Natl Acad Sci U S A. 2021.08; 118(35);
- 4. Fujii Shinya, Kikuchi Eriko, Suzuyama Honoka, Watanabe Yuko, Ishigami-Yuasa Mari, Masuno Hiroyuki, Mori Takayasu, Isobe Kiyoshi, Uchida Shinichi, Kagechika Hiroyuki. Structural Development of Salicylanilide-Based SPAK Inhibitors as Candidate Antihypertensive Agents CHEMMEDCHEM. 2021.07; 16(18); 2817-2822
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- Lin, Y.-W.; Nhieu, J.; Wei, C.-W.; Lin, Y.-L.; Kagechika, H.; Wei, L.-N.. Regulation of exosome secretion by cellular retinoic acid binding protein 1 contributes to systemic anti-inflammation Cell Commun. Signal.. 2021.06; 19(1); 69
- 7. Nagashima S, Maruyama J, Honda K, Kondoh Y, Osada H, Nawa M, Nakahama KI, Ishigami-Yuasa M, Kagechika H, Sugimura H, Iwasa H, Arimoto-Matsuzaki K, Nishina H, Hata Y. CSE1L promotes nuclear accumulation of transcriptional coactivator TAZ and enhances invasiveness of human cancer cells. The Journal of biological chemistry. 2021.05; 297(1); 100803
- 8. Kato, D.; Shiraishi, T.; Kagechika, H.; Hirano, T.. Design, synthesis and antitumor activity of phthalazine-1,4-dione-based menaquinone analogs Bioorg. Med. Chem. Lett.. 2021.04; 43; 128065
- 9. Cione, E.; Caroleo, M. C.; Kagechika, H.; Manetti, F.. Pharmacophore-guided repurposing of fibrates and retinoids as GPR40 allosteric ligands. J. Enzyme Inhibit. Med. Chem. 2021.02; 36(1); 377-383
- Kato Daiki, Shiraishi Takuya, Kagechika Hiroyuki, Hirano Tomoya. 6-Arylcoumarin as a Scaffold of Photofunctional Molecules with OFF-ON-OFF Type Regulation JOURNAL OF ORGANIC CHEMISTRY. 2021.02; 86(3); 2264-2270
- Arimura, M.; Tanaka, K.; Kanda, M.; Urushibara, K.; Fujii, S.*; Katagiri, K.; Azumaya, I.; Kagechika, H.; Tanatani, A.: Construction of Aromatic Multilayered Structures Based on the Conformational Properties of N,N' -Dimethylated Squaramide ChemPlusChem. 2021; 86(1); 198-205
- 12. Fujii, S.; Sekine, R.; Kano, A.; Masuno, H.; Kawachi, E.; Hirano, T.; Kagechika, H.. Synthesis and Structure-Activity Relationship Study of 1,12-Dicarba-closo-dodecaborane-based Triol Derivatives as Nonsecosteroidal Vitamin D Analogs Heterocycles. 2021; 103(1); 444-458

- 1. Shuichi Mori, Hiroto Iinuma, Takashi Murayama, Chin Xikun, Ryosuke Ishida, Nagomi Kurebayashi, Hiroyuki Kagechika. Structure development of ryanodine receptor 1(RyR1) inhibitor for activity and water-solubility. The 6th International Symposium on Biomedical Engineering (ISBE2021) 2021.12.02
- 2. Kotaro Ochiai, Hiroyuki Kagechika, Shinya Fujii. Design, Synthesis and Evaluation of Novel Androgen Receptor Ligand Bearing Ferrocene as the Hydrophobic Pharmacophore. The 6th International Symposium on Biomedical Engineering (ISBE2021) 2021.12.02
- 3. Nao Namba, Yuichiro Matsumoto, Yuichi Hashimoto, Tomomi Noguchi-Yachide, Hiroyuki Kagechika, Shinya Fujii. Structure Development of Silicon-Containing Derivatives of T0901317 as Novel Liver X Receptor (LXR) Ligands. The 6th International Symposium on Biomedical Engineering (ISBE2021) 2021.12.02
- 4. Yoshihara S., Sasaki H., Kawasaki H., Yoshihara A., Masuno H., Kanda Y., Kagechika H, Tanatani A.. Structure-activity Relationship of Lithocholic Acid As Novel Nonsecosteroidal Vitamin D Derivatives. The 6th International Symposium on Biomedical Engineering (ISBE2021) 2021.12.02
- 5. Kotaro Ochiai, Hiroyuki Kagechika, Shinya Fujii. Development of Androgen Receptor Ligands Bearing Ferrocene as the Hydrophobic Pharmacophore. AFMC International Medicinal Chemistry Symposium 2021 2021.11.29
- 6. Nao Namba, Yuichiro Matsumoto, Yuichi Hashimoto, Tomomi Noguchi-Yachide, Hiroyuki Kagechika, Shinya Fujii. Development of Subtype-Selective Liver X Receptor (LXR) Ligands Using Silicon Functionalities. AFMC International Medicinal Chemistry Symposium 2021 2021.11.29
- 7. Yoshihara S., Sasaki H., Kawasaki H., Yoshihara A., Masuno H., Kanda Y., Kagechika H, Tanatani A.. Structure-activity relationship of Lithocholic Acid as Novel Nonsecosteroidal Vitamin D Derivatives. AFMC International Medicinal Chemistry Symposium 2021 2021.11.29
- 8. Aya Tanatani, Chisaki Yoshioka, Hiroyuki Masuno, Nobutaka Numoto, Nobutoshi Ito, Hirata Naoya, Kanda Yasunari, Hiroyuki Kagechika. Development of Novel Lithocholic Acid Derivatives: Synthesis of Each Stereoisomer by Using Enzymatic Separation and The Vitamin D Activity. Symposium on Molecular Chirality 2021 2021.11.29 Hiroshima, Japan
- 9. Ishigami-Yuasa, M., Ekimoto, H., Kagechika, H.. Synergistic inhibition of several human cancer cell proliferations by a synthetic retinoid tamibarotene (Am80) in combination with the epigenetic modulators. FASEB meeting on retinoid Florida, USA
- 10. Tsuemoto, N., Mori, S., Kawachi, E., Kagechika, H.. Design and synthesis of novel RAR ligands containing pentafluorosulfanyl group. FASEB meeting on retinoid Florida, USA

Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Suguru Yoshida (-March)
Associate Professor	Takashi NIWA (October-)
Assistant Professor	Junpei TAGUCHI
Assistant Professor	Yuki SAKATA
Technical Assistant	Yuki HAZAMA, Satomi TOMITA,
	Miho Hanya
Graduate Students	Akihiro KOBAYASHI, Takumi OZAWA,
	Minori SUZUKI, Ryoto NABEKURA,
	Yohei OHATA, Yuta OMOTO,
	Kota KIMURA, Kento TOKUNAGA
Collaborators	Takumi OKUYAMA

(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. Development of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

(3) Publications

- 1. Niwa T, Uetake Y, Isoda M, Takimoto T, Nakaoka M, Hashizume D, Sakurai H, Hosoya T. Lewis acid-mediated Suzuki–Miyaura cross-coupling reaction. Nat Catal. 2021.12; 4(12); 1080-1088
- Takahashi K, Hosoya T, Onoe K, Mori T, Tazawa S, Mawatari A, Wada Y, Watanabe Y, Doi H, Watanabe Y. PET imaging of brain aromatase in humans and rhesus monkeys by ¹¹C-labeled cetrozole analogs. Sci Rep. 2021.12; 11(1); 23623
- Inouye S, Nakamura M, Hosoya T. Formation of Coelenteramine from 2-Peroxycoelenterazine in the Ca²⁺-Binding Photoprotein Aequorin. Photochem Photobiol. 2021.12;
- 4. Sakata Y, Yoshida S, Hosoya T. Synthesis of Azidoanilines by the Buchwald-Hartwig Amination. J Org Chem. 2021.11; 86(21); 15674-15688

- 5. Taguchi J, Kimura K, Igawa K, Tomooka K, Hosoya T. 3-Azidoarynes: Generation and Regioselective Reactions. Chem Lett. 2021.11; 51(2); 94-98
- Watanabe K, Terao N, Niwa T, Hosoya T. Direct 3-Acylation of Indolizines by Carboxylic Acids for the Practical Synthesis of Red Light-Releasable Caged Carboxylic Acids. J Org Chem. 2021.09; 86(17); 11822-11834
- 7. Aimi T, Meguro T, Kobayashi A, Hosoya T, Yoshida S. Nucleophilic transformations of azido-containing carbonyl compounds via protection of the azido group. Chem Commun. 2021.06; 57(49); 6062-6065
- 8. Kobayashi K, Matsuzawa T, Hosoya T, Yoshida S. Thioxanthone Synthesis from Benzoic Acid Esters through Directed *ortho*-Lithiation. Chem Lett. 2021.06; 50(9); 1624-1627
- Kobayashi T, Hosoya T, Yoshida S. Facile Synthetic Methods for Diverse N-Arylphenylalanine Derivatives via Transformations of Aryne Intermediates and Cross-Coupling Reactions. Bull Chem Soc Jpn. 2021.05; 94(7); 1823-1832
- 10. Nakajima H, Hazama Y, Sakata Y, Uchida K, Hosoya T, Yoshida S. Diverse diaryl sulfide synthesis through consecutive aryne reactions. Chem Commun. 2021.03; 57(21); 2621-2624
- 11. Minoshima M, Uchida K, Nakamura Y, Hosoya T, Yoshida S. Acylalkylation of Arynes Generated from *o*-Iodoaryl Triflates with Hydrosilanes and Cesium Fluoride. Org Lett. 2021.03; 23(5); 1868-1873
- 12. Matsuzawa T, Hosoya T, Yoshida S. Transition-Metal-Free Synthesis of *N*-Arylphenothiazines through an *N* and *S*-Arylation Sequence. Org Lett. 2021.03; 23(6); 2347-2352
- 13. Suzuki M, Kanemoto K, Nakamura Y, Hosoya T, Yoshida S. Palladium-Catalyzed Sulfinylation of Aryland Alkenylborons with Sulfinate Esters. Org Lett. 2021.03; 23(9); 3793-3797
- 14. M, Inoue A, Iida K, Denawa M, Kii I, Kadj F M Ni, Kishi T, Im D, Shimamura T, Onogi H, Yoshida S, Iwata S, Aoki J, Hosoya T, Hagiwara M. S1PR3–G₁₂-biased agonist ALESIA targets cancer metabolism and promotes glucose starvation. Cell Chem Biol. 2021.02; 28(8); 1132-1144
- 15. Nishiyama Y, Akiyama K, Sakata Y, Hosoya T, Yoshida S. Facile Synthesis of Tetraarylpyrazines by Sequential Cross-coupling Approach. Chem Lett. 2021.01; 50(1); 180-183
- Yoshida S, Sakata Y, Misawa Y, Morita T, Kuribara T, Ito H, Koike Y, Kii I, Hosoya T. Assembly of four modules onto a tetraazide platform by consecutive 1,2,3-triazole formations. Chem Commun. 2021.01; 57(7); 899-902
- 17. Isoda M, Uetake Y, Takimoto T, Tsuda J, Hosoya T, Niwa T. Convergent Synthesis of Fluoroalkenes Using a Dual-Reactive Unit. J Org Chem. 2021.01; 86(2); 1622-1632
- Inouye S, Sumida Y, Tomabechi Y, Taguchi J, Shirouzu M, Hosoya T. Chiral deaza-coelenterazine analogs for probing a substrate-binding site in the Ca2+-binding photoprotein aequorin. PloS one. 2021; 16(6); e0251743

[Misc]

1. Yoshida S, Hosoya T. Recent Insertion Reactions of Aryne Intermediates. Modern Aryne Chemistry (Ed. Biju AT). 2021.05; 111-148

- 1. Watanabe K, Terao N, Kii I, Nakagawa R, Niwa T, Hosoya T. Rapid uncaging of alcohols and carboxylic acids by red light-induced photooxidation of indolizines. Pacifichem 2021 2021.12.18 オンライン
- 2. Watanabe K, Terao N, Kii I, Nakagawa R, Niwa T, Hosoya T. Indolizines Enabling Rapid Uncaging of Alcohols and Carboxylic Acids by Red Light-Induced Photooxidation. ACS SPRING 2021 2021.04.15 オ ンライン
- 3. Kitakaze K, Taniuchi S, Kawano E, Hamada Y, Miyake M, Oyadomari M, Kojima H, Kosako H, Kuribara T, Yoshida S, Hosoya T, Oyadomari S. Identification of a chemical chaperone for mitigating protein aggregation and proteotoxicity during endoplasmic reticulum stress. Experimental Biology 2021 2021.04.02 オンライン

[Patents]

1. Benzothiophene compound, alternative autophagy-inducing agent and anticancer agent including the compound as active ingredient, and method for screening for compound having anticancer activity, Patent Number : US10954222

Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D. Assistant Professor Kohei TSUJI, Ph.D. Assistant Professor Takuya KOBAYAKAWA, Ph.D. Research Fellow Kento EBIHARA, Ph.D. Technical Assistant Ami MASUDA Technical Assistant Hiroko TAKAGI Technical Assistant Maiko HIRAYAMA Technical Assistant Mamiko HAYAKAWA Assistant Tomoe KAMEI

Graduate students

D3 Kento EBIHARA, Kofi Baffour-Awuah Owusu D2 WANG RONGYI D1 Takahiro ISHII M2 Tomoki KISHI, Chika AZUMA, Miyuki NAKAYAMA, Sayaka BOKU, LIU YIJIE, YANG TINGTING, Takato ONISHI, Akane KUDO, Hiroki NAKANO, Miki HORI, Naoya WADA, Syun KAWAKATSU, Yuki KISHIHARA, Yutaro MIURA Internal Collaborators ZHANG YAN, LI DONGRUI

External Collaborators Hideki SAGANO, Koki SHINOHARA

(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

- Kohei Tsuji, Takahiro Ishii, Takuya Kobayakawa, Nami Ohashi, Wataru Nomura & Hirokazu Tamamura. Fluorescence resonance energy transfer-based screening for protein kinase C ligands using 6-methoxynaphthalene-labeled 1,2-diacylglycerol-lactones. Organic & Biomolecular Chemistry. 2021.10; 19(38); 8264-8271
- 2. David Hymel, Kohei Tsuji, Robert A Grant, Ramesh M Chingle, Dominique L Kunciw, Michael B Yaffe, Terrence R Burke Jr. Design and synthesis of a new orthogonally protected glutamic acid analog and its

use in the preparation of high affinity polo-like kinase 1 polo-box domain - binding peptide macrocycles. Organic & Biomolecular Chemistry. 2021.09; 19(36); 7843-7854

- 3. Hasan Md Zahid, Takeo Kuwata, Shokichi Takahama, Yu Kaku, Shashwata Biswas, Kaho Matsumoto, Hirokazu Tamamura & Shuzo Matsushita. Functional Analysis of a Monoclonal Antibody Reactive against the C1C2 of Env Obtained from a Patient Infected with HIV-1 CRF02_AG. Retrovirology. 2021.08; 18(1); 23(article number)
- 4. Jan Vincent V. Arafiles, Hisaaki Hirose, Yusuke Hirai, Masashi Kuriyama, Maxwell Mamfe Sakyiamah, Wataru Nomura, Kazuhiro Sonomura, Miki Imanishi, Akira Otaka, Hirokazu Tamamura & Shiroh Futaki. Discovery of a Macropinocytosis-inducing Peptide Potentiated by Medium-mediated Intramolecular Disulfide Formation. Angewandte Chemie International Edition. 2021.05; 60(21); 11928-11936
- Takuya Kobayakawa, Chika Azuma, Yuki Watanabe, Shunsuke Sawamura, Atsuhiko Taniguchi, Yoshio Hayashi, Kohei Tsuji & Hirokazu Tamamura. Development of Methods for Convergent Synthesis of Chloroalkene Dipeptide Isosteres and Its Application. The Journal of Organic Chemistry. 2021.03; 86(7); 5091-5101
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- 7. Kohei Tsuji, Rongyi Wang, Takuya Kobayakawa, Kofi Baffour-Awuah Owusu, Masayuki Fujino, Moemi Kaneko, Naoki Yamamoto, Tsutomu Murakami, Hirokazu Tamamura. Potent leads based on CA-19L, an anti-HIV active HIV-1 capsid fragment. Bioorganic & Medicinal Chemistry. 2021.01; 30; 115923
- 8. Takuya Kobayakawa, Kohei Tsuji, Kiju Konno, Ai Himeno, Ami Masuda, Tingting Yang, Kohei Takahashi, Yusuke Ishida, Nami Ohashi, Takeo Kuwata, Kaho Matsumoto, Kazuhisa Yoshimura, Hiromi Sakawaki, Tomoyuki Miura, Shigeyoshi Harada, Shuzo Matsushita & Hirokazu Tamamura. Hybrids of Small-Molecule CD4 Mimics with Polyethylene Glycol Units as HIV Entry Inhibitors. Journal of Medicinal Chemistry. 2021.01; 64(3); 1481-1496
- 9. Kouki Matsuda, Takuya Kobayakawa, Ryusho Kariya, Kiyoto Tsuchiya, Kohei Tsuji, Takahiro Ishii, Hiroyuki Gatanaga, Kazuhisa Yoshimura, Seiji Okada, Hiroaki Mitsuya, Hirokazu Tamamura & Kenji Maeda. A Therapeutic Strategy to Combat HIV-1 Latently Infected Cells With a Combination of Latency-Reversing Agents Containing DAG-Lactone PKC Activators. Frontiers in Microbiology. 2021; 12; 636276

- 1. Hirokazu Tamamura. Bivalent Ligands of GPCR as Molecular Measures, Bioprobes for Cancer Cells and Anti-cancer Agents. The 2021 International Chemical Congress of Pacific Basin Societies (Pacifichem 2021) 2021.12.20 Online
- 2. Hirokazu Tamamura, Takuya Kobayakawa, Kento Ebihara, Tsutomu Murakami, Kohei Tsuji. Development of HIV-1 fusion inhibitors based on dimeric derivatives of the C34 peptide and its peptidomimetics. The 2021 International Chemical Congress of Pacific Basin Societies (Pacifichem 2021) 2021.12.18 Online
- 3. Kohei Tsuji, Rongyi Wang, Kofi Baffour-Awuah Owusu, Takuya Kobayakawa, Tsutomu Murakami, Hirokazu Tamamura. Explorative study in development of anti-HIV-1 peptides based on HIV-1 capsid protein segments. The 2021 International Chemical Congress of Pacific Basin Societies (Pacifichem 2021) 2021.12.15 Online
- 4. Takahiro Ishii, Takuya Kobayakawa, Kouki Matsuda, Kohei Tsuji, Kazuhisa Yoshimura, Hiroaki Mitsuya, Kenji Maeda, Hirokazu Tamamura. Development of protein kinase C activators for cure of HIV infectious diseases. The 2021 International Chemical Congress of Pacific Basin Societies (Pacifichem 2021) 2021.12.15 Online
- 5. Takuya Kobayakawa, Kohei Tsuji, Kiju Konno, Ami Masuda, Nami Ohashi, Takeo Kuwata, Kazuhisa Yoshimura, Tomoyuki Miura, Shigeyoshi Harada, Shuzo Matsushita, Hirokazu Tamamura. HIV entry inhibitors based on CD4 mimics with PEG units toward cure for HIV-infectious diseases. The 13th AFMC International Medicinal Chemistry Symposium 2021.12.02 Online

- 6. Takahiro Ishii, Takuya Kobayakawa, Kouki Matsuda, Kohei Tsuji, Kazuhisa Yoshimura, Hiroaki Mitsuya, Kenji Maeda, Hirokazu Tamamura. Structure-Activity Relationship Studies of Protein Kinase C Activators Derived from Diacylglycerol for Cure of HIV Infectious Diseases. The 13th AFMC International Medicinal Chemistry Symposium 2021.11.29 Online
- 7. Rongyi Wang, Kohei Tsuji, Yishan Liu, Takuya Kobayakawa, Tsutomu Murakami, Hirokazu Tamamura. HYBRID MOLECULES OF CD4 MIMIC AND HIV-1 GP41-RELATED PEPTIDES AS FUSION INHIBITORS. The 58th Japanese Peptide Symposium 2021.10.22 Online
- 8. Kohei Tsuji, Takuya Kobayakawa, Kento Ebihara, Takuma Kawada, Masayuki Fujino, Yuzuna Honda, Nami Ohashi, Tsutomu Murakami, Hirokazu Tamamura. DIMERIZED SMALL MOLECULE HIV-1 FUSION INHIBITORS WITH DRAMATIC ENHANCEMENT OF THEIR ANTI-HIV-1 ACTIVITIES. The 58th Japanese Peptide Symposium 2021.10.21 Online
- 9. Kohei Tsuji, Takahiro Ishii, Takuya Kobayakawa, Nami Ohashi, Wataru Nomura, Hirokazu Tamamura. A FRET-BASED ASSAY SYSTEM FOR PROTEIN KINASE C LIGAND SCREENING USING 1,2-DIACYLGLYCEROL-LACTONE DERIVATIVE. The 58th Japanese Peptide Symposium 2021.10.20 Online
- 10. Hirokazu Tamamura. Development of Anti-HIV and Anti-cancer Peptides. The 18th Akabori Conference: Japanese-German Symposium on Peptide Science 2021.03.08 Online
- 1. Tsutomu Murakami, Takuya Kobayakawa, Takato Onishi, Sayaka Boku, Osamu Kotani, Kohei Tsuji, Hironori Sato, and Hirokazu Tamamura. Elucidation of mechanism and derivative synthesis of a new anti-HIV-1 compound that targets the capsid dimerization interface. The 68th Annual Meeting of the Japanese Society for Virology 2021.11.16 Kobe
- 2. Takuya Kobayakawa, Kohei Tsuji, Kiju Konno, Ami Masuda, Nami Ohashi, Takeo Kuwata, Kazuhisa Yoshimura, Tomoyuki Miura, Shigeyoshi Harada, Shuzo Matsushita, Hirokazu Tamamura. CD4 mimics with PEG units as HIV entry inhibitors . The 15th Annual Meeting of Japanese Society for Chemical Biology 2021.06.23 Online

Metallic Biomaterials

Takao HANAWA Prof Maki ASHIDA Assist Prof Peng CHEN Assist Prof Akira UMISE Assist Prof 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 minimalize metal allergy

Countermeasure techniques for metal ion release from metallic biomaterials which causes metal allergy are investigated. Novel reagents of patch testing for the detection of sensitization to metal ions are developed.

(2) Lectures & Courses

Metallic biomaterials play an important role as medical devices. Our laboratory mainly deals with effects of crystal structure, process, and thermal treatment on mechanical properties (e.g. strength or toughness). We also focus on structure and property of nanometer-scaled surface phenomena: Formation of living tissue on metals, especially, reactions between biomolecules or cells and metals, changes in surface oxide layers in living tissues, and electrochemical property of metallic biomaterials. The aim of the education is perfect understanding of metallic biomaterials, enabling students to select a proper material for medical treatments or researches.

(3) Publications

- 1. Manaka T, Tsutsumi Y, Chen P, Ashida M, Katayama H, Hanawa T. Development of electrochemical surface treatment to visualize critical corrosion-inducing inclusions of Zr in chloride environments J Electrochem Soc. 2021.12; 168; 121505
- 2. Toriyabe A, Chiu WT, Umise A, Tahara M, Goto K, Kanetaka H, Hanawa T, Hosoda H. Mechanical property enhancement of the Ag–tailored Au–Cu–Al shape memory alloy via the ductile phase toughening Intermetallics. 2021.12; 139; 107349

- 3. Yun CS, Hanawa T, Hong MH, Min BK, Kwon TY. Biocompatibility of Ni–Cr alloys, with the same composition, prepared by two new digital manufacturing techniques Mater Lett. 2021.12; 305; 130761
- Yang, KR, Hanawa T, Kwon TY, Min BK, Hong MH. Mechanical property comparison of Ni–Cr–Mo alloys fabricated via one conventional and two new digital manufacturing techniques Appl Sci. 2021.10; 11(19); 9308
- Tsutsumi Y, Ishimoto T, Oishi T, Manaka T, Chen P, Ashida M, Doi K, Katayama H, Hanawa T, Nakano T. Crystallographic texture- and grain boundary density-independent improvement of corrosion resistance in austenitic 316 L stainless steel fabricated via laser powder bed fusion Additive Manufact. 2021.09; 45; 102066
- 6. Zhou W, Sun X, Tsutsumi Y, Nomura N, Hanawa T. Bioinspired low-magnetic Zr alloy with high strength and ductility Scripta Mater. 2021.07; 199; 113856
- Tsutsumi H, Tsutsumi Y, Shimabukuro M, Manaka T, Chen P, Ashida M, Ishikawa K, Katayama H, Hanawa T. Investigation of the long-term antibacterial properties of titanium by two-step micro-arc oxidation treatment Coatings. 2021.07; 11(7); 798
- Wai Cho HH, Takaichi A, Kajima Y, Htat HL, Kittikundecha N, Hanawa T, Wakabayashi N.. Effect of Post-Heat Treatment Cooling Conditions on Microstructures and Fatigue Properties of Cobalt Chromium Molybdenum Alloy Fabricated through Selective Laser Melting Metals. 2021.06; 11(7);
- Manaka T, Tsutsumi Y, Ashida M, Chen P, Katayama H, Hanawa T. Development of electrochemical surface treatment for improvement of localized corrosion resistance of zirconium in chloride environment Mater Trans. 2021.06; 62(6); 788-796
- Shimabukuro M, Tsutsumi H, Tsutsumi Y, Manaka T, Chen P, Ashida M, Ishikawa K, Katayama H, Hanawa T. Enhancement of antibacterial property of titanium by two-step micro arc oxidation treatment. Dent Mater J. 2021.05; 40(3); 592-598
- Hiji A, Hanawa T, Yokoi T, Chen P, Ashida M, Kawashita M. Time transient of calcium and phosphate ion adsorption by rutile crystal facets in Hanks' solution characterized by XPS Langmuir. 2021.03; 37; 3597-3604
- Sun XH, Liu DB, Chen MF, Zhou WW, Nomura N, Hanawa T. Combination of hot isostatic pressing and subsequent heat treatment for additively manufactured Zr-1Mo components Mater Lett. 2021.02; 285; 129123
- 13. Sun X, Liu D, Chen M, Zhou W, Nomura N, Hanawa T. Influence of annealing treatment on the microstructure, Mechanical performance and magnetic susceptibility of low magnetic Zr-1Mo parts manufactured via laser additive manufacturing Mater Sci Eng A. 2021.02; 804; 140740
- 14. Yoneyama T, Hanawa T. Reduction in nickel content of the surface oxide layer on Ni-Ti alloy by electrolytic treatment J Oral Sci. 2021.01; 63(1); 50-53

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1. Hanawa T. Metals and medicine Mater Trans. 2021.02; 62(2); 139-148

- 1. Manaka T, Tsutsumi Y, Ashida M, Chen P, Katayama H, Hanawa T. Effect of impurity elements on pitting corrosion of zirconium. MATERIALS RESEARCH MEETING 2021 (MRM2021) 2021.12.13 Yokohama, Japan
- 2. Zhou W, Tsutsumi Y, Nomura N, Hanawa T. Bioinspired low-magnetic Zr-1Mo alloy with high strength and ductility. MATERIALS RESEARCH MEETING 2021 (MRM2021) 2021.12.13 Yokohama, Japan
- 3. Chen P, Shinohara N, Ashida M, Sato Y, Tsukamoto M, Hanawa T. Regulation of preosteoblast behaviors by patterned titanium topography. The 43rd Annual Meeting of the Japanese Society for Biomaterials and The 8th Asian Biomaterials Congress 2021.11.28 Online

- 4. Chen P. Nanobiotechnology for smart surface designing of metallic dental implants. International Thin Film Conference 2021.11.15 Taipei, Taiwan
- 5. Uemura M, Nagai S, Fujii Y, Kubota Y, Kiguchi T, Konno T, Kuroda K, Tsukamoto M, Hanawa T, Ikoma T, Matsushita N. Controlling biodegradation rate of magnesium alloys by forming protective layers via hydrothermal treatment. The 12th International Conference on the Science and Technology for Advanced Ceramics (STAC12) 2021.07.06 Online (Yokohama, Japan)
- 6. Nishimoto J, Kubota Y, Wada T, Kato H, Kuroda K, Tsukamoto M, Hanawa T, Ikoma T, Natsushita N. Antibacterial nano-sized silver agent modified on titanate nanomesh intermediated by chitosan. The 12th International Conference on the Science and Technology for Advanced Ceramics (STAC12) 2021.07.06 Online (Yokohama, Japan)
- Ishimoto T, Sun SH, Hagihara K, Tsutsumi Y, Hanawa T, Nakano T. Crystallographic texture and material property control of 316L austenitic stainless steel via selective laser melting. Thermec'2021 2021.06.01 Online (Vienna, Austria)
- 8. Hanawa T. Biofunctionalization of metals meeting clinical demands. MATERIALS RESEARCH MEETING 2021 (MRM2021) 2021.12.13 Yokohama, Japan
- 9. Hanawa T. Metallic biomaterials from the viewpoint of surface reactions. The 5th Symposium for The Core Research Cluster for Materials Science and Spintronics, and the 4th Symposium on International Joint Graduate Program in Materials Science 2021.10.27 Online
- Hanawa T. Biofunctionalization of metals for regenerative medicine. Thermec'2021 2021.06.01 Online (Vienna, Austria)
- 11. Hanawa T. MRI-compatible alloy and biofunctionalization of metals. Biomaterials International 2021 (BMI2021) 2021.05.30 Online (Kenting, Taiwan)

Organic Biomaterials

Professor: Nobuhiko YUI Associate Professor: Atsushi TAMURA Assistant Professor: Yoshinori ARISAKA Secretary: Nanae NISHI

(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. 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

- 1. Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Delayed senescence of human vascular endothelial cells by molecular mobility of supramolecular biointerfaces Macromolecular Bioscience. 2021.12; 21(12); 2100216
- 2. Jun Kobayashi, Yoshinori Arisaka, Nobuhiko Yui, Masayuki Yamato, Teruo Okano. Preservation of heparin-binding EGF-like growth factor activity on heparin-modified poly(N-isopropylacrylamide)-grafted surfaces RSC Advances. 2021.11; 11(59); 37225-37232
- Ryo Mikami, Yoshinori Arisaka, Masahiro Hakariya, Takanori Iwata, Nobuhiko Yui. Improved epithelial cell-cell adhesion using molecular mobility of supramolecular surfaces. Biomaterials Science. 2021.10; 9(21); 7151-7158
- 4. Masahiro Hakariya, Yoshinori Arisaka, Hiroki Masuda, Atsushi Tamura, Tetsuya Yoda, Takanori Iwata, Nobuhiko Yui. Tissue adhesion-anisotropic polyrotaxane hydrogels bilayered with collagen Gels. 2021.10;

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- 5. Moe Ohashi, Atsushi Tamura, Nobuhiko Yui. Terminal structure of triethylene glycol-tethered chains on β -cyclodextrin-threaded polyrotaxanes dominates temperature-responsivity and biointeractions. Langmuir. 2021.09; 37(37); 11102-11114
- Tae Woong Kang, Atsushi Tamura, Yoshinori Arisaka, Nobuhiko Yui. Visible light-degradable supramolecular gels comprising cross-linked polyrotaxanes capped by trithiocarbonate groups. Polymer Chemistry. 2021.07; 12(26); 3794-3805
- 7. Shunyao Zhang, Atsushi Tamura, Nobuhiko Yui. Weakly acidic carboxy group-grafted β -cyclodextrin-threaded acid-degradable polyrotaxanes for modulating protein interaction and cellular internalization. Science and Technology of Advanced Materials. 2021.06; 22(1); 494-510
- 8. Azusa Kobayashi, Ayaka Ito, Ibuki Shirakawa, Atsushi Tamura, Susumu Tomono, Hideo Shindou, Per Niklas Hedde, Miyako Tanaka, Naotake Tsuboi, Takuji Ishimoto, Sachiko Akashi-Takamura, Shoichi Maruyama, Takayoshi Suganami. Dietary supplementation with eicosapentaenoic acid inhibits plasma cell differentiation and attenuates lupus autoimmunity. Frontiers in Immunology. 2021.06; 12; 650856
- 9. Yoshinori Arisaka, Masahiro Hakariya, Takanori Iwata, Hiroki Masuda, Tetsuya Yoda, Atsushi Tamura, Nobuhiko Yui. Surface-tethering of methylated polyrotaxanes with 4-vinylbenzyl groups onto poly(ether ether ketone) substrates for improving osteoblast compatibility. Dental Materials Journal. 2021.05; 40(3); 813-819
- Qutaiba Alsandi, Masaomi Ikeda, Yoshinori Arisaka, Toru Nikaido, Yumi Tsuchida, Alireza Sadr, Nobuhiko Yui, Junji Tagami. Evaluation of mechanical and physical properties of light and heat polymerized UDMA for DLP 3D printer Sensors. 2021.05; 21(10); 3331
- 11. Hiroki Masuda, Yoshinori Arisaka, Masahiro Hakariya, Takanori Iwata, Tetsuya Yoda, Nobuhiko Yui. Synergy of molecularly mobile polyrotaxane surfaces with endothelial cell co-culture for mesenchymal stem cell mineralization RSC Advances. 2021.05; 11(30); 18685-18692
- 12. Atsushi Tamura, Moe Ohashi, Asato Tonegawa, Tae Woong Kang, Shunyao Zhang, Nobuhiko Yui. Effect of alkyl chain length of acylated α -cyclodextrin-threaded polyrotaxanes on thermoresponsive phase transition behavior. Macromolecular Chemistry and Physics. 2021.03; 222(5); 2000420
- 13. Yoshinori Arisaka, Nobuhiko Yui. Anchoring α -cyclodextrin-based polyrotaxanes to biological tissues via riboflavin-mediated photo-crosslinking Materials Letters. 2021.03; 290; 129460
- 14. Sekiya-Aoyama R, Arisaka Y, Hakariya M, Masuda H, Iwata T, Yod T, Yui N. Dual effect of molecular mobility and functional groups of polyrotaxane surfaces on the fate of mesenchymal stem cells Biomaterials Science. 2021.02; 9(3); 675-684
- Yoshinori Arisaka, Nobuhiko Yui. Molecular mobility of polyrotaxane-based biointerfaces alters inflammatory responses and polarization in Kupffer cell lines Biomaterials science. 2021.02; 9(6); 2271-2278
- 16. Yoshinori Arisaka, Asato Tonegawa, Atsushi Tamura, Nobuhiko Yui. Terminally cross-linking polyrotaxane hydrogels applicable for cellular microenvironments. Journal of Applied Polymer Science. 2021.01; 138(3); 49706

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- 1. Daniel J. Klionsky, et al. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). Autophagy. 2021.02; 17(1); 1-382
- 2. Masahiko Terauchi, Atsushi Tamura, Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Cyclodextrin-based supramolecular complexes of osteoinductive agents for dental tissue regeneration. Pharmaceutics. 2021.01; 13(2); 136

- 1. Ruriko Sekiya-Aoyama, Yoshinori Arisaka, Nobuhiko Yui. Effect of polyrotaxane surfaces with fine-tuned molecular mobility on gene expression of myoblast. Pacifichem 2021 2021.12.20
- Ayaka Ito, Azusa Kobayashi, Ibuki Shirakawa, Atsushi Tamura, Susumu Tomono, Hideo Shindou, Per Niklas Hedde, Miyako Tanaka, Naotake Tsuboi, Takuji Ishimoto, Sachiko Akashi-Takamura, Shoichi Maruyama, Takayoshi Suganami. Dietary supplementation with eicosapentaenoic acid inhibits plasma cell differentiation and attenuates lupus autoimmunity. The 50th Annual Meeting of the Japanese Society for Immunology 2021.12.09 奈良春日野国際フォーラム, 奈良県奈良市
- 3. Shunyao Zhang, 田村篤志, 由井伸彦. Carboxyalkyl carbamate group-modified β-cyclodextrin polyrotaxane with different alkyl spacer lengths for modulating cellular internalization. 第 43 回日本 バイオマテリアル学会大会 2021.11.29 オンライン開催

Biomechanics

Hirokazu Kaji, Professor Takeshi Hori, Project Assistant Professor Akane Yamamoto, Technician

(1) Outline

We are developing micro/nanotechnologies minimally invasive to bio-derived materials and living bodiesbodies for next generation biomedical applications.

