Juntendo University

Research Highlights

Graduate School of Medicine,
Faculty of Medicine

Introduction

Juntendo is the oldest surviving private school of Western medicine in Japan, with a history dating back more than 180 years to 1838, when our founder, Sato Taizen, established Wadajuku as a school of Dutch (European) medicine in Edo's Yagenbori district.

While emphasizing the university motto jin (benevolence), based on Juntendo's guiding principle of continuously moving forward, we have established a school culture summed up in the phrase "sanmu shugi (the "three noes" principle)," which refers to our culture of not discriminating against people on the grounds of gender, nationality, or academic background. As a comprehensive health university and graduate school consisting, we are contributing to society and cultivating talent at the international level through education, research, medical care, and the liberal arts.

As a pioneer in advanced medicine, Juntendo University aims to remain a leader in all ages. We have created a booklet that introduces the main research subjects and highlights of our laboratories and courses with the aim of widely disseminating and further developing our research activities.

We expect this booklet to bolster the development of collaborative research with researchers who are active in academia and industry members, and to further stimulate discussions between researchers in different laboratories and courses on campus. Furthermore, we strive to release the research results back to the public and to contribute to the maintenance and improvement of people's health.

Graduate School of Medicine / Faculty of Medicine,
Juntendo University

Juntendo University Research Highlights 《 Graduate School of Medicine, Faculty of Medicine 》

INDEX

Basic Medicine

Clinical Medicine

INDEX

Clinical Medicine

Graduate School

Department of General Education

Department of

Anatomy and Life Structure

Chief Professor

Koichiro ICHIMURA

STAFF

Associate Professor
Hiroyuki Kudoh
Assistant Professor
Kota Kato

Assistant
Hidaka Anetai

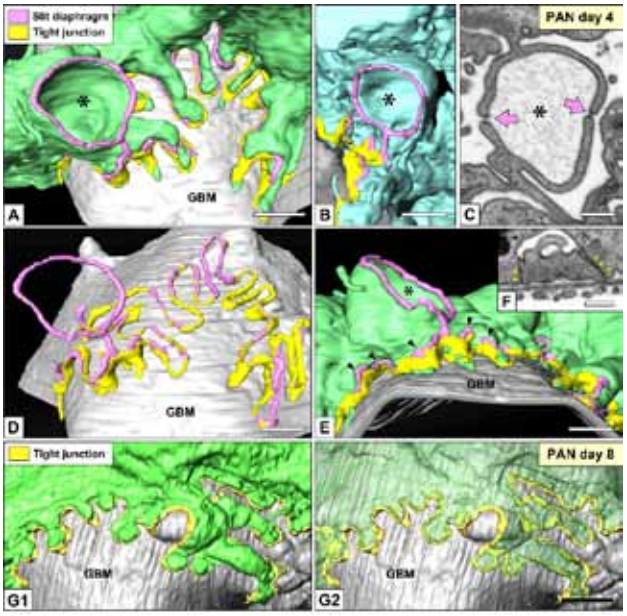
Main Research Subjects

1. **3D ultrastructural analysis of cell and tissue using volume electron microscopy**
2. **Cadaveric analysis of human anatomical structure.**

Research Highlights

3D structure of glomerular podocytes

Recently, our research group has clarified the entire process by which glomerular podocytes, which have complex projections, lose their projections during kidney disease (foot process effacement). In this study, we prepared high-resolution 3D reconstructed images of podocytes from their serial cross sectional images taken with an electron microscope called FIB-SEM. These results demonstrate the usefulness of FIB-SEM in the pathological evaluation of glomerular diseases. The study was published in the January 2019 issue of the Journal of the American Society of Nephrology (JASN).



Department of

Cell Biology and Neuroscience

Chief Professor

Masato KOIKE

STAFF

Associate Professor
Hiroyuki HIOKI

Assistant Professor
Yu-shin SODAKA
Mutsumi YOKOTA
Laxmi Kumar PARAJULI

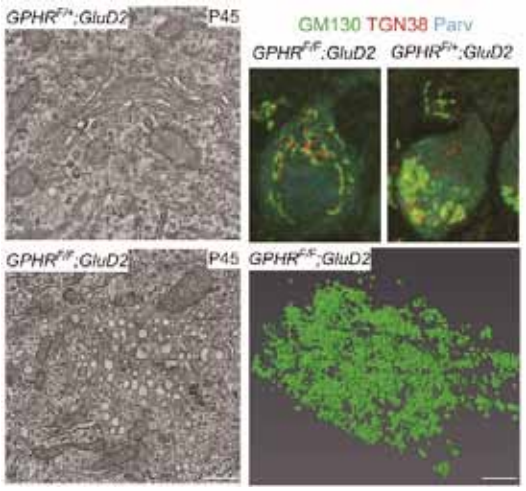
Main Research Subjects

1. **Understanding the mechanisms of neurodegeneration based on organellopathy**
2. **Establishing various correlative techniques bridging LM and EM observation**

Research Highlights

Cerebellar neurodegeneration and neuronal circuit remodeling in Golgi pH regulator-deficient mice

We generated Golgi pH regulator (GPHR) conditional knock-out mice. Purkinje cells (PCs) from the mutant mice exhibited vesiculation and fragmentation of the Golgi apparatus, followed by progressive cell loss, indicating that impairment of the Golgi luminal acidic condition triggers neurodegeneration.

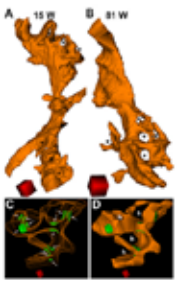


(Sou et al., 2019)

Three-dimensional structure of synapses revealed by volume electron microscopic techniques

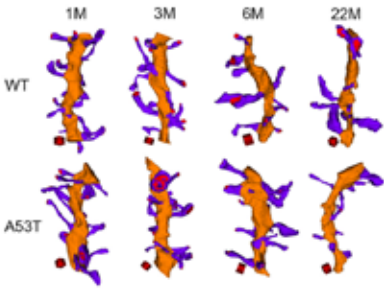
In normal mouse brains, we revealed the unique synaptic topography of crest-type synapses in the interpeduncular nucleus. Furthermore, we investigated developmental changes in dendritic spine morphology in the striatum and their alterations in an A53T α-synuclein BAC transgenic mouse model of Parkinson's disease.

Crest-synapse



(Parajuli et al., 2020a)

A53T mouse



(Parajuli et al., 2020b)

Department of

Physiology I

Chief Professor

Seiki KONISHI

STAFF

Associate Professor
Takahiro Osada

Assistant Professor
Akitoshi Ogawa

Main Research Subjects

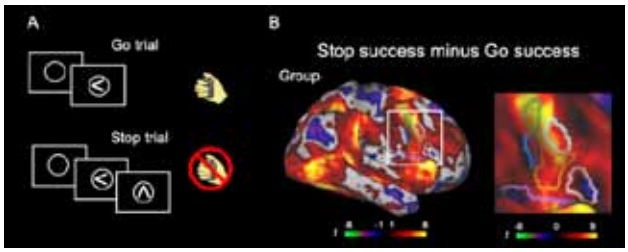
1. **fMRI of human cognitive functions**
2. **Functional intervention by TMS**
3. **fMRI of autonomic nervous systems**

Research Highlights

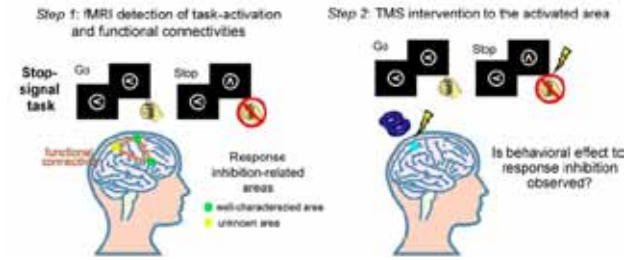
We investigate human brain functions by using neuroimaging. The main targets are higher cognitive functions and autonomic nervous systems. We also tackle with psychophysics, computational neuroscience, and research for patients.

We measure brain activity of human subjects by using functional magnetic resonance imaging (fMRI) while they perform cognitive tasks, such as response inhibition and memory. By identifying task-related brain areas, we aim to reveal neural circuit mechanisms that achieve higher cognitive functions. We also use transcranial magnetic stimulation (TMS) techniques to temporarily perturbate brain area activity. This helps to understand the causal effects of brain areas or neural networks.

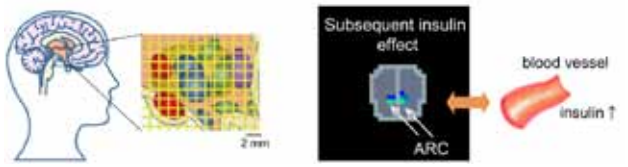
The hypothalamus is a center of autonomic nervous systems. By using high spatial resolution fMRI, we investigate human hypothalamus functions at the level of hypothalamic nuclei, and multi-organ network systems.



A response inhibition task (stop-signal task) and brain activation



Identification of task-related brain area and TMS intervention



Identification of hypothalamic nuclei with fMRI and activity in the arcuate nucleus associated with increase in blood insulin

Department of

Physiology II

Chief Professor

Masaaki KOMATSU

STAFF

Senior Associate Professor
Yoshinobu Ichimura

Associate Professor
Makino Watanabe

Lecturer
Hideaki Morishita

Assistant Professor
Shun Kageyama
Ryosuke Ishimura
Tomoko Ishii

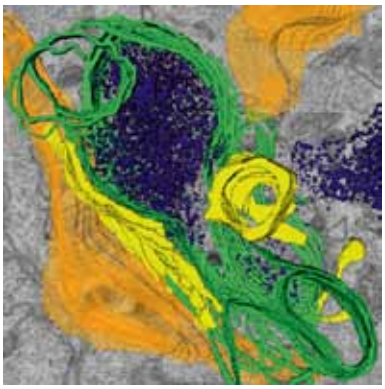
Main Research Subjects

1. **Molecular mechanism of selective autophagy**
2. **Physiological role of mammalian autophagy**
3. **ER-phagy mediated by the Ufm1-system**

Research Highlights

Though autophagy has been generally considered to be a non-selective degradation pathway, autophagy pathway has selectivity. It has become clear that soluble proteins, liquid-liquid phase separated granules, aggregates, nucleic acids, and organelles such as mitochondria and the endoplasmic reticulum are selectively recognized, sequestered and degraded. Like the ubiquitin-proteasome system, such selective degradation through autophagy is becoming clear to be involved in various vital events such as cellular differentiation, stem cell homeostasis and anti-aging. We aim to clarify the molecular mechanism of selective autophagy as well as the physiological roles in mammals.