(2) Research

- 1. Biofabrication technology
- 2. Drug delivery system
- 3. Cell delivery system
- 4. Micropysiological system (MPS)

(3) Lectures & Courses

Students will learn the latest trends in biomechanics and related research fields, as well as acquire fundamental knowledge and skills. In addition, students will aim to develop the ability to independently promote research in the field.

(4) **Publications**

[Original Articles]

- Violeta Carvalho, Inês Gonçalves, Teresa Lage, Raquel O. Rodrigues, Graça Minas, Senhorinha F.C.F Teixeira, Ana S. Moita, Takeshi Hori, Hirokazu Kaji, Rui A. Lima. 3D Printing Techniques and Their Applications to Organ-on-a-Chip Platforms: A Systematic Review Sensors. 2021.05; 21(9); 3304
- Bibek Raut, Li Jiun Chen, Takeshi Hori, Hirokazu Kaji. An open-source add-on evom® device for real-time transpithelial/endothelial electrical resistance measurements in multiple transwell samples Micromachines. 2021.03; 12(3); 1-13

[Conference Activities & Talks]

1. Takeshi Hori, Hiroaki Akae, Norio Kobayashi, Takahiro Arima, Hirokazu Kaji. A trophoblast stem cell-based model of the human placental barrier. MicroTAS 2021 2021.10.10 California, USA & Virtual

Molecular Cell Biology

Professor Hiroshi Shibuya Associate Professor Toshiyasu Goto Assistant Professor Masahiro Shimizu

(1) Research

Cancer stem cells (CSCs), also called tumor-initiating cells, are a subset of tumor cells that exhibit self-renewal ability and generate the diverse cells that comprise the tumor. CSCs show increased quiescence and poor responses to conventional chemotherapy strategies that primarily kill proliferating cells. Therefore, CSCs are correlated with chemoresistance, invasion and relapse of cancer cells. However, the underlying mechanisms of CSCs generation have not been completely elucidated.

Alterations of genes involved in the regulation of cell proliferation, such as oncogenes and tumor suppressor genes, may lead to cancer development. Therefore, it is possible that analyzes of reprogramming factors and cell growth regulators will lead to the elucidation of the mechanism of CSCs generation. However, cancer develops because of the acquisition of successive hallmark cancer capabilities in a multistep pathogenic process, and it is difficult to analyze the role of reprogramming factors in CSCs generation using established cancer cell lines. To solve these problems, we use normal cells expressing oncogenic mutants.

1. Oncogenic RAS induces SOX2-initiated CSCs generation.

Previously, we reported that oncogenic HRAS (HRAS G12V mutant: HRASV12) induced tumorigenic properties in p53-deficient mouse embryonic fibroblasts (p53 -/- MEFs), suggesting that HRASV12 promoted the generation of CSCs. To confirm this hypothesis, we generated HRASV12-expressing $p_{53} - /-$ MEFs and demonstrated that these cells formed tumors in nude mice. It has been reported that cancer cells with CSC-like properties will form spheres in low attachment culture conditions in medium containing growth factors. We next examined CSCs development of HRASV12-expressing $p_{53} - /-$ MEFs using sphere formation analysis, and found that approximately 0.4% of these cells developed spheres in low attachment plates. This demonstrates oncogenic RAS mutation generates CSCs. We also compared expression levels of reprograming factors such as OCT4, SOX2 and KLF4 between adherent HRASV12-expressing p_{53} -/- MEFs cells and p_{53} -/- MEFs control cells. Interestingly, the expression of only SOX2 was markedly enhanced in HRASV12-expressing p53 - /- MEFs cells, suggesting that it was possible that SOX2 functioned as an initiation factor for CSCs reprogramming. To test this hypothesis, we deleted the SOX2 gene in HRASV12-expressing $p_{53} - /-$ MEFs with three independent gRNAs using the CRISPR-Cas9 gene knockout system. We analysed the effect of SOX2 KO on the CSC properties found in HRASV12-expressing $p_{53} - / -$ MEFs, and showed that sphere-forming and tumor-initiating activities were not observed after SOX2 KO. These results suggest that SOX2 expression is required for CSCs generation by oncogenic RAS mutation.

2. SOX2 expression is induced by the RAF-MAPK-CDK1 pathway in HRASV12-expressing p53 - /- MEFs. RAS proteins directly activate the downstream effectors RAF and PI3K followed by the downstream activation of MAPK and AKT pathways, respectively. Therefore, we next examined whether these effectors were involved in promoting SOX2 expression. Constitutively active forms of RAF (BRAFV600E) and PI3K (PI3KCAAX) were stably expressed in p53 - /- MEFs. Although the increase in SOX2 mRNA expression was relatively weakly in PI3KCAAX-expressing cells, the levels of SOX2 and KLF4 mRNA in BRAFV600E-expressing cells were similar to that in HRASV12-expressing cells. Furthermore, SOX2 expression was significantly reduced by the MEK inhibitors U0126 and PD184352 but not by the PI3K inhibitor LY294002 in HRASV12-expressing p53 - /- MEFs. These results suggest that the RAF/MEK/ERK pathway is required for SOX2 induction. Activation of ERK enhances expression of cyclin D1, which binds to and activates cyclin-dependent kinase 4 and 6 (CDK4/6) during the G1 phase of the cell cycle. In addition to CDK4/6, the BRAF/MEK/MAPK pathway is also essential for some functions of CDK1 and CDK2. We next examined the effect of CDK4/6 inhibitor palbociclib and CDK1/2 inhibitor dinaciclib on SOX2 expression. As a result, although the expression of SOX2 mRNA and protein levels were slightly reduced in HRASV12-expressing p53 - /- MEFs after treatment with a high-dose of palbociclib, SOX2 mRNA and protein expression was strongly suppressed by dinaciclib. Moreover, the number of sphere-forming cells in HRASV12-expressing p53 - /- MEFs was largely suppressed by dinaciclib. To further analyse whether CDKs were essential for SOX2 expression, we analysed SOX2 levels in HRASV12-expressing p53 - /- MEFs after knockdown of CDK1 or CDK2 using siRNA, and confirmed requirement of only CDK1 for SOX2 induction. These results indicate that CDK1 activity is required for SOX2 expression in HRASV12-expressing p53 - /- MEFs.

3. Enhanced O-GlcNAc modification induced by the RAS/MAPK/CDK1 pathway is required for SOX2 protein expression and generation of cancer stem cells.

GlcNAcylation is the post-translational modification of N-acetylglucosamine (also known as GlcNAc) to serine or threenine residues of proteins that contributes to stability and activity of modified proteins. Previously, we reported that enhanced O-GlcNAcylation is important for SOX2 expression and maintenance of CSCs properties, including sphere- and tumour-forming activities, in colon and lung cancer cells. These findings suggested the possibility that O-GlcNAc modifications are involved in acquisition of CSCs properties. Therefore, we determined the O-GlcNAc levels in HRASV12-expressing p53 -/- MEFs and found elevated levels of protein O-GlcNAcylation compared with control p53 -/- MEFs. Next, we analyzed the cells after treatment with OSMI1, a cell-permeable, small molecule O-GlcNAc transferase inhibitor, and found that OSMI1 treatment suppressed total O-GlcNAcylation levels of proteins and SOX2 expression in HRASV12-expressing p53 -/-MEFs. Interestingly, the OSMI1-mediated reduction in SOX2 levels was attenuated by treatment with the proteasome inhibitor MG-132 and the mRNA levels of SOX2 in HRASV12-expressing p53 -/- MEFs were not significantly changed by OSMI1, indicating that O-GlcNAcylation regulated SOX2 expression at the post-transcriptional level. Consistent with these results, the numbers of sphere-forming cells decreased after treatment with OSMI1. These results suggest that increased O-GlcNAcylation is required for SOX2 protein expression and sphere-forming activity in these cells.

Finally, we analyzed the role of RAS/MAPK-activated CDK1 in the induction of O-GlcNAcylation. The elevated levels of O-GlcNAcylation in HRASV12-expressing p53 -/- MEFs were suppressed by dinaciclib in a dose dependent manner. Furthermore, knockdown of CDK1, but not CDK2, with siRNA inhibited O-GlcNAcylation levels in the cells. In addition, SOX2 expression and O-GlcNAcylation levels in KRAS-activated cancer cells including colon cancer cells HCT116, SW480 and DLD1 and lung cancer cells H460 and A549 were suppressed by dinaciclib treatment.

In conclusion, we show that RAS/RAF/MAPK pathway-induced CDK1 activation is important for induction of O-GlcNAcylation, and this activation pathway is required for SOX2 expression and subsequent CSC generation. Our results suggest the possibility that this signaling pathway is a therapeutic target for CSCs.

(2) 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.

(3) Publications

[Conference Activities & Talks]

1. Shimizu Masahiro, Tanaka Nobuyuki, Shibuya Hiroshi. Analysis of CXCR2 dependent regulation of cancer stem cells.. 2021.12.01

Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D. Lecturer Satoshi Kofuji, Ph.D. Assistant Professor Yasuhiro Nakano, Ph.D. Project Assistant Professor Taku Tanaka, Ph.D. Project Assistant Professor Jing Pu, Ph.D. Project Assistant Professor Keiko Kanayama, Ph.D. Technical Assistant Mizuki Kusaba Secretary Kaori Kofuji

(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

- Alifu Y, Kofuji S, Sunaga S, Kusaba M, Hirayama J, Nishina H. The Light-Inducible Genes Per2, Cry1a, and Cry2a Regulate Oxidative Status in Zebrafish. Biological & pharmaceutical bulletin. 2021.08; 44(8); 1160-1165
- 2. Sunaga S, Kofuji S, Nishina H. YAP drives cell competition by activating choline metabolism. Biochemical and biophysical research communications. 2021.08; 572; 178-184
- Alifu Yikelamu, Kofuji Satoshi, Sunaga Sachi, Kusaba Mizuki, Hirayama Jun, Nishina Hiroshi. The Light-Inducible Genes Per2, Cry1a, and Cry2a Regulate Oxidative Status in Zebrafish(和訳中) Biological & Pharmaceutical Bulletin. 2021.08; 44(8); 1160-1165

- Ikeda Y, Hirayama A, Kofuji S, Hirota Y, Kamata R, Osaka N, Fujii Y, Sasaki M, Ikeda S, Smith EP, Bachoo R, Soga T, Sasaki AT. SI-MOIRAI: A new method to identify and quantify the metabolic fate of nucleotides. Journal of biochemistry. 2021.07;
- Nagashima S, Maruyama J, Honda K, Kondoh Y, Osada H, Nawa M, Nakahama KI, Ishigami-Yuasa M, Kagechika H, Sugimura H, Iwasa H, Arimoto-Matsuzaki K, Nishina H, Hata Y. CSE1L promotes nuclear accumulation of transcriptional coactivator TAZ and enhances invasiveness of human cancer cells. The Journal of biological chemistry. 2021.05; 297(1); 100803
- Xinliang Jiang, Junichi Maruyama, Hiroaki Iwasa, Kyoko Arimoto-Matsuzaki, Hiroshi Nishina, Yutaka Hata. Heat shock induces the nuclear accumulation of YAP1 via SRC. Exp Cell Res. 2021.02; 399(1); 112439
- 7. Mayu Morishita, Kyoko Arimoto-Matsuzaki, Masami Kitamura, Kyohei Niimura, Hiroaki Iwasa, Junichi Maruyama, Yuichi Hiraoka, Kohei Yamamoto, Masanobu Kitagawa, Norio Miyamura, Hiroshi Nishina, Yutaka Hata. Characterization of mouse embryonic fibroblasts derived from Rassf6 knockout mice shows the implication of Rassf6 in the regulation of NF- κ B signaling. Genes Cells. 2021.12; 26(12); 999-1013
- 8. Keisuke Nakatani, Tomohiko Maehama, Miki Nishio, Junji Otani, Keiko Yamaguchi, Miki Fukumoto, Hiroki Hikasa, Shinji Hagiwara, Hiroshi Nishina, Tak Wah Mak, Teruki Honma, Yasumitsu Kondoh, Hiroyuki Osada, Minoru Yoshida, Akira Suzuki. Alantolactone is a natural product that potently inhibits YAP1/TAZ through promotion of reactive oxygen species accumulation. Cancer Sci. 2021.10; 112(10); 4303-4316
- 9. Takako Ooshio, Masahiro Yamamoto, Kiyonaga Fujii, Bing Xin, Kenji Watanabe, Masanori Goto, Yoko Okada, Akira Suzuki, Josef M Penninger, Hiroshi Nishina, Yuji Nishikawa. Hepatocyte Mitogen-Activated Protein Kinase Kinase 7 Contributes to Restoration of the Liver Parenchyma Following Injury in Mice. Hepatology. 2021.06; 73(6); 2510-2526
- Tadashi Shin, Yuichi Hiraoka, Tokiwa Yamasaki, Jamey D Marth, Josef M Penninger, Masami Kanai-Azuma, Kohichi Tanaka, Satoshi Kofuji, Hiroshi Nishina. MKK7 deficiency in mature neurons impairs parental behavior in mice. Genes Cells. 2021.01; 26(1); 5-17

[Misc]

1. Yasuhiro Nakano, Yutaka Inagaki. Treatment strategy for liver fibrosis by inducing deactivation of fibrogenic hepatic stellate cell Clinical Immunology & Allergology. 2021.08; 76(2); 113-119

[Conference Activities & Talks]

1. Yasuhiro Nakano, Atsushi Miyajima, Tohru Itoh. Behavior of Reactive Cholangiocytes in the Tissue Repair Stage from Chronic Liver Injury. APASL STC 2021 Osaka 2021.09.02

[Awards & Honors]

1. UJA Paper Award, United Japanese researchers Around the world, 2021.04

Immunology

Professor: Takeshi TSUBATA, M.D., Ph.D. Associate Professor: Takahiro ADACHI, Ph.D. Assistant Professor: Chizuru AKATSU, Ph.D. Assistant Professor: Cheryl Sophia SULTAN, Ph.D. Lecturer: Ji-Yang WANG, Ph.D. Researcher Amin Alborzian Deh Sheikh, Ph.D. Technician: Mikako AKAZAWA Secretary: Chikako SAWADA

Graduate Students:Hongrui YANG, Kyoko TAMEHIROGraduate Students:Wang LONG, Yuming HUANGGraduate Students:Shinji KUNITAKE, Ayaka OOKAMEGraduate Students:Kana MATSUMURA, Mizuki OOSUMIGraduate Students:Yang CUI, Yi DINGGraduate Students:Tianyi YANGGraduate Students:Hashadi Nadeesha WALAKULU GAMAGE

Research Student: Jixuan XU

Intern: Kennosuke KIYOTA Intern: Yutaka TSUNESHIGE

Collaborative Researcher: Wataru TAKASHIMA

(1) Outline

Education and research in the field of immunology from elucidation of basic mechanisms of antibody responses to development of novel therapies of immunological diseases and vaccines are conducted.

(2) Research

Antibody responses to non-protein antigens such as polysaccharides and nucleic acids play crucial roles in host defense against pathogens, and autoimmune diseases. The mechanisms for antibody responses to non-protein antigens are distinct from those to protein antigens, but are largely unknown. We are elucidating mechanisms for antibody responses and self-tolerence to non-protein antigens in normal immunity and autoimmunity, and also developing novel therapies and vaccines. Followings are our research subjects.

1) Study on the regulatory mechanisms of autoantibody production in systemic lupus erythematosus (SLE) and autoimmune neuropathy

2) Study on the B cell regulation by molecular interactions in glycocalyx

3) Study on the mechanisms for antibody production and self-tolernce to polysaccharides

4) Development of novel therapies for autoimmune diseases and vaccines

(3) Education

Department of Immunology 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.

(4) Lectures & Courses

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.

(5) Publications

[Original Articles]

- Li Y, Tang Y, Liu J, Meng X, Wang Y, Min Q, Hong R, Tsubata T, Hase K, Wang JY. Glia maturation factor- γ is involved in S1P-induced marginal zone B cell chemotaxis and optimal T-independent type II antigen-induced IgM production. International immunology. 2021.12; in press;
- Long, W., Kunitake, S., Sawada, S., Akiyoshi, K. and Tsubata, T. Protein antigen conjugated with cholesteryl amino-pullulan nanogel shows delayed degradation in dendritic cells and augmented immunogenicity. Vaccine. 2021.12; 39; 7526-7530
- Akatsu, C., Alborzian Deh Sheikh, A., Matsubara, N., Takematsu, H., Schweizer, A., Abdu-Allah, H. H. M., Tedder, T. F., Nitschke, L., Ishida, H. and Tsubata, T. Inhibitory co-receptor CD22 restores B cell signaling by developmentally regulating Cd45-/- immunodeficient B cells. Sci. Signal. 2021.12; in press;
- 4. Alborzian Deh Sheikh, A, Akatsu, C., Abdu-Allah, H. H. M., Suganuma, Y., Imamura, A., Ando, H., Takematsu, H., Ishida, H. and Tsubata, T. The protein tyrosine phosphatase SHP-1 (PTPN-6) but not CD45 (PTPR-C) is essential for the ligand-mediated regulation of CD22 in BCR-ligated B cells J. Immunol. 2021.06; 206(11); 2544-2551
- 5. Ballet, R., Brennan, M., Brandl, C., Feng, N., Berri, J., Cheng, J., Ocón, B., Alborzian Deh Sheikh, A., Marki, A., Bi,Y., Abram, C. L., Lowell, C. A., Tsubata, T., Greenberg, H. B., Macauley, M. S., Ley, K., Nitschke, L., Butcher. E. C. CD22-Shp1 phosphatase axis controls integrin β 7 display and B cell function in mucosal immunity Nature Immunology. 2021.02; 22; 381-390
- Alborzian Deh Sheikh, A., Gomaa, S., Li, X., Routledge, M., Saigoh, K., Numoto, N., Angata, T., Hitomi, Y., Takematsu, H., Tsuiji, M., Ito, N., Kusunoki, S., Tsubata, T. A Guillain-Barré syndrome-associated SIGLEC10 rare variant impairs its recognition of gangliosides. Journal of Autoimmunity. 2021.01; 116; 102571
- 7. Tsugawa, N., Yamada, D., Watabe, T., Onizawa, M., Wang, S., Nemoto, Y., Oshima, S., Tsubata, T., Adachi, T., Kawano, Y., Watanabe, M., Blumberg, RS., Okamoto, R., Nagaishi, T. CEACAM1 specifically suppresses B cell receptor signaling-mediated activation. Biochemical and Biophysical Research Communications. 2021.01; 535; 99-105

[Misc]

1. Tsubata, T. Role of inhibitory B cell co-receptors in B cell self-tolerance to non-protein antigens Immunological Reviews. 2021.12; in press;

- 1. Kana Matsumura, Takeshi Tsubata. Persistence of antigens in endosome/lysosome is essential for B cell response to TI-2 polysaccharide antigens. The 50th Annual Meeting of the Japanese Society for Immunology 2021.12.09 Nara+WEB
- 2. Chizuru Akatsu, Quan-Zhen Li, Hideharu Sekine, Teizo Fujita, Takeshi Tsubata. CD72 inhibits lupus-specific B cell autoimmunity caused by response to apoptotic cells through recognition of lupus-specific self-antigens. The 50th Annual Meeting of the Japanese Society for Immunology 2021.12.09 Nara+WEB
- 3. Takeshi Tsubata. Immunogenic Peptides Derived from SARS-CoV2. 19th Surugadai Symposium 2021.09.03 WEB
- 4. N. Numoto, K. Hirata, C. Akatsu, T. Tsubata, N. Ito. Molecular mechanism of self-antigen recognition by the ligand binding domain of B cell inhibitory co-receptor CD72. 25TH Congress and General Assembly of the International Union of Crystallography 2021.08.14 WEB
- 5. Amin Alborzian Deh Sheikh, Takeshi Tsubata, et al.. A Guillain-Barré syndrome-associated SIGLEC10 rare variant impairs its recognition of gangliosides. The 85th Annual Meeting of the Japanese Society of Interferon & Cytokine Research 2021.05.21 WEB
- 1. Takeshi Tsubata. Cross-talk between complement pathways and immune system. 2021.09.10
- 2. Takeshi Tsubata. Inhibitory B cell co-receptors and autoimmune diseases. The 85th Annual Meeting of the Japanese Society of Interferon & Cytokine Research 2021.05.21

Structural Biology

Professor Nobutoshi ITO Associate Professor Nobutaka NUMOTO Assistant Professor Yuya HANAZONO

(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) Rational design of PDZ domain inhibitors involved in regulation of intracellular signaling
- 5) Structural basis of giant hemoglobins
- 6) Molecular basis of suppression of HIV-1
- 7) Structure based drug design for protein kinases
- 8) Structural analysis including hydrogen atoms by ultra-high resolution crystallography
- 9) 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]

- Lensink MF, Brysbaert G, Mauri T, Nadzirin N, Velankar S, Chaleil RAG, Clarence T, Bates PA, Kong R, Liu B, Yang G, Liu M, Shi H, Lu X, Chang S, Roy RS, Quadir F, Liu J, Cheng J, Antoniak A, Czaplewski C, GiełdoN A, Kogut M, Lipska AG, Liwo A, Lubecka EA, Maszota-Zieleniak M, Sieradzan AK, Ślusarz R, Wesołowski PA, ZiEba K, Del Carpio Muñoz CA, Ichiishi E, Harmalkar A, Gray JJ, Bonvin AMJJ, Ambrosetti F, Honorato RV, Jandova Z, Jiménez-García B, Koukos PI, Van Keulen S, Van Noort CW, Réau M, Roel-Touris J, Kotelnikov S, Padhorny D, Porter KA, Alekseenko A, Ignatov M, Desta I, Ashizawa R, Sun Z, Ghani U, Hashemi N, Vajda S, Kozakov D, Rosell M, Rodríguez-Lumbreras LA, Fernandez-Recio J, Karczynska A, Grudinin S, Yan Y, Li H, Lin P, Huang SY, Christoffer C, Terashi G, Verburgt J, Sarkar D, Aderinwale T, Wang X, Kihara D, Nakamura T, Hanazono Y, Gowthaman R, Guest JD, Yin R, Taherzadeh G, Pierce BG, Barradas-Bautista D, Cao Z, Cavallo L, Oliva R, Sun Y, Zhu S, Shen Y, Park T, Woo H, Yang J, Kwon S, Won J, Seok C, Kiyota Y, Kobayashi S, Harada Y, Takeda-Shitaka M, Kundrotas PJ, Singh A, Vakser IA, DapkŪnas J, Olechnovič K, Venclovas Č, Duan R, Qiu L, Zhang S, Zou X, Wodak SJ. Prediction of protein assemblies, the next frontier: The CASP14-CAPRI experiment. Proteins. 2021.12; 89(12); 1800-1823
- 2. Tanaka H, Kondo K, Fujita K, Homma H, Tagawa K, Jin X, Jin M, Yoshioka Y, Takayama S, Masuda H, Tokuyama R, Nakazaki Y, Saito T, Saido T, Murayama S, Ikura T, Ito N, Yamamori Y, Tomii K, Bianchi ME, Okazawa H. HMGB1 signaling phosphorylates Ku70 and impairs DNA damage repair in Alzheimer's disease pathology. Commun Biol. 2021.10; 4(1); 1175
- 3. Kondo K, Ikura T, Tanaka H, Fujita K, Takayama S, Yoshioka Y, Tagawa K, Homma H, Liu S, Kawasaki R, Huang Y, Ito N, Tate SI, Okazawa H. Hepta-Histidine Inhibits Tau Aggregation. ACS Chem Neurosci. 2021.08; 12(16); 3015-3027
- 4. Yosuke Inoue, Yuya Hanazono, Kentaro Noi, Akihiro Kawamoto, Masato Kimatsuka, Ryuhei Harada, Kazuki Takeda, Ryoichi Kita, Natsuki Iwamasa, Kyoka Shibata, Keiichi Noguchi, Yasuteru Shigeta, Keiichi Namba, Teru Ogura, Kunio Miki, Kyosuke Shinohara, Masafumi Yohda. Split conformation of Chaetomium thermophilum Hsp104 disaggregase. Structure. 2021.07; 29(7); 721-730
- 5. Miho Emori, Nobutaka Numoto, Akane Senga, Gert-Jan Bekker, Narutoshi Kamiya, Yuma Kobayashi, Nobutoshi Ito, Fusako Kawai, Masayuki Oda. Structural basis of mutants of PET-degrading enzyme from Saccharomonospora viridis AHK190 with high activity and thermal stability. Proteins. 2021.05; 89(5); 502-511
- Momoka Iiyama, Nobutaka Numoto, Shuhei Ogawa, Masataka Kuroda, Hisayuki Morii, Ryo Abe, Nobutoshi Ito, Masayuki Oda. Molecular interactions of the CTLA-4 cytoplasmic region with the phosphoinositide 3-kinase SH2 domains. Mol Immunol. 2021.03; 131; 51-59
- Senga Akane, Numoto Nobutaka, Yamashita Mitsuaki, Iida Akira, Ito Nobutoshi, Kawai Fusako, Oda Masayuki. Multiple structural states of Ca2+-regulated PET hydrolase, Cut190, and its correlation with activity and stability The Journal of Biochemistry. 2021.02; 169(2); 207-213
- Alborzian Deh Sheikh, A., Gomaa, S., Li, X., Routledge, M., Saigoh, K., Numoto, N., Angata, T., Hitomi, Y., Takematsu, H., Tsuiji, M., Ito, N., Kusunoki, S., Tsubata, T. A Guillain-Barré syndrome-associated SIGLEC10 rare variant impairs its recognition of gangliosides. Journal of Autoimmunity. 2021.01; 116; 102571

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- 1. Masayuki Oda, Nobutaka Numoto, Gert-Jan Bekker, Narutoshi Kamiya, Fusako Kawai. Cutinases from thermophilic bacteria (actinomycetes): From identification to functional and structural characterization. Methods Enzymol. 2021.02; 648; 159-185
- Numoto N, Kamiya N, Kawai F, Oda M. Crystal Structures of Polyethylene Terephthalate-Degrading Enzyme Cut190 in Substrate-Bound States Reveal the Enzymatic Reaction Cycle Accelerated by Calcium Ion ACS Symposium Series "Green Polymer Chemistry and Sustainability." 2021;
- 1. Nobutaka Numoto. Structure Determination from Protein Crystal Clusters by Fully Automatic Data Collection Journal of the Crystallographic Society of Japan. 2021.08; 63(3);

- 1. Yuya Hanazono, Yu Hirano, Kazuki Takeda, Katsuhiro Kusaka, Taro Tamada, Kunio Miki. High-resolution structure of an electron-transfer protein by neutron crystallography. The 4th International Forum on Quantum Metrology and Sensing 2021.12.08 on-line
- 2. Nobutaka Numoto, Kunio Hirata, Chizuru Akatsu, Takeshi Tsubata, Nobutoshi Ito. Molecular mechanism of self-antigen recognition by the ligand binding domain of B cell inhibitory co-receptor CD72. 25th Congress and General Assembly of the International Union of Crystallography 2021.08.20 Prague / on-line hybrid meeting
- 3. Hafumi Nishi, Yuya Hanazono, Kengo Kinoshita. Comprehensive analysis of genetic variations on human SLC transporters. The 29th Conference on Intelligent Systems for Molecular Biology and the 20th European Conference on Computational Biology (ISMB/ECCB2021) 2021.07.25 on-line
- 1. Satoshi Omori, Yuya Hanazono, Hafumi Nishi, Kengo Kinoshita. Mechanism of the gating motion of SLC26A9 chloride ion transporter revealed by the molecular dynamics simulations. The 59th Annual Meeting of the Biophysical Society of Japan 2021.11.27 on-line
- 2. Nobutaka Numoto. A user review of automatic and remote measurement at SPring-8. 59th SPring-8 Advanced Utilization Technology Workshop / IPR Seminar 2021.03.23

Epigenetic Epidemiology

Professor: Masaaki MURAMATSU Associate Professor : Noriko SATO Assistant Professor : Chihiro Imai

Adjunct Instructor : Sumio Sugano, Tomio Arai

Graduate Student: Tadaaki Katsuta, Tong Daike Master Student: Fuko Yamada

(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. Developmental Origin of Health and Diseases
- 3. Role of nutrition on epigenetic modification and health
- 4. Genetic factors that affect the severity of pathological atherosclerosis and the development of cancer
- 5. Application of personal genome to preemptive & preventive medicine.

(3) Education

[Doctor course] Noriko Sato: Biomedical Science

[Master course] Noriko Sato: Molecular and Cellular Biology Noriko Sato: Introduction to Human Molecular Genetics

[Undergraduate] Noriko Sato: Bioinformatics Noriko Sato: Diet and Health

(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) Clinical Services & Other Works

[Japan Women's University] Noriko Sato: Lecturer

(6) Publications

[Original Articles]

- Sato N, Fudono A, Imai C, Takimoto H, Tarui I, Aoyama T, Yago S, Okamitsu M, Mizutani S, and Miyasaka N. Placenta mediates the effect of maternal hypertension polygenic score on offspring birth weight: a study of birth cohort with fetal growth velocity data BMC Medicine. 2021.11; 19(1); 260
- Fudono A, Imai C, Takimoto H, Tarui I, Aoyama T, Yago S, Okamitsu M, Muramatsu M, Sato N, Miyasaka N.. Trimester-specific associations between extracellular vesicle microRNAs and fetal growth. J Matern Fetal Neonatal Med. 2021.11; 1-7
- 3. Imai C, Takimoto H, Fudono A, Tarui I, Aoyama T, Yago S, Okamitsu M, Sasaki S, Mizutani S, Miyasaka N, Sato N. Application of the Nutrient-Rich Food Index 9.3 and the Dietary Inflammatory Index for assessing maternal dietary quality in Japan: a single-center birth cohort study Nutrients. 2021.08; 13; 2854

[Works]

1. DOHaD study for preemptive medicine (Noriko Sato), Other, http://www.tmd.ac.jp/ppepi/index.html, 2019.04 - Now

[Others]

- 1. Maternal genetic risk of hypertension associated with reduced placental weight, 2021.11 2 Minute Medicine
- 2. The Placenta the Smoking Gun in Cardiovascular Disease, 2021.12 AAAS EurekAlert! The Global Source for Science News
- 3. New the rapeutic targets for the treatment and prevention of hypertension, cardiov ascular diseases, 2021.12 The Medical News.

Department of Functional Genome Informatics

Professor NIKAIDO Itoshi

(1) **Outline**

We will develop human resources capable of development at an advanced level in molecular biology and data science technologies to measure genome function information at an unprecedented scale and accuracy and produce human resources that can promote the next generation of medicine creatively and proactively.

(2) Publications

[Original Articles]

- Yamada A, Hirasawa T, Nishimura K, Shimura C, Kogo N, Fukuda K, Kato M, Yokomori M, Hayashi T, Umeda M, Yoshimura M, Iwakura Y, Nikaido I, Itohara S, Shinkai Y. Derepression of inflammation-related genes link to microglia activation and neural maturation defect in a mouse model of Kleefstra syndrome. iScience. 2021.07; 24(7); 102741
- Ishihara S, Sasagawa Y, Kameda T, Yamashita H, Umeda M, Kotomura N, Abe M, Shimono Y, Nikaido I. Local states of chromatin compaction at transcription start sites control transcription levels. Nucleic acids research. 2021.07;
- 3. Mishina Tappei, Tabata Namine, Hayashi Tetsutaro, Yoshimura Mika, Umeda Mana, Mori Masashi, Ikawa Yayoi, Hamada Hiroshi, Nikaido Itoshi, Kitajima Tomoya S.. Single-oocyte transcriptome analysis reveals aging-associated effects influenced by life stage and calorie restriction AGING CELL. 2021.07; e13428
- 4. Morita Ritsuko, Sanzen Noriko, Sasaki Hiroko, Hayashi Tetsutaro, Umeda Mana, Yoshimura Mika, Yamamoto Takaki, Shibata Tatsuo, Abe Takaya, Kiyonari Hiroshi, Furuta Yasuhide, Nikaido Itoshi, Fujiwara Hironobu. Tracing the origin of hair follicle stem cells NATURE. 2021.06;
- 5. 二階堂 愛. High-throughput Transcriptome Analysis for Building Cell Atlas(和訳中) 日本循環器学会学術 集会抄録集. 2021.03; 85 回; ME08-4

- 1. Itoshi NIKAIDO. High-throughput transcriptome methods for building human cell atlas. The 5th Symposium of the inter-university Research Network for the trans-omics Medicine The future of transc-omics in the age of COVID-19. Web 2021.01.22
- 1. Itoshi NIKAIDO. Large-scale transcriptome analysis method for building human cell atlas. 2021.03.27
Medical Chemistry

Professor: Katsumori Segawa Assistant Professor: Yugo MIiyata Technical Staff: Risa Kuribayashi

(1) Outline

In the department of medical chemistry, we aim to understand cells with biochemistry and molecular genetics and, beyond that, life and disease.

(2) Research

The asymmetrical distribution of phospholipids in plasma membranes is a fundamental architecture that confines phosphatidylserine (PtdSer) and phosphatidylethanolamine (PtdEtn) to the inner leaflet and enriches phosphatidylcholine (PtdCho) and sphingomyelin (SM) in the outer leaflet. There are three types of phospholipid translocases (flippase, floppase, and scramblase) that transfer phospholipids across the membrane lipid bilayer. Flippases translocate PtdSer and PtdEtn from the outer to the inner leaflet, whereas the translocation of PtdCho and SM from the inner to the outer leaflet has been proposed to be mediated by floppase. These molecules create the asymmetrical distribution of phospholipids in an ATP-dependent manner, while scramblases disrupt it by providing a path for the non-specific phospholipid transport between the leaflets of the plasma membrane. We aim to identify various phospholipid translocases and elucidate their physiological and pathophysiological significances.

(3) Publications

[Original Articles]

 Katsumori Segawa, Atsuo Kikuchi, Tomoyasu Noji, Yuki Sugiura, Keita Hiraga, Chigure Suzuki, Kazuhiro Haginoya, Yasuko Kobayashi, Mitsuhiro Matsunaga, Yuki Ochiai, Kyoko Yamada, Takuo Nishimura, Shinya Iwasawa, Wataru Shoji, Fuminori Sugihara, Kohei Nishino, Hidetaka Kosako, Masahito Ikawa, Yasuo Uchiyama, Makoto Suematsu, Hiroshi Ishikita, Shigeo Kure, Shigekazu Nagata. A sublethal ATP11A mutation associated with neurological deterioration causes aberrant phosphatidylcholine flipping in plasma membranes. The Journal of clinical investigation. 2021.09; 131(18);

[Misc]

1. Shigekazu Nagata, Katsumori Segawa. Sensing and clearance of apoptotic cells. Current opinion in immunology. 2021.02; 68; 1-8

RIKEN Molecular and Chemical Somatology

Visiting Professor	Ichiro Taniuchi		
Visiting Professor	Mikiko Sodeoka		
Visiting Professor	Nobumoto Watanabe		
Visiting Professor	Shinya Hagihara		
Visiting Professor	Motomasa Tanaka		
Visiting Professor	Katsunori Tanaka		
Visiting Lecturer	Nobuhiko Miyasaka		
Visiting Lecturer	Takashi Kuromori		
Visiting Lecturer	Masanori Izumi		
Visiting Lecturer	Kosuke Dodo		
Visiting Lecturer	Ryo Endo		
Visiting Lecturer	Hideyuki Yoshida		
Visiting Lecturer	Yutaka Furutani		
Visiting Lecturer	Qin Xian-Yang		
Visiting Lecturer	Shunsuke Tagami		
Visiting Lecturer	Krzyzanowski Marek		
Graduate Students	D3	Ziyu Liu (1 月~12 月)	
	D2	Xintong Liu (1 月~12 月)	
	D2	Nayan Suryawanshi (1 月 \sim 12 月)	
	D2	Chang Jingjie (1 月~12 月)	
	D1	Shingo Tamai (4 月~12 月)	

(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
 - \cdot Regulatory mechanisms for lymphocyte development
- 5) Molecular Neuropathology
 - \cdot Molecular basis of neurodegenerative disorders and psychiatric diseases

(3) Publications

[Original Articles]

- Yamashita M, Kuehn HS, Okuyama K, Okada S, Inoue Y, Mitsuiki N, Imai K, Takagi M, Kanegane H, Takeuchi M, Shimojo N, Tsumura M, Padhi AK, Zhang KYJ, Boisson B, Casanova JL, Ohara O, Rosenzweig SD, Taniuchi I, Morio T. A Variant in human AIOLOS impairs adaptive immunity by interfering with IKAROS. *Nat Immunol.* 22:893 (2021).
- Hirai, G., <u>Kato, M.</u>, Koshino, H., <u>Nishizawa, E.</u>, Oonuma, K., Ota, E., Watanabe, T., Hashizume, D., Tamura, Y., <u>Okada, M.</u>, Miyagi, T., Sodeoka, M. Ganglioside GM3 Analogues Containing Monofluoromethylene-linked Sialoside: Synthesis, Stereochemical Effects, Conformational Behavior, and Biological Activities. *JACS Au*, 1,:137 (2021).
- 3. Nagayoshi Y., Chujo T., Hirata S., Nakatsuka H., Chen CW., Takakura M., Miyauchi K., Ikeuchi Y., Carlyle B.C., Kitchen R.R., Suzuki T., Katsuoka F., Yamamoto M., Goto Y., Tanaka M., Natsume K., Nairn A.C., Suzuki T., Tomizawa K., Wei F.Y. Loss of Ftsj1 perturbs codon-specific translation efficiency in the brain and is associated

with X-linked intellectual disability. *Science Adv.*, 7(13), eabf3072 (2021).

- 4. Wilke J, Kawamura T, Xu H, Brause A, Friese A, Metz M, Schepmann D, Wünsch B, Artacho-Cordón A, Nieto FR, Watanabe N, Osada H., Ziegler S, Waldmann H Discovery of a σ1 receptor antagonist by combination of unbiased cell painting and thermal proteome profiling. *Cell Chem. Biol.* 28: 848 (2021).
- K. Vong, T. Tahara, S. Urano, I. Nasibullin, K. Tsubokura, Y. Nakao, A. Kurbangalieva, H. Onoe, Y. Watanabe, K. Tanaka, Disrupting tumor onset and growth via selective cell tagging (SeCT) therapy, Sci. Adv., 7, eabg4038 (2021).

[Review Articles]

- Taniuchi, I."Novel pathogenesis of human primary immunodeficiency by mis-sense variants in transcription factors" 14th International Symposium on Nanomedicine (ISNM 2021) Nov 18, 2021. Online
- Chang Jingjie. "T- and B-cell abnormalities associated with an IKZF3 miss-sense mutation" The 50th Annual Meeting of the Japanese Society for Immunology, Dec 5,2021, Nara,Japan
- Tanaka, M. "Short disordered protein segment regulates cross-species transmission of a yeast prion" IUBMB Focused Meeting on Neurodegenerative Diseases, Apr 22, 2021, Taipei (Taiwan), Hybrid
- Tanaka, M."Deciphering mental disorders by profiling mRNA translation in neurons" CMHA International Symposium, May 28, 2021, Kumamoto (Japan), Online
- 5. Tanaka, M."Deciphering mental disorders by profiling mRNA translation in neurons" The 1st CJK International Meeting, Jul 29, 2021, Kobe (Japan), Hybrid
- Liu, X., Osada, H., Watanabe, N."Screening of ligands of 8-TrCP for Protac complex to efficiently degrade the target protein." The 80th Annual Meeting of the Japanese Cancer Association (JCA2021) Oct 1, 2021. Yokohama, Japan
- Liu, Z., Ishikawa, K., Semba, K., Osada, H., Watanabe, N. "Screening for c-Myc inhibitors from natural resources" The 80th Annual Meeting of the Japanese Cancer Association (JCA2021) Oct 2, 2021. Yokohama, Japan
- Katsunori Tanaka, Renovation of in vivo cancer targeting by low-affinity glycan ligands, Pacifichem 2021, 2021.12.17 (Online)
- 9.

NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA		
Visiting Professor	Kenkichi MASUTOMI		
Visiting Professor	Ryuji HAMAMOTO		
Visiting Professor	Masahiro	YASUNAGA	
Visiting Associate P	rofessor	Yasushi UEMURA	
Visiting Associate P	rofessor	Yoshikatsu KOGA	
Visiting Lecturer	Kazunori	AOKI	
Visiting Lecturer	Naoto TSUCHIYA		
Visiting Lecturer	Hiroyosh	i NISHIKAWA	
Visiting Lecturer	Issay KI	FABAYASHI	
Visiting Lecturer	Tadashi I	KONDO	
Graduate Students	D3 I	Kazuma KOBAYASHI	
		Eri HASHIMOTO	
		Yamato OGIWARA	
	,	Takahiro SHIRAI	
	D2 A	Akira SAKAI	
		Norio SHINKAI	
	M2	Masako TSUDUKIHASHI	
		Ai SASAKI	
		Yuma TAKAMOTO	
		Rie SAWADO	
	,	Tomomasa TANIYAMA	

(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. Futamura M, Tokumaru Y, Takabe K, Arakawa H, Asano Y, Mori R, Mase J, Nakakami A, Yoshida K. MIEAP, a p53-downstream gene, is associated with suppression of breast cancer cell proliferation and better survival. *Am J Cancer Res.* 11(12) : 6060-6073, 2021.

2. Nakano T, Fujimoto K, Tomiyama A, Takahashi M, Achiha T, Arita H, Kawauchi D, Yasukawa M, Masutomi K, Kondo A, Narita Y, Maehara T, Ichimura K. Eribulin prolongs survival in an orthotopic xenograft mouse model of malignant meningioma. *Cancer Sci.* 113: 697-708, 2021.

3. Kobayashi K, Hataya R, Kurose Y, Miyake M, Takahashi M, Nakagawa A, Harada T, Hamamoto R. Decomposing normal and abnormal features of medical images for content-based image retrieval of glioma imaging. *Med Image Anal.* 74:102227, 2021.

4. Kobayashi K, Miyake M, Takahashi M, Hamamoto R. Observing Deep Radiomics for the Classification of Glioma Grades. *Sci Rep.* 11(1):10942, 2021.

5. Takashima H, Koga Y, Manabe S, Ohnuki K, Tsumura R, Anzai T, Iwata N, Wang Y, Yokokita T, Komori Y, Mori D, Usuda S, Haba H, Fujii H, Matsumura Y, Yasunaga M. Radioimmunotherapy with an 211 At-labeled anti-tissue factor antibody protected by sodium ascorbate. *Cancer Sci.* 112:1975-1986, 2021.

6. Tsumura R, Anzai T, Manabe S, Takashima H, Koga Y, Yasunaga M, Matsumura Y. Antitumor effect of humanized anti-tissue factor antibody-drug conjugate in a model of

peritoneal disseminated pancreatic cancer. Oncol Rep. 45:329-336, 2021.

7. Manabe S, Takashima H, Ohnuki K, Koga Y, Tsumura R, Iwata N, Wang Y, Yokokita T, Komori Y, Usuda S, Mori D, Haba H, Fujii H, Yasunaga M, Matsumura Y. Stabilization of an 211At-Labeled Antibody with Sodium Ascorbate. *ACS Omega.* 6(23): 14887-14895, 2021.

8. Shiraishi T, Ikeda K, Tsukada Y, Nishizawa Y, Sasaki T, Ito M, Kojima M, Ishii G, Tsumura R, Saijou S, Koga Y, Yasunaga M, Matsumura Y. High expression of TMEM180, a novel tumour marker, is associated with poor survival in stage III colorectal cancer. *BMC Cancer.* 21:302, 2021.

9. Mizuhashi S, Kubo Y, Fukushima S, Kanemaru H, Nakahara S, Miyasita A, Ishibashi T, Kuriyama H, Kimura T, Masuguchi S, Zhang R, Iwama T, Nakatsura T, Uemura Y, Senju S, Ihn H. Immune cell therapy against disseminated melanoma by utilizing induced pluripotent stem cell-derived myeloid cell lines producing interferon-beta or interleukin-15/interleukin-15 receptor alpha. *J Dermatol Sci.* 102(2):133-136, 2021.

10. Wang B, Iriguchi S, Waseda M, Ueda N, Ueda T, Xu H, Minagawa A, Ishikawa A, Yano H, Ishi T, Ito R, Goto M, Takahashi R, Uemura Y, Hotta A, Kaneko S. Generation of hypoimmunogenic T cells from genetically engineered allogeneic human induced pluripotent stem cells. *Nat. Biomed. Eng.* 5:429-440, 2021.

11. Kudo-Saito C, Ogiwara Y, Imazeki H, Boku N, Uemura Y, Zhang R, Kawano-Nagatsuma A, Kojima M, Ochiai A. CD11b+DIP2A+LAG3+ cells facilitate immune dysfunction in colorectal cancer. *Am J Cancer Res.* 11(11):5428-5439, 2021.

12. Imazeki H, Ogiwara Y, Mami Kawamura M, Boku N, Kudo-Saito C. CD11b+CTLA4+ myeloid cells are a key driver of tumor evasion in colorectal cancer. *Journal for ImmunoTherapy of Cancer.* 9:e002841, 2021.

[Reviews Articles]

1. Asada K, Kaneko S, Takasawa K, Machino H, Takahashi S, Shinkai N, Shimoyama R, Komatstu M, Hamamoto R. Integrated Analysis of Whole Genome and Epigenome Data Using Machine Learning Technology: Toward the Establishment of Precision Oncology. *Front Oncol.* 11:666397, 2021.

2. Komatsu M, Sakai A, Dozen A, Shozu A, Yasutomi S, Machino H, Asada K, Kaneko S,

Hamamoto R. Towards Clinical Application of Artificial Intelligence in Ultrasound Imaging. *Biomedicines*. 9(7):720, 2021.

 Kamakura D, Asano R, Yasunaga M. T Cell Bispecific Antibodies: An Antibody-Based Delivery System for Inducing Antitumor Immunity. Pharmaceuticals (Basel). 14:1172, 2021.

4. Zhang R, Liu T, Tsuchiya N, Mashima H, Kobayashi T, Nakatsura T, Ohdan H, Endo I, Senju S, Uemura Y. Induced pluripotent stem cell-derived, genetically engineered myeloid cells as unlimited cell source for dendritic cell-related cancer immunotherapy. *J Immunol Reg Med.* 12: 100042, 2021.

5. Kudo-Saito C, Ozaki Y, Imazeki H, Hayashi H, Masuda J, Ozawa H, Ogiwara Y. Targeting oncoimmune drivers of cancer metastasis. *Cancers*. 13:554, 2021

[Conference Activities & Talks]

1. Ryuji Hamamoto. Development of the integrated medical system using AI: Towards the realization of Precision Medicine. 14th Meeting of the Asia Pacific Federation of Pharmacologists, Taipei (Taiwan), November 2021.

2. Yasunaga M, Development of bispecific antibody using DDS and molecular imaging. 9th Annual Immuno-Oncology Summit. Boston(Online), October 2021.

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.

Division of Integrative Molecular Biomedicine

(5) Publications

- 1. Junya Hasegawa, Lois S. Weisman, Junko Sasaki, Takehiko Sasaki. A new insights into the roles of phosphoinositides in lysosomal function. The 44th Annual Meeting of the Molecular Biology Society of Japan 2021.11.03
- 2. Yixin Zhang, Toshiyoshi Yamamoto, Takehiko Sasaki, Junko Sasaki. Biology of phosphoinositide acyl chains. 次世代を担う若手のためのファーマ・バイオフォーラム 2021.08.28

Division of Data Science Algorithm Design and Analysis

Professor BANNAI Hideo Assistant Professor KOEPPL Dominik

(1) Outline

The department of Data Science Algorithm Design and Analysis studies algorithms, which are an essential component of data science, especially for handling large data sets. Our aim is to design algorithms and data structures that are both effective and efficient, in order to help manage and analyze various types of medical data.

(2) Publications

[Original Articles]

- 1. Ryo Sugahara, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Efficiently computing runs on a trie Theoretical Computer Science. 2021.10; 887; 143-151
- Hideo Bannai, Mitsuru Funakoshi, Tomohiro I, Dominik Köppl, Takuya Mieno, Takaaki Nishimoto. A Separation of \$\gamma\$ and \$b\$ via Thue–Morse Words String Processing and Information Retrieval. 2021.10; 167-178
- 3. Tooru Akagi, Dominik Köppl, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Grammar Index by Induced Suffix Sorting String Processing and Information Retrieval. 2021.10; 85-99
- Tomohiro I, Robert W. Irving, Dominik Köppl, Lorna Love. Extracting the Sparse Longest Common Prefix Array from the Suffix Binary Search Tree String Processing and Information Retrieval. 2021.10; 143-150
- 5. Kosuke Fujita, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Longest Common Rollercoasters String Processing and Information Retrieval. 2021.10; 21-32
- Kazuya Tsuruta, Dominik Köppl, Shunsuke Kanda, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. c-trie++: A Dynamic Trie Tailored for Fast Prefix Searches Information and Computation. 2021.08; 104794
- Hideo Bannai, Juha Kärkkäinen, Dominik Köppl, Marcin Piatkowski. Constructing the Bijective and the Extended Burrows-Wheeler Transform in Linear Time 32nd Annual Symposium on Combinatorial Pattern Matching (CPM 2021). 2021.07; 7:1-7:16
- 8. Hideo Bannai, Shunsuke Inenaga, Neerja Mhaskar. Longest previous overlapping factor array Information Processing Letters. 2021.06; 168; 106097
- 9. Noriki Fujisato, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. The Parameterized Suffix Tray 12th International Conference on Algorithms and Complexity. 2021.05; 258-270
- 10. Dominik Köppl. Reversed Lempel–Ziv Factorization with Suffix Trees Algorithms. 2021.05; 14(6); 161

- 11. Shiori Mitsuya, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Compressed Communication Complexity of Hamming Distance Algorithms. 2021.04; 14(4); 116
- Christina Boucher, Travis Gagie, Tomohiro I, Dominik Köppl, Ben Langmead, Giovanni Manzini, Gonzalo Navarro, Alejandro Pacheco, Massimiliano Rossi 0001. PHONI: Streamed Matching Statistics with Multi-Genome References. 2021.04; 193-202
- Mitsuru Funakoshi, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Computing longest palindromic substring after single-character or block-wise edits Theoretical Computer Science. 2021.03; 859; 116-133
- 14. Hideo Bannai, Momoko Hirayama, Danny Hucke, Shunsuke Inenaga, Artur Jez, Markus Lohrey, Carl Philipp Reh. The Smallest Grammar Problem Revisited IEEE Transactions on Information Theory. 2021.01; 67(1); 317-328
- 15. Köppl, Dominik. Non-Overlapping LZ77 Factorization and LZ78 Substring Compression Queries with Suffix Trees Algorithms. 2021.01; 14(2);

- 1. Extracting the Sparse Longest Common Prefix Array from the Suffix Binary Search Tree. SPIRE 2021.10
- 2. Computation of Variations of the LZ77 factorization and the LPF Array with Suffix Trees. WCTA 2021.10
- 3. Hideo Bannai. Repetitions in strings: a "constant" problem. 32nd Annual Symposium on Combinatorial Pattern Matching (CPM 2021) 2021.07.07 Wroclaw, Poland / Online
- 4. Open Problems on the BBWT. StringMasters 2021.07
- 5. Constructing the Bijective and the Extended Burrows-Wheeler Transform in Linear Time. CPM 2021.07
- 6. PHONI: Streamed Matching Statistics with Multi-Genome References. DSB2021 (Data Structures in Bioinformatics) 2021.02

Department of AI Technology Development

Heewon Park

(1) **Outline**

The department of AI Technology Development studies statistical methodologies and artificial intelligence technique that play a key role in uncovering disease mechanism based on complex biomedical data. Our mission is to develop novel AI and machine learning methodologies that attain statistical accuracy and better interpretability, simultaneously.

- 1. Statistical theory and data-analytic approaches
- 2. Explainable AI technologies for systematic understanding of diseases
- 3. Analysis of omics data for healthcare
- 4. Network biology for uncovering gene regulatory networks

(2) Research

We are research on statistical modeling and AI techniques for medical data analysis.

1)Statistical modeling and AI techniques for personalized medicine.

In recent years, genomic personalized medicine has been drawn a large amount of attention to identify individual genomic characteristics for each sample. One of our research topics is theoretical and practical studies on statistical modeling and AI technique to extract evidences and understand the mechanisms of disease. 2) Network Biology

Gene regulatory network is a crucial tool for identifying biomarkers having essential biological functions and uncover mechanism of disease. We are studying on gene network estimation and interpretation of the constructed network based on statistical and AI methodologies to understand complex mechanism of disease, find drug target, predict drug sensitivity, etc.

(3) Education

We are educating undergraduate and graduated students on the fields of data science and AI methodologies based on Mathematics and Statistics for analysis of data obtained from medical and dental area.

(4) Lectures & Courses

We aim to study knowledge for understanding statistical modeling and artificial intelligence, and encourages students to learn analysis of complex data obtained from medical and healthcare area based on the statistical and AI methodologies.

(5) Clinical Services & Other Works

Research support

We are providing support/ counseling data analysis of clinical data.

(6) **Publications**

[Original Articles]

1. Heewon Park, Koji Maruhashi, Rui Yamaguchi, Seiya Imoto, Satoru Miyano. Correction: Global gene network exploration based on explainable artificial intelligence approach. PLoS One. 2021.01; 16(1); e0246380

[Misc]

 Heewon Park, Koji Maruhashi, Rui Yamaguchi, Satoru Miyano. "Launch of new data-driven science": Realization of personal genome medicine/prevention by explainable AI Igakuno Ayumi. 2021.02; 276(9); 849-853

- 1. Park Heewon, Maruhashi Koji, Yamaguchi Rui, Imoto Seiya, Miyano Satoru. がん研究におけるビッグデー タ 説明可能な AI に基づく包括的な遺伝子制御ネットワーク解析 (Comprehensive gene regulatory network analysis based on explainable AI). 日本癌学会総会記事 2021.09.01
- 1. Heewon Park. Data science and AI strategies for precision medicine. 16th Tokyo-4Univ. Lecture 2021.11.06

Department of Anatomical and Physiological Science

Professor Osamu Hoshi Assistant Professor Hitomi Fujishiro (Master's Programs)Ryusuke Kobayashi, Miki Azumaya (Graduate Research Student)Miku Nakai, Kumi Inoue

(1) Outline

Anatomy and physiology are the primary disciplines taught in the field of anatomy and physiological sciences. Anatomy explores the morphology and structure of the human body from the organ to cellular and molecular levels. It is the most fundamental area of medical science. Physiology investigates what kind of mechanism is needed for each structural component of the human body to function, and how such components are integrated into the whole human body. Anatomy and physiology function like two wheels of a cart for the scientific understanding of the human body. These two subjects lay down the foundation required to study advanced subjects. The teaching team is committed to providing students with education that helps them master the basics of the subjects and successfully transition to the clinic.

(2) Research

Morphology and biological information analysis uses various microscopic techniques including electron microscopy for observing the microstructure of the living tissue, with the primary aim of gaining new scientific knowledge. Cutting-edge research has been conducted in this area, such as the development of new imaging technologies and applying atomic force microscopy to biomedicine.

(3) Education

Examination for Technology Stream: Human Anatomy Lecture, Human Anatomy Practicum, Physiological Examination Lecture I, Physiological Examination Practicum I, Electron Microscopy, Theory of Advanced Medical Technology, General Lecture, Graduate Research Project

Examination for Nursing Stream: Anatomy, Physiology, Joint Practicum with Advanced and Basic Students (anatomy practicum)

Examination for Science Stream: Morphology and Biological Information Analysis Special Lecture A, Morphology and Biological Information Analysis Experiment A, Morphology and Biological Information Analysis Special Lecture

(4) Lectures & Courses

The teaching team provides students with education and research instructions that help them grow their interest to study and research in the field of medicine. The team simultaneously reviews feedback from students to improve the method of conducting lectures and practicums.

(5) Publications

[Original Articles]

1. Saito Masumi, Makino Yumi, Inoue Kumi, Watanabe Yoshino, Hoshi Osamu, Kubota Tetsuo. Anti-DNA antibodies cross-reactive with β 2-glycoprotein I induce monocyte tissue factor through the TLR9 pathway. Immunological Medicine. 2021.06; 44(2); 124-135

Department of Molecular and Cellular Biology

Nobuharu Suzuki, Associate Professor

(1) Outline

In 2021, the 4th year for our department, Assoc. Prof. Suzuki and 5 graduate students were the members and performed various activities in research and education. Regarding our research, our main project was the elucidation of the molecular mechanism of myelination in the central nervous system, particularly, about the mechanisms of cell adhesion and cytoskeletal organization as well as of the pericellular microenvironment organized by extracellular matrix proteins. In terms of education, we taught graduate and undergraduate students at many lectures and laboratory classes of basic biochemistry/molecular biology, particularly related to medical technologies. In addition, Suzuki was a member of the administrative offices of Lab Safety and of Open Innovation for Research and of many other committees and contributed to their activities.

(2) Research

In the central nervous system, myelin is formed by oligodendrocytes and is essential for the rapid propagation of neuronal signal. Therefore, defects in the functions of myelin cause neurological disorders, such as multiple sclerosis and leukodystrophy. In addition, it has been recently revealed that the myelin functions are critically associated with mental disorders and dementia. Thus, the study regarding myelin functions will give new insights in brain science and better understanding of the mechanisms and new strategies of the treatments for the diseases. In our department, we investigate its cellular and molecular mechanisms using the mutant mouse line that develops hypomyelination in the central nervous system and try to expand our research to application studies. In 2021, we revealed that the mechanism of axon degeneration after the myelin defect in the mutant mice, indicating that this mouse line is useful for understanding the mechanism and for developing the treatment for axonal loss in the related diseases. We further identified the molecular structure of the extracellular domain of teneurin-4, which is required for the interaction between myelin and axons. Also, the downstream signaling for cytoskeletal organization was analyzed. Moreover, the promoting effect of laminin and fibulin on the morphological maturation of oligodendrocytes was observed in our experiments. We reported the summary of these results in a review and in presentations at expertise meetings.

(3) Education

In 2021, for undergraduate students, Suzuki was a responsible organizer for "Biochemistry", "Biochemistry, Lecture", "Medical Genetics and Human Genome Science, Lecture", "Biochemistry, Laboratory", "Medical Genetics, Laboratory", and "Medical Ethics, Laws and Regulations", and taught parts of the lectures of "Advanced Laboratory Sciences", "Practice of Medical Science", and "General Medical Technology". For graduate students, Suzuki taught parts of "Medical Technology I", "Development of Novel Technologies for Clinical Tests" (Ph.D. course), and "Biomedical Laboratory Science Seminar I" (master and Ph.D. courses). In addition, Suzuki organized many times of lectures and journal clubs for students in the laboratory/department.

(4) Lectures & Courses

Our concept for education is to explain well about 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

In 2021, Suzuki worked as a topic editor in 2 international scientific journals. In one of them, Frontiers in Cell and Developmental Biology, Suzuki organized an article collection together with co-editors in US and Germany. Suzuki was Special Volunteer at National Institutes of Health (NIH) and contributed to international relationships between the research institutes and universities. 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 Japanese Society for Neurochemistry (JSN), The Japanese Society for Matrix Biology and Medicine (JSMBM), and the Japanese Society for Myelin Study and contributed to their activities.

(6) Publications

[Misc]

1. Chikako Hayashi, Momona Yamada, Miho Iwase, Nobuharu Suzuki. The regulation of axonal homeostasis by myelin: From studies with genetically engineered mice 2021.03; 36(4); 353-357

- 1. Riko Takahashi, Hinako Saito, Yukina Hosoda, Chikako Hayashi, Nobuharu Suzuki. The maintenance of unmyelinated small diameter axons in the CNS. 第 44 回日本分子生物学会年会 2021.12.03
- 2. Momona Yamada, Miho Iwase, Chikako Hayashi, de Vega Susana, Nobuharu Suzuki. The extracellular matrix protein Fibulin-7 relates to the cell interaction for myelination in CNS. 第 44 回日本分子生物学会 年会 2021.12.03
- 3. Riko Takahashi, Hinako Saito, Yukina Hosoda, Chikako Hayashi, Nobuharu Suzuki. The maintenance of small diameter axons after myelination defect in the CNS. 第 64 回日本神経化学会大会 2021.09.30
- 4. Miho Iwase, Momona Yamada, Chikako Hayashi, Nobuharu Suzuki. The expression pattern and functional analysis of Arpc1a controlling actin cytoskeleton at the initial stage of myelination. 第 64 回日本神経化学 会大会 2021.09.30
- 5. Momona Yamada, Miho Iwase, Chikako Hayashi, de Vega Susana, Nobuharu Suzuki. The extracellular matrix protein fibulin-7 regulates cellular interaction for CNS myelination. 第 64 回日本神経化学会大会 2021.09.30

Department of Molecular Pathology

Professor: Motoji Sawabe Junior Associate Professor(Career Track): Yurie Soejima

Graduate student Doctoral Program Graduated in March 2021: Yuichi Koyama, Yoshifumi Morita Enrolled in 2021: Mizuho Sato, Mayumi Kinoshita, Akiya Tatsumi, Minami Kikuchi, HATTHAKONE THAVISOUK

Graduate student Master's Program Graduated in March 2021: Nao Miyamoto, KO PO JUI, SAKHA SUJATA Enrolled in 2021: Shiori Watabe, 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

 \cdot 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 contributes 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.

 \cdot 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.

 \cdot 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

 \cdot In the Pathology department of the Medical hospital, Sawabe participates in the pathological diagnosis of autopsy cases, Soejima participates in the cytological diagnosis.

 \cdot Soejima provided education on practical training of pathological examination as a part-time instructor at Bunkyo Gakuin University.

(6) **Publications**

[Original Articles]

- 1. Morita Y, Kurano M, Sakai E, Sawabe M, Aoki J, Yatomi Y. Simultaneous analyses of urinary eicosanoids and related mediators identified tetranor-prostaglandin E metabolite as a novel biomarker of diabetic nephropathy. Journal of lipid research. 2021.09; 100120
- 2. Sato Mizuho, Tsumoto Hiroki, Toba Ayumi, Soejima Yurie, Arai Tomio, Harada Kazumasa, Miura Yuri, Sawabe Motoji. Proteome analysis demonstrates involvement of endoplasmic reticulum stress response in human myocardium with subclinical left ventricular diastolic dysfunction GERIATRICS & GERONTOLOGY INTERNATIONAL. 2021.07; 21(7); 577-583

- Soejima Y, Takeuchi M, Miyamoto N, Sawabe M, Fukusato T. ITGB6-Knockout Suppresses Cholangiocarcinoma Cell Migration and Invasion with Declining PODXL2 Expression. International journal of molecular sciences. 2021.06; 22(12); 6303
- 濱松 晶彦, 沢辺 元司, 千田 宏司, 北岡 裕章. Chronological Changes of Coronary Artery Stenosis: Autopsy Examination at the Tokyo Metropolitan Medical Examiner's Office(和訳中) 日本循環器学会学術集会抄録 集. 2021.03; 85 回; OJ36-4
- 5. Tatsumi Akiya, Sawabe Motoji, Aida Junko. Chronic sun exposure shortens telomeres of the epidermis(和 訳中) Journal of Medical and Dental Sciences. 2021; 68; 75-83

- Minami Kikuchi, Motoji Sawabe, Haruyo Aoyagi, Kosho Wakae, Koichi Watashi, Satoru Hattori, Naoto Kawabe, Kentaro Yoshioka, Junko Tanaka, Masamichi Muramatsu, Takaji Wakita, Hideki Aizaki. Development of a community-based intervention system for linkage to care and follow-up for hepatitis virus-positive individuals cooperating with health care providers. Global hepatitis summit 2020/2021 2021.06.18 Taipei (hybrid)
- 2. Yurie Soejima, Miho Takeuchi, Nao Miyamoto, Motoji Sawabe, Toshio Fukusato. Analysis of function and gene expression in ITGB6 knockout cholangiocarcinoma cells. The 110th Annual Meeting of the Japanese Society of Pathology 2021.04.22 Tokyo (web)
- 3. 濱松晶彦, 沢辺元司, 千田宏司, 北岡裕章. Chronological Changes of Coronary Artery Stenosis: Autopsy Examination at the Tokyo Metropolitan Medical Examiner's Office. 第 85 回日本循環器学会学術集会 2021.03.26 横浜 (hybrid)

Department of Biofunctional System Engineering

Professor ITO Minami Assistant Professor HONMA Satoru Visiting Lecturer AKAZAWA Kouhei Visiting Lecturer SATO Tomoaki

(1) Outline

Biological measurements tell a lot about functions of the human bodies. Norbert Wiener, known as a founder of cybernetics, indicated that our body is a kind of control mechanism. Thus, our goal is to understand mechanisms underlying our complex biological systems and to control them for improving our life. Here, we have explored the visual information processing underlying contour integration and material perception, by combining behavioral studies indicating animals' percept, electrophysiological studies at the level of a single unit, and computational studies with mathematical models. On the other hand, we have developed a temperature control system in hypothermia based on a heat conduction model of the brain.

(2) Research

1) Mathematical models for context dependent visual information processing

2) Neural mechanisms underlying context dependent visual information processing

Our visual perception mechanism is well flexible to reveal stable recognition of the external information even under various environments. Furthermore, it realizes dynamics given by the surrounding situation, past experiences and learning processes. Our goal is to reveal the mechanism underlying such flexible visual information processing, by studying the process of integrating fragmentary information into the contour of objects or the process of material representation on an object surface, in middle stages of the cerebral visual cortex. Especially, by performing behavioral study with a method of psychophysics and electrophysiological recordings mainly from a single cell in an animal, we may reveal causal relationships between them.

So far, we have trained three Japanese monkeys to conduct our material discrimination tasks. Five materials (metal, fabric, gel sheet, wood bark, fur) were used as reference stimuli, which represent categories of material discrimination. Then, the second task was introduced, combining haptic inspection of material cues and visual inspection of correct response levers. Under the covid19 situation, the training was continued to keep animals' performance. Then, animals performed the material discrimination task using a sample of 95 other materials, to examine a stability of the material perception over a long period of training and task changes. 3) Developing methods to monitor vital information with aid of mathematical models

Our goal is to develop new devices of to control functions in living bodies, which can be introduced into the medical treatment or rehabilitation. Toward this end, we are studying comprehensive methods to understand the interactions among multiple biological functions and the mathematical methods to express the non-linearity, individuality, temporal changes and their environmental conditions of biological phenomena, and an adaptive control system to overcome such complexity of human mechanisms. So, we have developed a brain temperature control system for the brain hypothermia. The heat conduction in the head tissue was reproduced using a physical model, and the validity of the temperature control system using different control methods was compared and verified by simulation. Now, we started more realistic simulations by using a simulation head model that

assumes occurrence of local inflammation and circulatory disorders and examined several control programs.

(3) Education

1) Undergraduate school

Under the covid19 situation, remote lectures were carried out via on-line programs or tutoring via an e-mail. The practices were carried out with sever precaution against the covid19, separating students into two classes. Clinical Laboratory Management; students learn about the basic management methods in the medical laboratory sciences.

Medical Measurement System and Information (1); students learn the frequency-filters and amplification systems of electrical signals, in order to understand the principle of the physiological measurements and to conduct them safely.

Medical Measurement, System and Information (2); students learn about basic concepts of (1) informatics, (2) computer and network, information security, and (3) the hospital information systems. In practice, students learn some of logical ways to build up some programing rules and programing tools to achieve some calculation programs in C language.

Principles and Practice of Medical Information Processing (1)&(2); students learn statistical tests to compare data with a spreadsheet software, the evidence based medicine (EBM), database, experimental designs for biological experiments, the regression analysis and some recent topics covering the multivariate analysis and the Baysian inference.

2) Graduate school

Students learn the way to collect necessary information and to solve their problems to advance their own research projects. Through intensive reading of original articles and text books in English, students learn basic ideas of the central nervous system, underlying mechanisms, and the way of logical thinking. Health care informatics; this is a joint course with Nursing Innovation Science Track. Invited lecturers give omnibus-style lectures on a wide range of topics, following group discussion. Biomedical Laboratory Sciences Seminar: 4 joint seminar with all members of the biomedical laboratory science track. In a part of special lectures, we discussed the system neuroscience, visual information processing in the brain, and relationships with the artificial intelligence.

(4) Lectures & Courses

Rapid progress of the medical technology change the role of a medical technologist. Introduction of the systematic management system, IT technology, auto measurement devices, new measurement methods, new statistical analysis, demand diverse knowledge across a wide range of fields from medicine/life sciences to engineering.

1) Undergraduate school. Not only acquiring practical techniques necessary as a clinical laboratory technician, students learn the background, principle and mechanism of biological measurement. They also learn about the advantages and disadvantages of the current measurement technologies. Our purpose is to train new type laboratory technicians with a broad perspective suitable for the healthcare and medical field, a high degree of expertise and versatility, who can be a bridge between engineering and life sciences,

2) Graduate school. Our purpose is to train autonomous researchers with a broad perspective suitable for the life science and medical science who are capable of working in an international and interdisciplinary environment. Students learn the way of preparing, organizing and conducting research projects. We also encourage students to use English, which is necessary for activities in international community.