Blue: p62-liqud droplet
Green: autophagosome
Yellow: ER



Ultrastructure and three-dimensional models of autophagic membranes around p62-liquid droplet.
Provided by Eeva-Liisa Eskelinen (Univ of Turku).

Selected publications

1. Kageyama S,…*Komatsu M. p62/SQSTM1-droplet serves as a platform for autophagosome formation and anti-oxidative stress response. ***Nat Commun***. In press.
2. Sánchez-Martín P, … *Komatsu M. NBR1-mediated p62-liquid droplets enhance the Keap1-Nrf2 system. ***EMBO Rep***. 2020 Jan 9:e48902.
3. Saito T, … *Komatsu M. Autophagy regulates lipid metabolism through selective turnover of NCoR1. ***Nat Commun***. 2019 Apr 5;10(1):1567.
4. Ueno T, *Komatsu M. Autophagy in the liver: functions in health and disease. ***Nat Rev Gastroenterol Hepato***l. 2017 Mar;14(3):170-184.
5. *Mizushima N, *Komatsu M. Autophagy: renovation of cells and tissues. ***Cell***. 2011 Nov 11;147(4):728-41.

Department of

Biochemistry I

Chief Professor

Takehiko YOKOMIZO

STAFF

Senior Associate Professor
Masathugu Ohora

Associate Professor
Kazuko Saeki
Toshiaki Okuno

Assistant Professor
Airi Jo
Hyeon-Cheol Lee-Okada

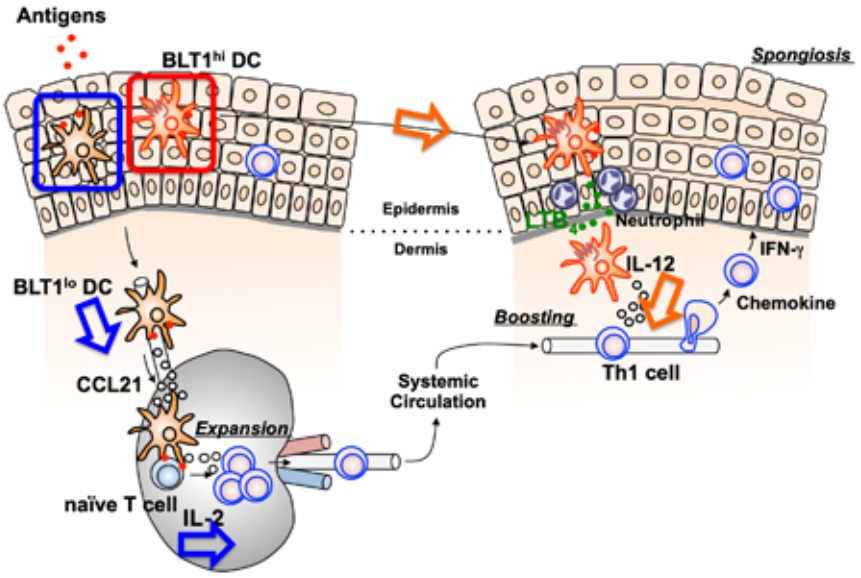
Main Research Subjects

1. **Roles of bioactive lipids and their receptors**
2. **Roles of polyunsaturated fatty acids**
3. **Bioactive lipids and inflammation/immunity**

Research Highlights

Novel dendritic cell (DC) subsets

We identified novel EC subsets defined by the expression of Leukotriene B_4 receptor 1 (BLT1). We found that BLT1^{hi} and BLT1^{lo} DCs differentially migrated toward LTB_4 and CCL21, a lymph node-homing chemoattractant, respectively. BLT1^{hi} DC stays at the inflammatory sites and enhances inflammation by releasing IL-12. Thus, Leukotriene B_4 receptor controls immune response and inflammation.



Cell Mol Immunol (2020) I
doi: 10.1038/s41423-020-00559-7.

Department of

Biochemistry II

STAFF

Associate Professor
Akimasa Someya

Assistant Professor
Kaori Suzuki
Yumi Kumagai

Main Research Subjects

1. **Molecular mechanisms for the anti-inflammatory actions of glucosamine**
2. **Functions of neutrophil-derived extracellular vesicles in amelioration of sepsis pathophysiology**
3. **Involvement of antimicrobial a-helical peptide LL-37 in atherosclerosis**

Research Highlights

1. Molecular mechanisms for the anti-inflammatory actions of glucosamine

Glucosamine has the anti-inflammatory action, which is thought to be involved in the joint health. Associate Professor Someya *et al*. investigate the mechanisms by which glucosamine exerts its anti-inflammatory effect. His group revealed that glucosamine inhibits a transcription factor NF-κB which is involved a pivotal role in the expression of inflammatory molecules, via *O*-linked-*N*-acetylglucosamine (*O*-GlcNAc) modification of proteins, and thereby reducing the production of pro-inflammatory cytokines (Fig. 1).

2. Functions of neutrophil-derived extracellular vesicles in amelioration of sepsis pathophysiology

Assistant Professor Kumagai *et al*. revealed that LL-37, a human host-defense peptide, stimulates neutrophils to release extracellular vesicles (EV) containing antimicrobial molecules and that the neutrophil-derived EVs possess antibacterial activity. Her group also showed that administration of LL-37-induced EVs reduced the bacterial load and improved the survival of septic mice (Fig. 2).

3. Involvement of antimicrobial α-helical peptide LL-37 in atherosclerosis

LL-37 is an α-helical antimicrobial peptide produced by neutrophils etc. In recent years, it has been reported that LL-37 interacts with amyloid proteins or forms self-aggregates, which is involved in diseases. Since LL-37 is found to accumulate in atherosclerotic lesions, Assistant Professor Suzuki *et al*. plan to elucidate the involvement of LL-37 in the onset and progression of atherosclerosis.

Fig. 1. Molecular mechanisms for the anti-inflammatory action of glucosamine

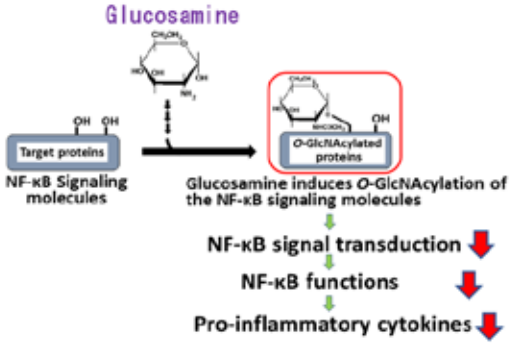
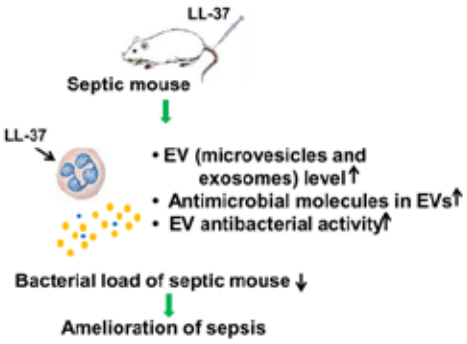


Fig. 2. LL-37 ameliorates sepsis through inducing antimicrobial extracellular vesicles from neutrophils



Department of

Pharmacology

STAFF

Associate Professor
Takashi Murayama
Yohei Okubo
Yuji Kamikubo

Lecturer
Naoya Yamashita, Nagomi Kurebayashi

Assistant Professor
Taku Kashiyama, Chigure Suzuki,
Hakushun Sakairi

Main Research Subjects

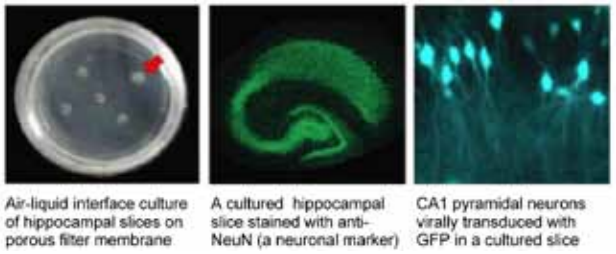
1. **Pathophysiological mechanisms of neurodegeneration**
2. **Neuronal signaling via axonal transport**
3. **Development of RyR-specific modulators**

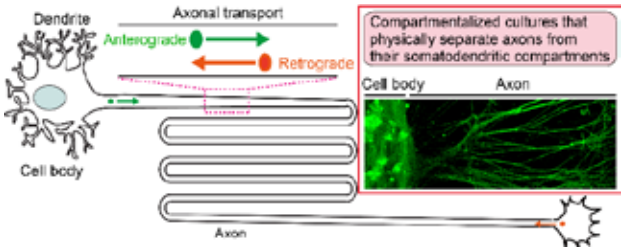
Research Highlights

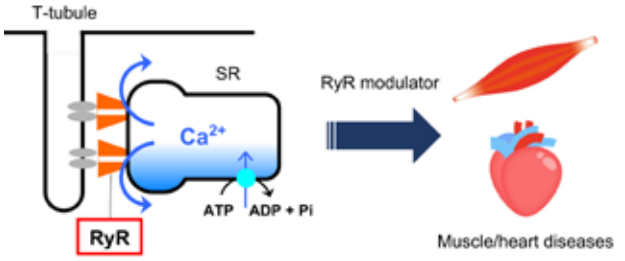
1. Most neurodegenerative diseases, including Alzheimer's disease, progress slowly and appear to have long, relatively asymptomatic prodromal phases. To analyze the early pathological events in disease progression, we established an *ex vivo* model, using organotypic slice cultures of the brain, which can maintain *in vivo* tissue architecture and neuronal circuits for months.