(5) Publications

[Original Articles]

1. Satoru HONMA. Portable C-language learning system with graphics library The Transactions of the Institute of Electrical Engineers of Japan A. 2021.06; 141(6); 360-366

[Misc]

1. Minami Ito. extrastriate cortex 2021.09;

Department of Respiratory and Nervous System Science

Professor: Yuki Sumi, MD, PHD.
Assistant Professor: Miho Akaza, MD, PHD.
Part-time: Keiko Hara, MD, PHD. Sayaka Aritake, MT, PHD.
Mina Ako, MT, PHD. Osamu Takahashi, MT, PHD.
Yoko Soroida, MT, PHD. Akihiko Tajima, MT, PHD.
Jyunji Endo, MD, PHD. Yuri Ichikawa, MT, PHD.
Yutaka Yatomi, MD, PHD. Mitsuru Murata, MD, PHD.
Yoshiaki Adachi, PHD. Yuko Kato, MT, PHD.
Master's: Ryusuke Mizuguchi MT. Luna Okubo MT, Yuka Hosoya MT, Chiune Funaita MT, Gengen Ko MT.
Students: Izumi Koshi, Haruka Tsukamoto, Maina Oshige, Shunsuke Machida.

(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.

Previously, 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 diagnosis 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, 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.

In addition, the educational effort equal to or higher than the lecture training in our Department is given to the 1st to 6th grade medical students and residents. (Details omitted)

The Ministry of Education, Culture, Sports, Science and Technology (MEXT) has set 2025 as the target year in its "AI Strategy 2019" for (1) all university and technical college students, regardless of their background, to acquire elementary level skills and (2) university and technical college students to acquire basic skills for application in their own specialized fields. The University has developed a model curriculum and teaching materials for mathematics, DS, and AI education in the fields of medicine and dentistry, and has newly established "Introduction to Medicine, AI, and Big Data" as a university-wide common subject, aiming to incorporate it into the University's curriculum and disseminate it to medical and dental schools across the country. In addition, "AI Practical Exercise" was offered to those who wished to take it. (Details are omitted.)

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 educates 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 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 Pharmaco-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.

(6) Clinical Performances

Dr. Sumi is a specialist in general internal medicine from the Japanese Society of Internal Medicine, an advisor and specialist in respiratory medicine from the Japanese Society of Respiratory Medicine, and a specialist in allergy from the Japanese Society of Allergy.

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. Takayuki Kuroda, Miho Akaza, Kazunori Miki, Shoko Fujii, Yousuke Yagi, Tadashi Kanouchi, Nobuo Sanjo, Kazutaka Sumita, Takanori Yokota. Sacral dural arteriovenous fistula mimicking multiple mononeuropathy. Clin Neurol Neurosurg. 2021.10; 210; 106993

Department of Clinical and Diagnostic Laboratory Science

Professor Sei Kakinuma, M.D., Ph.D. (June, 2020-)

Graduate Students, Doctoral Program. Hiroaki Komuro, M.S. (Biomedical Science and Engineering Track) Jun Tsuchiya, M.D., Taro Shimizu, M.D., Keiya Watakabe, M.D., Tomohiro Mochida, M.D. (in collaboration with Department of Gastroenterology and Hepatology, Medical and Dental Science Track)

Undergraduate Students. 4th grade, Rion Kamimae, Mayumi Itakura. 3rd grade, Nana Shibayama, Ayaka Suga, Kai Suzuki, Kyoko Chino, Momoko Furue.

(1) Outline

Patients died from chronic liver diseases, including liver cancer, are about 40,000 persons per a year in Japan. Liver transplantation remains the only effective treatment available to patients with end-stage liver diseases. Because of a serious shortage of donors for allogeneic liver transplantation, an alternative therapy is needed. Prevention of hepatocarcinogenesis and hepatic fibrosis is also necessary for patients with chronic liver disease, and the development of effective treatment for progressive liver diseases has been quite essential. Moreover, patients died from biliary and pancreatic cancer are more than 50,000 persons per a year in Japan. It is still difficult to detect such diseases at early stages and to establish the standard therapeutic strategy for them. It is urgently needed to address this issue as well as that of chronic liver diseases.

We believe that an essential role of departments in the Graduate school in Division of Biomedical Laboratory Sciences, TMDU, in medical science is to provide a basis for the innovative medical examination and to establish the treatment in next generation. To achieve our mission, both basic research lead by clinical concepts and development of novel therapeutic strategy established upon basic research are required.

Our department is founded in 2020, which is standing by such principles. Our research projects focus on hepatology, including the field of hepato-biliary-pancreatic diseases. The goal of our education is to promote students to become a well-developed hepatologist, and also leading experts in the field of hepato-biliary-pancreatic diseases and medical technology.

(2) Research

Our principle of research is to achieve studies evoked from various clinical problems, and also directs to launch innovative diagnostic and therapeutic procedures. We focus on the basic studies of novel disease models using human iPS cells to elucidate the pathophysiology. We also focus on analysis of cell-to-cell interaction regulating development and progression of hepatobiliary diseases. We focus other projects described as below, and promote them using molecular and cellular biologic approaches. We are collaborating with Department of Gastroenterology and Hepatology (Medical and Dental Science Track, Graduate school, TMDU), a lot of departments in TMDU, and several departments in other universities in Japan.

Research Projects:

(1) Development of novel disease models using human iPS cells to elucidate the pathophysiology

- (2) Analysis of cell-to-cell interaction regulating development and progression of hepatobiliary diseases
- (3) Development of hepatobiliary and pancreatic disease models using organoid culture system

(4) Molecular mechanisms regulating homeostasis of stem/progenitor cells in gastrointestinal, hepatobiliary, and pancreatic tissue

(5) Research on molecular mechanisms regulating liver regeneration and hepatic fibrosis

(3) Education

Undergraduate students.

We are teaching the courses of physiological function tests and clinical pathophysiology for undergraduate students of medical technologists in School of Medicine, TMDU. We also teach about basic techniques and scientific thinking necessary to advance the scientific research of undergraduate students in TMDU.

Graduate students

Primary goal for education of graduate students is to train highly educated and experienced clinical and technological scientists in the field of hepatology, including the field of hepato-biliary-pancreatic diseases. Our goal for education of graduate students is to produce clinical and technological scientists thinking from a wide perspective and to bring up leaders of hepatologist in next generation.

(4) Lectures & Courses

Undergraduate students.

- # Clinical Medicine (II)
- # Physiological Laboratory Science
- # Advanced physiological function
- # Analysis of Electrocardiogram

Graduate students.

Clinical and Diagnostic Laboratory Science

Our lectures and courses are collaboration with Department of Respiratory and Nervous System Science in undergraduate course, and with Department of Gastroenterology and Hepatology in graduate course. We also educate residents and medical technologist in Medical Hospital of TMDU.

Goals for education in scientific research

#1. Students should master the strategy of research for molecular, regenerative, and stem cell biology to reveal the pathophysiology of Hepato-Biliary-Pancreatic diseases.

#2. Students should master the theory and techniques about physiological laboratory and diagnostic imaging in the field of Hepato-Biliary-Pancreatic diseases.

#3. Students should learn about the research strategy to develop a novel diagnostic and therapeutic methods.

(5) Clinical Services & Other Works

We pursue development 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 clinical study collaborating with the Department of Gastroenterology and Hepatology in TMDU.

We participate in eight research projects for treatment and eradiation of hepatitis virus and one for cancer research and clinical evolution, funded by Japan Agency for Medical Research and Development (AMED). We published a lot of studies in peer-reviewed international journals and presented the recent works in a lot of international and domestic conferences as described below. 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 contribute to the management of the activities and academic meetings held by the American Association

for the Study of Liver Disease, the Japanese Society of Gastroenterology, the Japanese Society of Hepatology, the Japanese Society for Regenerative Medicine, and the Japanese Society for the Research of Hepatic cells.

(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 established the outpatient section specialized for chronic hepatitis, cirrhosis, and HCC. We are operating several multicenter studies about hepatitis and liver cancer, including one named as "Ochyanomizu Liver Conference". More than 2000 patients with viral hepatitis were enrolled in such studies, and they have clarified the clinical factors predicting accurately the therapeutic prognosis and risk for development of HCC. We are developing the screening programs for the early detection of HCC in patients with chronic hepatitis after eradication of viruses utilizing non-invasive elastography, novel serum biomarkers, and dynamic contrast-enhanced ultrasonography.

(7) Publications

[Conference Activities & Talks]

1. Mina Nakagawa, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhiro Asahina. Factors associated with HCC development and patients' survival in patients with an SVR. JSH International Liver Conference 2021 2021.10.03

Department of Analytical Laboratory Chemistry

Professor: • 2021.1-12 : Ryunosuke Ohkawa

Assistant Professor: • 2021.1-12 : Takahiro Kameda

Contract Lecturer · 2021.4-12 : Yuna Horiuchi

Graduate Students: (Master students) · 2021.1-3 : Ayuko Hara, Yume Mutsuda · 2021.4-12 : Ayuko Hara, Yume Mutsuda, Mei Ogino, Rina Kawaguchi, Marino Shibuya, Motoki Nakamura, Takako Yamada

(Doctoral Students) • 2021.1-3 : Yuna Horiuchi

Adult Graduate Students: • 2021.1-3 : Tamaki Kobayashi • 2021.4-12 : Azusa Yamazaki, Masamichi Mikame

Research Students: • 2021.1-3 : Shao Jui Lai, Sun Chengman • 2021.4-12 : Sun Chengman, Motoki Nakamura

Under Graduate Students: (Senior) • 2021.4-12 : Wakana Okabayashi, Riho Shimizu, Yuna Hakii, Tsunehiro Miyakoshi (Junior) • 2021.11-12 : Sayaka Okuma, Yuto Kikuchi, Honoka Sedutu, Yuwa Someya, Taichi Hasimoto

(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), antioxidant ability and anti-inflammatory effect of high-density lipoprotein (HDL) 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). Moreover, it is known that HDL is not structurally homogeneous but heterogeneous in size, density and chemical composition. We are investigating the mechanism of the HDL diversification through the interactions with other lipoproteins and tissue, and its effect on the HDL character and functions. We are further studying the red blood cell-related lipids metabolism.

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 above mechanisms 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
- \cdot $\,$ $\,$ Mechanism of HDL diversification and its effect on the character and function $\,$
- \cdot ~ Molecular mechanism of red blood cell-related lipids metabolism

(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. Out 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. Takahiro Kameda, Yuna Horiuchi, Shitsuko Shimano, Kouji Yano, Shao-Jui Lai, Naoya Ichimura, Shuji Tohda, Yuriko Kurihara, Minoru Tozuka, Ryunosuke Ohkawa. N-homocysteinylation of high-density lipoprotein on endothelial repair function. Biol Chem. 2021.08;
- Tamaki Kobayashi, Makoto Kurano, Mai Nanya, Tomo Shimizu, Ryunosuke Ohkawa, Minoru Tozuka, Yutaka Yatomi. Glycation of HDL Polymerizes Apolipoprotein M and Attenuates Its Capacity to Bind to Sphingosine 1-Phosphate. J Atheroscler Thromb. 2021.07; 28(7); 730-741
- 3. Azusa Yamazaki, Ryunosuke Ohkawa, Yuka Yamagata, Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Naoya Ichimura, Shuji Tohda, Minoru Tozuka. Apolipoprotein C-II and C-III preferably transfer to both high-density lipoprotein (HDL)2 and the larger HDL3 from very low-density lipoprotein (VLDL). Biol Chem. 2021.05; 402(4); 439-449
- 4. Yasunori Iwata, Shinji Kitajima, Junya Yamahana, Shuji Shimomura, Shiori Yoneda-Nakagawa, Norihiko Sakai, Kengo Furuichi, Hisayuki Ogura, Koichi Sato, Tadashi Toyama, Yuta Yamamura, Taro Miyagawa, Akinori Hara, Miho Shimizu, Ryunosuke Ohkawa, Makoto Kurano, Yutaka Yatomi, Takashi Wada. Higher serum levels of autotaxin and phosphatidylserine-specific phospholipase A1 in patients with lupus nephritis Int J Rheum Dis. 2021.02; 24(2); 231-239

5. Shitsuko Shimano, Ryunosuke Ohkawa, Mayu Nambu, Mai Sasaoka, Azusa Yamazaki, Yuki Fujii, Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Naoya Ichimura, Koji Fujita, Shuji Tohda, Minoru Tozuka. Marked Changes in Serum Amyloid A Distribution and High-Density Lipoprotein Structure during Acute Inflammation. Biomed Res Int. 2021; 2021; 9241259

- Horiuchi Y., Kameda T., Ichimura N., Kina K., Miyake K., Tohda S., Tozuka M., Miida T., and Ohkawa R. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: validation of condition in polyethylene glycol precipitation procedure.. The 19th International Symposium on Atherosclerosis 2021.10.24 Kyoto
- 2. Mutsuda Y., Kameda T., Tanaka H., Takahashi J., Okazaki M., Ai M., and Ohkawa R. Analysis of apolipoproteins distribution in subdivided lipoprotein fractions applying LipoSEARCH system. The 19th International Symposium on Atherosclerosis 2021.10.24 Kyoto
- 3. Kotoko Yamatani, Satoshi Hirayama, Yuna Horiuchi, Astushi Hori, Takashi Miida. Delay of pre β 1-high-density lipoprotein metabolism in patients with chronic kidney disease not on hemodialysis. the 19th International Symposium on Atherosclerosis (ISA2021) 2021.10.24 Kyoto
- 4. Ohkawa R.. Education for international activities and international joint research. 日本医療検査科学会第 53 回大会 2021.10.10 横浜

Department of Laboratory Molecular Genetics of Hematology

Associate professor : Miwako NISHIO

Adjunct Lecturer : Kumiko SAEKI, Ken-ichi IMADOME, Yoichi NAKAYAMA

Graduate Student : Yuki KUMAKI, Ayaka Mimura, Masato YAMAGUTI, Minori SAITO

(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

4.Development of new treatment methods using regenerative medicine technology

5. Functional Analysis of human iPS cells derived Brown Adipocytes

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. 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.

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]

- Yoshimori M, Nishio M, Ohashi A, Tateishi M, Mimura A, Wada N, Saito M, Shimizu N, Imadome KI, Arai A. Interferon-γ Produced by EBV-Positive Neoplastic NK-Cells Induces Differentiation into Macrophages and Procoagulant Activity of Monocytes, Which Leads to HLH. Cancers. 2021.10; 13(20);
- Yoshimori M, Shibayama H, Imadome KI, Kawano F, Ohashi A, Nishio M, Shimizu N, Kurata M, Fujiwara S, Arai A. Antineoplastic and anti-inflammatory effects of bortezomib on systemic chronic active EBV infection. Blood advances. 2021.04; 5(7); 1805-1815

[Misc]

1. Miwako Nishio, Kumiko Saeki.. Evolving Concept of Brown Adipose Tissue in Humans Endocrinology and metabolism. 2021.01; 5(1); 155

- A. Arai, M. Yamamoto, M. Sato, Y. Onishi, Y. Sasahara, H. Sano, M. Masuko, H. Nakamae, K. Matsuoka T. Ara, K. Washio, M. Onizuka, K. Watanabe, T. Hirakawa, M. Nishio, C. Sakashita, T. Kobayashi, A. Sawada, T. Ichinohe, T. Fukuda, Y. Hashii, Y. Atsuta. The outcomes of sCAEBV Treatment by allo-HSCT: An Analysis of Japanese Registry Data. the 63rd ASH Annual Meeting 2021.12.13
- 2. Mayumi Yoshimori, Megumi Tateishi, Ayaka Ohashi, Ayaka Mimura, Ken-Ichi Imadome, Norio Shimizu, Miwako Nishio, Ayako Ara. IFN-r, which is Produced by EBV-Positive Neoplastic NK-Cells Induces Macrophage Differentiation and Upregulates Blood Coagulation of which Both Causing HLH. 19th International Symposium on EBV and associated diseases 2021.07.29
- 3. Ayaka Ohashi, Yu Uemura, Mayumi Yoshimori, Naomi Wada, Ken-Ichi Imadome, Miwako Nishio, and Ayako Arai. Plasma level of IL-1 β in Chronic Active EBV Infection can be a biomarker of angiopathy. 19th International Symposium on EBV and associated diseases 2021.07.29

Department of Molecular Microbiology

Professor: Ryoichi Saito Assistant Professor: Yusuke Ota Graduate Student (doctor's course): Isaac Prah, Samiratu Mahazu Graduate Student (master's course): Runa Furuya, Kei Yasunaga, Kayo Yamada, Kotono Nagasawa Short-term graduate research student: Yikeshan Yalikun

(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. Research on the resistance mechanism of multidrug-resistant bacteria with whole-genome sequencing

2. Research on the regulation system of virulence in Neisseria meningitidis, Clostridioides difficile, and Clostridium perfringens

3. Research on clarifying the interaction between microorganisms and environments with metagenomics and transcriptomics

4. Development of rapid assay methods for detecting globally important bacteria

(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. Yusuke Ota, Natsune Hongou, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Evaluation of polymerase chain reaction-based open reading frame typing method for the clonality investigation of Clostridioides difficile isolates. Anaerobe. 2021.12; 72; 102462
- 2. Yusuke Ota, Natsune Hongou, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Evaluation of polymerase chain reaction-based open reading frame typing method for the clonality investigation of Clostridioides difficile isolates. Anaerobe. 2021.12; 72; 102462
- 3. Hideyuki Takahashi, Masaki Nakamura, Yuko Matsumoto, Shuji Yoshino, Tetsuya Kakita, Ken Shimuta, Hajime Kamiya, Ryoichi Saito, Makoto Ohnishi. Development of a simple and cost-effective gel-based duplex PCR method to identify both encapsulated and unencapsulated Neisseria meningitidis applicable under resource-limited conditions. J Infect Chemother. 2021.05; 27(5); 773-777
- 4. Yusuke Ota, Kazuki Furuhashi, Nachi Hirai, Jinko Ishikawa, Osanori Nagura, Katsumasa Yamanaka, Masato Maekawa. Evaluation of MBT STAR-Cepha and MBT STAR-Carba kits for the detection of extended-spectrum β -lactamases and carbapenemase producing microorganisms using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. Journal of Microbiological Methods. 2021.04; 183(106166);
- 5. Yusuke Ota, Kazuki Furuhashi, Wataru Hayashi, Nachi Hirai, Jinko Ishikawa, Osanori Nagura, Katsumasa Yamanaka, Kazuto Katahashi, Kotaro Aoki, Noriyuki Nagano, Masato Maekawa. Daptomycin resistant Enterococcus faecalis has a mutation in liaX, which encodes a surface protein that inhibits the LiaFSR systems and cell membrane remodeling. Journal of infection and chemotherapy. 2021.01; 27; 90-93
- 6. Samiratu Mahazu, Isaac Prah, Alafate Ayibieke, Wakana Sato, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Possible Dissemination of Escherichia coli Sequence Type 410 Closely Related to B4/H24RxC in Ghana. Front Microbiol. 2021.12; 12; 770130
- 7. Isaac Prah, Alafate Ayibieke, Samiratu Mahazu, Chihiro Tani Sassa, Takaya Hayashi, Shoji Yamaoka, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Emergence of oxacillinase-181 carbapenemase-producing diarrheagenic Escherichia coli in Ghana. Emerg Microbes Infect. 2021.12; 10(1); 865-873
- Ayuka Kobayashi, Jun Nakajima, Takeshi Otsuka, Masami Iigusa, Yuichiro Sakai, Akira Sata, Takeya Ohshiro, Koji Kikuchi, Shun Kikuchi, Yuko Matsumoto, Seina Miyahara, Masato Miyahira, Hajime Kamiya, Hideyuki Takahashi, Shuji Tohda, Ryoichi Saito. Assessment of different storage conditions for Neisseria meningitidis survival The Journal of the Japanese Society for Clinical Microbiology. 2021.01; 31(2); 108-112

[Conference Activities & Talks]

- 1. Isaac Prah, Alafate Ayibieke, Samiratu Mahazu, Chihiro Tani Sassa, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Shoji Yamaoka, Anthony Ablordey, Ryoichi Saito. Emergence of Oxacillinase-181Carbapenemase-producing Diarrheagenic Escherichia coli in Ghana. World Microbe Forum 2021 2021.06.20
- 2. Samiratu Mahazu, Wakana Sato, Alafate Ayibieke, Isaac Prah, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Genetic Features of Extended-spectrum Beta-lactamase Producing Escherichia coli from TwoHospitals in Ghana. World Microbe Forum 2021 2021.06.20
- 3. Alafate Ayibieke, Kayo Yamada, Kageto Yamada, Shinji Ogihara, Yoshibumi Aiso, Yoshiro Hadano, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Molecular characterization of S. epidermidis bloodstream isolates from two hospitals in Tokyo. 第 32 回日本臨床微生物学会総会 2021.01.29 東京
- 4. Isaac Prah, Alafate Ayibieke, Samiratu Mahazu, Chihiro Tani Sassa, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Shoji Yamaoka, Anthony Ablordey, Ryoichi Saito. Whole-genome characterization of OXA-181 carbapenemase producing Escherichia coli from diarrheic patients in Ghana. 第 32 回日本臨床 微生物学会総会 2021.01.29 東京
- 1. Yusuke Ota, Natsune Hongou, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Evaluation of polymerase chain reaction-based open reading frame typing method for the clonality investigation of Clostridioides difficile isolates. The 70th Annual Meeting of the Japanese association for infectious diseases 2021.10.27 Tokyo, Japan
- 2. Ryoichi Saito, Hajime Kamiya, Shuji Toda, Hideyuki Takahashi. Antimicrobial susceptibility of Neisseria meningitidis strains isolated from meningitis cases. The 95th Annual Meeting of the Japanese association for infectious diseases 2021.05.07 Tokyo, Japan

[Awards & Honors]

1. Eimi Hasegawa, The Biomedical Research Award (Master's Program), Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, 2021.03

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]

- Sasaki Y, Yamada T, Tanaka S, Sekizawa A, Hirose T, Suzumori N, Kaji T, Kawaguchi S, Hasuo Y, Nishizawa H, Matsubara K, Hamanoue H, Fukushima A, Endo M, Yamaguchi M, Kamei Y, Sawai H, Miura K, Ogawa M, Tairaku S, Nakamura H, Sanui A, Mizuuchi M, Okamoto Y, Kitagawa M, Kawano Y, Masuyama H, Murotsuki J, Osada H, Kurashina R, Samura O, Ichikawa M, Sasaki R, Maeda K, Kasai Y, Yamazaki T, Neki R, Hamajima N, Katagiri Y, Izumi S, Nakayama S, Miharu N, Yokohama Y, Hirose M, Kawakami K, Ichizuka K, Sase M, Sugimoto K, Nagamatsu T, Shiga T, Tashima L, Taketani T, Matsumoto M, Hamada H, Watanabe T, Okazaki T, Iwamoto S, Katsura D, Ikenoue N, Kakinuma T, Hamada H, Egawa M, Kasamatsu A, Ida A, Kuno N, Kuji N, Ito M, Morisaki H, Tanigaki S, Hayakawa H, Miki A, Sasaki S, Saito M, Yamada N, Sasagawa T, Tanaka T, Hirahara F, Kosugi S, Sago H, Japan N. I. P. T. Consortium.. Evaluation of the clinical performance of noninvasive prenatal testing at a Japanese laboratory. The journal of obstetrics and gynaecology research. 2021.08; 47(10); 3437-3446
- 2. Ikeda Sadakatsu, Kudo Ryo, Yamashita Yamato, Noji Rika, Yokobori Jyunko, Ohki Mika, Takamine Eriko, Kobayashi Yumi, Egawa Makiko, Ebana Yusuke, Kimura Koichiro, Yokoyama Kohta, Onishi Iichiro, Takemoto Akira, Kirimura Susumu, Kinowaki Yuko, Tanimoto Kosuke, Miya Fuyuki, Kano Yoshihito, Yoshida Masayuki, Miyake Satoshi. Clinical utility of multi-disciplinary expert panel discussion in precision cancer medicine ANNALS OF ONCOLOGY. 2021.07; 32; S287
- 3. Dewan SMR, Osaka M, Deushi M, Yoshida M. Complement C5a-triggered differentiated HL-60 stimulates migration of THP-1 monocytic leukocytes via secretion of CCL2. FEBS open bio. 2021.03;
- 4. Dewan Syed Masudur Rahman, Osaka Mizuko, Deushi Michiyo, Yoshida Masayuki. C5a-stimulated Neutrophil-like Differentiated HL-60 Induced Migration of Monocytic THP-1 through the Secretion of MCP-1(和訳中) 日本循環器学会学術集会抄録集. 2021.03; 85回; OE029-5
- 5. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. Complement Factor D Facilitates the Development of Fatty Liver under Long-term but not Short-term High-fat Diet-feeding Conditions(和訳中) 日本循環器学 会学術集会抄録集. 2021.03; 85 回; OE113-3

6. Osaka M, Deushi M, Aoyama J, Funakoshi T, Ishigami A, Yoshida M. High-Fat Diet Enhances Neutrophil Adhesion in LDLR-Null Mice Via Hypercitrullination of Histone H3. JACC. Basic to translational science. 2021.06; 6(6); 507-523

Department of Lifetime Clinical Immunology

MORI Masaaki KIMURA Naoki SASAKI Hirokazu IRABU Hitoshi

(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.

(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 Rhewumatology 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]

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Department of Child Health and Development

Professor: Hirokazu KANEGANE Junior Assistant Professor: Masaki SHIMIZU

(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

4. Etiologic and pathophysiological analysis of cytokine storm syndrome, especially of macrophage activation syndrome.

5. Etiologic and pathophysiological analysis of juvenile idiopathic arthritis (JIA), the most common type of pediatric rheumatic diseases.

6.Registry study on pediatric kidney disease in Kashiwa city.

(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.

Our university hospital is one of the largest core centers for pediatric rheumatic diseases in Japan. Pediatric rheumatologists, adult rheumatologists, pediatric orthopedic surgeons and pediatric ophthalmologists cooperatively provide seamless medical cares for pediatric rheumatic diseases from children to adults.

(7) **Publications**

[Original Articles]

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- 1. Kento Inoue, Hirokazu Kanegane. Defects in innate immunity : vulnerability to virus and bacterial infections 2021.02; (53); 777-82
- 2. Hirokazu Kanegane, Kay Tanita. Primary immunodeficiencies predisposing to Epstein-Barr virus including X-linked lymphoproliferative 2021.02; (53); 749-57

- 1. Hirokazu Kanegane. Updates in Primary antibody deficiencies. 16th Congress of Asian Society for Pediatric Research (ASPR 2021) 2021.12.11 Web 開催
- 2. Hirokazu Kanegane. Tips of hematopoietic cell transplantation for inborn errors of immunity. Chinese PID Summer School 2021 2021.09.25 Web 開催
- 3. Hirokazu Kanegane. Revisiting X-linked agammaglobulinemia. 12th International Congress of Immunodeficiency Diseases(ICID) 2021.04.27 Web 開催
- 1. Successful TCRABCD 19-depleted hematopoietic cell transplantation for a patient with Artemis deficiency. 2021.11.25
- 2. Epstein-Barr Virus-negative granulomatous disease due to SAP deficiency; a case report. 2021.11.25
- 3. A study of adenosine deaminase 2 deficiency by multi-omics analysis. 2021.02.07
- 4. Delayed recovery of chimeric status after non-myeloablative cord blood transplantation in a patient with DNA ligase IV deficiency. 2021.02.06

Department of Women's Health

Professor Masakazu Terauchi MD PhD Assistant Professor Tamami Odai MD PhD

(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 serton in 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 insomina 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]

- Makiko Tomida, Rei Otsuka, Chikako Tange, Yukiko Nishita, Tomomi Kimura, Matthias Stoelzel, Keiko Tanaka-Amino, Hiroshi Shimokata, Masakazu Terauchi. Vasomotor symptoms, sleep problems, and depressive symptoms in community-dwelling Japanese women. J Obstet Gynaecol Res. 2021.10; 47(10); 3677-3690
- Haruka Enomoto, Masakazu Terauchi, Tamami Odai, Kiyoko Kato, Makoto Iizuka, Mihoko Akiyoshi, Naoyuki Miyasaka. Independent association of palpitation with vasomotor symptoms and anxiety in middle-aged women. Menopause. 2021.07; 28(7); 741-747
- 3. Kiyoshi Takamatsu, Mariko Ogawa, Satoshi Obayashi, Takashi Takeda, Masakazu Terauchi, Tsuyoshi Higuchi, Kiyoko Kato, Toshiro Kubota. A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Investigate the Effects of Kamishoyosan, a Traditional Japanese Medicine, on Menopausal Symptoms: The KOSMOS Study Evidence-Based Complementary and Alternative Medicine. 2021.02; 2021; ID 856149
- 4. Kawaguchi Ryuji, Matsumoto Koji, Ishikawa Tetsuya, Ishitani Ken, Okagaki Ryugo, Ogawa Mariko, Oki Toshimichi, Ozawa Nobuaki, Kawasaki Kaoru, Kuwabara Yoshimitsu, Koga Kaori, Sato Yuichi, Takai Yasushi, Tanaka Kyoko, Tanebe Kyoko, Terauchi Masakazu, Todo Yukiharu, Nose-Ogura Sayaka, Noda Tsuneo, Baba Tsukasa, Fujii Eriko, Fujii Takuma, Miyazaki Hiroaki, Yoshino Osamu, Yoshimura Kazuaki, Maeda Tsugio, Kudo Yoshiki, Kobayashi Hiroshi, Japan Society of Obstetrics and Gynecology, Japan Association of Obstetricians and Gynecologists. Guideline for Gynecological Practice in Japan: Japan Society of Obstetricians and Gynecology and Japan Association of Obstetricians and Gynecology and Japan Association of Obstetricians and Gynecology Research. 2021.01; 47(1); 5-25

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- 1. Masakazu Terauchi. Postmenopausal hormone therapy protects kidneys Menopause Live. 2021.10;
- 2. Kiyoko Kato, Masakazu Terauchi. Annual report of the Women's Healthcare Committee, Japan Society of Obstetrics and Gynecology, 2021. The journal of obstetrics and gynaecology research. 2021.10;

- 1. Masakazu Terauchi. Special Session "Challenges in the Management of Menopause during the Pandemic". 8th Scientific Meeting of the Asia Pacific Menopause Federation 2021.10.15 web
- 2. Masakazu Terauchi. Plenary Symposium 2: Features of National Menopause Guideline for Countries in the Asia Pacific Region "Japan Guidelines for Menopause Practice: Office Gynecology Guideline & Menopausal Hormone Therapy Guideline". 8th Scientific Meeting of the Asia Pacific Menopause Federation 2021.10.15 web

- 3. Odai Tamami, Terauchi Masakazu, Miyasaka Naoyuki. Frequent urination in middle-aged and elderly women is associated with low intake of beta-carotene(和訳中). The Journal of Obstetrics and Gynaecology Research 2021.08.01
- 4. Masakazu Terauchi. Plenary 6 "Management of Menopausal Women in Japan". Malaysian International Conference on Menopause and Women's Health 2021.07.11 web
- 5. Masakazu Terauchi, Tamami Odai, Naoyuki Miyasaka. Body mass index and percentage body fat are negatively associated with severe dyspareunia in post-menopausal women. The 73rd Annual Congress of the Japan Society of Obstetrics and Gynecology 2021.04.23 Niigata, Japan

Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA Junior Associate Professor Keiko KONDO Specially Appointed Assistant Professor Masayuki TOI Specially Appointed Assistant Professor Risako MIKAKMI(from November) Graduate Student Nami ISHIZAKA Resident Keiji KOMATSU(until Octorber)

(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 oralpathology 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) :antimicrobila activity and effects to eukaryotic cells (induction of anti-oxydant 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 oralpathology 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 oralpathology 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. Yuka Shichiri-Negoro, Chiaki Tsutsumi-Arai, Kazuhito Satomura, Shinichi Arakawa, Noriyuki Wakabayashi. Ozone ultrafine bubble water inhibits the early formation of Candida albicans biofilms PLOS ONE. 2021.12; Online ahead of print, doi.org/10.1371/journal.pone.0261180
- 2. Keiko Kondo, Ryoko Kanenaga, Yoshinori Tanaka, Kunimoto Hotta, and Shinichi Arakawa. The neutralizing effect of mouth rinsing with alkaline electrolyzed water on different regions of the oral cavity acidified by acidic beverages Journal of Oral Science. 2021.09; 64(1); 17-21
- 3. Mikami R, Mizutani K, Shioyama H, Matsuura T, Aoyama N, Suda T, Kusunoki Y, Takeda K, Izumi Y, Aida J, Aoki A, Iwata T. Influence of aging on periodontal regenerative therapy using enamel matrix derivative: A 3-year prospective cohort study. Journal of clinical periodontology. 2021.09; 49(2); 123-133
- 4. Kawasaki M, Ikeda Y, Ikeda E, Takahashi M, Tanaka D, Nakajima Y, Arakawa S, Izumi Y, Miyake S. Oral infectious bacteria in dental plaque and saliva as risk factors in patients with esophageal cancer. Cancer. 2021.02; 127(4); 512-519

[Books etc]

1. Shinichi Arakawa. Ultrafine Bubbles. Jenny Stanford Publishing Pte., 2021.11 (ISBN : 978-1-003-14195-2)

[Conference Activities & Talks]

1. 遠井 政行、近藤 真啓、荒川 真一、網干 博文. ショウジョウバエの糖質摂食を誘導するドパミン作動 性ニューロンの探索. 2021 年度第 44 回日本分子生物学会年会 2021.12.01 横浜

Oral Care for Systemic Health Support

Professor Yuhji Kabasawa Assistant Professor Kanade Ito Postgraduate student(Master's course) Shiori Tokura

(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

[Original Articles]

- Hsu YJ, Chen YH, Lin KD, Lee MY, Lee YL, Yu CK, Kabasawa Y, Huang HL. Clinical Outcomes and Oral Health-Related Quality of Life after Periodontal Treatment with Community Health Worker Strategy in Patients with Type 2 Diabetes: A Randomized Controlled Study. International journal of environmental research and public health. 2021.08; 18(16);
- Nami Koida, Yuji Kabasawa. Clinico-Statistical Study of Postoperative Delirium in Patients with Malignant Tumors in the Oral and Maxillofacial Region Pharmacology and Pharmacogenomics. 2021.08; 4(1); 107-111
- 3. Kabasawa Yuji, Ito Kanade, Tokura Shiori, Takazawa Itsuki, Kimura Rio, Nakanishi Tohko, Akiyama Kikue, Onuma Yuki, Adachi Toshiko, Komiya Ruri, Harada Hiroyuki, Nojima Hitomi, Miura Masahiko, Yoshimura Ryoichi. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer 日本口腔ケア学会雑誌. 2021.04; 15(3); 264
- Lin YC, Du JK, Lin PC, Kabasawa Y, Lin PL, Hsiao SY, Huang HL. Association between the dental occlusion and perceived ability to eat foods of Taiwanese older adults. Journal of oral rehabilitation. 2021.02;

- Yuji Kabasawa, Kanade Ito, Shiori Tokura, Itsuki Takazawa, Rio Kimura, Tohko Nakanishi, Kikue Akiyama, Yuki Onuma, Toshiko Adachi, Ruri Komiya, Hiroyuki Harada, Hitomi Nojima, Masahiko Miura, Ryoichi Yoshimura. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. The 1st Annual Meeting of the International Society of Oral Care 2021.04.18 東京
- Kabasawa Yuji, Ito Kanade, Tokura Shiori, Takazawa Itsuki, Kimura Rio, Nakanishi Tohko, Akiyama Kikue, Onuma Yuki, Adachi Toshiko, Komiya Ruri, Harada Hiroyuki, Nojima Hitomi, Miura Masahiko, Yoshimura Ryoichi. 頭頸部がんへの放射線化学療法時に発症する口腔粘膜炎に対して、エピシル口腔用液 が及ぼす効果に関するの臨床研究 (Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer). 日本口腔ケア学会雑誌 2021.04.01
- 3. Kabasawa Yuji, Ito Kanade, Tokura Shiori, Takazawa Itsuki, Kimura Rio, Nakanishi Tohko, Akiyama Kikue, Onuma Yuki, Adachi Toshiko, Komiya Ruri, Harada Hiroyuki, Nojima Hitomi, Miura Masahiko,

Yoshimura Ryoichi. 頭頸部がんへの放射線化学療法時に発症する口腔粘膜炎に対して、エピシルロ腔用液 が及ぼす効果に関するの臨床研究 (Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer). 日本口腔ケア学会雑誌 2021.04.01

1. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. 2021.04.18

Preventive Oral Health Care Sciences

Professor Kayoko SHINADA Assistant Professor Naoko ADACHI

Part-time lecturer Atsushi OHYAMA, Kenichi TANAKA, Kanako TODA, Chie YOSHIZU, Mamoru MURATA

Graduate Students Master Course Miyu YASUI(-March), HSU CHEN WEI(-March), WANG LIYANG, Yuko HIROTA (April-) Graduate Students(research) Yuko HIROTA (-March), WANG RAN,

(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. Suzuki H, Sugimoto K, Kubota-Miyazawa A, Noritake K, Umemori S, Araki K, Adachi N, Otsuka H, Yoshida N. A survey of oral health status, subjective oral symptoms and oral health behaviors among first-year dental students at a Japanese university. Journal of oral science. 2021.12; 64(1); 85-90

1. YASUDA Miyu, TODA Kanako, SHINADA Kayoko . Comparison of the effects of non-alcohol mouthrinses on oral malodor The Journal of Japan Society for Dental Hygiene . 2021.02; 15(2); 80-90

- 1. Adachi Naoko, Shinada Kayoko. Association between tooth loss and dyslipidemia: a four-year longitudinal study. 第 80 回日本公衆衛生学会総会 2021.12.21 オンデマンド開催
- 2. Liyang WANG, 安達 奈穂子, 品田 佳世子. コロナ禍における学生のマスク着用や生活の変化が口腔保健へ 及ぼす影響について. 第 86 回口腔病学会学術大会 2021.12.04 オンライン開催
- 1. A study of oral health behavior of students in COVID-19 pandemic. 2021.12.04

Oral Health Sciences for Community Welfare

Professor Koichiro MATSUO Assistant Professor Rena HIDAKA Graduate Student Itsuki TASAKA

(1) **Outline**

The Vision of department of Oral Health Sciences for Community Welfare is:

To establish the basis of human resource development where dental professionals can manage the needs of older adults who have various characteristics.