2. Neurons have long axons that commonly extend for more than several centimeters. Long-distance communication between axons and their cell bodies is, therefore, one of the fundamental features for regulating the formation and maintenance of neuronal circuits. Using compartmentalized cultures, we investigated how axonal transport regulates axon-cell body communication in health and disease.

3. Ryanodine receptor (RyR) is a Ca^{2+} release channel in the sarcoplasmic reticulum in skeletal and cardiac muscles, and is implicated in various muscle and arrhythmogenic heart diseases. We are searching for compounds that specifically modulate RyR function (activators and inhibitors), as potential therapeutic candidates for these diseases.







Department of

Pathology and Oncology

Chief Professor

Akira ORIMO

STAFF

Associate Professor
Toshiyuki Kobayashi
Takehiro Yasukawa

Assistant Professor
Yoshinobu Sugitani
Kazunari Yamashita
Kana Tominaga

Main Research Subjects

1. **Elucidate molecular mechanisms by which cancer-associated fibroblasts (CAFs) promote tumor progression**
2. **Investigate the mechanism for maintenance of tumor-promoting ability of CAFs and their cellular plasticity**
3. **Development of novel cancer treatments targeting the tumor stroma**

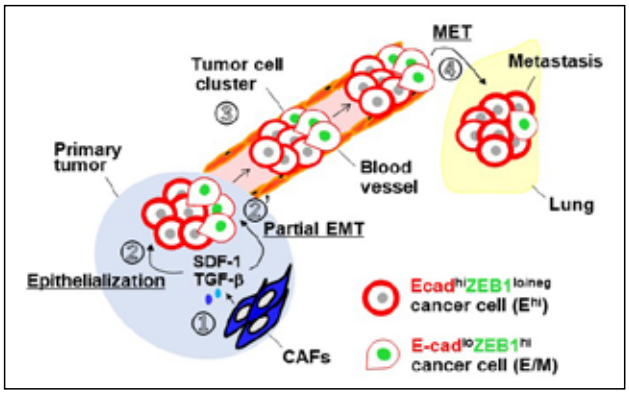
Research Highlights

1. Elucidation of the mechanism for promoting tumor progression of CAFs

It is not clear whether a single cancer cell that has undergone (complete) epithelial-mesenchymal transition (EMT) or a cancer cell population (cluster) that has cell adhesion ability is the primary contributor to cancer invasion / metastasis. In recent years, multiple groups have reported that cancer cell clusters enhance cell death resistance and are essential for invasion and metastasis. In addition, although it is known that signals from the tumor microenvironment promote invasion and metastasis of cancer cells, there are almost no reports concerning the formation of cancer cell clusters. What is more, many things remain unclear regarding the mechanism by which CAFs promote tumor invasion and metastasis.

Under these circumstances, we have shown that CAFs induce partial EMT of cancer cells, and promote tumor invasion and metastasis through formation of cancer cell clusters (Fig. 1; Matsumura, et al. Life Sci Alliance, 2019). We extracted cancer cells transplanted from tumor mass formed by co-transplanting human breast cancer cells and CAFs into immunodeficient mice. These cancer cells had acquired properties of the E^{hi} type of cancer cells (E-cadherin^{hi}ZEB1$^{lo/neg}$) that exhibit epithelial characteristics due to the CAF-derived SDF-1 and TGF-β, as well as the properties of the E/M type of cancer cells (E-cadherin^{lo}ZEB1^{hi}) that exhibit both epithelial and mesenchymal characteristics by being positive for E-cadherin and ZEB1.
We found that by forming clusters, these two types of breast cancer cells acquired the abilities to resist cell death, invade extensively and metastasize. Furthermore, the E/M-type cancer cells that metastasized to the lungs promoted metastatic colony formation by returning to the epithelial E^{hi} phenotype (Fig. 1). It has also been shown that the E/M- and E^{hi}–type phenotypes, as well as the capacities for extensive invasion and metastasis induced by CAFs are maintained in a stable manner in the cancer cells.

Research to further elucidate the molecular mechanism by which CAFs induce heterogeneity in cancer cells (at least E^{hi}, E/M-type) and the epigenetic reprogramming that takes place to maintain the highly invasive and metastatic capacities in cancer cells in a stable manner is underway.



(Matsumura, et al. Life Sci Alliance, 2019)

Fig. 1: Discovery of a novel mechanism through which CAFs promote breast cancer metastasis

① CAFs produce large amounts of the cytokines SDF-1 and TGF-β.
② Stimulation by these cytokines produce epithelial, E^{hi}-type breast cancer cells.
②' At the same time, CAFs produce E/M type breast cancer cells with enhanced invasive capacity that exhibit both epithelial and mesenchymal characteristics through partial epithelial-mesenchymal transition (EMT).
③ These breast cancer cells form clusters, undergo local invasion, and pass through blood vessels to metastasize into the lungs.
④ E/M-type cancer cells that have metastasized to the lungs promote metastatic colony formation by returning to the epithelial phenotype through mesenchymal-epithelial transition (MET).

Department of

Microbiology

Chief Professor

Teruo KIRIKAE

STAFF

Associate Professor

Kyoko Kuwahara
Tadashi Baba
Tatsuya Tada

Assistant Professor

Satoshi Oshiro
Mari Tohya

Main Research Subjects

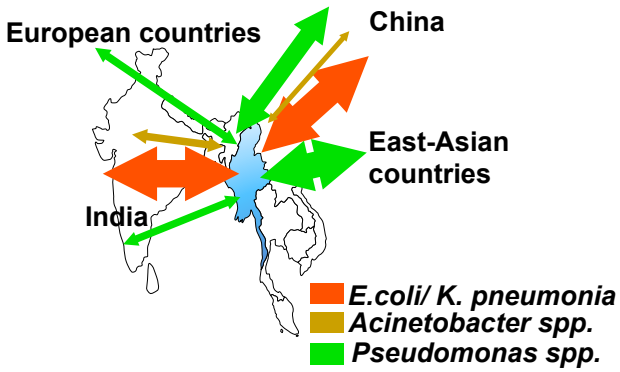
1. **Molecular epidemiology of multidrug-resistant Gram-negative bacteria**
2. **Development of infectious diseases diagnostic method**
3. **Infection controls with microbiome analysis**

Research Highlights

Expanding the SATREPS project in the medial field in Myanmar

It is of the highest priority to overcome the global spread of antimicrobial resistance (AMR) with the joint effort of all mankind.

We conducted an international collaboration study on AMR molecular epidemiology in Myanmar (2015-2017). As a result, we found that AMR strains isolated in Myanmar had various AMR characteristics of those isolated in India, China and Eurasia continent (Fig). We will start another five-year international collaboration project, **SATREPS**, from 2021 in Myanmar. The object of this study is to establish a comprehensive AMR surveillance network system collaborating with NHL (National Health Laboratory, Yangon) and 16 core hospitals.



Reference

Antimicrob Agents Chemother. 2019; 63: e02397-18,
Antimicrob Agents Chemother. 2019; 63: e00475-19,
mSphere. 2020; 5: e00054-20.

Department of

Tropical Medicine and Parasitology

Chief Professor

Toshihiro MITA

STAFF

Associate Professor
Makoto Hirai

Assistant Professor
Naoko Yoshida

Main Research Subjects

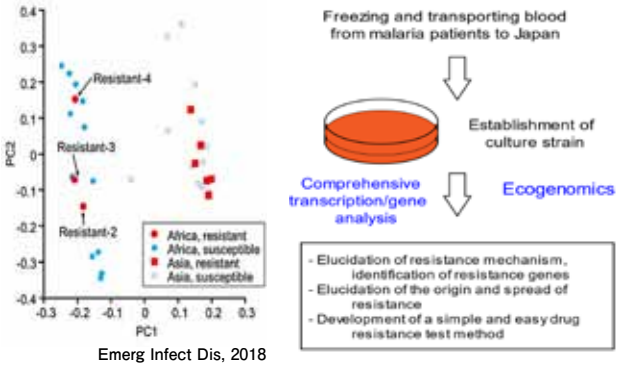
1. **Molecular epidemiology of drug-resistant malaria: Elucidation of the mechanism of emergence and spread of resistance**
2. **Development of genome diagnostic procedures to elucidate the evolution of malaria drug resistance**
3. **Development of new antimalarial drugs**

Research Highlights

Development of new tools to help fight drug-resistant malaria through field-based research

Malaria is one of the world's three major infectious diseases. Drug resistance has caused a serious situation. We are advancing "offensive" epidemiology, basic and applied research to solve this problem.

- Artemisinin is currently the first drug of choice. We have conducted regular field surveys of drug resistance in the Republic of Uganda and discovered for the first time in the world that malaria parasites resistant to artemisinin have emerged in Africa. This resistant malaria had a unique appearance in Africa.
- We have created transgenic parasites that evolve 38 times faster than normal malaria parasites by genetic modification. This makes it possible to produce drug-resistant malaria in the laboratory in a few weeks to a few months, which can provide effective diagnosis and treatment before they emerge in endemic areas.



Emerg Infect Dis, 2018

Department of

Immunology

Chief Professor

Sachiko MIYAKE

STAFF

Senior Associate Professor
Hideo Yagita

Associate Professor
Hisaya Akiba
Asako Chiba
Daisuke Noto

Main Research Subjects

1. **Mechanisms of autoimmunity**
2. **Pathomechanisms of neuroinflammatory diseases**
3. **Analysis of function of costimulatory molecules that control T cell functions**

Research Highlights

Mechanisms of autoimmunity

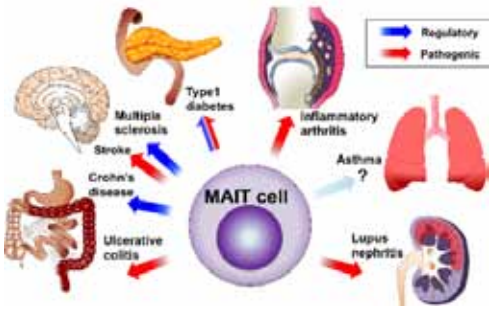
We have reported that are mucosal-associated invariant T (MAIT) cells are activated in autoimmune diseases and demonstrated that MAIT cells can be therapeutic targets in murine lupus (Murayama G, et al. Front Immunol, 2019). We also found that STING pathway is augmented in monocytes from lupus patients and this may be associated with enhanced type I IFN production in lupus(Murayama G, et al. Rheumatology, 2020).

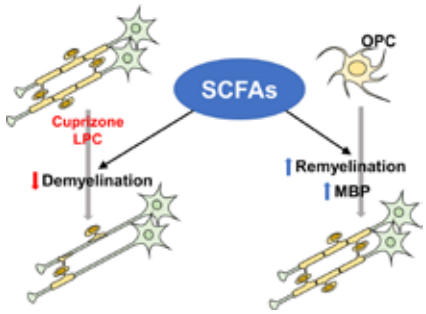
Pathomechanisms of Neuroinflammatory diseases

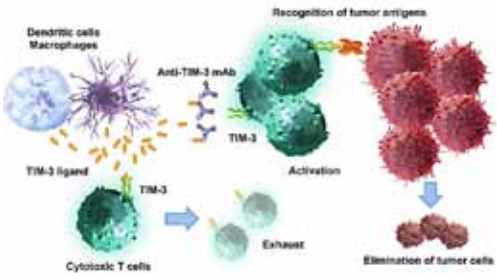
Noto group is investigating about the roles of immune system and glia cells in neuroinflammatory diseases. We revealed that short chain fatty acids (SCFAs), which are major metabolites of gut microbiota, suppress symptoms of animal model of multiple sclerosis (Mizuno M, et al. PLoS One. 2017), and SCFAs act on oligodendrocytes directly, suppress demyelination and enhance remyelination (Chen T, et al. J Neuroinflammation, 2019).

Analysis of function of costimulatory molecules that control T cell functions

While neutralizing antibodies against the coinhibitory molecule PD-1, which suppresses T cell function, improve treatment for malignant tumors as an immune checkpoint inhibitor. On the other hand, side effects have also become a clinical problem. Akiba group showed that anti-TIM-3 antibody has an antitumor effect as a new immune checkpoint inhibitor, and also showed a risk of developing and exacerbating the side effect of interstitial pneumonia. It is necessary to fully consider this side effect in clinical application (Isshiki T, et al. J Immunol. 2017).







Department of

Epidemiology and Environmental Health

STAFF

Associate Professor
Michiko Kurosawa
Fumihiko Kitamura

Assistant Professor
Hiroaki Itoh
Mayuko Hosokawa
Takehisa Matsukawa

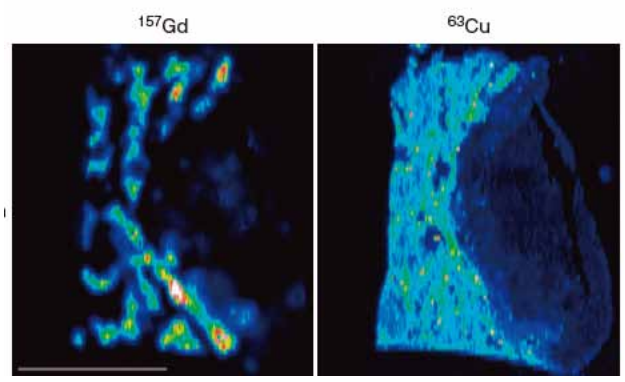
Main Research Subjects

1. **Epidemiological Studies**
2. **Occupational Health**
3. **Environmental health**

Research Highlights

Research on the application of "metallomics" in the field of environmental medicine

We focus on the concept of "metallomics", as well as genomics and proteomics. We applicate of "metallomics" methodologies in the field of environmental health. Our research aims to establish a comprehensive method to elucidate (1) the distribution of multiple elements, (2) the location of each element in the body, and (3) the chemical forms and isotope ratios of each element. We are developing and improving various analytical methods and developing methods to analyze the mechanisms of biological functions of various trace elements.



Quantitative gadolinium imaging of rabbit VX-2 cancer in liver*
Quantitative image of ^{157}Gd (left). Images of ^{63}Cu distribution in rabbit hepatic cancer (right).

*KUBOTA, et al. *Juntendo Medical Journal* 65.5 (2019): 461-467.

Department of

Public Health

Chief Professor

Takeshi TANIGAWA

STAFF

Senior Associate Professor
Hiroo WADA

Associate Professor
Motoyuki YUASA
Ai NODA, Motoki ENDO,
Naohiro YONEMOTO

Assistant Professor
Kiyohide TOMOOKA
Setsuko SATO

Main Research Subjects

1 Community-based Epidemiological Study
(CIRCS, The Toon Health Study, Sleep Study on Child's SDB and Behavioral Problem)

2 Epidemiological Study of Occupational Health
(SDB in Working Women, Health-related Accident Prevention in Professional Drivers, the Fukushima Nuclear Energy Workers' Support Project study, Study on the Work Style Reform for Japanese Physicians)

3 Other Studies
(Employment Support for Patients, Global Health)

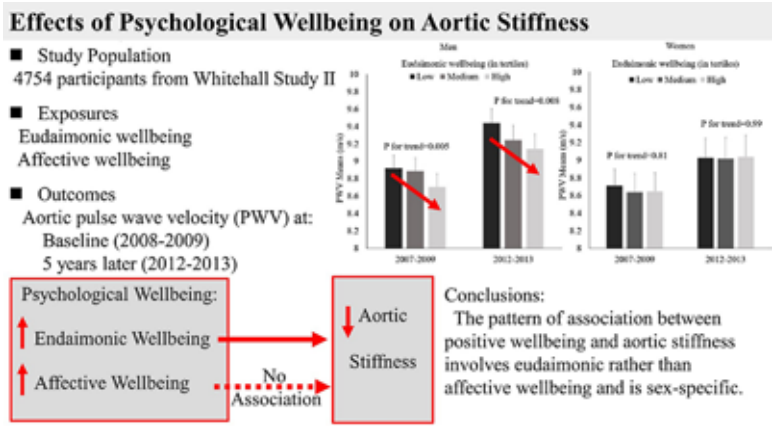
Research Highlights

Psychological Wellbeing and Aortic Stiffness: Longitudinal Study

Summary

In older men, higher levels of eudaimonic wellbeing were associated with lower long-term levels of arterial stiffness. We found no significant associations of affective wellbeing with PWV and no associations among women. The pattern of association between positive wellbeing and cardiovascular health outcomes involves eudaimonic rather than affective wellbeing and is sex-specific.

Ikeda A, et al. *Hypertension*, 2020



Department of

Forensic Medicine

Chief Professor

Kazuyuki SAITO

STAFF

Associate Professor
Hiroaki Nakanishi

Assistant Professor
Takehisa Matsukawa

Main Research Subjects

1. **Forensic pathology of sudden death due to cardiovascular diseases**
2. **Practical realization of DNA profiling in Japan**
3. **Development of DNA analysis method for animal crude drugs**
4. **Relationship between coronary artery spasm and oxidative stress**

Research Highlights

Forensic pathology of sudden death

We are pathologically analyzing sudden death cases due to cardiovascular diseases such as myocardial infarction, coronary artery spasms, eosinophilic coronary periarteritis, and SIDS.

Practical realization of DNA profiling in Japan

We are trying to develop "Mainland-Okinawa plex" that can distinguish between Mainland-Japanese and Okinawa-Japanese by using some SNPs.

Development of DNA analysis method for animal crude drugs

We are trying to develop a method that can detect each animal species of origin for crude drugs derived from multiple animal species based on massively parallel sequencing analysis of mitochondrial genes.

Relationship between coronary artery spasm and oxidative stress

This theme is collaborated with Kanazawa Medical University. We are in charge of measuring 3-nitrotyrosine and 4-hydoxy-2-nonenal by our original methods.

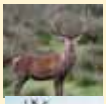
<DNA analysis for animal crude drugs>

We can't identify counterfeit crude drugs in which the original animals differ from those required by the regulations, especially those in powdered form or Kampo drug formulations.

Left; Antler Velvet originated by red deer (real)
Right; Antler Velvet originated by reindeer (fake)

ATTAATATAT・・・

GTTGATATAT・・・



Gene of red deer

Gene of reindeer

Next generation sequencer (NGS)

This method can identify origin animals by each sequences that are detected separately by NGS.

This method can estimate roughly mixture ratio of origin animals by detected genes ratio.

Department of

Medical History

STAFF

Visiting Professor
Yamada Hiromichi
Okubo Takeshi

Assistant Professor
Sawai Tadashi

Part-time Research Assistant
Murakami Ayumi

Main Research Subjects

1. **History of Western Medicine (Traditional and Modern)**
2. **History of Japanese Medicine (after Edo Era)**
3. **History of Medial Education (incl. Juntendo)**

Research Highlights

Only one in Japan, Department of Medical History

Professor Sakai Shizu, the leading figure of the Medical History in Japan, published the beloved "Yamaiga Kataru Nihonshi (Japanese history dialogued through diseases)" (2008) and many other books.

Professor Sakai Tatsuo collectively studied the medical books in the history, and published newly the academic "History of Medicine illustrated" (2019) and the popular "Total History of Medicine" (2020). It was clarified that the Western Traditional Medicine was taught in four courses and had different construction from the Western Modern Medicine divided into the basic and clinical medicine, and that the scientific research was restricted to the anatomy in the former, but widely performed in many disciplines of the basic medicine in the latter. On the history of medical education, the "History of Medical Education in Japan" (2012) and the "History of Medical Education, in old / new and in East / West" (2020) were published.

Professor Sakai T. and Assistant Professor Sawai Tadashi organized the Galen Research Group to translate and interpret the Greek medical text of Galen, and published "Galen Anatomical Treatises" (2011) and "Galen Usefulness of the Parts of the Body I" (2016).