We engage in the activities with the Mission below:

To conduct practice, research and education to nurture human resources who act vigorously as oral health professional, working together with the other health professionals in acute care to community welfare

Please contact us if you are interested in the graduate school or collaborative research (matsuo.ohcw at tmd.ac.jp)

(2) Research

- 1. Invention of oral frail preventive program for community dwelling older adults
- 2. Invention of monitoring system for eating behavior in dependent older adults
- 3. Innovative food technology systems for independent senior living
- 4. Establishment of oral management system during stroke recovery
- 5. Invention of peri-operative oral management system for cancer patients
- 6. Multidisciplinary Oral management system

(3) Education

Under-graduate course

Gerodontology/Welfare for older adults/Nursing-care for older adults/Prosthodontics/Home visiting dentistry/Community dental care/ Social work

Post-graduate course Welfare and Oral Health Care for older adults

(4) Lectures & Courses

The education policy of our department is: To educate dental professionals who will acquire the competency below: Knowledge, skill and experience to work in medical and health care fields Communication skill to educate the other health professionals Activities with self-intent Interest in international academic activities with positive research mind

Clinical Services & Other Works (5)

Japanese Society of Gerodontology: Specialist, Instructor, Executive Board Member (International Affair) Japanese Association of Dentistry and Oral Health: Specialist, Instructor, Board Member (International Affair) Japanese Society of Dysphagia Rehabilitation

Japanese Society for Clinical Nutrition and Metabolism

Asian Association of Dentistry and Oral Health: Board member International Association of Dentistry and Oral Health: Councilor, International Advisory Committee

(6) Publications

[Original Articles]

- 1. Suzuki H, Furuya J, Hidaka R, Miyajima S, Matsubara C, Ohwada G, Asada T, Akazawa C, Sato Y, Tohara H, Minakuchi S.. Patients with mild cognitive impairment diagnosed at dementia clinic display decreased maximum occlusal force: a cross-sectional study. BMC Oral Health. 2021.12; 21(1); 665
- 2. Furuya J, Suzuki H, Hidaka R, Nakagawa K, Yoshimi K, Nakane A, Yamaguchi K, Shimizu Y, Itsui Y, Saito K, Sato Y, Tohara H, Minakuchi S. Factors Related to Oral Intake of Food by Hospitalized Patients with Malnutrition under the Care of a Nutrition Support Team. Int J Environ Res Public Health. 2021.11; 18(21); 11725
- 3. Matsuo Koichiro, Sekimoto Yu, Okamoto Mieko, Shibata Seiko, Otaka Yohei. Association between oral health status and oral food intake level in subacute stroke patients admitted to a convalescent rehabilitation unit GERODONTOLOGY. 2021.08; 39(1); 67-73
- 4. Furuya J, Suzuki H, Hidaka R, Akatsuka A, Nakagawa K, Yoshimi K, Nakane A, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Oral health status and its association with nutritional support in malnourished patients hospitalised in acute care. Gerodontology. 2021.07;
- 5. Kobayashi Yoshikazu, Okui Taro, Tsujimoto Masakazu, Ikeda Hirotaka, Satoh Koji, Kanamori Daisuke, Fujii Naoko, Toyama Hiroshi, Matsuo Koichiro. Effect of morphological findings in computed tomography on the quantitative values in single-photon emission computed tomography for patients with antiresorptive agent-related osteonecrosis of the jaw: a cross-sectional study ANNALS OF NUCLEAR MEDICINE. 2021.05; 35(7); 853-860
- 6. Matsuo K, Kito N, Ogawa K, Izumi A, Kishima M, Itoda M, Masuda Y. Improvement of oral hypofunction by a comprehensive oral and physical exercise programme including textured lunch gatherings. Journal of oral rehabilitation. 2021.04; 48(4); 411-421
- 7. Hidaka R, Furuya J, Nishiyama A, Suzuki H, Aoyagi M, Matsubara C, Yoshizumi Y, Yoshimi K, Nakane A, Tohara H, Sato Y, Minakuchi S. Structural Equation Modeling of Tongue Function and Tongue Hygiene in Acute Stroke Patients. International journal of environmental research and public health. 2021.04; 18(9);
- 8. Horibe Yasuhiro, Matsuo Koichiro, Ikebe Kazunori, Minakuchi Shunsuke, Sato Yuji, Sakurai Kaoru, Ueda Takayuki. Relationship between two pressure-sensitive films for testing reduced occlusal force in diagnostic criteria for oral hypofunction GERODONTOLOGY. 2021.02;

Oral Health Care Education

Professor Naomi Yoshida Assistant Professor

Hitomi Suzuki

(1) Research

- 1) Research on oral health behabior
- 2) Research on oral health management
- 3) Research on interprofessional education and work
- 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. Sekiya T, Sugimoto K, Kubota A, Tsuchihashi N, Oishi A, Yoshida N. Assessment of psychological changes in young children during dental treatment: Analysis of the autonomic nervous activity and electroencephalogram. International journal of paediatric dentistry. 2021.09;
- Yuko Yamamoto, Yoshiaki Nomura, Ayako Okada, Erika Kakuta, Naomi Yoshida ,Noriyasu Hosoya ,Nobuhiro Hanada and Noriko Takei . Improvement of Workplace Environment That Affects Motivation of Japanese Dental Hygienists International Journal of Environment Research and Public Health. 2021.02;
- Tsuchihashi Natsumi, Uehara Naoko, Miwa Zenzo, Yoshida Naomi, Sugimoto Kumiko. Perception of pungent, gustatory and olfactory stimuli in patients with congenital insensitivity to pain with anhidrosis JOURNAL OF ORAL SCIENCE. 2021.01; 63(1); 104-106
- Makoto Arakawa, Jun Kaneko, Vivianne Cruz de Jesus, Hidekazu Sonoda, Naomi Yoshida, Junji Tagami. Relationship between taste sensitivity and dental caries Journal of Medical and Dental Sciences. 2021.01; 68; 85-89

5. Arakawa Makoto, Kaneko Jun, Cruz de Jesus Vivianne, Sonoda Hidekazu, Yoshida Naomi, Tagami Junji. 味覚感度と齲蝕症の関連性 (Relationship between taste sensitivity and dental caries) Journal of Medical and Dental Sciences. 2021; 68; 85-89

- 1. Akiko Oshiro, Masako Okada, Naomi Yoshida, Jun Aida, Kayoko Shinada. Approaches at training for dental hygienists reinstatement and new graduate in Japan. AAPD 2021.10.01
- 1. Dental treatment needs of inpatients in convalescent ward . 2021.08.19

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 pharmaceutics.

Subjects and contents.

• Structure and function of human body I and II: anatomy, histology, physiology, embryology, oral anatomy, oral histology, oral physiology.

• Mechanism of disease and promotion of recovery process: pathology, oral pathology, microbiology, immunology, pharmacology.

- Dental pharmacology and pharmaceutics.
- Graduation thesis:

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).

Medical and Dental Science and Technology

(4) Publications

[Original Articles]

1. Sakamoto Yujiro. The branching pattern of the middle temporal artery and the relation with the temporal fascia. SURGICAL AND RADIOLOGIC ANATOMY. 2021.11; 43(11); 1867-1874

Basic Oral Health Engineering

Professor Kazuhiro Aoki Associate Professor Meiko Oki Assistant Professor Shingo Kamijo Technical Assistant Masud Khan

(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 novel bone anabolic reagents targeting RANKL (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 objective evaluation methods for tooth carving
- 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

 \cdot Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects

Medical and Dental Science and Technology

 \cdot Making dental and maxillofacial prostheses

(5) Publications

[Original Articles]

- 1. Yuna Hirohashi, Shingo Kamijo, Masud Khan, Masaomi Ikeda, Meiko Oki, Khairul Matin, Fatma Rashed, Kazuhiro Aoki. Tetracycline, an appropriate reagent for measuring bone-formation activity in the murine model of the Streptococcus mutans-induced bone loss Frontiers in Cellular and Infection Microbiology Microbiome in Health and Disease. 2021.09; 11; 714366
- 2. Gao Jing, Muroya Ryusuke, Huang Fei, Nagata Kengo, Shin Masashi, Nagano Ryoko, Tajiri Yudai, Fujii Shinsuke, Yamaza Takayoshi, Aoki Kazuhiro, Tamura Yukihiko, Inoue Mayuko, Chishaki Sakura, Kukita Toshio, Okabe Koji, Matsuda Miho, Mori Yoshihide, Kiyoshima Tamotsu, Jimi Eijiro. Bone morphogenetic protein induces bone invasion of melanoma by epithelial-mesenchymal transition via the Smad1/5 signaling pathway LABORATORY INVESTIGATION. 2021.09; 101(11); 1475-1483
- Nakai H, Inokoshi M, Nozaki K, Komatsu K, Kamijo S, Liu H, Shimizubata M, Minakuchi S, Van Meerbeek B, Vleugels J, Zhang F. Additively Manufactured Zirconia for Dental Applications. Materials (Basel). 2021.07; 14(13);
- 4. Okawara H, Arai Y, Matsuno H, Marcián P, Borák L, Aoki K, Wakabayashi N. Effect of load-induced local mechanical strain on peri-implant bone cell activity related to bone resorption and formation in mice: An analysis of histology and strain distributions. Journal of the mechanical behavior of biomedical materials. 2021.01; 116; 104370

[Misc]

1. Rashed Fatma, Kamijyo Shingo, Shimizu Yuri, Hirohashi Yuna, Khan Masud, Sugamori Yasutaka, Murali Ramachandran, Aoki Kazuhiro. The Effects of Receptor Activator of NF-kappa B Ligand-Binding Peptides on Bone Resorption and Bone Formation FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY. 2021.07; 9; 648084

- 1. Hein Linn Htat, Kajima Yuka, Takaichi Atsushi, Hla Htoot Wai Cho, Kamijo Shingo, Hanawa Takao, Wakabayashi Noriyuki. Effect of post-heat treatments on metal-ceramic bond properties of Co-Cr-Mo-W alloy fabricated by selective laser melting. The 77th General Session of the Japanese Society for Dental Materials and Devices 2021.04.10
- 2. Nakai H, Inokoshi M, Nozaki K, Kamijo S, Shimizubata M, Liu H, Minakuchi S. Crystallography and flexural strength of additive manufactured zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
- 1. Yuna KANAMORI, Rena TAKAHASHI, Masaomi IKEDA, Shingo KAMIJO, Shin ROZAN, Kanako NORITAKE, Ken-ichi TONAMI, Hiroshi NITTA, Toru NIKAIDO, Yasushi SHIMADA, Junji TAGAMI. The effect of resin coating technique on internal fit of CAD/CAM composite resin crowns. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Web

Oral Prosthetic Engineering

Professor Noriyuki WAKABAYASHI Junior Associate Professor Masaomi IKEDA Assistant Professor Maho SHIOZAWA Assistant Professor Maiko IWAKI

(1) Outline

Oral Health Information Technology educates deepen understanding of the production of the dental prosthesis using the latest computer science and cultivate basics power to new technology development. This course cultivates the ability to offer high quality medical technology taking advantage of expertise or knowledge. And the purpose of this section is to educate professional dental technologists who has ability to apply newly developed materials and technologies and who is able to contribute in not only clinical situation but also research institution or educational organization at international levels. Presently, the latest technologies such as dental implant and dental CAD/CAM etc became popular by the development of materials and the progress in technologies among dental treatment. Therefore, it is necessary to understand and lean knowledge about newly developed materials and technologies for properly control the dental laboratory works. Furthermore, It is necessary that the communication skill for report information about the materials and technologies to dentists and dental hygienists. Based on these evidences, it is an education in which specialists are raised to not be bound by classification as technologist and have ambition.

(2) Research

- 1) 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. Tabata Miyuki, Ratanaporncharoen Chindanai, Ishihara Nouboru, Masu Kazuya, Sriyudthsak Mana, Kitasako Yuichi, Ikeda Masaomi, Tagami Junji, Miyahara Yuji. Surface analysis of dental caries using a

wireless pH sensor and Raman spectroscopy for chairside diagnosis TALANTA. 2021.12; 235; 122718

- Takada Seira, Ogata Yasuko, Yumoto Yoshie, Ikeda Masaomi. Implementation of an Advance Care Planning Inventory and Its Possible Effect on Quality of Dying: A Nationwide Cross-Sectional Study in Group Homes for Persons with Dementia in Japan Healthcare. 2021.12;
- Akane Chin, Masaomi Ikeda, Tomohiro Takagaki, Toru Nikaido, Alireza Sadr, Yasushi Shimada, Junji Tagami. Effects of Immediate and Delayed Cementations for CAD/CAM Resin Block after Alumina Air Abrasion on Adhesion to Newly Developed Resin Cement. Materials (Basel). 2021.11; 14(22); 7058
- 4. Sayaka Tada, Manabu Kanazawa, Anna Miyayasu, Maiko Iwaki, Murali Srinivasan, Shunsuke Minakuchi, Gerald McKenna. Patient preferences for different tooth replacement strategies for the edentulous mandible: A willingness-to-pay analysis. J Prosthodont Res. 2021.10; 65(4); 535-540
- Hosaka Keiichi, Tichy Antonin, Araoka Daisuke, Wurihan Wuriham, Shibata Yo, Ikeda Masaomi, Klein Celoso Afonso Jr, Tagami Junji, Nakajima Masatoshi. Eight-year Microtensile Bond Strength to Dentin and Interfacial Nanomechanical Properties of a One-step Adhesive. The Journal Adhesive Dentistry. 2021.10; 23(5); 461-467
- 6. Nanako Ueda, Tomohiro Takagaki, Toru Nikaido, Rena Takahashi, Masaomi Ikeda, Junji Tagami. The effect of different ceramic surface treatments on the repair bond strength of resin composite to lithium disilicate ceramic. Dental Materials Journal. 2021.09; 40(5); 1073-1079
- 7. Saki Uchiyama, Rena Takahashi, Takaaki Sato, Shin Rozan, Masaomi Ikeda, Masanao Inokoshi, Toru Nikaido, Junji Tagami. Effect of a temporary sealing material on the bond strength of CAD/CAM inlay restorations with resin-coating technique. Dental Materials Journal. 2021.09; 40(5); 1122-1128
- 8. Yuna Hirohashi, Shingo Kamijo, Masud Khan, Masaomi Ikeda, Meiko Oki, Khairul Matin, Fatma Rashed, Kazuhiro Aoki. Tetracycline, an appropriate reagent for measuring bone-formation activity in the murine model of the Streptococcus mutans-induced bone loss Frontiers in Cellular and Infection Microbiology Microbiome in Health and Disease. 2021.09; 11; 714366
- Nasiry Khanlar L, Revilla-León M, Barmak AB, Ikeda M, Alsandi Q, Tagami J, Zandinejad A. Surface roughness and shear bond strength to composite resin of additively manufactured interim restorative material with different printing orientations. The Journal of prosthetic dentistry. 2021.09;
- 10. Hosaka Keiichi, Kubo Shisei, Tichy Antonin, Ikeda Masaomi, Shinkai Koichi, Maseki Toshio, Rikuta Akitomo, Sasazaki Hiromi, Satoh Kaori, Fujitani Morioki, Hanabusa Masao, Yamamoto Takatsugu, Yoshikawa Kazushi, Morigami Makoto, Uno Shigeru, Sugizaki Junpei, Yatani Hirofumi, Nikaido Toru. Clinical effectiveness of direct resin composite restorations bonded using one-step or two-step self-etch adhesive systems: A three-year multicenter study(和訳中) Dental Materials Journal. 2021.09; 40(5); 1151-1159
- 11. Uchiyama Saki, Takahashi Rena, Sato Takaaki, Rozan Shin, Ikeda Masaomi, Inokoshi Masanao, Nikaido Toru, Tagami Junji. Effect of a temporary sealing material on the bond strength of CAD/CAM inlay restorations with resin-coating technique(和訳中) Dental Materials Journal. 2021.09; 40(5); 1122-1128
- 12. Ueda Nanako, Takagaki Tomohiro, Nikaido Toru, Takahashi Rena, Ikeda Masaomi, Tagami Junji. The effect of different ceramic surface treatments on the repair bond strength of resin composite to lithium disilicate ceramic(和訳中) Dental Materials Journal. 2021.09; 40(5); 1073-1079
- Hayashi Meiken, Kubo Shisei, Pereira Patricia N. R., Ikeda Masaomi, Takagaki Tomohiro, Nikaido Toru, Tagami Junji. Progression of non-carious cervical lesions: 3D morphological analysis CLINICAL ORAL INVESTIGATIONS. 2021.08;
- Martina Vicheva, Takaaki Sato, Tomohiro Takagaki, Yuuta Baba, Masaomi Ikeda, Michael F Burrow, Toru Nikaido, Junji Tagami. Effect of repair systems on dentin bonding performance. Dental Materials Journal. 2021.07; 40(4); 903-910
- Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S.. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. Journal of Dental Sciences. 2021.07;

- 16. Hasegawa Mayu, Tichy Antonin, Hosaka Keiichi, Kuno Yusuke, Ikeda Masaomi, Nozaki Kosuke, Chiba Ayaka, Nakajima Masatoshi, Tagami Junji. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents(和訳中) Dental Materials Journal. 2021.07; 40(4); 877-884
- 17. Vicheva Martina, Sato Takaaki, Takagaki Tomohiro, Baba Yuuta, Ikeda Masaomi, Burrow Michael F., Nikaido Toru, Tagami Junji. Effect of repair systems on dentin bonding performance(和訳中) Dental Materials Journal. 2021.07; 40(4); 903-910
- 18. Yuta Baba, Takaaki Sato, Tomohiro Takagaki, Martina Vicheva, Ayaka Sato, Masaomi Ikeda, Toru Nikaido, Junji Tagami. Effects of Different Tooth Conditioners on the Bonding of Universal Self-etching Adhesive to Enamel. The Journal of Adhesive Dentistry. 2021.06; 23(3); 233-242
- 19. Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S. Patient-reported outcomes with immediate-loaded two-implant-supported mandibular overdentures: Results of a 5-year prospective study. Journal of Dental Sciences. 2021.06;
- Alsandi Qutaiba, Ikeda Masaomi, Arisaka Yoshinori, Nikaido Ru, Tsuchida Yumi, Sadr Alireza, Yui Nobuhiko, Tagami Junji. Evaluation of Mechanical and Physical Properties of Light and Heat Polymerized UDMA for DLP 3D Printer SENSORS. 2021.05; 21(10);
- 21. Kitasako Yuichi, Ikeda Masaomi, Takagaki Tomohiro, Burrow Michael F., Tagami J.. The prevalence of non-carious cervical lesions (NCCLs) with or without erosive etiological factors among adults of different ages in Tokyo CLINICAL ORAL INVESTIGATIONS. 2021.05;
- 22. Ishikawa Kyoko, Yamauti Monica, Tichy Antonin, Ikeda Masaomi, Ueno Takeshi, Wakabayashi Noriyuki, Thanatvarakorn Ornnicha, Prasansuttiporn Taweesak, Klein-Junior Celso Afonso, Takahashi Akifumi, Takagaki Tomohiro, Nakajima Masatoshi, Tagami Junji, Hosaka Keiichi. UV-Mediated Photofunctionalization of Indirect Restorative Materials Enhances Bonding to a Resin-Based Luting Agent BIOMED RESEARCH INTERNATIONAL. 2021.05; 2021; 9987860
- 23. Takaaki Sato, Rena Takahashi, Shin Rozan, Saki Uchiyama, Yuta Baba, Martina Vicheva, Ayaka Sato, Masaomi Ikeda, Tomohiro Takagaki, Toru Nikaido, Junji Tagami. The effect of temporary sealing materials and cleaning protocols on the bond strength of resin cement applied to dentin using the resin-coating technique. Dental Materials Journal. 2021.05; 40(3); 719-726
- 24. Khanlar LN, Takagaki T, Abdou A, Inokoshi M, Ikeda M, Takahashi A, Yoshihara K, Nagaoka N, Nikaido T, Blatz MB, Tagami J. Effect of Air-Particle Abrasion Protocol and Primer on The Topography and Bond Strength of a High-Translucent Zirconia Ceramic. J Prosthodont. 2021.04;
- 25. Hasegawa M, Tichy A, Hosaka K, Kuno Y, Ikeda M, Nozaki K, Chiba A, Nakajima M, Tagami J. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents. Dental Materials Journal. 2021.03; 40(4); 877-884
- 26. Luz Madrigal Erick, Tichy Antonin, Hosaka Keiichi, Ikeda Masaomi, Nakajima Masatoshi, Tagami Junji. The effect of curing mode of dual-cure resin cements on bonding performance of universal adhesives to enamel, dentin and various restorative materials(和訳中) Dental Materials Journal. 2021.03; 40(2); 446-454
- Soeda Y, Kanazawa M, Hada T, Arakida T, Iwaki M, Minakuchi S. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. The Journal of prosthetic dentistry. 2021.03;
- Dwiandhany WS, Abdou A, Tichy A, Yonekura K, Ikeda M, Hosaka K, Tagami J, Nakajima M. Additive effects of touch-activated polymerization and extended irradiation time on bonding of light-activated adhesives to root canal dentin. The Journal of prosthetic dentistry. 2021.01; 3913(20); 30742-30743
- 29. Aung Swe Zin, Takagaki Tomohiro, Ikeda Masaomi, Nozaki Kosuke, Burrow Michael F., Abdou Ahmed, Nikaido Toru, Tagami Junji. The effect of different light curing units on Vickers microhardness and degree of conversion of flowable resin composites(和訳中) Dental Materials Journal. 2021.01; 40(1); 44-51
- Yumika Soeda, Manabu Kanazawa, Tamaki Hada, Toshio Arakida, Maiko Iwaki, Shunsuke Minakuch. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. 2021;
- 1. BUI Ngoc Huyen Trang. CED-IADR/NOF Oral Health Research Congress in Brussels. CED-IADR/NOF Oral Health Research Congress in Brussels 2021.09.16
- 1. Yuna KANAMORI, Rena TAKAHASHI, Masaomi IKEDA, Shingo KAMIJO, Shin ROZAN, Kanako NORITAKE, Ken-ichi TONAMI, Hiroshi NITTA, Toru NIKAIDO, Yasushi SHIMADA, Junji TAGAMI. The effect of resin coating technique on internal fit of CAD/CAM composite resin crowns. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Web
- 2. Otake R, Kanazawa M, et al.. A prospective study of digital complete dentures using customized disc method.. 2021.06.19 online
- 3. Soeda Y, Kanazawa M, Iwaki M, Arakida T, Hada T, Otake R, Katheng A, Akiyama Y, Ando K, Minakuchi S. Trueness and precision of artificial teeth in CAD/CAM milled complete dentures with custom disks of prefabricated frame. 2021.04.24

Digital Dentistry

Professor: Hidekazu Takahashi (-Mar) Manabu Kanazawa (May-) Assistant Professor: Naohiko Iwasaki Assistant Professor: Yumi Tsuchida

Graduate Student (Master): Ha Rou Bing

(1) Outline

Department of Digital Dentistry was founded on May 1, 2021, and is responsible for digital dentistry research, clinical practice, and teaching. "Digital dentistry" is an interdisciplinary field consisting of dentistry and engineering. This department provides a smooth connection between clinical dentistry and digital devices (hardware and software) in the field of engineering, and educates and trains individuals in research, clinical practice, and education.

(2) Research

1) Milled Complete Base Denture

Traditional complete denture manufacturing entails a high number of visits, varying treatment quality due to dentist competence variances, and contamination resistance issues due to the use of acrylic resin. To address these issues, we developed a denture fabrication process based on CAD/CAM technology that reduces the number of visits, improves treatment quality uniformity, and improves the physical qualities of dentures. In the traditional milled denture, only the denture base was milled and the artificial teeth were connected thereafter, resulting in issues such as the adhesive surface of the artificial teeth deteriorating. As a result, we invented the TMDU custom disk method, in which a personalized disk is generated for each patient and the denture base is milled as a single piece with artificial teeth. This custom disk is the subject of a patent application, as well as an application for an overseas patent with the help of the Industry-University Collaboration Office. In a prospective clinical study of complete dentures with CAD/CAM technology, which began in 2019, the findings of employing the TMDU custom disk method revealed better cost-effectiveness compared to fabricating complete dentures using the conventional method. The digital denture fabrication process we've developed incorporates a workflow that starts with an intraoral scanner optical impression of the edentulous jaw crest, then denture design and fabrication on a computer. To further digitalize the process, we intend to integrate AI-assist in denture design in the future. In addition, the company collaborates with manufacturer of milling machine and cutting tool on the creation of milling discs, which are required for milling digital dentures, as well as the verification of acceptable milling machine settings.

2) Digital partial denture

The digital partial denture has not been applied in clinical practice compared to the digital complete denture, because there are few research reports. One reason for this could be that partial dentures must accept a wide range of defect and support methods, and are made comprised of metal and resin materials in a variety of forms to do so. While it is possible to fabricate metal frames using the Selective Laser Melting (SLM), subsequent fabrication processes such as artificial teeth placement and polymerization are still carried out using traditional partial denture fabrication procedures, making it difficult to say that all processes have been digitized. As a result, we developed a method for fabricating a custom plate for partial dentures in which a metal frame created

using the SLM method and ready-made artificial tooth is embedded for each patient by adapting the TMDU custom disc method for complete dentures. This allowed for the milling of the artificial tooth, metal frame, and denture base all in one piece, overcoming the issues with traditional digital partial dentures. Dry milling machine is used to create this digital partial denture, but a wet milling machine might be utilized to create partial dentures of any size in the future. In the future, appropriate designs for custom plates will be considered, and fabrication of partial dentures for various defect configurations is assessed.

3) Implant overdenture

For a long period, implant overdentures (IOD) for edentulous mandible patients have been explored. Many research were undertaken in Europe and the United States in the 1980s and 1990s, and many evidence has been amassed in this field since a consensus statement was issued in 2002. We began our clinical research in 2008 at Tokyo Medical and Dental University Hospital, and we now have over 100 patients, with the longest case being followed for over ten years. To date, the following IOD studies have been conducted.

- 1) Prospective clinical study of 2-IOD using ball attachment (2008-)
- 2) RCT comparing normal and immediate loading of 2-IOD using magnetic attachments (2011-)
- 3) Prospective clinical study of mini-IODs using mini-implants (2013-2014 McGill University)
- 4) Prospective clinical studies of 1-IOD (2015-)
- 5) Joint clinical research with Showa University on implant-assisted partial denture (IARPD) (2017-)
- 6) Model experiments on IOD implant placement location and denture movement

On the other hand, only a few clinical trials on maxillary IOD have been conducted worldwide. Based on the evidence of mandibular 2-IOD and our knowledge of edentulous prosthodontics, we believe that if the jaw crest conditions are selected, maxillary IOD can be maintained with two implants, and that this will be an effective treatment choice in the super-aging society. To demonstrate proof, we plan to conduct clinical research of 2-IOD employing two implants as the maintenance source in the maxilla as well as in the mandible to establish evidence.

4) Medical device program

Software intended for illness diagnosis and treatment can now be sold on a stand-alone basis and is regulated as a "medical device program," thanks to the passage of legislation in 2014. This has resulted in the development of medical device programs in a variety of fields. We are currently developing applications (medical device programs) to support oral myofunctional therapy for patients with malocclusion and periodontal disease treatment in our department, and we intend to test their clinical effectiveness, including synergistic effects, with face-to-face examinations.

(3) Education

Under graduate: In charge of the following lectures and practical training, focusing on the basics of dental technology, complete denture fabrication methods, and digital dentistry.

Basic Technology of Manufacturing, Teeth Morphological Carving, Advanced Teeth Morphological Carving, Sciences of Oral Biomaterials, Sciences of Oral Biomaterials Practice, Dental Precise Casting Practice, Complete Denture Prosthodontic Practice, Removable Partial Prosthodontic Practice 1, Basic Fixed Prosthodontic Practice, Advanced Fixed Prosthodontics Practice, Aesthetic Dentistry Practice, CAD/CAM System Technology Practice, Process Device Engineering, Graduation Reseach 1, CAD/CAM System Technology Practice, Oral and Maxillofacial Radiology, Graduation Reseach 2.

Graduate: In charge of research guidance and lectures "Oral Health Engineering" for the master's program of the graduate school.

(4) Lectures & Courses

Undergraduate: Provide education on cutting-edge technology, particularly in the field of digital dentistry, in order to create digital dental technicians and scientists.

Graduate: Provide professional education in clinical and cutting-edge technologies in the field of digital dentistry, as well as build research skills.

(5) Clinical Performances

Center for Advanced Interdisciplinary Dentistry: Charge of digital dentistry and prosthetic dentistry as a specialist of denture.

Prosthodontics: A unique intraoral assessment and denture design must be conducted in order to repair the morphological and functional alterations induced by the unique intraoral condition of the edentulous jaw and retention with a complete denture. Complete dentures, in particular, cannot rely on teeth to keep them in oral cavity, instead relying on saliva-mediated adhesion between the oral mucosa and the denture base surface. The subfloor mucosa supports the occlusal stresses on a complete denture through the denture base. It is necessary to retention the denture base, take into account the opposing relationship between the upper and lower jaw crests, and organize the artificial teeth and occlusal style in accordance with jaw movement. The denture should be in a form that harmonizes with the morphology and dynamics of the surrounding muscles and associated soft tissues and improves denture retention in order to restore the significant changes in the facial appearance of edentulous individuals due to missing teeth and tooth-supporting tissues. In addition, when dealing with patients, the psychological impact of tooth loss and the installation of massive prostheses in the mouth should be considered. These alterations in general health, including mental status, are likely to cause changes in the oral mucosa, which will affect denture retention, stability, and function. As a result, periodic recalls are conducted, and the patient's subjective evaluation of the denture and function gained by interview and VAS is continually studied to verify that the recovered function is maintained and enhanced over time. Furthermore, we have created our own evaluation standards to objectively assess the efficacy of prosthetic procedures based on EBM as well as patient subjective opinions.