Department of

Medical Education

STAFF

Professor
Okada T, Takeda Y, Tomiki Y
Senior Associate Professor
Suzuki T, Wada H, Nishizaki Y
Associate Professor
Watanabe M
Assistant Professor
Sekine M

Main Research Subjects

1. **Health inequities and social determinants of health**
2. **Factors associated with students' academic achievement**
3. **Postgraduate training and career strategies**

Research Highlights

Considering the social inequality and disparity, clinicians need a more profound understanding of people in the social-cultural context. We have developed an elective program for students to understand the social determinants of health (SDH) by participating in community activities to support marginalized people. We believe the program will equip students with social empathy and we are developing a scale to analyze and measure the effect.

To bridge the gap due to the language barrier as a cause of health inequity, we have implemented an "Plain Japanese" communication class for medical students. We have developed educational materials for healthcare professionals to practice "Plain Japanese" in clinical settings (https://easy-japanese.info/archives/391).

Role-play with overseas students practicing "Plain Japanese"

We are the first medical school to introduce "Plain Japanese" to the formal curriculum.

https://www.juntendo.ac.jp/co-core/education/yasashii-nihongo202011.html

Department of

Cardiovascular Biology and Medicine

Chief Professor

Tohru MINAMINO

STAFF

Associate Professor

Kikuo Isoda, Shinya Okazaki, Hakuo Konish, Shinichiro Fujimoto, Takatoshi Kasai, Hiroshi Iwata, Hidemori Hayashi, Sakiko Miyazaki, Tomotaka Dohi, Yuya Matsue

Assistant Professor

Miho Yokoyama, Iwao Okai, Haruna Tabuchi, Kazuhisa Takamura, Yoshiteru Kato, Yoshifumi Fukushima, Kiyoshi Takasu, Shinichiro Doi, Yusuke Joki, Hirohisa Endo, Takao Kato

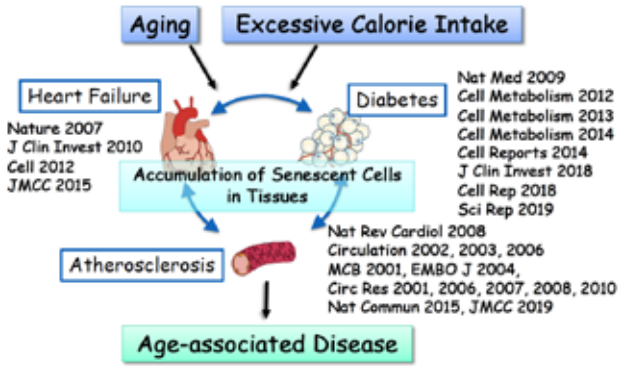
Main Research Subjects

1. **Development of therapeutic strategy for age-associated disease by targeting senescent cells**
2. **Development of therapeutic strategy by regulating seno-metabolites**
3. **Elucidation of molecular mechanisms underlying endogenous senolysis**

Research Highlights

Therapeutic strategy for age-associated disease by targeting senescent cells

One of our research goals is to develop therapeutic strategy for age-associated disease by targeting senescent cells. We have demonstrated that age and/or metabolic stress promotes accumulation of senescent cells in various tissues, thereby leading to the onset and progression of age-associated disease. Recently, we have identified senolytic agents (senolytics) that specifically could eliminate senescent cells and improve pathological aging such as atherosclerosis and diabetes. More recently, we have identified several seno-antigens that are specifically expressed by senescent cells. We have developed senolytic vaccine that could target seno-antigens and eliminate senescent cells. The treatment with senolytic vaccine could improve dietary atherosclerosis and metabolic dysfunction in obese mice, improve frailty in aged mice, and extend lifespan of mice with premature aging syndrome. We also have identified several seno-metabolites that play a critical role in regulating pathological aging phenotypes.



Department of

Gastroenterology

Professor

Akihito NAGAHARA

STAFF

Professor
Kenichi Ikejima, Hiromichi Isayama

Senior Associate Professor
Tatsuo Ogihara, Mariko Hojo, Syunhei Yamashina

Associate Professor
Tomoyoshi Shibuya, Kazuyoshi Kon, Nobuko Serizawa, Kenshi Matsumoto, Akira Uchiyama, Dai Ishikawa, Toshiro Fujisawa, Hiroya Ueyama, Hiromichi Fukada, Kouhei Matsumoto

Assistant Professor
Kyoko Fukuhara, Reiko Yaginuma, Kumiko Ueda, Shino Uchida, Eisuke Nakadera, Tsutomu Takeda, Osamu Nomura, Hirofumi Fukushima, Takashi Murakami, Youichi Akazawa, Keiichi Haga

Main Research Subjects

1. Antibiotic fecal microbiota transplantation for ulcerative colitis
2. Pathophysiological analysis of special-type gastric cancer and search for new therapeutic targets
3. Development of artificial intelligence (AI) system in endoscopic diagnosis of gastric cancer
5. Clinicopathological and molecular study of the serrated neoplasia pathway of colorectal tumors
6. Molecular mechanisms involved in lipotoxicity in Nonalcoholic Steatohepatitis
7. Role of the small intestinal flora in Alcohol-related Liver Disease
8. Function of lipid droplet-organelle interactions in pathogenesis of NASH
9. The pathophysiological role of autophagy in NAFLD Analysis of the Role of Gut Flora on the Development of PSC
11. Elucidation of the Mechanism of IL13Ra2 in Invasion and Metastasis of Pancreatic Cancer
12. Elucidation of the Effects of Persistent Microbial Infection on Bilio-pancreatic Carcinogenesis
13. Elucidation of the Pathogenesis and related genes of non-alcoholic early chronic pancreatitis.
14. Development of a Novel Stent in Biliary-Pancreas Endoscopy
15. Development of New Procedures in Interventional EUS.
16. Development of Antitumor Therapy for Biliary-Pancreas Cancer

Research Highlights

① We demonstrate new FMT method called (Antibiotic FMT:A-FMT) for ulcerative colitis (Fig. 1) We have recently found that the relationship between patients with ulcerative colitis and their fecal donors is associated with therapeutic effect. Favorable, long-term therapeutic effects of FMT can be expected if the donor is a sibling of the patient or both patient and donor are in the same generation. Findings can lead to the development of individualized stool transplant for which a donor will be selected for each patient.

⑤ Clinicopathological and molecular study of the serrated neoplasia pathway of colorectal tumors (Fig. 2) We have reported that activation of the WNT signal pathway might be associated with methylation of the associated genes (i.e. MCC, AXIN2) in the serrated neoplasia pathway. Furthermore, we showed that SSLs might be associated with both MSI-high and MSS cancer, which might be distinguished by distinct molecular biological features such as FBXW7 mutations and TP53 mutations.

⑥ Imbalance of fatty acid profile contribute to the progression of nonalcoholic steatohepatitis (Fig. 3) Investigation of the pathophysiology of non-alcoholic steatohepatitis (NASH) and alcohol-related liver disease is one of the most important theme for us. We revealed that aged mice easily developed steatohepatitis induced by high-fat diet compared to young mice, caused by imbalance of lipid metabolism, in collaboration with Prof. Yokomizo's group of Department of Molecular and Cellular Biochemistry.

⑨ The pathophysiological role of autophagy in NAFLD (Fig. 4) We reported that hepatic steatosis causes autophagic dysfunction via suppression of lysosomal acidification and autophagic induction. (Inami et al.BBRC2011, Nakadera et al. BBRC2016) Autophagy specific substrate p62 is accumulated in hepatocytes from NAFLD and ASH patients, revealing that autophagy dysfunction is involved in the development and progression of these liver diseases.(Fukuo et al. Hepatol Res. 2014, Fukushima et al. Hepatol Res.2018) Recently, we identified insoluble nuclear proteins accumulated by autophagic dysfunction. Since these proteins are involved in liver carcinogenesis and cell damage, we are evaluating if these proteins are effective as new therapeutic targets to liver diseases.

⑩ Prof. Isayama serves as Chairman of the Study Group on PSC, Ministry of Health, Labour and Welfare. Therefore, our hospital is the head hospital of the PSC study. We are studying the relationship between the intestinal bacterial flora and the mechanism of the disease to link the research results to clinic.

⑪ We found that IL13Ra2, one of the cancer-specific antigens, is positively involved in the invasion and metastasis of pancreatic cancer (Fig. 5), and reported that the prognosis of the high expression group was significantly shorter (Fig. 6). We are conducting research to suppress invasion & metastasis via reducing IL13Ra2.

⑫–⑭ Pathogens in bile and pancreas are analyzed using next-generation sequencers to examine their association with carcinogenesis. We collaborate with Dr. Shin Watanabe of the Microbiome Research for sequencing and Prof. Toshiaki Shimizu of pediatrics for identifying genes related to early chronic pancreatitis.

⑮–⑯ In the field of endoscopes, we are working with companies to develop endoscope systems and fluoroscopes, as well as to design new therapeutic devices such as stents. We are also conducting multi-center prospective trials to evaluate the usefulness of biliary stent and interventional EUS for obstructive jaundice.

Fig.1

Fig.2

Fig.3

Increased lipid synthesis/decreased unsaturatedization with age enhances lipotoxicity and exacerbates NASH.