(6) Publications

[Original Articles]

- 1. Yoko Uehara, Manabu Kanazawa, Anna Miyayasu, Masataka Watanabe, Awutsadaporn Katheng, Daisuke Sato, Shunsuke Minakuchi. Comparison of general satisfaction, oral health-related quality of life, and patient's self-assessment between mandibular single-implant overdentures and experimental removable complete dentures: A randomized crossover clinical trial. Journal of Dentistry. 2021.12;
- Sayaka Tada, Manabu Kanazawa, Anna Miyayasu, Maiko Iwaki, Murali Srinivasan, Shunsuke Minakuchi, Gerald McKenna. Patient preferences for different tooth replacement strategies for the edentulous mandible: A willingness-to-pay analysis. J Prosthodont Res. 2021.10; 65(4); 535-540
- Negoro M, Kanazawa M, Sato D, Shimada R, Miyayasu A, Asami M, Katheng A, Kusumoto Y, Abe Y, Baba K, Minakuchi S. Patient-reported outcomes of implant-assisted removable partial dentures with magnetic attachments using short implants: A prospective study. Journal of prosthodontic research. 2021.07;
- 4. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Correction: Aung et al. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications. Polymers 2021, 13, 1879 POLYMERS. 2021.07; 13(14); 2280
- 5. Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S.. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. Journal of Dental Sciences. 2021.07;
- 6. Katheng A, Kanazawa M, Komagamine Y, Miyayasu A, Uehara Y, Sato D. Masticatory performances and maximum occlusal forces of immediate and conventional loaded two-implant supported overdentures retained by magnetic attachments: preliminary study of randomized controlled clinical trial. International Journal of Implant Dentistry. 2021.06; 7(1); 1-9
- Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S. Patient-reported outcomes with immediate-loaded two-implant-supported mandibular overdentures: Results of a 5-year prospective study. Journal of Dental Sciences. 2021.06;

- 8. Hada T, Kanazawa M, Iwaki M, Katheng A, Minakuchi S. Comparison of Mechanical Properties of PMMA Disks for Digitally Designed Dentures. Polymers. 2021.05; 13(11);
- 9. Alsandi Qutaiba, Ikeda Masaomi, Arisaka Yoshinori, Nikaido Ru, Tsuchida Yumi, Sadr Alireza, Yui Nobuhiko, Tagami Junji. Evaluation of Mechanical and Physical Properties of Light and Heat Polymerized UDMA for DLP 3D Printer SENSORS. 2021.05; 21(10);
- Soeda Y, Kanazawa M, Hada T, Arakida T, Iwaki M, Minakuchi S. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. The Journal of prosthetic dentistry. 2021.03;
- 11. Chaiamornsup P, Iwasaki N, Tsuchida Y, Takahashi H. Effects of build orientation on adaptation of casting patterns for three-unit partial fixed dental prostheses fabricated by using digital light projection. The Journal of prosthetic dentistry. 2021.02;
- 12. Doke M, Komagamine Y, Kanazawa M, Iwaki M, Suzuki H, Miyazaki Y, Mizuno T, Okayasu K, Minakuchi S. Effect of dental intervention on improvements in metabolic syndrome patients: a randomized controlled clinical trial. BMC oral health. 2021.01; 21(1); 4
- 13. Ryo Shimada, Manabu Kanazawa, Anna Miyayasu, Mari Asami, Thuy V. Lam, Khaing M. Thu, Daisuke Sato, Shunsuke Minakuchi. A preliminary comparison of marginal bone-level changes, survival rates, and prosthodontic maintenances between immediately and conventionally loaded two-implant overdentures with magnetic attachments. Journal of Medical and Dental Sciences. 2021.01; 68; 9-16
- 14. Watanabe M, Kanazawa M, Miyayasu A, Shimada R, Negoro M, Uehara Y, Sato D, Sato Y, Minakuchi S. Comparison of masticatory performance between immediately loaded and conventionally loaded mandibular 2-implant overdentures with magnetic attachments The Journal of the Japanese Society of Magnetic Applications in Dentistry. 2021; 29(2); 19-23
- Hao J, Murakami N, Yamazaki T, Iwasaki N, Yatabe M, Takahashi H, Wakabayashi N. Flexural and fatigue properties of polyester disk material for milled resin clasps Dental Materials Journal. 2021; 40(6); 1359-1364

- 1. Manabu Kanazawa. Scan in digital denture. Japan Denture Professional 2021.11.18
- 2. Li C, Churei H, Aung TK, Tsuchida Y, Takahashi H, Ueno T. Impact absorption and distribution ability of 3D printed mouthguard material in contrasting orientations. 第78回日本歯科理工学会学術講演会 2021.10.17
- 3. Bui Ngoc Huyen Trang, Manabu Kanazawa, Natsuko Murakami, Noriyuki Wakabayashi, Awutsadaporn Katheng, Sai Tun Naing, Sahaprom Namano, Maiko Iwaki, Shunsuke Minakuchi. Stress Distribution of One-Piece and Two-Piece Mini-Implant Overdentures (Various Attachments). CED-IADR/NOF Oral Health Research Congress in Brussels 2021.09.16
- 4. Manabu Kanazawa. Applied concepts & digital advancements in implantology. The Roundtable 2021.08.17
- 5. Manabu Kanazawa. One day direct denture restorations using hard and soft relining materials. Essential Expertise for Clinical Dentistry 7 2021.08.17
- 6. Sai Tun Naing, Manabu Kanazawa, Tamaki Hada, Shunsuke Minakuchi. Effect of implant position on the stress distribution of IARPD. IADR general session, Boston, 2021 2021.07.21
- 7. Ha RB, Tsuchida Y, Iwasaki N, Takahashi H. 多層 CAD/CAM 冠用コンポジットレジンブロックの厚みが 色の見え方に与える影響. 第 77 回日本歯科理工学会学術講演会 2021.04.10 東京
- 1. Otake R, Kanazawa M, et al.. A prospective study of digital complete dentures using customized disc method.. 2021.06.19 online
- 2. Soeda Y, Kanazawa M, Iwaki M, Arakida T, Hada T, Otake R, Katheng A, Akiyama Y, Ando K, Minakuchi S. Trueness and precision of artificial teeth in CAD/CAM milled complete dentures with custom disks of prefabricated frame. 2021.04.24

Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA Junior Associate Professor Keiko KONDO Specially Appointed Assistant Professor Masayuki TOI Specially Appointed Assistant Professor Risako MIKAKMI(from November) Graduate Student Nami ISHIZAKA Resident Keiji KOMATSU(until Octorber)

(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 oralpathology 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) :antimicrobila activity and effects to eukaryotic cells (induction of anti-oxydant 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 oralpathology 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 oralpathology 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. Yuka Shichiri-Negoro, Chiaki Tsutsumi-Arai, Kazuhito Satomura, Shinichi Arakawa, Noriyuki Wakabayashi. Ozone ultrafine bubble water inhibits the early formation of Candida albicans biofilms PLOS ONE. 2021.12; Online ahead of print, doi.org/10.1371/journal.pone.0261180
- 2. Keiko Kondo, Ryoko Kanenaga, Yoshinori Tanaka, Kunimoto Hotta, and Shinichi Arakawa. The neutralizing effect of mouth rinsing with alkaline electrolyzed water on different regions of the oral cavity acidified by acidic beverages Journal of Oral Science. 2021.09; 64(1); 17-21
- 3. Mikami R, Mizutani K, Shioyama H, Matsuura T, Aoyama N, Suda T, Kusunoki Y, Takeda K, Izumi Y, Aida J, Aoki A, Iwata T. Influence of aging on periodontal regenerative therapy using enamel matrix derivative: A 3-year prospective cohort study. Journal of clinical periodontology. 2021.09; 49(2); 123-133
- 4. Kawasaki M, Ikeda Y, Ikeda E, Takahashi M, Tanaka D, Nakajima Y, Arakawa S, Izumi Y, Miyake S. Oral infectious bacteria in dental plaque and saliva as risk factors in patients with esophageal cancer. Cancer. 2021.02; 127(4); 512-519

[Books etc]

1. Shinichi Arakawa. Ultrafine Bubbles. Jenny Stanford Publishing Pte., 2021.11 (ISBN : 978-1-003-14195-2)

[Conference Activities & Talks]

1. 遠井 政行、近藤 真啓、荒川 真一、網干 博文. ショウジョウバエの糖質摂食を誘導するドパミン作動 性ニューロンの探索. 2021 年度第 44 回日本分子生物学会年会 2021.12.01 横浜

Oral Care for Systemic Health Support

Professor Yuhji Kabasawa Assistant Professor Kanade Ito Postgraduate student(Master's course) Shiori Tokura

(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

[Original Articles]

- Hsu YJ, Chen YH, Lin KD, Lee MY, Lee YL, Yu CK, Kabasawa Y, Huang HL. Clinical Outcomes and Oral Health-Related Quality of Life after Periodontal Treatment with Community Health Worker Strategy in Patients with Type 2 Diabetes: A Randomized Controlled Study. International journal of environmental research and public health. 2021.08; 18(16);
- Nami Koida, Yuji Kabasawa. Clinico-Statistical Study of Postoperative Delirium in Patients with Malignant Tumors in the Oral and Maxillofacial Region Pharmacology and Pharmacogenomics. 2021.08; 4(1); 107-111
- 3. Kabasawa Yuji, Ito Kanade, Tokura Shiori, Takazawa Itsuki, Kimura Rio, Nakanishi Tohko, Akiyama Kikue, Onuma Yuki, Adachi Toshiko, Komiya Ruri, Harada Hiroyuki, Nojima Hitomi, Miura Masahiko, Yoshimura Ryoichi. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer 日本口腔ケア学会雑誌. 2021.04; 15(3); 264
- Lin YC, Du JK, Lin PC, Kabasawa Y, Lin PL, Hsiao SY, Huang HL. Association between the dental occlusion and perceived ability to eat foods of Taiwanese older adults. Journal of oral rehabilitation. 2021.02;

- Yuji Kabasawa, Kanade Ito, Shiori Tokura, Itsuki Takazawa, Rio Kimura, Tohko Nakanishi, Kikue Akiyama, Yuki Onuma, Toshiko Adachi, Ruri Komiya, Hiroyuki Harada, Hitomi Nojima, Masahiko Miura, Ryoichi Yoshimura. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. The 1st Annual Meeting of the International Society of Oral Care 2021.04.18 東京
- Kabasawa Yuji, Ito Kanade, Tokura Shiori, Takazawa Itsuki, Kimura Rio, Nakanishi Tohko, Akiyama Kikue, Onuma Yuki, Adachi Toshiko, Komiya Ruri, Harada Hiroyuki, Nojima Hitomi, Miura Masahiko, Yoshimura Ryoichi. 頭頸部がんへの放射線化学療法時に発症する口腔粘膜炎に対して、エピシル口腔用液 が及ぼす効果に関するの臨床研究 (Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer). 日本口腔ケア学会雑誌 2021.04.01
- 3. Kabasawa Yuji, Ito Kanade, Tokura Shiori, Takazawa Itsuki, Kimura Rio, Nakanishi Tohko, Akiyama Kikue, Onuma Yuki, Adachi Toshiko, Komiya Ruri, Harada Hiroyuki, Nojima Hitomi, Miura Masahiko,

Yoshimura Ryoichi. 頭頸部がんへの放射線化学療法時に発症する口腔粘膜炎に対して、エピシルロ腔用液 が及ぼす効果に関するの臨床研究 (Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer). 日本口腔ケア学会雑誌 2021.04.01

1. Clinical Investigation of Episil Oral Solution for Oral Mucositis during Radiochemical Treatment for Head and Neck Cancer. 2021.04.18

Preventive Oral Health Care Sciences

Professor Kayoko SHINADA Assistant Professor Naoko ADACHI

Part-time lecturer Atsushi OHYAMA, Kenichi TANAKA, Kanako TODA, Chie YOSHIZU, Mamoru MURATA

Graduate Students Master Course Miyu YASUI(-March), HSU CHEN WEI(-March), WANG LIYANG, Yuko HIROTA (April-) Graduate Students(research) Yuko HIROTA (-March), WANG RAN,

(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. Suzuki H, Sugimoto K, Kubota-Miyazawa A, Noritake K, Umemori S, Araki K, Adachi N, Otsuka H, Yoshida N. A survey of oral health status, subjective oral symptoms and oral health behaviors among first-year dental students at a Japanese university. Journal of oral science. 2021.12; 64(1); 85-90

1. YASUDA Miyu, TODA Kanako, SHINADA Kayoko . Comparison of the effects of non-alcohol mouthrinses on oral malodor The Journal of Japan Society for Dental Hygiene . 2021.02; 15(2); 80-90

- 1. Adachi Naoko, Shinada Kayoko. Association between tooth loss and dyslipidemia: a four-year longitudinal study. 第 80 回日本公衆衛生学会総会 2021.12.21 オンデマンド開催
- 2. Liyang WANG, 安達 奈穂子, 品田 佳世子. コロナ禍における学生のマスク着用や生活の変化が口腔保健へ 及ぼす影響について. 第 86 回口腔病学会学術大会 2021.12.04 オンライン開催
- 1. A study of oral health behavior of students in COVID-19 pandemic. 2021.12.04

Oral Health Sciences for Community Welfare

Professor Koichiro MATSUO Assistant Professor Rena HIDAKA Graduate Student Itsuki TASAKA

(1) **Outline**

The Vision of department of Oral Health Sciences for Community Welfare is:

To establish the basis of human resource development where dental professionals can manage the needs of older adults who have various characteristics.

We engage in the activities with the Mission below:

To conduct practice, research and education to nurture human resources who act vigorously as oral health professional, working together with the other health professionals in acute care to community welfare

Please contact us if you are interested in the graduate school or collaborative research (matsuo.ohcw at tmd.ac.jp)

(2) Research

- 1. Invention of oral frail preventive program for community dwelling older adults
- 2. Invention of monitoring system for eating behavior in dependent older adults
- 3. Innovative food technology systems for independent senior living
- 4. Establishment of oral management system during stroke recovery
- 5. Invention of peri-operative oral management system for cancer patients
- 6. Multidisciplinary Oral management system

(3) Education

Under-graduate course

Gerodontology/Welfare for older adults/Nursing-care for older adults/Prosthodontics/Home visiting dentistry/Community dental care/ Social work

Post-graduate course Welfare and Oral Health Care for older adults

(4) Lectures & Courses

The education policy of our department is: To educate dental professionals who will acquire the competency below: Knowledge, skill and experience to work in medical and health care fields Communication skill to educate the other health professionals Activities with self-intent Interest in international academic activities with positive research mind

Clinical Services & Other Works (5)

Japanese Society of Gerodontology: Specialist, Instructor, Executive Board Member (International Affair) Japanese Association of Dentistry and Oral Health: Specialist, Instructor, Board Member (International Affair) Japanese Society of Dysphagia Rehabilitation

Japanese Society for Clinical Nutrition and Metabolism

Asian Association of Dentistry and Oral Health: Board member International Association of Dentistry and Oral Health: Councilor, International Advisory Committee

(6) Publications

[Original Articles]

- 1. Suzuki H, Furuya J, Hidaka R, Miyajima S, Matsubara C, Ohwada G, Asada T, Akazawa C, Sato Y, Tohara H, Minakuchi S.. Patients with mild cognitive impairment diagnosed at dementia clinic display decreased maximum occlusal force: a cross-sectional study. BMC Oral Health. 2021.12; 21(1); 665
- 2. Furuya J, Suzuki H, Hidaka R, Nakagawa K, Yoshimi K, Nakane A, Yamaguchi K, Shimizu Y, Itsui Y, Saito K, Sato Y, Tohara H, Minakuchi S. Factors Related to Oral Intake of Food by Hospitalized Patients with Malnutrition under the Care of a Nutrition Support Team. Int J Environ Res Public Health. 2021.11; 18(21); 11725
- 3. Matsuo Koichiro, Sekimoto Yu, Okamoto Mieko, Shibata Seiko, Otaka Yohei. Association between oral health status and oral food intake level in subacute stroke patients admitted to a convalescent rehabilitation unit GERODONTOLOGY. 2021.08; 39(1); 67-73
- 4. Furuya J, Suzuki H, Hidaka R, Akatsuka A, Nakagawa K, Yoshimi K, Nakane A, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Oral health status and its association with nutritional support in malnourished patients hospitalised in acute care. Gerodontology. 2021.07;
- 5. Kobayashi Yoshikazu, Okui Taro, Tsujimoto Masakazu, Ikeda Hirotaka, Satoh Koji, Kanamori Daisuke, Fujii Naoko, Toyama Hiroshi, Matsuo Koichiro. Effect of morphological findings in computed tomography on the quantitative values in single-photon emission computed tomography for patients with antiresorptive agent-related osteonecrosis of the jaw: a cross-sectional study ANNALS OF NUCLEAR MEDICINE. 2021.05; 35(7); 853-860
- 6. Matsuo K, Kito N, Ogawa K, Izumi A, Kishima M, Itoda M, Masuda Y. Improvement of oral hypofunction by a comprehensive oral and physical exercise programme including textured lunch gatherings. Journal of oral rehabilitation. 2021.04; 48(4); 411-421
- 7. Hidaka R, Furuya J, Nishiyama A, Suzuki H, Aoyagi M, Matsubara C, Yoshizumi Y, Yoshimi K, Nakane A, Tohara H, Sato Y, Minakuchi S. Structural Equation Modeling of Tongue Function and Tongue Hygiene in Acute Stroke Patients. International journal of environmental research and public health. 2021.04; 18(9);
- 8. Horibe Yasuhiro, Matsuo Koichiro, Ikebe Kazunori, Minakuchi Shunsuke, Sato Yuji, Sakurai Kaoru, Ueda Takayuki. Relationship between two pressure-sensitive films for testing reduced occlusal force in diagnostic criteria for oral hypofunction GERODONTOLOGY. 2021.02;

Oral Health Care Education

Professor Naomi Yoshida Assistant Professor

Hitomi Suzuki

(1) Research

- 1) Research on oral health behabior
- 2) Research on oral health management
- 3) Research on interprofessional education and work
- 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. Sekiya T, Sugimoto K, Kubota A, Tsuchihashi N, Oishi A, Yoshida N. Assessment of psychological changes in young children during dental treatment: Analysis of the autonomic nervous activity and electroencephalogram. International journal of paediatric dentistry. 2021.09;
- Yuko Yamamoto, Yoshiaki Nomura, Ayako Okada, Erika Kakuta, Naomi Yoshida ,Noriyasu Hosoya ,Nobuhiro Hanada and Noriko Takei . Improvement of Workplace Environment That Affects Motivation of Japanese Dental Hygienists International Journal of Environment Research and Public Health. 2021.02;
- Tsuchihashi Natsumi, Uehara Naoko, Miwa Zenzo, Yoshida Naomi, Sugimoto Kumiko. Perception of pungent, gustatory and olfactory stimuli in patients with congenital insensitivity to pain with anhidrosis JOURNAL OF ORAL SCIENCE. 2021.01; 63(1); 104-106
- Makoto Arakawa, Jun Kaneko, Vivianne Cruz de Jesus, Hidekazu Sonoda, Naomi Yoshida, Junji Tagami. Relationship between taste sensitivity and dental caries Journal of Medical and Dental Sciences. 2021.01; 68; 85-89

5. Arakawa Makoto, Kaneko Jun, Cruz de Jesus Vivianne, Sonoda Hidekazu, Yoshida Naomi, Tagami Junji. 味覚感度と齲蝕症の関連性 (Relationship between taste sensitivity and dental caries) Journal of Medical and Dental Sciences. 2021; 68; 85-89

- 1. Akiko Oshiro, Masako Okada, Naomi Yoshida, Jun Aida, Kayoko Shinada. Approaches at training for dental hygienists reinstatement and new graduate in Japan. AAPD 2021.10.01
- 1. Dental treatment needs of inpatients in convalescent ward . 2021.08.19

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 pharmaceutics.

Subjects and contents.

• Structure and function of human body I and II: anatomy, histology, physiology, embryology, oral anatomy, oral histology, oral physiology.

• Mechanism of disease and promotion of recovery process: pathology, oral pathology, microbiology, immunology, pharmacology.

- Dental pharmacology and pharmaceutics.
- Graduation thesis:

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).

Medical and Dental Science and Technology

(4) Publications

[Original Articles]

1. Sakamoto Yujiro. The branching pattern of the middle temporal artery and the relation with the temporal fascia. SURGICAL AND RADIOLOGIC ANATOMY. 2021.11; 43(11); 1867-1874

Basic Oral Health Engineering

Professor Kazuhiro Aoki Associate Professor Meiko Oki Assistant Professor Shingo Kamijo Technical Assistant Masud Khan

(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 novel bone anabolic reagents targeting RANKL (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 objective evaluation methods for tooth carving
- 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

 \cdot Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects

Medical and Dental Science and Technology

 \cdot Making dental and maxillofacial prostheses

(5) Publications

[Original Articles]

- 1. Yuna Hirohashi, Shingo Kamijo, Masud Khan, Masaomi Ikeda, Meiko Oki, Khairul Matin, Fatma Rashed, Kazuhiro Aoki. Tetracycline, an appropriate reagent for measuring bone-formation activity in the murine model of the Streptococcus mutans-induced bone loss Frontiers in Cellular and Infection Microbiology Microbiome in Health and Disease. 2021.09; 11; 714366
- 2. Gao Jing, Muroya Ryusuke, Huang Fei, Nagata Kengo, Shin Masashi, Nagano Ryoko, Tajiri Yudai, Fujii Shinsuke, Yamaza Takayoshi, Aoki Kazuhiro, Tamura Yukihiko, Inoue Mayuko, Chishaki Sakura, Kukita Toshio, Okabe Koji, Matsuda Miho, Mori Yoshihide, Kiyoshima Tamotsu, Jimi Eijiro. Bone morphogenetic protein induces bone invasion of melanoma by epithelial-mesenchymal transition via the Smad1/5 signaling pathway LABORATORY INVESTIGATION. 2021.09; 101(11); 1475-1483
- Nakai H, Inokoshi M, Nozaki K, Komatsu K, Kamijo S, Liu H, Shimizubata M, Minakuchi S, Van Meerbeek B, Vleugels J, Zhang F. Additively Manufactured Zirconia for Dental Applications. Materials (Basel). 2021.07; 14(13);
- 4. Okawara H, Arai Y, Matsuno H, Marcián P, Borák L, Aoki K, Wakabayashi N. Effect of load-induced local mechanical strain on peri-implant bone cell activity related to bone resorption and formation in mice: An analysis of histology and strain distributions. Journal of the mechanical behavior of biomedical materials. 2021.01; 116; 104370

[Misc]

1. Rashed Fatma, Kamijyo Shingo, Shimizu Yuri, Hirohashi Yuna, Khan Masud, Sugamori Yasutaka, Murali Ramachandran, Aoki Kazuhiro. The Effects of Receptor Activator of NF-kappa B Ligand-Binding Peptides on Bone Resorption and Bone Formation FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY. 2021.07; 9; 648084

- 1. Hein Linn Htat, Kajima Yuka, Takaichi Atsushi, Hla Htoot Wai Cho, Kamijo Shingo, Hanawa Takao, Wakabayashi Noriyuki. Effect of post-heat treatments on metal-ceramic bond properties of Co-Cr-Mo-W alloy fabricated by selective laser melting. The 77th General Session of the Japanese Society for Dental Materials and Devices 2021.04.10
- 2. Nakai H, Inokoshi M, Nozaki K, Kamijo S, Shimizubata M, Liu H, Minakuchi S. Crystallography and flexural strength of additive manufactured zirconia. The 7th Biennial Joint Congress of JPS-CPS-KAP 2021.02.19 web
- 1. Yuna KANAMORI, Rena TAKAHASHI, Masaomi IKEDA, Shingo KAMIJO, Shin ROZAN, Kanako NORITAKE, Ken-ichi TONAMI, Hiroshi NITTA, Toru NIKAIDO, Yasushi SHIMADA, Junji TAGAMI. The effect of resin coating technique on internal fit of CAD/CAM composite resin crowns. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Web

Oral Prosthetic Engineering

Professor Noriyuki WAKABAYASHI Junior Associate Professor Masaomi IKEDA Assistant Professor Maho SHIOZAWA Assistant Professor Maiko IWAKI

(1) Outline

Oral Health Information Technology educates deepen understanding of the production of the dental prosthesis using the latest computer science and cultivate basics power to new technology development. This course cultivates the ability to offer high quality medical technology taking advantage of expertise or knowledge. And the purpose of this section is to educate professional dental technologists who has ability to apply newly developed materials and technologies and who is able to contribute in not only clinical situation but also research institution or educational organization at international levels. Presently, the latest technologies such as dental implant and dental CAD/CAM etc became popular by the development of materials and the progress in technologies among dental treatment. Therefore, it is necessary to understand and lean knowledge about newly developed materials and technologies for properly control the dental laboratory works. Furthermore, It is necessary that the communication skill for report information about the materials and technologies to dentists and dental hygienists. Based on these evidences, it is an education in which specialists are raised to not be bound by classification as technologist and have ambition.

(2) Research

- 1) 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. Tabata Miyuki, Ratanaporncharoen Chindanai, Ishihara Nouboru, Masu Kazuya, Sriyudthsak Mana, Kitasako Yuichi, Ikeda Masaomi, Tagami Junji, Miyahara Yuji. Surface analysis of dental caries using a

wireless pH sensor and Raman spectroscopy for chairside diagnosis TALANTA. 2021.12; 235; 122718

- Takada Seira, Ogata Yasuko, Yumoto Yoshie, Ikeda Masaomi. Implementation of an Advance Care Planning Inventory and Its Possible Effect on Quality of Dying: A Nationwide Cross-Sectional Study in Group Homes for Persons with Dementia in Japan Healthcare. 2021.12;
- Akane Chin, Masaomi Ikeda, Tomohiro Takagaki, Toru Nikaido, Alireza Sadr, Yasushi Shimada, Junji Tagami. Effects of Immediate and Delayed Cementations for CAD/CAM Resin Block after Alumina Air Abrasion on Adhesion to Newly Developed Resin Cement. Materials (Basel). 2021.11; 14(22); 7058
- 4. Sayaka Tada, Manabu Kanazawa, Anna Miyayasu, Maiko Iwaki, Murali Srinivasan, Shunsuke Minakuchi, Gerald McKenna. Patient preferences for different tooth replacement strategies for the edentulous mandible: A willingness-to-pay analysis. J Prosthodont Res. 2021.10; 65(4); 535-540
- Hosaka Keiichi, Tichy Antonin, Araoka Daisuke, Wurihan Wuriham, Shibata Yo, Ikeda Masaomi, Klein Celoso Afonso Jr, Tagami Junji, Nakajima Masatoshi. Eight-year Microtensile Bond Strength to Dentin and Interfacial Nanomechanical Properties of a One-step Adhesive. The Journal Adhesive Dentistry. 2021.10; 23(5); 461-467
- 6. Nanako Ueda, Tomohiro Takagaki, Toru Nikaido, Rena Takahashi, Masaomi Ikeda, Junji Tagami. The effect of different ceramic surface treatments on the repair bond strength of resin composite to lithium disilicate ceramic. Dental Materials Journal. 2021.09; 40(5); 1073-1079
- 7. Saki Uchiyama, Rena Takahashi, Takaaki Sato, Shin Rozan, Masaomi Ikeda, Masanao Inokoshi, Toru Nikaido, Junji Tagami. Effect of a temporary sealing material on the bond strength of CAD/CAM inlay restorations with resin-coating technique. Dental Materials Journal. 2021.09; 40(5); 1122-1128
- 8. Yuna Hirohashi, Shingo Kamijo, Masud Khan, Masaomi Ikeda, Meiko Oki, Khairul Matin, Fatma Rashed, Kazuhiro Aoki. Tetracycline, an appropriate reagent for measuring bone-formation activity in the murine model of the Streptococcus mutans-induced bone loss Frontiers in Cellular and Infection Microbiology Microbiome in Health and Disease. 2021.09; 11; 714366
- Nasiry Khanlar L, Revilla-León M, Barmak AB, Ikeda M, Alsandi Q, Tagami J, Zandinejad A. Surface roughness and shear bond strength to composite resin of additively manufactured interim restorative material with different printing orientations. The Journal of prosthetic dentistry. 2021.09;
- 10. Hosaka Keiichi, Kubo Shisei, Tichy Antonin, Ikeda Masaomi, Shinkai Koichi, Maseki Toshio, Rikuta Akitomo, Sasazaki Hiromi, Satoh Kaori, Fujitani Morioki, Hanabusa Masao, Yamamoto Takatsugu, Yoshikawa Kazushi, Morigami Makoto, Uno Shigeru, Sugizaki Junpei, Yatani Hirofumi, Nikaido Toru. Clinical effectiveness of direct resin composite restorations bonded using one-step or two-step self-etch adhesive systems: A three-year multicenter study(和訳中) Dental Materials Journal. 2021.09; 40(5); 1151-1159
- 11. Uchiyama Saki, Takahashi Rena, Sato Takaaki, Rozan Shin, Ikeda Masaomi, Inokoshi Masanao, Nikaido Toru, Tagami Junji. Effect of a temporary sealing material on the bond strength of CAD/CAM inlay restorations with resin-coating technique(和訳中) Dental Materials Journal. 2021.09; 40(5); 1122-1128
- 12. Ueda Nanako, Takagaki Tomohiro, Nikaido Toru, Takahashi Rena, Ikeda Masaomi, Tagami Junji. The effect of different ceramic surface treatments on the repair bond strength of resin composite to lithium disilicate ceramic(和訳中) Dental Materials Journal. 2021.09; 40(5); 1073-1079
- Hayashi Meiken, Kubo Shisei, Pereira Patricia N. R., Ikeda Masaomi, Takagaki Tomohiro, Nikaido Toru, Tagami Junji. Progression of non-carious cervical lesions: 3D morphological analysis CLINICAL ORAL INVESTIGATIONS. 2021.08;
- Martina Vicheva, Takaaki Sato, Tomohiro Takagaki, Yuuta Baba, Masaomi Ikeda, Michael F Burrow, Toru Nikaido, Junji Tagami. Effect of repair systems on dentin bonding performance. Dental Materials Journal. 2021.07; 40(4); 903-910
- Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S.. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. Journal of Dental Sciences. 2021.07;

- 16. Hasegawa Mayu, Tichy Antonin, Hosaka Keiichi, Kuno Yusuke, Ikeda Masaomi, Nozaki Kosuke, Chiba Ayaka, Nakajima Masatoshi, Tagami Junji. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents(和訳中) Dental Materials Journal. 2021.07; 40(4); 877-884
- 17. Vicheva Martina, Sato Takaaki, Takagaki Tomohiro, Baba Yuuta, Ikeda Masaomi, Burrow Michael F., Nikaido Toru, Tagami Junji. Effect of repair systems on dentin bonding performance(和訳中) Dental Materials Journal. 2021.07; 40(4); 903-910
- 18. Yuta Baba, Takaaki Sato, Tomohiro Takagaki, Martina Vicheva, Ayaka Sato, Masaomi Ikeda, Toru Nikaido, Junji Tagami. Effects of Different Tooth Conditioners on the Bonding of Universal Self-etching Adhesive to Enamel. The Journal of Adhesive Dentistry. 2021.06; 23(3); 233-242
- 19. Komagamine Y, Kanazawa M, Sato D, Iwaki M, Miyayasu A, Minakuchi S. Patient-reported outcomes with immediate-loaded two-implant-supported mandibular overdentures: Results of a 5-year prospective study. Journal of Dental Sciences. 2021.06;
- Alsandi Qutaiba, Ikeda Masaomi, Arisaka Yoshinori, Nikaido Ru, Tsuchida Yumi, Sadr Alireza, Yui Nobuhiko, Tagami Junji. Evaluation of Mechanical and Physical Properties of Light and Heat Polymerized UDMA for DLP 3D Printer SENSORS. 2021.05; 21(10);
- 21. Kitasako Yuichi, Ikeda Masaomi, Takagaki Tomohiro, Burrow Michael F., Tagami J.. The prevalence of non-carious cervical lesions (NCCLs) with or without erosive etiological factors among adults of different ages in Tokyo CLINICAL ORAL INVESTIGATIONS. 2021.05;
- 22. Ishikawa Kyoko, Yamauti Monica, Tichy Antonin, Ikeda Masaomi, Ueno Takeshi, Wakabayashi Noriyuki, Thanatvarakorn Ornnicha, Prasansuttiporn Taweesak, Klein-Junior Celso Afonso, Takahashi Akifumi, Takagaki Tomohiro, Nakajima Masatoshi, Tagami Junji, Hosaka Keiichi. UV-Mediated Photofunctionalization of Indirect Restorative Materials Enhances Bonding to a Resin-Based Luting Agent BIOMED RESEARCH INTERNATIONAL. 2021.05; 2021; 9987860
- 23. Takaaki Sato, Rena Takahashi, Shin Rozan, Saki Uchiyama, Yuta Baba, Martina Vicheva, Ayaka Sato, Masaomi Ikeda, Tomohiro Takagaki, Toru Nikaido, Junji Tagami. The effect of temporary sealing materials and cleaning protocols on the bond strength of resin cement applied to dentin using the resin-coating technique. Dental Materials Journal. 2021.05; 40(3); 719-726
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- 25. Hasegawa M, Tichy A, Hosaka K, Kuno Y, Ikeda M, Nozaki K, Chiba A, Nakajima M, Tagami J. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents. Dental Materials Journal. 2021.03; 40(4); 877-884
- 26. Luz Madrigal Erick, Tichy Antonin, Hosaka Keiichi, Ikeda Masaomi, Nakajima Masatoshi, Tagami Junji. The effect of curing mode of dual-cure resin cements on bonding performance of universal adhesives to enamel, dentin and various restorative materials(和訳中) Dental Materials Journal. 2021.03; 40(2); 446-454
- Soeda Y, Kanazawa M, Hada T, Arakida T, Iwaki M, Minakuchi S. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. The Journal of prosthetic dentistry. 2021.03;
- Dwiandhany WS, Abdou A, Tichy A, Yonekura K, Ikeda M, Hosaka K, Tagami J, Nakajima M. Additive effects of touch-activated polymerization and extended irradiation time on bonding of light-activated adhesives to root canal dentin. The Journal of prosthetic dentistry. 2021.01; 3913(20); 30742-30743
- 29. Aung Swe Zin, Takagaki Tomohiro, Ikeda Masaomi, Nozaki Kosuke, Burrow Michael F., Abdou Ahmed, Nikaido Toru, Tagami Junji. The effect of different light curing units on Vickers microhardness and degree of conversion of flowable resin composites(和訳中) Dental Materials Journal. 2021.01; 40(1); 44-51
- Yumika Soeda, Manabu Kanazawa, Tamaki Hada, Toshio Arakida, Maiko Iwaki, Shunsuke Minakuch. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. 2021;

- 1. BUI Ngoc Huyen Trang. CED-IADR/NOF Oral Health Research Congress in Brussels. CED-IADR/NOF Oral Health Research Congress in Brussels 2021.09.16
- 1. Yuna KANAMORI, Rena TAKAHASHI, Masaomi IKEDA, Shingo KAMIJO, Shin ROZAN, Kanako NORITAKE, Ken-ichi TONAMI, Hiroshi NITTA, Toru NIKAIDO, Yasushi SHIMADA, Junji TAGAMI. The effect of resin coating technique on internal fit of CAD/CAM composite resin crowns. The 155th Meeting of the Japanese Society of Conservative Dentistry 2021.10.28 Web
- 2. Otake R, Kanazawa M, et al.. A prospective study of digital complete dentures using customized disc method.. 2021.06.19 online
- 3. Soeda Y, Kanazawa M, Iwaki M, Arakida T, Hada T, Otake R, Katheng A, Akiyama Y, Ando K, Minakuchi S. Trueness and precision of artificial teeth in CAD/CAM milled complete dentures with custom disks of prefabricated frame. 2021.04.24

Digital Dentistry

Professor: Hidekazu Takahashi (-Mar) Manabu Kanazawa (May-) Assistant Professor: Naohiko Iwasaki Assistant Professor: Yumi Tsuchida

Graduate Student (Master): Ha Rou Bing

(1) Outline

Department of Digital Dentistry was founded on May 1, 2021, and is responsible for digital dentistry research, clinical practice, and teaching. "Digital dentistry" is an interdisciplinary field consisting of dentistry and engineering. This department provides a smooth connection between clinical dentistry and digital devices (hardware and software) in the field of engineering, and educates and trains individuals in research, clinical practice, and education.

(2) Research

1) Milled Complete Base Denture

Traditional complete denture manufacturing entails a high number of visits, varying treatment quality due to dentist competence variances, and contamination resistance issues due to the use of acrylic resin. To address these issues, we developed a denture fabrication process based on CAD/CAM technology that reduces the number of visits, improves treatment quality uniformity, and improves the physical qualities of dentures. In the traditional milled denture, only the denture base was milled and the artificial teeth were connected thereafter, resulting in issues such as the adhesive surface of the artificial teeth deteriorating. As a result, we invented the TMDU custom disk method, in which a personalized disk is generated for each patient and the denture base is milled as a single piece with artificial teeth. This custom disk is the subject of a patent application, as well as an application for an overseas patent with the help of the Industry-University Collaboration Office. In a prospective clinical study of complete dentures with CAD/CAM technology, which began in 2019, the findings of employing the TMDU custom disk method revealed better cost-effectiveness compared to fabricating complete dentures using the conventional method. The digital denture fabrication process we've developed incorporates a workflow that starts with an intraoral scanner optical impression of the edentulous jaw crest, then denture design and fabrication on a computer. To further digitalize the process, we intend to integrate AI-assist in denture design in the future. In addition, the company collaborates with manufacturer of milling machine and cutting tool on the creation of milling discs, which are required for milling digital dentures, as well as the verification of acceptable milling machine settings.

2) Digital partial denture

The digital partial denture has not been applied in clinical practice compared to the digital complete denture, because there are few research reports. One reason for this could be that partial dentures must accept a wide range of defect and support methods, and are made comprised of metal and resin materials in a variety of forms to do so. While it is possible to fabricate metal frames using the Selective Laser Melting (SLM), subsequent fabrication processes such as artificial teeth placement and polymerization are still carried out using traditional partial denture fabrication procedures, making it difficult to say that all processes have been digitized. As a result, we developed a method for fabricating a custom plate for partial dentures in which a metal frame created

using the SLM method and ready-made artificial tooth is embedded for each patient by adapting the TMDU custom disc method for complete dentures. This allowed for the milling of the artificial tooth, metal frame, and denture base all in one piece, overcoming the issues with traditional digital partial dentures. Dry milling machine is used to create this digital partial denture, but a wet milling machine might be utilized to create partial dentures of any size in the future. In the future, appropriate designs for custom plates will be considered, and fabrication of partial dentures for various defect configurations is assessed.

3) Implant overdenture

For a long period, implant overdentures (IOD) for edentulous mandible patients have been explored. Many research were undertaken in Europe and the United States in the 1980s and 1990s, and many evidence has been amassed in this field since a consensus statement was issued in 2002. We began our clinical research in 2008 at Tokyo Medical and Dental University Hospital, and we now have over 100 patients, with the longest case being followed for over ten years. To date, the following IOD studies have been conducted.

- 1) Prospective clinical study of 2-IOD using ball attachment (2008-)
- 2) RCT comparing normal and immediate loading of 2-IOD using magnetic attachments (2011-)
- 3) Prospective clinical study of mini-IODs using mini-implants (2013-2014 McGill University)
- 4) Prospective clinical studies of 1-IOD (2015-)
- 5) Joint clinical research with Showa University on implant-assisted partial denture (IARPD) (2017-)
- 6) Model experiments on IOD implant placement location and denture movement

On the other hand, only a few clinical trials on maxillary IOD have been conducted worldwide. Based on the evidence of mandibular 2-IOD and our knowledge of edentulous prosthodontics, we believe that if the jaw crest conditions are selected, maxillary IOD can be maintained with two implants, and that this will be an effective treatment choice in the super-aging society. To demonstrate proof, we plan to conduct clinical research of 2-IOD employing two implants as the maintenance source in the maxilla as well as in the mandible to establish evidence.

4) Medical device program

Software intended for illness diagnosis and treatment can now be sold on a stand-alone basis and is regulated as a "medical device program," thanks to the passage of legislation in 2014. This has resulted in the development of medical device programs in a variety of fields. We are currently developing applications (medical device programs) to support oral myofunctional therapy for patients with malocclusion and periodontal disease treatment in our department, and we intend to test their clinical effectiveness, including synergistic effects, with face-to-face examinations.

(3) Education

Under graduate: In charge of the following lectures and practical training, focusing on the basics of dental technology, complete denture fabrication methods, and digital dentistry.

Basic Technology of Manufacturing, Teeth Morphological Carving, Advanced Teeth Morphological Carving, Sciences of Oral Biomaterials, Sciences of Oral Biomaterials Practice, Dental Precise Casting Practice, Complete Denture Prosthodontic Practice, Removable Partial Prosthodontic Practice 1, Basic Fixed Prosthodontic Practice, Advanced Fixed Prosthodontics Practice, Aesthetic Dentistry Practice, CAD/CAM System Technology Practice, Process Device Engineering, Graduation Reseach 1, CAD/CAM System Technology Practice, Oral and Maxillofacial Radiology, Graduation Reseach 2.

Graduate: In charge of research guidance and lectures "Oral Health Engineering" for the master's program of the graduate school.

(4) Lectures & Courses

Undergraduate: Provide education on cutting-edge technology, particularly in the field of digital dentistry, in order to create digital dental technicians and scientists.

Graduate: Provide professional education in clinical and cutting-edge technologies in the field of digital dentistry, as well as build research skills.

(5) Clinical Performances

Center for Advanced Interdisciplinary Dentistry: Charge of digital dentistry and prosthetic dentistry as a specialist of denture.

Prosthodontics: A unique intraoral assessment and denture design must be conducted in order to repair the morphological and functional alterations induced by the unique intraoral condition of the edentulous jaw and retention with a complete denture. Complete dentures, in particular, cannot rely on teeth to keep them in oral cavity, instead relying on saliva-mediated adhesion between the oral mucosa and the denture base surface. The subfloor mucosa supports the occlusal stresses on a complete denture through the denture base. It is necessary to retention the denture base, take into account the opposing relationship between the upper and lower jaw crests, and organize the artificial teeth and occlusal style in accordance with jaw movement. The denture should be in a form that harmonizes with the morphology and dynamics of the surrounding muscles and associated soft tissues and improves denture retention in order to restore the significant changes in the facial appearance of edentulous individuals due to missing teeth and tooth-supporting tissues. In addition, when dealing with patients, the psychological impact of tooth loss and the installation of massive prostheses in the mouth should be considered. These alterations in general health, including mental status, are likely to cause changes in the oral mucosa, which will affect denture retention, stability, and function. As a result, periodic recalls are conducted, and the patient's subjective evaluation of the denture and function gained by interview and VAS is continually studied to verify that the recovered function is maintained and enhanced over time. Furthermore, we have created our own evaluation standards to objectively assess the efficacy of prosthetic procedures based on EBM as well as patient subjective opinions.

(6) Publications

[Original Articles]

- 1. Yoko Uehara, Manabu Kanazawa, Anna Miyayasu, Masataka Watanabe, Awutsadaporn Katheng, Daisuke Sato, Shunsuke Minakuchi. Comparison of general satisfaction, oral health-related quality of life, and patient's self-assessment between mandibular single-implant overdentures and experimental removable complete dentures: A randomized crossover clinical trial. Journal of Dentistry. 2021.12;
- Sayaka Tada, Manabu Kanazawa, Anna Miyayasu, Maiko Iwaki, Murali Srinivasan, Shunsuke Minakuchi, Gerald McKenna. Patient preferences for different tooth replacement strategies for the edentulous mandible: A willingness-to-pay analysis. J Prosthodont Res. 2021.10; 65(4); 535-540
- Negoro M, Kanazawa M, Sato D, Shimada R, Miyayasu A, Asami M, Katheng A, Kusumoto Y, Abe Y, Baba K, Minakuchi S. Patient-reported outcomes of implant-assisted removable partial dentures with magnetic attachments using short implants: A prospective study. Journal of prosthodontic research. 2021.07;
- 4. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Correction: Aung et al. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications. Polymers 2021, 13, 1879 POLYMERS. 2021.07; 13(14); 2280
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- 6. Katheng A, Kanazawa M, Komagamine Y, Miyayasu A, Uehara Y, Sato D. Masticatory performances and maximum occlusal forces of immediate and conventional loaded two-implant supported overdentures retained by magnetic attachments: preliminary study of randomized controlled clinical trial. International Journal of Implant Dentistry. 2021.06; 7(1); 1-9
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- 8. Hada T, Kanazawa M, Iwaki M, Katheng A, Minakuchi S. Comparison of Mechanical Properties of PMMA Disks for Digitally Designed Dentures. Polymers. 2021.05; 13(11);
- 9. Alsandi Qutaiba, Ikeda Masaomi, Arisaka Yoshinori, Nikaido Ru, Tsuchida Yumi, Sadr Alireza, Yui Nobuhiko, Tagami Junji. Evaluation of Mechanical and Physical Properties of Light and Heat Polymerized UDMA for DLP 3D Printer SENSORS. 2021.05; 21(10);
- Soeda Y, Kanazawa M, Hada T, Arakida T, Iwaki M, Minakuchi S. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures with custom disks. The Journal of prosthetic dentistry. 2021.03;
- 11. Chaiamornsup P, Iwasaki N, Tsuchida Y, Takahashi H. Effects of build orientation on adaptation of casting patterns for three-unit partial fixed dental prostheses fabricated by using digital light projection. The Journal of prosthetic dentistry. 2021.02;
- 12. Doke M, Komagamine Y, Kanazawa M, Iwaki M, Suzuki H, Miyazaki Y, Mizuno T, Okayasu K, Minakuchi S. Effect of dental intervention on improvements in metabolic syndrome patients: a randomized controlled clinical trial. BMC oral health. 2021.01; 21(1); 4
- 13. Ryo Shimada, Manabu Kanazawa, Anna Miyayasu, Mari Asami, Thuy V. Lam, Khaing M. Thu, Daisuke Sato, Shunsuke Minakuchi. A preliminary comparison of marginal bone-level changes, survival rates, and prosthodontic maintenances between immediately and conventionally loaded two-implant overdentures with magnetic attachments. Journal of Medical and Dental Sciences. 2021.01; 68; 9-16
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- 2. Li C, Churei H, Aung TK, Tsuchida Y, Takahashi H, Ueno T. Impact absorption and distribution ability of 3D printed mouthguard material in contrasting orientations. 第78回日本歯科理工学会学術講演会 2021.10.17
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- 4. Manabu Kanazawa. Applied concepts & digital advancements in implantology. The Roundtable 2021.08.17
- 5. Manabu Kanazawa. One day direct denture restorations using hard and soft relining materials. Essential Expertise for Clinical Dentistry 7 2021.08.17
- 6. Sai Tun Naing, Manabu Kanazawa, Tamaki Hada, Shunsuke Minakuchi. Effect of implant position on the stress distribution of IARPD. IADR general session, Boston, 2021 2021.07.21
- 7. Ha RB, Tsuchida Y, Iwasaki N, Takahashi H. 多層 CAD/CAM 冠用コンポジットレジンブロックの厚みが 色の見え方に与える影響. 第 77 回日本歯科理工学会学術講演会 2021.04.10 東京
- 1. Otake R, Kanazawa M, et al.. A prospective study of digital complete dentures using customized disc method.. 2021.06.19 online
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Urology

(1) Publications

[Original Articles]

- Yuki Arita, Soichiro Yoshida, Thomas C Kwee, Hirotaka Akita, Shigeo Okuda, Yuki Iwaita, Kiyoko Mukai, Shunya Matsumoto, Ryo Ueda, Ryota Ishii, Ryuichi Mizuno, Yasuhisa Fujii, Mototsugu Oya, Masahiro Jinzaki. Diagnostic value of texture analysis of apparent diffusion coefficient maps for differentiating fat-poor angiomyolipoma from non-clear-cell renal cell carcinoma. Eur J Radiol. 2021.10; 143; 109895
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- 4. Yoshida S, Matsuoka Y, Toda K, Uehara S, Tanaka H, Yokoyama M, Saito K, Yoshimura R, Fujii Y. Nonmetastatic castration-resistant prostate cancer treated with salvage focal brachytherapy after external beam radiotherapy. IJU case reports. 2021.07; 4(4); 228-230
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- 7. Kimura Koichiro, Yoshida Soichiro, Tsuchiya Junichi, Yamada Ichiro, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Tateishi Ukihide, Fujii Yasuhisa. Usefulness of texture features of apparent diffusion coefficient maps in predicting chemoradiotherapy response in muscle-invasive bladder cancer EUROPEAN RADIOLOGY. 2021.06;
- 8. Yamazaki A, Ito T, Sugimoto M, Yoshida S, Honda K, Kawashima Y, Fujikawa T, Fujii Y, Tsutsumi T. Patient-specific virtual and mixed reality for immersive, experiential anatomy education and for surgical planning in temporal bone surgery. Auris, nasus, larynx. 2021.05;

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- 13. Yoshida S, Fujii Y. Editorial Comment to Utility of whole-body diffusion-weighted magnetic resonance imaging in the management of treatment-related neuroendocrine prostate cancer. IJU case reports. 2021.03; 4(2); 73-74
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- 15. Yoshida Soichiro, Fujii Yasuhisa. Editorial Comment to Utility of whole-body diffusion-weighted magnetic resonance imaging in the management of treatment-related neuroendocrine prostate cancer(和訳中) IJU Case Reports. 2021.03; 4(2); 73-74
- 16. Tanaka H, Fujii Y. Editorial Comment. The Journal of urology. 2021.02; 101097JU00000000000154902
- 17. Yoshida Soichiro, Takahara Taro, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Can progressive site-directed therapy prolong the efficacy of subsequent androgen receptor axis-targeted drugs in oligometastatic castration-resistant prostate cancer? International Journal of Urology. 2021.02; 28(2); 241-242
- 18. Fukuda S, Saito K, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Kageyama Y, Fujii Y. Impact of C-reactive protein flare-response on oncological outcomes in patients with metastatic renal cell carcinoma treated with nivolumab. Journal for immunotherapy of cancer. 2021.02; 9(2);
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- 20. Fukushima Hiroshi, Yoshida Soichiro, Kijima Toshiki, Nakamura Yuki, Fukuda Shohei, Uehara Sho, Yasuda Yosuke, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Fujii Yasuhisa. Combination of Cisplatin and Irradiation Induces Immunogenic Cell Death and Potentiates Postirradiation Anti-PD-1 Treatment Efficacy in Urothelial Carcinoma INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES. 2021.01; 22(2);
- 21. Tanaka Hajime, Fujii Yasuhisa. Editorial Comment to Lymph node dissection for bladder cancer: Current standards and the latest evidence INTERNATIONAL JOURNAL OF UROLOGY. 2021.01; 28(1); 16
- 22. Yoshida Soichiro, Takahara Taro, Arita Yuki, Toda Kazuma, Yamada Ichiro, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Genuine- and induced-oligometastatic castration-resistant prostate cancer: clinical features and clinical outcomes after progressive site-directed therapy INTERNATIONAL UROLOGY AND NEPHROLOGY. 2021.01;
- 23. Matsuoka Yoh, Uehara Sho, Yoshida Soichiro, Tanaka Hajime, Yokoyama Minato, Fujii Yasuhisa. Three-dimensional analysis of systematic biopsy-derived prostate cancer upgrading over targeted biopsy: Potential of target margin and surrounding region sampling using magnetic resonance-ultrasound image fusion systems INTERNATIONAL JOURNAL OF UROLOGY. 2021.01; 28(1); 127-129

- 24. Yoshida S, Matsushima H, Fujii Y. Classification of oligometastatic prostate cancer with additional consideration for hormone sensitivity. World journal of urology. 2021.01;
- 25. Matsuoka Yoh, Uehara Sho, Yoshida Soichiro, Tanaka Hajime, Yokoyama Minato, Fujii Yasuhisa. Three-dimensional analysis of systematic biopsy-derived prostate cancer upgrading over targeted biopsy: Potential of target margin and surrounding region sampling using magnetic resonance-ultrasound image fusion systems(和訳中) International Journal of Urology. 2021.01; 28(1); 127-129
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Clinical Laboratory

General Manager -Professor : Shuji Tohda

Associate Manager -Junior Associate Professor : Tadashi Kanouchi

Assistant Professor : Ayako Nogami Assistant Professor : Sayuri Nitta Assistant Professor : Mie Ochida Medical Staff : Hirokazu Natsui

(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.
- 9) Typing of SARS-CoV-2 variants by PCR.

(3) Education

We lecture on clinical laboratory medicine and give technical training on clinical laboratory tests and physiolosical 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 14 junior residents of university hospital in 2021.

(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. Takahiro Kameda, Yuna Horiuchi, Shitsuko Shimano, Kouji Yano, Shao-Jui Lai, Naoya Ichimura, Shuji Tohda, Yuriko Kurihara, Minoru Tozuka, Ryunosuke Ohkawa. N-homocysteinylation of high-density lipoprotein on endothelial repair function. Biol Chem. 2021.08;
- Nagano K, Tani-Sassa C, Iwasaki Y, Takatsuki Y, Yuasa S, Takahashi Y, Nakajima J, Sonobe K, Ichimura N, Nukui Y, Takeuchi H, Tanimoto K, Tanaka Y, Kimura A, Tohda S. SARS-CoV-2 R.1 lineage variants prevailed in Tokyo in March 2021. Journal of medical virology. 2021.07;
- 3. Takahiro Mitsumura, Tsukasa Okamoto, Tsuyoshi Shirai, Yuki Iijima, Rie Sakakibara, Takayuki Honda, Masahiro Ishizuka, Junichi Aiboshi, Tomoya Tateishi, Meiyo Tamaoka, Hidenobu Shigemitsu, Hirokuni Arai, Yasuhiro Otomo, Shuji Tohda, Tatsuhiko Anzai, Kunihiko Takahashi, Shinsuke Yasuda, Yasunari Miyazaki. Predictors associated with clinical improvement of SARS-CoV-2 pneumonia. J Infect Chemother. 2021.06; 27(6); 857-863
- 4. Azusa Yamazaki, Ryunosuke Ohkawa, Yuka Yamagata, Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Naoya Ichimura, Shuji Tohda, Minoru Tozuka. Apolipoprotein C-II and C-III preferably transfer to both high-density lipoprotein (HDL)2 and the larger HDL3 from very low-density lipoprotein (VLDL). Biol Chem. 2021.05; 402(4); 439-449
- 5. Sonoda Y, Itoh M, Tohda S. Effects of HOXA9 Inhibitor DB818 on the Growth of Acute Myeloid Leukaemia Cells. Anticancer Research. 2021.04; 41(4); 1841-1847
- 6. Yamazaki Azusa, Ohkawa Ryunosuke, Yamagata Yuka, Horiuchi Yuna, Lai Shao-Jui, Kameda Takahiro, Ichimura Naoya, Tohda Shuji, Tozuka Minoru. Apolipoprotein C-II and C-III preferably transfer to both high-density lipoprotein (HDL)(2) and the larger HDL3 from very low-density lipoprotein (VLDL) BIOLOGICAL CHEMISTRY. 2021.03; 402(4); 439-449
- 7. Shitsuko Shimano, Ryunosuke Ohkawa, Mayu Nambu, Mai Sasaoka, Azusa Yamazaki, Yuki Fujii, Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Naoya Ichimura, Koji Fujita, Shuji Tohda, Minoru Tozuka. Marked Changes in Serum Amyloid A Distribution and High-Density Lipoprotein Structure during Acute Inflammation. Biomed Res Int. 2021; 2021; 9241259

[Conference Activities & Talks]

1. Mina Nakagawa, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhiro Asahina. Factors associated with HCC development and patients' survival in patients with an SVR. JSH International Liver Conference 2021 2021.10.03

- 2. 野上 彩子, 岡田 啓五, 本村 鷹多朗, 吉藤 康太, 東田 修二, 長尾 俊景. Inhibition of USP14 induces apoptosis in FLT3-ITD-positive AML cells through upregulation of Nrf-2(和訳中). 日本血液学会学術集会 2021.09.01
- 3. 吉藤 康太, 本村 鷹多朗, 野上 彩子, 岡田 啓五, 東田 修二, 長尾 俊景. Involvement of TPL2/p105/STAT3 axis in tumorigenesis of ABC-DLBCL(和訳中). 日本血液学会学術集会 2021.09.01
- 4. 木村 萌, 西山 優, 上田 浩樹, 有松 朋之, 久保木 麻衣, 高畑 篤, 斎藤 真貴子, 東田 修二, 野上 彩子. Perioperative management of a PNH patient treated with ravulizumab: in case of gallstone disease(和訳中). 日本血液 学会学術集会 2021.09.01
- 1. Inhibition of USP14 induces apoptosis in FLT3-ITD-positive AML cells through upregulation of Nrf-2. 2021.09.23
- 2. Moyu KIMURA,Yu NISHIYAMA,Hiroki UEDA,Tomoyuki ARIMATSU,Mai KUBOKI,Atsushi TAKAHATA,Makiko SAITO,Shuji TOHDA,Ayako NOGAMI. Perioperative management of a PNH patient treated with ravulizumab: in case of gallstone disease. The 83rd Annual Meeting of the Japanese Society of Hematology 2021.09.23 Sendai

Hyperbaric Medical Center

Senior Director and Clinical Professor; Kazuyoshi YAGISHITA Assistant Professor ; Toshiyuki OHHARA Specially Appointed Assistant Professor ; Mikio SHIODA(~2021.3) ,Naoki YAMAMOTO(~2021.3) , Takashi HOSHINO Adjunct Lecturer; Yasushi KOJIMA, Yumi NIIZEKI,Tkuya OYAIZU Researcher; Masaki HORIE, Toshihiro KONDOH, Naohiro MITSUMOTO Staff Assistant; Kiyomi ITOH

(1) **Outline**

Hyperbaric oxygen therapy (HBO), which can dissolve oxygen in serum in population to atomic pressure and transport oxygen to ischemic tissue, is an established therapy for treatment of several conditions, including decompression illness, carbon monoxide poisoning, acute arterior 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 2021, 1,617 times hyperbaric oxygen therapy (HBO) in 185 $\,$ $\,$ patients were performed in the university hospital.

(5) Publications

[Original Articles]

- 1. Naoki Yamamoto, Ryohei Takada, Takuma Maeda, Toshitaka Yoshii, Atsushi Okawa, Kazuyoshi Yagishita. Microcirculation and tissue oxygenation in the head and limbs during hyperbaric oxygen treatment. Diving Hyperb Med. 2021.12; 51(4); 338-344
- 2. Hirohata K, Aizawa J, Ohmi T, Ohji S, Yagishita K. Characteristics of ground reaction force and frontal body movement during failed trials of single-leg lateral drop jump-landing task. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.10; 26; 8-14
- 3. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Jinno T, Koga H, Yagishita K. Characteristics of landing impact in athletes who have not returned to sports at the pre-injury competition level after anterior cruciate ligament reconstruction. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.07; 25; 47-52
- 4. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Injury-related fear in athletes returning to sports after anterior cruciate ligament reconstruction A quantitative content analysis of an open-ended questionnaire. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.07; 25; 1-7
- 5. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. The psychological readiness to return to sports of patients with anterior cruciate ligament reconstruction preoperatively and 6 months postoperatively PHYSICAL THERAPY IN SPORT. 2021.07; 50; 114-120
- 6. Aizawa Junya, Hirohata Kenji, Ohji Shunsuke, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Correlations between isokinetic knee torques and single-leg hop distances in three directions in patients after ACL reconstruction BMC SPORTS SCIENCE MEDICINE AND REHABILITATION. 2021.04; 13(1); 38
- 7. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Jinno T, Koga H, Yagishita K. Single-leg hop distance normalized to body height is associated with the return to sports after anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2021.04; 8(1); 26
- Ohji S, Aizawa J, Hirohata K, Mitomo S, Ohmi T, Jinno T, Koga H, Yagishita K. Athletic identity and sport commitment in athletes after anterior cruciate ligament reconstruction who have returned to sports at their pre-injury level of competition. BMC sports science, medicine & rehabilitation. 2021.04; 13(1); 37
- 9. Naoki Yamamoto, Takuya Oyaizu, Kazuyoshi Yagishita, Mitsuhiro Enomoto, Masaki Horie, Atsushi Okawa. Multiple and early hyperbaric oxygen treatments enhance muscle healing after muscle contusion injury: a pilot study. Undersea Hyperb Med. 2021.04; 48(3); 227-238
- 10. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Single-leg hop can result in higher limb symmetry index than isokinetic strength and single-leg vertical jump following anterior cruciate ligament reconstruction. The Knee. 2021.02; 29; 160-166

[Others]

 Multiplace Hyperbaric Chambers of Japan: RCN Bulletin Issue 5: February 2021, 2021.02 Newsletter of the DAN Recompression Chamber Network RCN Bulletin Issue 5: February 2021 https://dan.org/safety-prevention/chamber-operation-safety/safety-resources-chamber-operators/
Sports Medicine Center

Director and Clinical Professor; Kazuyoshi YAGISHITA Head Physical Therapist ; Kenji HIROHATA Assistant Professor ; Toshiyuki OHHARA Specially Appointed Assistant Professor ; Mikio SHIOTA (~ 2021.3) , Takashi HOSHINO (2021.4~) , Etsuko MATSUMURA (2021.4~) Physical Therapist ; Takehiro OHMI, Sho MITOMO, Shunsuke OHJI Adjunct Lecturer ; Tomohiko TATEISHI Staff Assistant; Kiyomi ITOH

(1) **Publications**

- 1. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Yuji Kohno, Ichiro Sekiya. Surgical Repair of Symptomatic Wrisberg Variant Discoid Lateral Mensicus with Pull-Out Repair and Capsulodesis. Arthrosc Tech. 2021.12; 11(1); e61-e68
- 2. Hirohata K, Aizawa J, Ohmi T, Ohji S, Yagishita K. Characteristics of ground reaction force and frontal body movement during failed trials of single-leg lateral drop jump-landing task. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.10; 26; 8-14
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- 4. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Injury-related fear in athletes returning to sports after anterior cruciate ligament reconstruction - A quantitative content analysis of an open-ended questionnaire. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.07; 25; 1-7
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- 6. Aizawa Junya, Hirohata Kenji, Ohji Shunsuke, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Correlations between isokinetic knee torques and single-leg hop distances in three directions in patients after ACL reconstruction BMC SPORTS SCIENCE MEDICINE AND REHABILITATION. 2021.04; 13(1); 38
- 7. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Jinno T, Koga H, Yagishita K. Single-leg hop distance normalized to body height is associated with the return to sports after anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2021.04; 8(1); 26
- Ohji S, Aizawa J, Hirohata K, Mitomo S, Ohmi T, Jinno T, Koga H, Yagishita K. Athletic identity and sport commitment in athletes after anterior cruciate ligament reconstruction who have returned to sports at their pre-injury level of competition. BMC sports science, medicine & rehabilitation. 2021.04; 13(1); 37

- 9. J-S An, K Tsuji, H Onuma, N Araya, M Isono, T Hoshino, K Inomata, J Hino, M Miyazato, H Hosoda, K Kangawa, Y Nakagawa, H Katagiri, K Miyatake, I Sekiya, T Muneta, H Koga. Inhibition of fibrotic changes in infrapatellar fat pad alleviates persistent pain and articular cartilage degeneration in monoiodoacetic acid-induced rat arthritis model. Osteoarthritis Cartilage. 2021.03; 29(3); 380-388
- 10. Weiding Cui, Yusuke Nakagawa, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Takashi Hoshino, Aritoshi Yoshihara, Ichiro Sekiya, Hideyuki Koga. Knee laxity, lateral meniscus tear and distal femur morphology influence pivot shift test grade in ACL injury patients. Knee Surg Sports Traumatol Arthrosc. 2021.02; 29(2); 633-640
- Kinjo Rio, Wada Takahiro, Churei Hiroshi, Ohmi, Takehiro, Hayashi Kairi, Yagishita Kazuyoshi, Uo Motohiro, Ueno Toshiaki. Development of a Wearable Mouth Guard Device for Monitoring Teeth Clenching during Exercise Sensors. 2021.02; 21(4); 1503
- 12. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Single-leg hop can result in higher limb symmetry index than isokinetic strength and single-leg vertical jump following anterior cruciate ligament reconstruction. The Knee. 2021.02; 29; 160-166

Center for Transfusion Medicine and Cell Therapy

Director: Ichiro Sekiya (Center for Stem Cell and Regenerative Medicine/Professor)

Vise Director: Michiko Kajiwara (Center for Transfusion Medicine and Cell Therapy/Junior Associate Professor) Vise Director: Hisako Katano (Center for Stem Cell and Regenerative Medicine/Junior Associate Professor) Quality control manager: Norio Shimizu (Center for Stem Cell and Regenerative Medicine/Associate Professor) Product manager: Mitsuru Mizuno (Center for Stem Cell and Regenerative Medicine/Project Assistant Professor) Specially Appointed Assistant Professor: Shihoko Suwa(Center for Transfusion Medicine and Cell Therapy) Project Researcher: Kei-ichiro Komori (Center for Stem Cell and Regenerative Medicine)

Head Medical Technologist: Naoki Ohtomo

Section Chief Medical Technologist: Keiko Aikawa

Assisitant Section Chief Medical Technologist: Yukiko Ohishi

Medical Technologist: Yukari Usui, Chihiro Itoh, Tomoko Kamiyama, Miho Yamasaki, Misaki Chiba,

Akiko Shiraishi, Mei Tanaka, Yukiko Kuroki, Sumire Fujiki

Technician: Ayako Tsuji, Yuri Kohno

Clerical Assistant: Jun Kusano, Saki Nishimura

(1) Outline

Center for Transfusion Medicine and Cell Therapy provides "Blood Transfusion", "Cell Therapy" and "Regenerative Medicine" to assist and regenerate dysfunctional tissues and organs.

In the Blood Transfusion group, Japan Society of Blood Transfusion and Cell Therapy Association certified doctors, certified blood transfusion laboratory stuffs, and cell therapy certified administrators enroll. We cover blood transfusion testing, blood product management, safety measures up to the implementation of blood transfusion including blood transfusion certification, and blood transfusion history management. We perform safe and appropriate blood transfusion therapy and hematopoietic stem cell transplantation.

In the Cell Therapy group, we set up a cell processing facility with the aim of putting the world's top level of regenerative medicine and cell therapy into practical use. Japan Society of Regenerative Medicine certified doctors and clinical culture specialists process cells for clinical research and trials there. We support the practical application of useful regenerative medicine procedures inside and outside our university.

(2) Research

· Blood Transfusion group

1)The practice of safe and appropriate transfusion therapy

(including prevention of medical accident related transfusion)

2)Basic and clinical research of hematopoietic stem cell transplantation

 \cdot Cell Therapy group

1)Development of innovative techniques for quality assurance of cell products

2)Development of a novel measure for rapid and sensitive detection of multiple pathogens

3)Development of multi-virus specific T lymphocytes for adoptive immunotherapy

(Department of Pediatrics and Developmental Biology)

4)Research on a regeneration system of the cartilage from the synovial membrane (Department of Orthopedic Surgery) 5)Development of novel peptide-pulsed dendritic therapy for adult T-cell leukemia (Department of Immunotherapeutics/ Department of Hematology)

6)Development of organoid-based therapy for inflammatory bowel disease

(Department of Gastroenterology & Hepatology, Advanced Research Institute)

(3) Education

· Blood Transfusion group

Transfusion therapy is supplementation of the blood component, but it also has aspects of cell therapy and transplantation. So, it is important to practice safe and appropriate transfusion therapy. Clinical tests of transfusion, such as blood type test, are the most basic immunological test technique. The accurate understanding and practice of these tests is also necessary for the safety of the medical treatment. From this point of view, we educate the students of the school of medicine, school of allied health sciences, a graduate school of medical and dental sciences, medical doctors, and co-medicals.

· Cell Therapy group

Center of Cell Therapy assist to prepare standard operation procedure (SOP) and offer on-the-job training for cell processing/ manipulating procedures and that for quality assurance at the center. Facility for the education and training were recently installed at the CPC annex.

(4) Clinical Services & Other Works

Blood transfusion Services (The result of 2021)

- 1) The number of blood products used
 - Red cell component products 8,820 Units (4,468 bags)
 Platelet concentration 20,415 Units (1,780 bags)
 Fresh frozen plasma 5,801 Units (2,862 bags)
 Allogenic cryoprecipitate 144 Units (36 bags)
- 2) Autologous blood collection and transfusion Autologous blood collection 195 cases (283 times, 554Units) Autologous blood transfusion 174 cases (448 Units)

 3) The number of clinical tests of transfusion Blood typing 7,255 Anti-red blood cell antibody test 4,560 Crossmatch tests 5,648

- Cell Therapy Services (The result of 2021)
- 1) Hematopoietic stem cell harvest
 - Autologous peripheral blood stem cell harvest 13cases 16 times Allogenic peripheral blood stem cell harvest 5 cases 5 times Allogenic bone marrow harvest 9 cases 9 times (Including Japan Marrow Donor Program donors)
- 2) Cryopreservation of hematopoietic stem cells 22 times
- 3) Hematopoietic stem cell transplantation
- (The evaluation and preservation of the stem cells were done in our department) Autologous peripheral blood stem cell transplantation 8 cases 8 times Allogenic peripheral blood stem cell transplantation 4 cases 4 times Allogenic bone marrow transplantation 12 cases 12 times Allogenic umbilical cord blood transplantation 1 case 1 time
- 4) Donor lymphocyte infusion 2 cases 4 times
- 5) CAR-T therapy
 - Obtained Kymriah facility certification at the end of October 2019 2021 Autologous peripheral blood mononuclear cell collection 9 cases 9 times Tisagen Recleucell administration 10 cases 10 times

The cell products currently prepared in our center include

- #1 Synovium-derived mesenchymal stem cells
- #2 Regenerative Medicine (HeartSheet) 1 case 1 time
- #3 Autologous Protein Solution (APS: concentrated Platelet-Rich Plasma) 5 cases 5 times

(5) Clinical Performances

· Blood Transfusion group

We provide safe and wide of variation transfusion therapy. We cope with highly urgent blood transfusion of critical care center and blood transfusion with a high specialty such as NICU. In the area of hematopoietic stem cell transplantation, we closely cooperate with the clinical department. Transfusion medicine staffs mainly conduct collection, evaluation, processing, and storage of cells.

\cdot Cell Therapy group

Our center in TMDU Medical Hospital was renovated and re-started operation as of March 2015. We have five Central Clinical Facilities independent cell processing rooms (class 10,000 clean rooms). All the rooms are equipped with a bio-safety cabinet. The hardware, as well as software used in our center, fulfills all the guidelines that are required for the preparation of cell products of clinical grade.