Fig.4

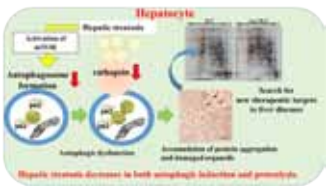
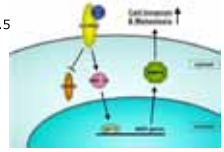
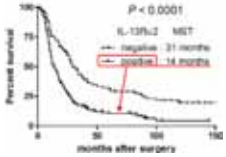


Fig.5



Signaling pathway of IL13Ra2 in pancreatic cancer invasion

Fig. 6



Worse prognosis in high IL13Ra2 expression

Department of

Diagnostic Imaging and Interventional Oncology

Chief Professor

Shuichiro SHIINA

STAFF

Associate Professor
Hitoshi Maruyama
Hiroaki Nagamatsu

Assistant Professor
Shigeto Ishii

Main Research Subjects

1. **Diagnosis and minimally invasive treatment of liver cancer**
2. **Treatment of advanced liver cancer with molecular targeted therapy and IVR**
3. **Comprehensive management of portal hypertension**

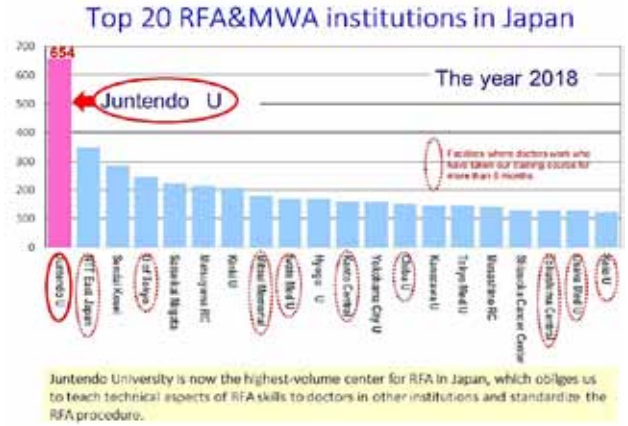
Research Highlights

In our department, imaging diagnosis and minimally invasive treatment of gastroenterological diseases are the main axes. The number of annual ablation (radiofrequency/microwave) for liver cancer has been the highest in Japan since 2013. Since Japanese technique is at the top in the world, it can be said that our achievements are highest. Its background factors are Professor Shiina's outstanding achievement, advanced equipment, skilled staff, and devices developed with companies.

Ablation has become standard treatment modalities for liver cancer. However, its outcomes and skills are significantly different among facilities. To improve these circumstances and to disseminate skills and know-hows for ablation, we have held domestic training programs 14 times in which 237 doctors participated and international versions 7 times, which were successfully completed with 111 participants.

Regarding advanced liver cancer, we actively use molecular targeted therapy and vascular intervention, such as hepatic arterial infusion chemotherapy.

We also perform comprehensive management of patients with portal hypertension based on hemodynamic assessment using interventional radiology. As for basic research, we have started a project to detect the acoustic identification index for histological change of muscle in order to introduce the non-invasive ultrasound-based imaging (for sarcopenia and glucose/lipid metabolism) which may extend the healthy life expectancy.



週間朝日 MOOK2019

Department of

Respiratory Medicine

Chief Professor

Kazuhisa TAKAHASHI

STAFF

Senior Associate Professor
Kuniaki Seyama

Associate Professor
Fumiyuki Takahashi, Yuzo Kodama, Shinsaku Togo, Tetsutaro Nagaoka, Satomi Shioda, Norihiro Harada, Tadashi Sato

Lecturer
Ken Tajima

Assistant Professor
Takehito Shukuya, Jun Ito, Yoichiro Mitsuishi, Motoyasu Kato, Ryo Ko, Tetsuhiko Asao, Shoichi Okamoto

Main Research Subjects

Research theme 1 (lung cancer, mesothelioma, thymic cancer)

1. Analysis of EGFR-tyrosine kinase inhibitor (TKI) resistant cancer stem cells in non-small cell lung cancer
2. Search for new therapeutics targeting epigenetics in mesothelioma and small cell lung cancer
3. Oxidative stress response system in lung cancer and its potential as a therapeutic target
4. Analysis of circulating tumor cells (CTC)
5. Analysis of cancer-associated fibroblasts (CAF)
6. Search for differential markers in thymic tumors (Type B3 and type C)
7. Clinical research/clinical trials (lung cancer, advanced thymic cancer)

Research theme 2 (LAM, BHDS, COPD, asthma, pulmonary hypertension, Interstitial lung disease, and sleep apnea syndrome)

1. Research of lymphangioleiomyomatosis (LAM), Birt-Hogg-Dubé syndrome (BHDS), α1-antitrypsin deficiency, and cystic lung disease.
2. Elucidation of chronic obstructive pulmonary disease (COPD) pathology using smoke exposure/aging mice model.
3. Exosome analysis for COPD treatment with microRNA.
4. Analysis of innate lymphoid cells and mucosal-associated invariant T (MAIT) cells in asthma pathology.
5. Search for biomarkers that predict the effects of biologics on asthma
6. Pathological analysis of pulmonary arterial hypertension (PAH).
7. Verification of multi-tyrosine kinase inhibitor using PAH rat models.
8. Clinical study of idiopathic pulmonary fibrosis, drug-induced lung injury, and connective tissue disease-interstitial lung disease：CTD-ILD.
9. Development of new therapies targeting epithelial-mesenchymal transition.
10. Clinical studies related to sleep apnea, respiratory failure, and respiratory physiology.
11. Examination of the involvement of Alzheimer's disease in sleep apnea using mice with intermittent hypoxia exposure.

Research Highlights

Research theme 1

Our department conducts basic research on lung cancer (non-small cell lung cancer, small cell lung cancer), malignant pleural mesothelioma, and thymic carcinoma. These research projects are undertaken mainly by Kazuhisa Takahashi, Fumiyuki Takahashi, Shinsaku Togo, Ken Tajima, Yoichiro Mitsuishi, as well as graduate and overseas students under their guidance. Simultaneously, Kazuhisa Takahashi, Takehito Shukuya, Ryo Ko, Tetsuhiko Asao, and others are also promoting clinical research on lung cancer and advanced thymic carcinoma.

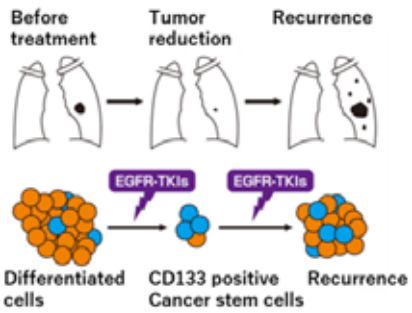


Figure: Analysis of EGFR-TKI-resistant lung cancer stem cells (CD133; lung cancer stem cell marker)

Research theme 2

We undertake the following projects: the research of LAM/BHDS, and cystic lung disease by Kuniaki Seyama, Shoichi Okamoto; COPD using a smoke exposure model by Tadashi Sato, Yuzo Kodama; bronchial asthma by Norihiro Harada, Jun Ito; pulmonary arterial hypertension by Tetsutaro Nagaoka; interstitial lung disease by Shinsaku Togo, Motoyasu Kato; and sleep apnea syndrome and respiratory failure by Satomi Shioda.

Department of
Nephrology

Chief Professor

Yusuke SUZUKI

STAFF

Senior Associate Professor
Tomohito GOHDA, Hitoshi SUZUKI

Associate Professor
Seiji UEDA (Graduate School)
Junichiro NAKATA, Masao KIHARA,
Maki MURAKOSHI

Assistant Professor
Satoshi MANO, Miyuki TAKAGI,
Takashi KOBAYASHI, Daisuke SATO,
Nao NOHARA, Masayuki MAIGUMA,
Koji SATO, Yuko MAKITA, Akiko TAKAHATA,
Toshiki KANO

Main Research Subjects

1. **Pathogenesis of IgA Nephropathy**
   "Stop the incidence of dialysis due to IgA Nephropathy"
2. **Pathogenesis of Chronic Kidney Disease induced by lifestyle-related diseases**
3. **Clinical Research in patients with hemodialysis and peritoneal dialysis**

Research Highlights

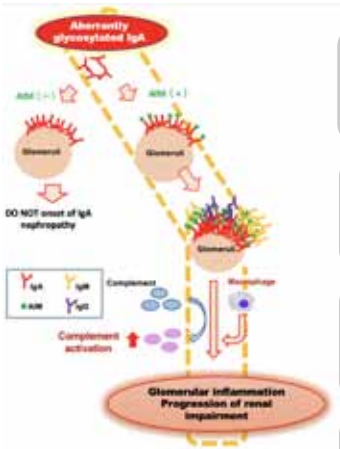
Identified a key molecule that causes glomerular inflammation in IgA nephropathy

～ Apoptosis inhibitor of macrophage (AIM) induces IgG/IgM deposition and subsequent inflammation in IgA nephropathy ～

Our research group, Akiko TAKAHATA and Yusuke SUZUKI, detected a key molecule of inflammation in IgA Nephropathy. This work is a joint research with Professsor MIYAZAKI of Laboratory of Molecular Biomedicine for Pathogenesis, Center for Disease Biology and Integrative Medicine in the University of Tokyo.

We elucidated that glomerular IgA deposition alone does not induce IgA nephropathy. Apoptosis inhibitor of macrophage (AIM) is essential for deposited IgA to bind to IgM or IgG, which leads to initiation and progression of glomerular inflammation. This research is recently published in *Journal of the American Society of Nephrology* (J Am Soc Nephrol. 2020 Sep; 31(9):2013-2024).

Our department takes place various joint research. Members in our department have various research subjects about kidney disease and are trained hard through reserch activity to offer better medical care.



Glomerular IgA deposition alone does not induce glomerular injury. AIM is essential for deposited IgA to bind to IgM or IgG and this binding leads to glomerular inflammation and progression of renal impairment.

Our research groups

IgA Nephropathy
Pathogenesis of IgA Nephropathy

Hypertention
Hypertension and endothelial injury
Multiple Organ Crosstalk

Diabetic Kidney Disease
Pathogenesis and Biomarkers of Diabetic Kidney Disease

Renal Replacement Therapy
Clinical Research in patients with hemodialysis and peritoneal dialysis

Dept. of Nephrology
Juntendo University

Department of

Internal Medicine and Rheumatology

Chief Professor

Naoto TAMURA

STAFF

Professor
Ken Yamaji

Associate Professor
Hirofumi Amano, Kazuhisa Nozawa, Michihiro Ogasawara
Masakazu Matsushita, Kurisu Tada

Assistant Professor
Makio Kusaoi, Toshio Kawamoto, Kentaro Minowa, Yoshiyuki Abe, Eri Hayashi, Goh Murayama, Tomoko Miyashita

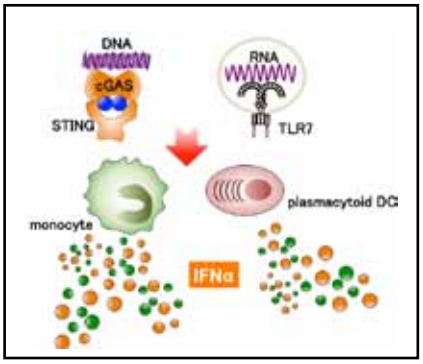
Main Research Subjects

1. **Detection of specific serum biomarkers for SLE patients with severe manifestations**
2. **Establishment of new treatment for interstitial lung disease with anti-MDA5 antibody**
3. **Elucidating the mechanism of interferon-α overproduction in systemic lupus erythematosus**

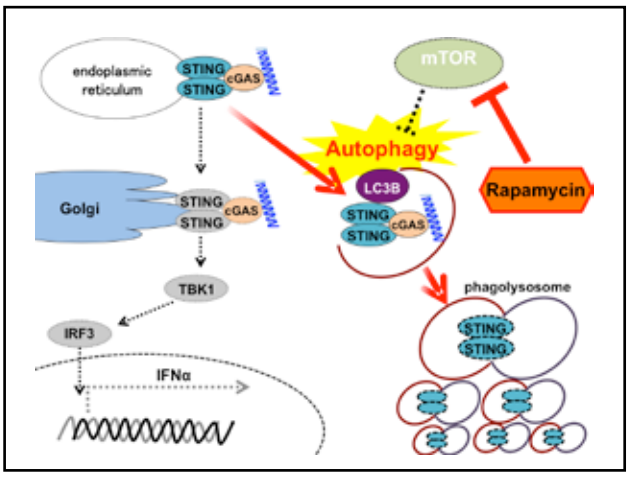
Research Highlights

An autophagy inducer suppresses the overproduction of IFN-α from monocytes via STING in systemic lupus erythematosus.

It has previously been demonstrated that interferon-α (IFN-α) is involved in the development and pathogenesis of systemic lupus erythematosus (SLE). Several studies have reported the increased production of IFN-α from the immunocompetent cells; however, IFN-α -producing cells or IFN-α production pathway that are directly associated with the pathogenesis of SLE have not been identified yet. We have been working in collaboration with the Department of Immunology in Juntendo University for elucidating the mechanism of IFN-α overproduction in SLE. We analyzed IFN-α production of the peripheral blood mononuclear cells derived from SLE patients. We found the overproduction of IFN-α from plasmacytoid dendritic cells (pDCs) via Toll-like receptor (TLR)-7, which are intracellular RNA receptor, in SLE patients. We have published this finding in Arthritis Research & Therapy in 2017. Similarly, we also found that, in severe SLE patients, significantly large amount of IFN-α is produced from monocytes via the stimulator of interferon genes (STING), which is an intracellular DNA receptor. Moreover, we focused on understanding the metabolism of STING via autophagy. We used the autophagy inducer, rapamycin, to verify if the production of IFN-α is decreased by reducing the expression of STING in monocytes derived from SLE patients. These results suggested that rapamycin can be potentially a new therapeutic reagent for SLE by reduction of IFN-α production. These findings were published in Rheumatology (Oxford) in 2020.



In SLE, production of IFN-α from pDCs via TLR7 as well as that from monocytes via STING is increased.



Rapamycin decreases the production of IFN-α in the STING pathway by uptake and degradation of STING in autophagosomes.

Department of

Hematology

Chief Professor

Norio KOMATSU

STAFF

Senior Associate Professor
Makoto Sasaki, Jun Ando

Associate Professor
Yasuharu Hamano, Miki Ando, Tomoiku Takaku, Hajime Yasuda, Yutaka Tsukune, Yoshinori Hashimoto, Yoko Edahiro

Assistant Professor
Miyuki Tsutsui, Shuichi Shirane, Naoki Watanabe, Tomonori Ochiai, Sakiko Harada, Tadahiro Honda

Main Research Subjects

1. **Development of iPSC-derived antigen-specific cytotoxic T cell therapy**
2. **Development of next-generation chimeric antigen receptor T cell (CAR T cell) therapy**

Research Highlights

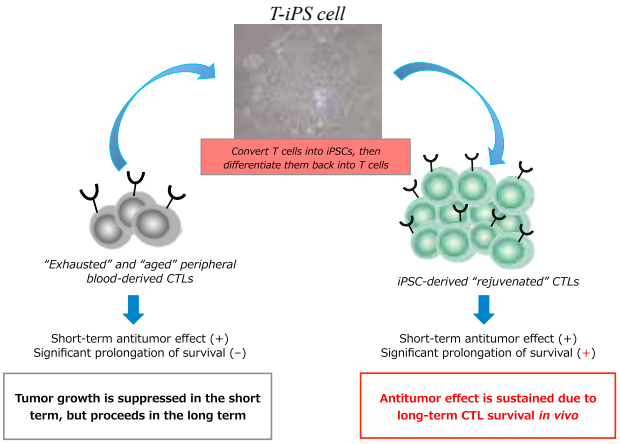
Malignant lymphoma successfully cured with iPSC-derived cytotoxic T cells (CTLs) — Promising new cell therapy for refractory NK-cell lymphoma —

At the Department of Hematology at Juntendo University School of Medicine, iPSC technology is being used to pursue research into the functional "rejuvenation" of cytotoxic T lymphocytes (CTLs) from an "exhausted" state, while maintaining their antigen specificity, and their use to treat refractory tumors.

Unlike peripheral blood CTLs, functionally rejuvenated iPSC-derived CTLs have been demonstrated to survive for prolonged periods in mice *in vivo* as immature memory T cells. Functionally rejuvenated iPSC-derived CTLs strongly suppressed the growth of an EBV positive NK-cell lymphoma (an extremely refractory lymphoma) for a prolonged period before successfully eradicating the lymphoma. This finding could open an important door to the development of new therapies using iPSC-derived CTLs in recurrent and severe cases of refractory lymphoma (Ando et al., *Haematologica*, 2020).

iPSC-derived T cells that exhibit prolonged survival *in vivo* are also being used to develop next-generation CAR-T cell therapies. Our aim is to bridge the gap between fundamental experimental research and clinical practice.

This technology is being used for hematological malignancies and solid tumors. iPSC-derived human papillomavirus (HPV) antigen-specific CTLs were successfully created to target cervical cancer, known as the "mother killer." In a mouse model, these iPSC-derived HPV-specific CTLs were demonstrated to strongly suppress the growth of cervical cancer *in vivo* and prolong survival for significantly longer than peripheral blood CTLs. This research shows that iPSC banking will allow for a stable supply of iPSC-derived CTLs effective against cervical cancer and opens an important door to development of new therapies using immune cells (Honda et al., *Molecular Therapy*, 2020).



Department of

Metabolism & Endocrinology

STAFF

Senior Associate Professor
Hiroaki Sato, Yoshifumi Tamura (Center of Sportology)

Associate Professor
Akio Kanazawa, Takeshi Ogihara, Takeshi Miyatsuka, Toyoyoshi Uchida, Tomoya Mita, Yuya Nishida, Hiromasa Goto, Junko Sato

Assistant Professor
Hitoshi Iida, Takashi Funayama, Hideyoshi Kaga, Satoshi Kadowaki, Kenichi Nakajima, Miwa Himuro

Main Research Subjects

1. **Mechanism of Pancreatic β cell differentiation, regeneration and dysfunction**
2. **Pathophysiology of insulin resistance in Asians**
3. **Pathophysiology of diabetic vascular complication**

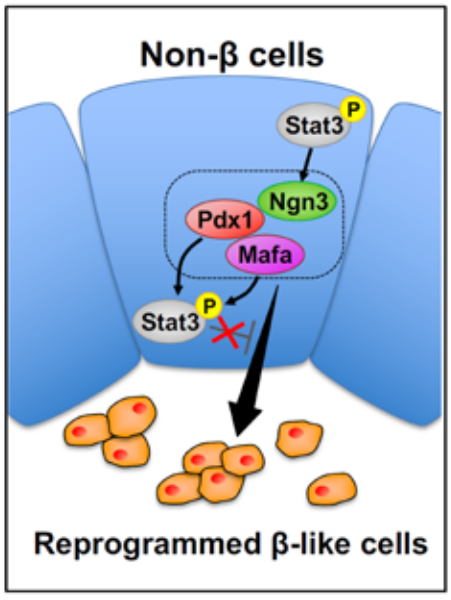
Research Highlights

In diabetes, a decrease in the number of insulin-producing pancreatic β-cells is considered to be an main pathophysiology. Therefore, treatment to replace the reduced pancreatic β-cells is ideal. Until now, it has been known that simultaneous expression of transcription factors Pdx1, Neurog3, and Mafa in pancreatic exocrine cells induces differentiation into pancreatic β-cells, thus, in the future, direct reprogramming from cells in the body to β-cells is expected to be a novel treatment for diabetes, but for that purpose, it is necessary to further improve the efficiency of differentiation induction.

For this purpose, we have been conducting our own studies with the aim of improving the efficiency of differentiation induction. As a result, we noticed that STAT3 activation occurs when the transcription factors Pdx1, Neurog3, and Mafa are expressed in mPAC cells, an exocrine pancreatic cell line. Examining this event in detail, we found that STAT3 activation did not occur, especially in differentiated pancreatic β-cells, and that suppression of STAT3 activation promoted β-cell differentiation in cell lines.

Next, in order to investigate whether reprogramming efficiency is improved by similar STAT3 suppression in vivo, mice expressing the transcription factors Pdx1, Neurog3, and Mafa with the deletion of STAT3 gene in pancreatic exocrine cells were prepared. By deleting STAT3 gene in this mice, the number of new β-cells with cell maturation markers increased and pancreatic islet-like structure in which multiple new β-cells were clustered was frequently found. Furthermore, hyperglycemia was improved by adenovirus mediated expression of Pdx1, Neurog3, and Mafa in the pancreas with the administering a STAT3 inhibitor in alloxan diabetic model mice.

In summary, we clarified a new molecular mechanism in which the STAT3 signal negatively regulates reprogramming from non-β cells to β cells, and it became possible to induce β cell differentiation by suppressing the STAT3 signal. The results of this research were published in "Ebio Medicine".