(6) **Publications**

- 1. Katsuaki Yanagisawa, Toshifumi Watanabe, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta, Tetsuya Jinno. Do the distal femur and the proximal tibia have narrower aspect ratios in smaller knees? : A morphological analysis of osteoarthritic knees in the Japanese population using computed tomography. Knee. 2021.12; 33; 84-92
- 2. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Yuji Kohno, Ichiro Sekiya. Surgical Repair of Symptomatic Wrisberg Variant Discoid Lateral Mensicus with Pull-Out Repair and Capsulodesis. Arthrosc Tech. 2021.12; 11(1); e61-e68
- 3. Mitsuru Mizuno, Kentaro Endo, Hisako Katano, Naoki Amano, Masaki Nomura, Yoshinori Hasegawa, Nobutake Ozeki, Hideyuki Koga, Naoko Takasu, Osamu Ohara, Tomohiro Morio, Ichiro Sekiya. Transplantation of human autologous synovial mesenchymal stem cells with trisomy 7 into the knee joint and 5 years of follow-up. Stem Cells Transl Med. 2021.11; 10(11); 1530-1543
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- 8. Hisako Katano, Nobutake Ozeki, Yuji Kohno, Yusuke Nakagawa, Hideyuki Koga, Toshifumi Watanabe, Tetsuya Jinno, Ichiro Sekiya. Trends in arthroplasty in Japan by a complete survey, 2014-2017. J Orthop Sci. 2021.09; 26(5); 812-822

- 9. Tsubasa Okano, Akira Nishimura, Kento Inoue, Takuya Naruto, Shown Tokoro, Takahiro Tomoda, Takahiro Kamiya, Asami Simbo, Yuko Akutsu, Keisuke Okamoto, Tzuwen Yeh, Takeshi Isoda, Masakatsu Yanagimachi, Michiko Kajiwara, Kohsuke Imai, Hirokazu Kanegane, Masaaki Mori, Tomohiro Morio, Masatoshi Takagi. Somatic mutation in RUNX1 underlies mucocutaneus inflammatory manifestations Rheumatology (Oxford). 2021.09;
- Misaki Yagi, Mitsuru Mizuno, Ryota Fujisawa, Hisako Katano, Kentaro Endo, Nobutake Ozeki, Yuriko Sakamaki, Hideyuki Koga, Ichiro Sekiya. Optimal Pore Size of Honeycomb Polylactic Acid Films for In Vitro Cartilage Formation by Synovial Mesenchymal Stem Cells. Stem Cells Int. 2021.08; eCollection; 2021:9239728
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- 21. Kiyotaka Horiuchi, Mitsuru Mizuno, Hisako Katano, Kentaro Endo, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Optimal initial cell density that yields the highest number of primary synovial mesenchymal stem cells in a clinical setting. J Med Dent Sci. 2021.04; 68; 17-26

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- 25. Toshifumi Watanabe, Kazuyoshi Gamada, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta, Tetsuya Jinno. Characteristic kinematics of floor-sitting activities after posterior-stabilized total knee arthroplasty determined using model-based shape-matching techniques. Knee. 2021.03; 29; 571-579
- 26. Weiding Cui, Yusuke Nakagawa, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Takashi Hoshino, Aritoshi Yoshihara, Ichiro Sekiya, Hideyuki Koga. Knee laxity, lateral meniscus tear and distal femur morphology influence pivot shift test grade in ACL injury patients. Knee Surg Sports Traumatol Arthrosc. 2021.02; 29(2); 633-640
- 27. Nobutake Ozeki, Yuji Kohno, Yoshihisa Kushida, Naoto Watanabe, Mitsuru Mizuno, Hisako Katano, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Synovial mesenchymal stem cells promote the meniscus repair in a novel pig meniscus injury model. J. Orthop. Res. 2021.01; 39(1); 177-183
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- 2. Nobutake Ozeki, Hiroki Katagiri, Yusuke Nakagawa , Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga.. Ramp lesions in anterior cruciate ligament deficient knees.. 2nd International Knee Day 2021.03.18 WEB
- 3. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Yuji Kohno, Hisako Katano, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya.. 3D MRI Analysis For Cartilage In Anterior Cruciate Ligament Deficient Knees Using Radially Projected Images.. Orthopaedic Research Society 2021 Annual Meeting 2021.02.12 California, USA
- 4. Yugo Miura, Nobutake Ozeki, Yuji Kohno, Hisako Katano, Hayato Aoki, Noriya Okanouchi, Makoto Tomita, Kenji Suzuki, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya.. Difference In The Joint Space Of The Medial Knee Compartment Between Full Extension And Rosenberg Weight-bearing Radiographs.. Orthopaedic Research Society 2021 Annual Meeting 2021.02.12 California,USA
- 1. SHIMIZU Norio. Study of blood diseases caused by EB virus-infected T/NK cells.. 20th Hematological Malignancy Webinar 2021.09.15 Tokyo Japan.

Dental Clinic for Sleep Disorders (Apnea and Snoring)

Junior Associate Professor (Clinic Chief) Masayuki HIDESHIMA Hospital Staff Mai MIYACHI Hospital Staff Akitake HATTORI Minoru FURUHATA Adjunct Assistant Professor Adjunct Assistant Professor Nanami SAITOH Adjunct Assistant Professor Shuhei NAKAMURA Project Assistant Professor Hiroyuki ISHIYAMA (concurrently with TMJ CLinic) Adjunct Assistant Professor Yuko MITSUMA (concurrently with Oral Diagnosis and General Dentistry) Dental technician Hisashi MATSUBARA (concurrently with Dental Laboratory) Dental technician Tatsu SUZUKI (concurrently with Dental Laboratory) Dental technician Koichi ENOMOTO (concurrently with Dental Laboratory) Assistant Clerk Naoko OBATA

(1) Outline

This clinic was established in October 2012 and provides dental treatment for relatively mild patients with obstructive sleep apnea who repeats apnea and snoring during sleep. Currently, about 230,000 people are diagnosed with OSA and are being treated in Japan, and the number of potential patients is said to be as high as 2 million. Since OSA patients sleep lightly, they do not only interfere with their daily lives such as strong drowsiness during the day and lack of concentration, but also have a high risk of diseases such as hypertension, diabetes, myocardial infarction, and cerebrovascular accident.

For OSA with apnea and hypopnea frequency (Apnea Hypopnea Index: AHI) of 20 or more per hour during sleep, wear a nasal mask called CPAP (Continuous Positive Airway Pressure) at the medical hospital to support breathing. The treatment is covered by social medical insurance in Japan. On the other hand, if AHI is less than 20, CPAP cannot be covered by social insurance, so in dentistry, a mouthpiece (sleep sprint) called Oral Appliance (OA) is delivered to protrude the lower jaw, preventing from the tongue sinking, enlarge the pharyngeal airway and make it easier to breathe. Therefore, CPAP is usually applied to relatively severe OSA, and OA is usually applied to mild OSA.

However, even if OA is not as effective as CPAP, it has the advantages of excellent portability and less discomfort during sleep. It is often used in patients who cannot continue to use CPAP even if AHI is 20 or more. Also, it is often used in patients with severe OSA who has pollinosis or business trips.

In this way, in order to treat diseases in the medical field across multiple fields of medicine and dentistry, cooperation with many clinical departments is indispensable. In Tokyo medical and dental university, the sleep apnea center cooperates with the department of respiratory, psychiatry, and otorhinolaryngology cooperates with dental clinic for sleep disorder which cooperate with dental prosthetics department, general dentistry, TMD department, and engineering department work together. We provide collaborative medical care with outpatients, hold regular conferences, and consider more effective treatment methods.

(2) Research

At the conference with sleep apnea medical center, we are planning and discussing research, making presentations at specialized academic societies, planning symposiums, formulating clinical practice guidelines, and conducting activities such as applying for research funds.

The outline of the research is as follows.

- Transition of outpatient SAS cases and clinical usefulness of OA therapy.
- Effects of Nursing Home on Temporomandibular Joint Pain for Obstructive Sleep Apnea Syndrome Using OA. Double-Blind Randomized Comparative Study
- Effects of long-term use of upper and lower integrated OA on the orofacial in OSA patients
- Development of a system for determining the therapeutic effect of OA on OSA patients
- Development and application of OA treatment prediction model for OSA patients
- Effects of lifestyle factors on the rapeutic effect in her OA therapy for OSA patients
- Development of non-contact screening methods for OSA patients
- An open study of the effects of hyperbaric oxygen therapy on sleep

(3) Education

In order to provide OA treatment by insurance for OSA patients in a dental clinic for sleep disorder, it is necessary to perform a sleep test at a medical hospital and diagnose sleep apnea syndrome by physician. No insurance treatment is available in dentistry without a referral letter and a summary of sleep test.

To fabricate OA, the maxillary and mandibular impressions are taken, the bite registration with mandibular anterior positions taken, and the upper and lower OA are prepared separately, and trial fitting and adjustment are performed in the oral. If OA covered by insurance, it is necessary to glue the upper and lower OA pieces with an immediate polymerization resin and attach them together. On the other hand, in OA that is not covered by insurance, the maxilla and mandibulae are separated, and there is a freedom in the range of movement without retracting the lower jaw, so there is less burden on the TMJ, snoring and apnea are reduced, and patient can be obtained more comfortable sleep.

If dentist adjust OA, and a patient can wear it every night, it is necessary to refer a patient to medical hospital to take sleep study test.

Medical treatments are coordinated in both medical and dental clinic, and conferences are held regularly to consider more effective treatment methods. In addition, dental clinic for sleep disorder accepts patient requests from off-campus medical sleep clinics, and proceed with OA treatment, requesting referrals to primary physician, and provide regular examinations.

(4) Clinical Services & Other Works

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(5) Clinical Performances

Taking advantage of the characteristics of our university, which has both medical and dentistry, we carry out close collaborative medical treatment and information exchange between the sleep apnea center and dental clinic for sleep disorder, and practice tailor-made treatment suitable for each case.

In dental clinic for sleep disorder, the staff of the dental prosthetics department, general dentistry, TMD department, and engineering department, which specialize in dental prosthodontics, oral diagnosis, orofacial

pain control, and dental engineering, cooperate to OA treatment of OSA patients.

Although it is difficult to fabricate OA for edentulous or partial missing teeth dentition even in dentistry, OA can be applied to these cases because the specialist of the prosthesis department and engineering department handles it, and it is possible to improve general health and QOL of OSA patient.

In addition, OA therapy, in which the mandibula is fixed forward during bed time, may cause side effect such as temporomandibular joint pain. However Specialized staff in TMD department provide treatment for pain and preventive therapy to maintain OA compliance.

(6) **Publications**

[Original Articles]

1. Hiroyuki Ishiyama, Masayuki Hideshima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki. Evaluation of Respiratory Resistance as a Predictor for Oral Appliance Treatment Response in Obstructive Sleep Apnea: A Pilot Study. Journal of Clinical Medicine. 2021.03; 10(6); 1255-1268

[Misc]

- 1. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part12 PSG/OCST for The Objective Effect Measurement of Oral Appliance and The Instructive and Coaching Methods for Its Habit Training. the Quintessence. 2021.12; 40(12); 212-219
- 2. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part11 Jaw Exercises, Subjective Assessments of Oral Appliance, and Mandibular Advancement Titration. the Quintessence. 2021.11; 40(11); 190-199
- 3. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part10 The Fabrication, Adjustment and Delivery of the OA. the Quintessence. 2021.10; 40(10); 212-221
- 4. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part9 Protrusive Bite Fundamentals in Preparation of Oral Appliance. the Quintessence. 2021.09; 40(9); 204-211
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part8 Perfect Techniques for Impression Taking in Preparation of Oral Appliances. the Quintessence. 2021.08; 40(8); 196-201
- 6. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part7 The Treatment Planning and Consultation in Dental Sleep Medicine. the Quintessence. 2021.07; 40(7); 220-227
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part6 The Preprocedural Testing of Sleep-Related Breathing Disorders Necessary to Make Oral Appliances. the Quintessence. 2021.06; 40(6); 228-239
- Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part5 The Testing of Sleep Apnea Syndrome and the Exploratory Data Analysis Method for Its Outcomes. the Quintessence. 2021.05; 40(5); 250-260
- 9. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part4 How to Counsel Someone with Sleep Disorders. the Quintessence. 2021.04; 40(4); 254-264
- 10. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part3 The Definition and Description of Sleep and of sleep disorders. the Quintessence. 2021.03; 40(3); 224-231
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[Conference Activities & Talks]

- 1. Mai Miyachi. Approach for the side effects of Mandibular Advanced Device treatment for Obstructive Sleep Apnea in the United States. The 20th Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2021.11.28 Kitakyuusyuu Convention Center
- NORITAKE Kanako, SUNAGA Masayo, EBIHARA Arata, HIDESHIMA Masayuki, TONAMI Ken-ichi, UMEMORI Sachi, KANAMORI Yuna, KINOSHITA Atsuhiro, NITTA Hiroshi. A Trial of Online Examination for Recruitment of Dental Residents at Dental Hospital, Tokyo Medical and Dental University. 2021.11.20
- 3. KANAMORI Yuna, NORITAKE Kanako, KIMURA Yasuyuki, KIDO Daisuke, EBIHARA Arata, HIDESHIMA Masayuki, TONAMI Ken-ichi, UMEMORI Sachi, NITTA Hiroshi. TMDU dental trainee residents' ability to evaluate abutment tooth preparation. The 40th General and Scientific Meeting of the Japanese Dental Education Association 2021.11.20 online
- 4. Mai Miyachi. Medical and dental cooperation in sleep apnea treatment, Practice and problems of medical and dental cooperation: Perspective of general dentistry. Japanese Society of Sleep Research 46th Annual Meeting 2021.09.23 Fukuoka Convention Center
- 5. Mai Miyachi. Approach for the side effects of Mandibular Advanced Device treatment for Obstructive Sleep Apnea in the United States. Japanese Society of Sleep Research 46th Annual Meeting 2021.09.23 Fukuoka Convention Center
- 6. Masayuki Hideshima, Takeshi Suganuma, Kentaro Okuno, Eri Makihara. Symposium "Oral appliance therapy for obstructive sleep apnea (OSA)". The 130th Commemorative Scientific Meeting of the Japan Prosthodontic Society 2021.06.20

[Others]

1. Prognosis model of treatment effect for sleep apnea - Non-contacting evaluation of oral appliance therapy -, 2021.04

Masayuki HIDESHIMA Grant-in-Aid for Scientific Research(C) 2018 Research No. 18K09678 Research Period 2018-2021 Principal Investigator Masayuki HIDESHIMA Research Fund \3,500,000

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 (~ 2021.3 月) Physical therapy operator chief ; Kenji HIROHATA Physiotherapist; Takehiro OHMI,Sho MITOMO,Shunsuke OHJI Staff Assistant; Rento HAYASHI,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
- \bigcirc 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 2021 to December 2021)
 Section of out-patient clinic: 3,098
 Section of athletic rehabilitation: 3,788

○ Sports Medicine/Dentistry, Sports dentistry clinic

Sports dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered dental diseases and traumatic injuries. Custom-fitted protective gears such as mouthguard and faceguard against sports-related dental and maxillofacial trauma are also handled for participants in contact sports such as a boxing, American football, rugby football, hockey, lacrosse, and martial art.

(4) **Publications**

- 1. Hiroshi Churei, Ruman Uddin Chowdhury, Yuriko Yoshida, Gen Tanabe, Shintaro Fukasawa, Takahiro Shirako, Takahiro Wada, Motohiro Uo, Hidekazu Takahashi, Toshiaki Ueno. Use of the fiberglass reinforcement method in thermoplastic mouthguard materials to improve flexural properties for enhancement of functionality. Dent Mater J. 2021.12; 40(6); 1338-1344
- 2. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Yuji Kohno, Ichiro Sekiya. Surgical Repair of Symptomatic Wrisberg Variant Discoid Lateral Mensicus with Pull-Out Repair and Capsulodesis. Arthrosc Tech. 2021.12; 11(1); e61-e68
- 3. Naoki Yamamoto, Ryohei Takada, Takuma Maeda, Toshitaka Yoshii, Atsushi Okawa, Kazuyoshi Yagishita. Microcirculation and tissue oxygenation in the head and limbs during hyperbaric oxygen treatment. Diving Hyperb Med. 2021.12; 51(4); 338-344
- 4. Gonda T, Yasui T, Maeda Y, Ishigami K, Ueno T, Matsumoto M, Takamata T, Koide K, Kawara M. Application of sensors to oral appliances: possibilities, problems and prospects International Journal of Sports Dentistry. 2021.10; 14(1); 34-37
- 5. Gonda T, Yasui T, Maeda Y, Ishigami K, Ueno T, Matsumoto M, Takamata T, Koide K, Kawara M. Literature review on relationship between body balance and occlusal status International Journal of Sports Dentistry. 2021.10; 14(1); 38-58
- 6. Gonda T, Yasui T, Maeda Y, Ishigami K, Ueno T, Matsumoto M, Takamata T, Koide K, Kawara M. Proposal for social insurance coverage of sports mouthguards in Japan: survey of oral health professionals International Journal of Sports Dentistry. 2021.10; 14(1); 59-62
- Hirohata K, Aizawa J, Ohmi T, Ohji S, Yagishita K. Characteristics of ground reaction force and frontal body movement during failed trials of single-leg lateral drop jump-landing task. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.10; 26; 8-14
- 8. Kairi Hayashi, Ruman Uddin Chowdhury, Nafees Uddin Chowdhury, Abhishekhi Shrestha, Ishan Pradhan, Sharika Shahrin, Yukako Toyoshima, Gen Tanabe, Yuriko Yoshida, Kaito Togawa, Hiroshi Churei, Toshiaki Ueno. Thickness change and deformation of custom-made mouthguards after two years of use by Bangladeshi field hockey players. Dent Traumatol. 2021.08; 37(4); 617-622

- 9. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Correction: Aung et al. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications. Polymers 2021, 13, 1879 POLYMERS. 2021.07; 13(14); 2280
- 10. Tanabe G, Hasunuma T, Inai Y, Takeuchi Y, Kobayashi H, Hayashi K, Shimizu S, Kamiya N, Churei H, Sumita Y, Suzuki K, Moriya N, Ueno T. Potential assessment of dehydration during high-intensity training using a capacitance sensor for oral mucosal moisture: evaluation of elite athletes in a field-based survey. Chemosensors. 2021.07; 9(8); 196
- 11. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Jinno T, Koga H, Yagishita K. Characteristics of landing impact in athletes who have not returned to sports at the pre-injury competition level after anterior cruciate ligament reconstruction. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.07; 25; 47-52
- 12. Tanabe G, Churei H, Takeuchi Y, Hayashi K, Kanasaki A, Yoshida Y, Toma J, Araie Y, Ueno T. Antibacterial effect of a disinfectant spray for sports mouthguards on Streptococcus sobrinus Dental research journal. 2021.07; 18; 59
- Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Injury-related fear in athletes returning to sports after anterior cruciate ligament reconstruction - A quantitative content analysis of an open-ended questionnaire. Asia-Pacific journal of sports medicine, arthroscopy, rehabilitation and technology. 2021.07; 25; 1-7
- 14. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. The psychological readiness to return to sports of patients with anterior cruciate ligament reconstruction preoperatively and 6 months postoperatively PHYSICAL THERAPY IN SPORT. 2021.07; 50; 114-120
- 15. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications POLYMERS. 2021.06; 13(11); 1879
- 16. Hayashi K, Churei H, Shrestha A, Suzuki T, Matsubara H, Otomaru T, Sumita YI, Uddin Chowdhury R, Uddin Chowdhry N, Ueno T. Fabrication technique of obturator-type sports mouthguard for a patient who had undergone maxillectomy and its speech intelligibility assessment: A case report. Journal of Prosthodontic Research. 2021.06; 65(2); 261-265
- 17. Aizawa Junya, Hirohata Kenji, Ohji Shunsuke, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Correlations between isokinetic knee torques and single-leg hop distances in three directions in patients after ACL reconstruction BMC SPORTS SCIENCE MEDICINE AND REHABILITATION. 2021.04; 13(1); 38
- 18. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Jinno T, Koga H, Yagishita K. Single-leg hop distance normalized to body height is associated with the return to sports after anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2021.04; 8(1); 26
- Ohji S, Aizawa J, Hirohata K, Mitomo S, Ohmi T, Jinno T, Koga H, Yagishita K. Athletic identity and sport commitment in athletes after anterior cruciate ligament reconstruction who have returned to sports at their pre-injury level of competition. BMC sports science, medicine & rehabilitation. 2021.04; 13(1); 37
- Naoki Yamamoto, Takuya Oyaizu, Kazuyoshi Yagishita, Mitsuhiro Enomoto, Masaki Horie, Atsushi Okawa. Multiple and early hyperbaric oxygen treatments enhance muscle healing after muscle contusion injury: a pilot study. Undersea Hyperb Med. 2021.04; 48(3); 227-238
- Toshiaki Ueno, Yukako Toyoshima. The Relationship Between the State of Engagement in Exercise/ Sports and Medical Evaluations: Dental Evaluations Japan Sport Association/ Follow up study on the TOKYO1964 Olympians. 2021.03; 26-27

- 22. Weiding Cui, Yusuke Nakagawa, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Takashi Hoshino, Aritoshi Yoshihara, Ichiro Sekiya, Hideyuki Koga. Knee laxity, lateral meniscus tear and distal femur morphology influence pivot shift test grade in ACL injury patients. Knee Surg Sports Traumatol Arthrosc. 2021.02; 29(2); 633-640
- 23. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Ohmi, Takehiro, Hayashi Kairi, Yagishita Kazuyoshi, Uo Motohiro, Ueno Toshiaki. Development of a Wearable Mouth Guard Device for Monitoring Teeth Clenching during Exercise Sensors. 2021.02; 21(4); 1503
- 24. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Single-leg hop can result in higher limb symmetry index than isokinetic strength and single-leg vertical jump following anterior cruciate ligament reconstruction. The Knee. 2021.02; 29; 160-166
- 25. Nana Shiota, Atsuhiro Kinoshita, Masayo Sunaga, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tomoko Fukai, Masaru Matsumoto, Toshikazu Yasui, Toshiaki Ueno. Effectiveness of computer-assisted learning in sports dentistry: Studies over a multiple-year period and at two universities. Eur J Dent Educ. 2021.01; Online ahead of print;

- 1. Aung TK, Churei H, Tanabe G, Kinjo R, Li C, Tun PS, Ueno T. Shock absorption of 3D-printed ABS and fabric for sports faceguard. FDI 2021 World Dental Congress 2021.09.26 Virtual online
- Tanabe G, Hattori M, Obata S, Takahashi Y, Sumita YI, Ueno T. Psychoacoustic analysis of a clarinet performance with soft type custom-made lip shield to prevent mucosal erosion of lower lip: A case study. 39th Annual PAMA International Symposium 2021.06.24 Live Event on Virtual Platform
- 3. Hattori M, Tanabe G, Nishiyama A, Churei H, Tanase R, Sumita YI. Use of 4D facial scanner in dentistry for musician: Facial surface analysis while recorder playing. 39th Annual PAMA International Symposium 2021.06.24 Live Event on Virtual Platform

Sports Dentistry

(1) Publications

- 1. Hiroshi Churei, Ruman Uddin Chowdhury, Yuriko Yoshida, Gen Tanabe, Shintaro Fukasawa, Takahiro Shirako, Takahiro Wada, Motohiro Uo, Hidekazu Takahashi, Toshiaki Ueno. Use of the fiberglass reinforcement method in thermoplastic mouthguard materials to improve flexural properties for enhancement of functionality. Dent Mater J. 2021.12; 40(6); 1338-1344
- 2. Kairi Hayashi, Ruman Uddin Chowdhury, Nafees Uddin Chowdhury, Abhishekhi Shrestha, Ishan Pradhan, Sharika Shahrin, Yukako Toyoshima, Gen Tanabe, Yuriko Yoshida, Kaito Togawa, Hiroshi Churei, Toshiaki Ueno. Thickness change and deformation of custom-made mouthguards after two years of use by Bangladeshi field hockey players. Dent Traumatol. 2021.08; 37(4); 617-622
- 3. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Correction: Aung et al. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications. Polymers 2021, 13, 1879 POLYMERS. 2021.07; 13(14); 2280
- 4. Tanabe G, Hasunuma T, Inai Y, Takeuchi Y, Kobayashi H, Hayashi K, Shimizu S, Kamiya N, Churei H, Sumita Y, Suzuki K, Moriya N, Ueno T. Potential assessment of dehydration during high-intensity training using a capacitance sensor for oral mucosal moisture: evaluation of elite athletes in a field-based survey. Chemosensors. 2021.07; 9(8); 196
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- 6. Tanabe G, Hasunuma T, Inai Y, Takeuchi Y, Kobayashi H, Hayashi K, Shimizu S, Kamiya N, Churei H, Sumita Y, Suzuki K, Moriya N, Ueno T. Potential Assessment of Dehydration during High-Intensity Training Using a Capacitance Sensor for Oral Mucosal Moisture: Evaluation of Elite Athletes in a Field-Based Survey. CHEMOSENSORS. 2021.07; 9(8);
- 7. Aung Thet Khaing, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Togawa Kaito, Li Chenyuan, Tsuchida Yumi, Tun Phyu Sin, Hlaing Shwe, Takahashi Hidekazu, Ueno Toshiaki. Air Permeability, Shock Absorption Ability, and Flexural Strength of 3D-Printed Perforated ABS Polymer Sheets with 3D-Knitted Fabric Cushioning for Sports Face Guard Applications POLYMERS. 2021.06; 13(11); 1879
- Kinjo Rio, Wada Takahiro, Churei Hiroshi, Ohmi, Takehiro, Hayashi Kairi, Yagishita Kazuyoshi, Uo Motohiro, Ueno Toshiaki. Development of a Wearable Mouth Guard Device for Monitoring Teeth Clenching during Exercise Sensors. 2021.02; 21(4); 1503
- 9. Nana Shiota, Atsuhiro Kinoshita, Masayo Sunaga, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tomoko Fukai, Masaru Matsumoto, Toshikazu Yasui, Toshiaki Ueno. Effectiveness of computer-assisted learning in sports dentistry: Studies over a multiple-year period and at two universities. Eur J Dent Educ. 2021.01; Online ahead of print;

Life Science and Bioethics Research Center

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

- Ishisaka Y, Nosaka N, Mishima Y, Masuda T, Nagashima M, Tanaka Y, Yamamoto K, Yoshida M, Shigemitsu H. COVID-19 case of ventilator-induced lung injury on extracorporeal membrane oxygenation: Physicians' clinical struggle and ethical conflict in a novel pandemic. Clinical case reports. 2021.12; 9(12); e05223
- Aoyama J, Osaka M, Deushi M, Hosoya S, Ishigami A, Maehara T, Yoshida M. CXCL1-Triggered PAD4 Cytoplasmic Translocation Enhances Neutrophil Adhesion through Citrullination of PDIA1. Journal of atherosclerosis and thrombosis. 2021.12;
- Aoyama J, Osaka M, Deushi M, Hosoya S, Ishigami A, Maehara T, Yoshida M. CXCL1-Triggered PAD4 Cytoplasmic Translocation Enhances Neutrophil Adhesion through Citrullination of PDIA1. Journal of atherosclerosis and thrombosis. 2021.12;
- 4. Yusuke Ebana, Sou Hee Yang, Megumu Yokono, Masayuki Yoshida. Establishment of the Certified Research Ethics Professionals: An Ethical Review Expert -Translated in English from Japanese Version. JMA J. 2021.10; 4(4); 405-408
- Ebana Y, Yang SH, Yokono M, Yoshida M. Establishment of the Certified Research Ethics Professionals: An Ethical Review Expert -Translated in English from Japanese Version. JMA journal. 2021.10; 4(4); 405-408
- 6. Ebana Yusuke, Yang Sou Hee, Yokono Megumu, Yoshida Masayuki. Establishment of the Certified Research Ethics Professionals: An Ethical Review Expert: Translated in English from Japanese Version(和 訳中) JMA Journal. 2021.10; 4(4); 405-408

- Masuda T, Uchimido R, Nosaka N, Akiyama H, Kamisato A, Yoshida M. Concerns in Methodology for Self-Administered Questionnaire: Needs for Involvement of Social Scientists. Chest. 2021.07; 160(1); e92-e93
- 8. Ikeda Sadakatsu, Kudo Ryo, Yamashita Yamato, Noji Rika, Yokobori Jyunko, Ohki Mika, Takamine Eriko, Kobayashi Yumi, Egawa Makiko, Ebana Yusuke, Kimura Koichiro, Yokoyama Kohta, Onishi Iichiro, Takemoto Akira, Kirimura Susumu, Kinowaki Yuko, Tanimoto Kosuke, Miya Fuyuki, Kano Yoshihito, Yoshida Masayuki, Miyake Satoshi. Clinical utility of multi-disciplinary expert panel discussion in precision cancer medicine ANNALS OF ONCOLOGY. 2021.07; 32; S287
- 9. Ikeda Sadakatsu, Kudo Ryo, Yamashita Yamato, Noji Rika, Yokobori Jyunko, Ohki Mika, Takamine Eriko, Kobayashi Yumi, Egawa Makiko, Ebana Yusuke, Kimura Koichiro, Yokoyama Kohta, Onishi Iichiro, Takemoto Akira, Kirimura Susumu, Kinowaki Yuko, Tanimoto Kosuke, Miya Fuyuki, Kano Yoshihito, Yoshida Masayuki, Miyake Satoshi. Clinical utility of multi-disciplinary expert panel discussion in precision cancer medicine ANNALS OF ONCOLOGY.. 2021.07;
- 10. Myunghee Hong, Yusuke Ebana, Jaemin Shim, Eue-Keun Choi, Hong Euy Lim, Inseok Hwang, Hee Tae Yu, Tae-Hoon Kim, Jae-Sun Uhm, Boyoung Joung, Seil Oh, Moon-Hyoung Lee, Young-Hoon Kim, Sun Ha Jee, Hui-Nam Pak. Ethnic similarities in genetic polymorphisms associated with atrial fibrillation: Far East Asian vs European populations. Eur J Clin Invest. 2021.05; e13584
- Nagaoka E, Arai H, Ugawa T, Masuda T, Ochiai K, Tamaoka M, Kurashima N, Oi K, Fujiwara T, Yoshida M, Shigemitsu H, Otomo Y. Efficacy of Multidisciplinary Team Approach with Extracorporeal Membrane Oxygenation for COVID-19 in Low Volume ECMO center. Artificial organs. 2021.03;
- 12. Dewan SMR, Osaka M, Deushi M, Yoshida M. Complement C5a-triggered differentiated HL-60 stimulates migration of THP-1 monocytic leukocytes via secretion of CCL2. FEBS open bio. 2021.03;
- 13. Dewan Syed Masudur Rahman, Osaka Mizuko, Deushi Michiyo, Yoshida Masayuki. C5a-stimulated Neutrophil-like Differentiated HL-60 Induced Migration of Monocytic THP-1 through the Secretion of MCP-1(和訳中) 日本循環器学会学術集会抄録集. 2021.03; 85 回; OE029-5
- 14. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. Complement Factor D Facilitates the Development of Fatty Liver under Long-term but not Short-term High-fat Diet-feeding Conditions(和訳中) 日本循環器学 会学術集会抄録集. 2021.03; 85 回; OE113-3
- 15. Osaka M, Deushi M, Aoyama J, Funakoshi T, Ishigami A, Yoshida M. High-Fat Diet Enhances Neutrophil Adhesion in LDLR-Null Mice Via Hypercitrullination of Histone H3. JACC. Basic to translational science. 2021.06; 6(6); 507-523

[Misc]

1. Yusuke Ebana, Tetsushi Furukawa. Up-to-date knowledge for genetic diagnosis of inherited arrhythmia syndrome Heart View. 2021.07; 25(7); 648-651

- 1. 青山 二郎, 大坂 瑞子, 吉田 雅幸. CXCL1 誘導性好中球接着亢進に好中球 Peptidylarginine deiminase 4 に よる細胞 質シトルリン化を介する integrin 活性化が 関与する. 第 29 回日本血管生物医学会学術集会 (心血 管代謝週間 2021) 2021.12.10 web
- Dewan Syed Masudur Rahman, Osaka Mizuko, Deushi Michiyo, Yoshida Masayuki. C5a 刺激により好 中球様細胞に分化した HL-60 が MCP-1 分泌を介して単球性 THP-1 の遊走を誘発する (C5a-stimulated Neutrophil-like Differentiated HL-60 Induced Migration of Monocytic THP-1 through the Secretion of MCP-1). 日本循環器学会学術集会抄録集 2021.03.01
- 3. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. 補体 D 因子は長期高脂肪食条件下で脂肪肝の発生を 促進する (Complement Factor D Facilitates the Development of Fatty Liver under Long-term but not Short-term High-fat Diet-feeding Conditions). 日本循環器学会学術集会抄録集 2021.03.01

[Others]

- Grant-in-Aid for Young Scientists (B) JSPS KAKENHI (16K19048) S-nitrosylation, a novel posttranslational protein modification, mediated glycolipid metabolism disorder and chronic inflammation. 2016-2017
- 2. Takeda Science Foundation for Medical Research The missing link between the metabolic syndrome pathogenesis and chronic inflammation. 2016-2018
- 3. Grant-in-Aid for Exploratory Research JSPS KAKENHI (16K15120) Elucidation of a role of de-nitrosylation in septic myocardial injury and development for therapeutic drugs. PI: Toshihiro Tanioka. Role on Project: Co- Investigator 2016-2017

Center for Experimental Animals

(1) Publications

[Original Articles]

- Hirate Yoshikazu, Hayakawa Kana, Nakano Yuki, Kumazawa Shiori, Miura Kento, Kanai Yoshiakira, Kanai-Azuma Masami. Role of SOX17 in crypt formation and regulation of SOX9 and AREG expression at the implantation site. Experimental Animals. 2021.06; 70(Suppl.); S61
- Seki H, Fujiwara T, Hijikata W, Murashige T, Tahara T, Yokota S, Ogata S, Ohuchi K, Mizuno T, Arai H. Evaluation of real-time thrombus detection method in a magnetically levitated centrifugal blood pump using a porcine left ventricular assist circulation model. Artif Organs. 2021.01; 45(7); 726-735
- 3. Kitazawa M., Sutani A., Kaneko-Ishino T. and Ishino F.. The role of eutherian-specific RTL1 in the nervous system and its implications for the Kagami-Ogata and Temple syndromes. Genes to cells. 2021.01;
- Okiko Habara, Catriona Y Logan, Masami Kanai-Azuma, Roeland Nusse, Hinako M Takase. WNT signaling in pre-granulosa cells is required for ovarian folliculogenesis and female fertility. Development. 2021.05; 148(9);
- Yoshikazu Hirate, Kana Hayakawa, Yuki Nakano, Shiori Kumazawa, Kento Miura, Yoshiakira Kanai, Masami Kanai-Azuma. Early Crypt Formation Defects in the Uterine Epithelia of Sox17 Heterozygous Mice. Sex Dev. 2021.03; 14(1-6); 40-50
- 6. Tadashi Shin, Yuichi Hiraoka, Tokiwa Yamasaki, Jamey D Marth, Josef M Penninger, Masami Kanai-Azuma, Kohichi Tanaka, Satoshi Kofuji, Hiroshi Nishina. MKK7 deficiency in mature neurons impairs parental behavior in mice. Genes Cells. 2021.01; 26(1); 5-17
- 7. Kasane Imura-Kishi, Aya Uchida, Naoki Tsunekawa, Hitomi Suzuki, Hinako M Takase, Yoshikazu Hirate, Masami Kanai-Azuma, Ryuji Hiramatsu, Masamichi Kurohmaru, Yoshiakira Kanai. Low retinoic acid levels mediate regionalization of the Sertoli valve in the terminal segment of mouse seminiferous tubules. Sci Rep. 2021.01; 11(1); 1110

- 1. Hirate Yoshikazu, Hayakawa Kana, Nakano Yuki, Kumazawa Shiori, Miura Kento, Kanai Yoshiakira, Kanai-Azuma Masami. Role of SOX17 in crypt formation and regulation of SOX9 and AREG expression at the implantation site. Experimental Animals 2021.06.01
- Yuki Tanaka, Yosikazu Hirate, Yoshifumi Fujioka, Kenya Imaimatsu, Tsutomu Endo, Hideki Hatanaka, Masami Kanai-Azuma. Identification of embryo-derived serine proteases that regulate the initiation of implantation. The 44th Annual Meeting of the Molecular Biology Society of Japan 2021.12.03
- 2. Gerel Melig, Ikuo Nobuhisa, Kiyoka Saito, Ryota Tsukahara, Ayumi Itabashi, Yoshiakira Kanai, Masami Kanai, Tetsuya Taga. Rasip1 preserves the maintenance of the hematopoietic activity of cluster forming cells in E10.5 mouse embryos. The 44th Annual Meeting of the Molecular Biology Society of Japan 2021.12.01 Pacifico Yokohama

- 3. Ryuichi Yamada, Akira Oguri, Katsunori Fujiki, Katsuhiko Shirahige, Yoshikazu Hirate, Masami Kanai-Azuma, Hirotaka Takezoe, Yoshihiro Akimoto, Naoki Takahashi, Yoshiakira Kanai. Identification of molecular and cellular events immediately downstream of Mab21/1 action in murine lens placode. 2021.12.01
- 4. Hiroshi Yomogita, Yoshiki Takamine, Hikaru Ito, Yoshikazu Hirate, Toshiaki Fkushima, Masayuki Komada, Yoshiakira Kanai, Naoyuki Miyasaka, Masami Kanai-Azuma. Relationship between delivery delay and Nrk gene expression in mouse and huma placenta. 2021.12.01