Department of

General Medicine

Chief Professor

Toshio NAITO

STAFF

Professor
Hiroshi Fukuda, Chieko Hamada, Gautam A. Deshpande

Senior Associate Professor
Hirohide Yokokawa,Yang Kwang-seok, Akihiro Inui

Associate Professor
Kazutoshi Fujibayashi, Mizue Saita, Yukiko Fukui, Mai Suzuki, Hirotake Mori, Miki Kanai

Assistant Professor
Takako Sasayama, Yuichi Takahashi, Taiju Miyagami, Sayato Fukui

Main Research Subjects

1. **Improvement for the delivery system of HIV infection treatment using ICT (Information and Communication Technology)**
2. **Diagnosis and treatment of COVID-19**
3. **Association between glycemic control and health literacy in patients with diabetes in Vietnam**
4. **Efficacy of the pneumococcal vaccine using database**

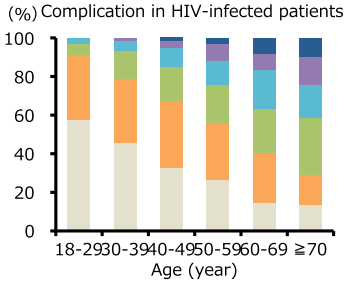
Research Highlights

Development of HIV infected-patients' care system for general physicians/primary care physicians, utilizing an ICT-based education system, a remote medication support network, and an alert system.

The life expectancy of HIV-infected patients has improved with the rapid development of anti-HIV drugs. Consequently, the aging of them and their comorbidities subsequent to aging have a significant impact on their prognosis.

It is necessary to establish a medical system that includes general physician/primary care physicians in addition to HIV specialists for the long-term management of their patients. Naito et al. has established an ICT-based education system and remote medication support network, which are enable general physician/primary care physicians to conduct HIV treatment and improved medication adherence, which was not possible with face-to-face consultations.

We aim to build a more precise medical system by utilizing the alert system.



Patients with HIV infection have more chronic complications compared to those without (67.3% vs. 34.9%). Therefore, comprehensive medical care is important.
(Database study of 17 million people, JIC, 2019)
Currently, we are conducting research for chronic complication management and early detection of HIV infection using the national database.

Medication management and consultation using App.

Online case study conference using App.

An electronic medical record alert system for early detection of HIV infection (warning to test for HIV if hepatitis or shingles are present).

Department of

Psychiatry

STAFF

Senior Associate Professor
Tohru Ohnuma

Associate Professor
Chihiro Kakiuchi, Masanobu Ito, Narimasa Katsuta, Tsuneyoshi Ota

Lecturer
Yoshihide Takeshita

Assistant Professor
Yasuhito Nagai, Hiroki Yamashita, Yui Kurosawa, Hiromi Takagi

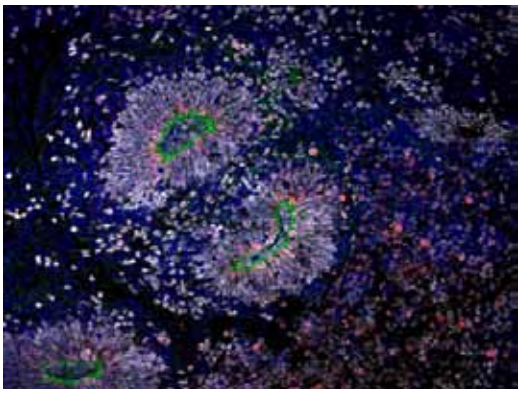
Main Research Subjects

1. **Revealing the cause of bipolar disorder and developing new treatment**
2. **Revealing the pathology of schizophrenia and developing new treatment**
3. **Revealing the cause of autism spectrum disorder and developing new treatment**

Research Highlights

Revealing the causes of psychiatric illnesses and developing new treatment

Professor Tadafumi Kato, who joined a new post in April 2020, has long been engaged in the neurobiological study of bipolar disorder at the RIKEN Center for Brain Science. After proposing the mitochondrial dysfunction hypothesis of bipolar disorder, Dr. Kato went on to develop a mouse model exhibiting recurrent depression-like episodes based on this hypothesis and identified the paraventricular thalamic nucleus as the candidate of causative brain region of bipolar disorder (*Molecular Psychiatry* 2016). He also demonstrated that imbalance in the differentiation of excitatory and inhibitory neurons contributes to the onset of psychiatric illnesses through single-cell RNA sequence analysis of cerebral organoids derived from iPS cells of discordant monozygotic twins. Dr. Kato's other discoveries include the involvement of de novo mutations in bipolar disorder and the contribution of brain somatic mutations in psychiatric illnesses (*Neuron* 2014). He is involved in an international research collaboration on the postmortem brain (*Nature Neuroscience* 2008) and in international consortia on genome research (ConLiGen, Bipolar Sequencing Consortium, etc.; *NEJM* 2014, *Lancet* 2016). On October 1st, the Department of Molecular Pathology of Mood Disorders was launched and a joint research with Sumitomo Dainippon Pharma has started. He will continue his research into causes and treatments of bipolar disorder and other mood disorders in collaboration with the Center for Mood Disorders established on September 1st. Senior Associate Professor Toru Onuma is studying schizophrenia seeking to reveal its pathology, develop treatment methods, and explore biomarkers. Associate Professor Masanobu Ito is studying the effects of prenatal exposure to psychotropic drugs and working on drug development research using animal models of autism spectrum disorder induced by prenatal exposure to valproic acid with the support of AMED. The department is also pursuing joint research with the radiology department seeking to reveal the brain pathology of psychiatric disorders and develop diagnostic methods using new magnetic resonance imaging techniques.



Press Release
Developmental excitation-inhibition imbalance underlying psychoses revealed by single-cell analyses of discordant twin-derived cerebral organoids
(Aug 7th, 2020) (Sawada et al, *Molecular Psychiatry* 2020)

Department of
Neurology

Chief Professor

Nobutaka HATTORI

STAFF

Associate Professor
Taiji Tsunemi, Shigeto Sato, Taku Hatano, Shinji Saiki, Kenya Nishioka, Yuji Ueno, Genko Oyama, Noriko Nishikawa, Nobukazu Miyamoto, Yuji Tomizawa

Lecturer
Kazumasa Yokoyama

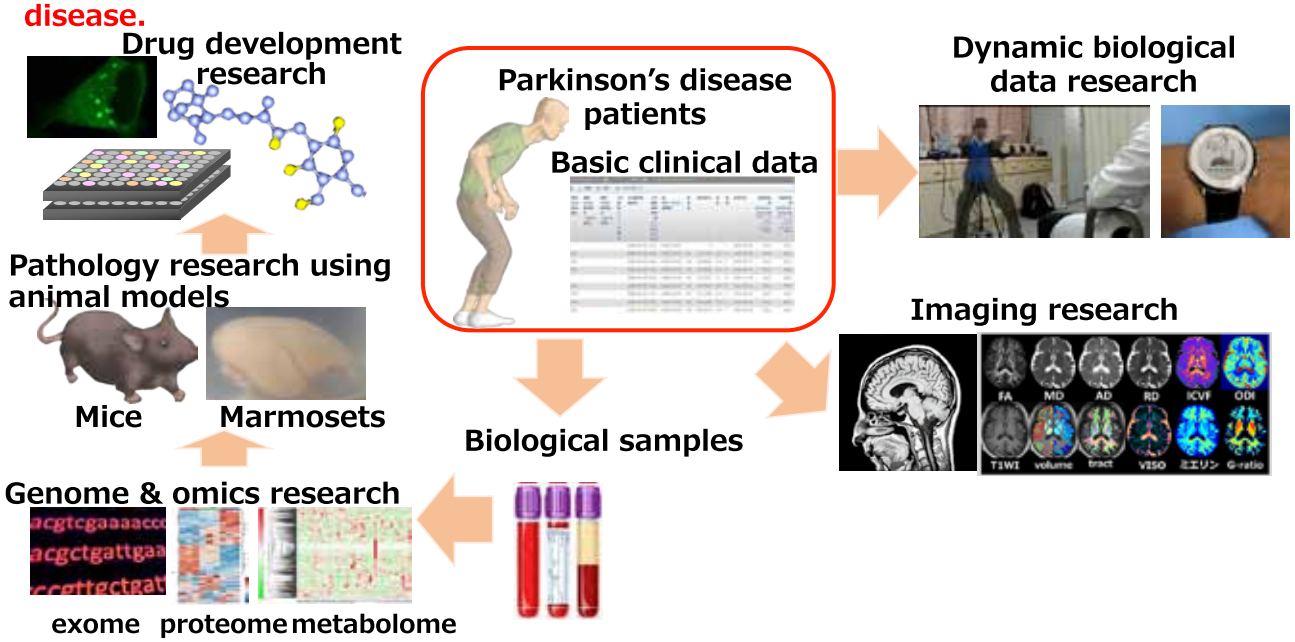
Assistant Professor
Yutaka Oji, Kenichiro Hira

Main Research Subjects

1. **Research on the diagnosis and treatment of Parkinson's disease**
2. **Research on the pathology of Parkinson's disease**
3. **Foundational and clinical research on cerebrovascular disorders**

Research Highlights

Our lab is engaged in diverse research into new approaches to curing Parkinson's disease.



Major achievements of the past 5 years

Ann Neurol 2019; *Autophagy* 2020; *Brain* 2019; *Lancet Neurol* 2016; *Mov Disord* 2017, 2018, 2020; *J Neurosci* 2020; *Neurology* 2018; *PNAS* 2019

Department of

Pediatrics

Chief Professor

Toshiaki SHIMIZU

STAFF

Senior Associate Professor
Ken TAKAHASHI

Associate Professor
M Kishiro, N Takubo, H Shoji, T Kudo, K Hisata, J Fujimura, H Haruna, M Suzuki, S Abe, K Matsui

Assistant Professor
H Fukunaga, T Furukawa, M Ikeno, A Endo, K Jimbo, T Ikuse, E Inage, N Saito, O Tomita, T Ishibashi

Main Research Subjects

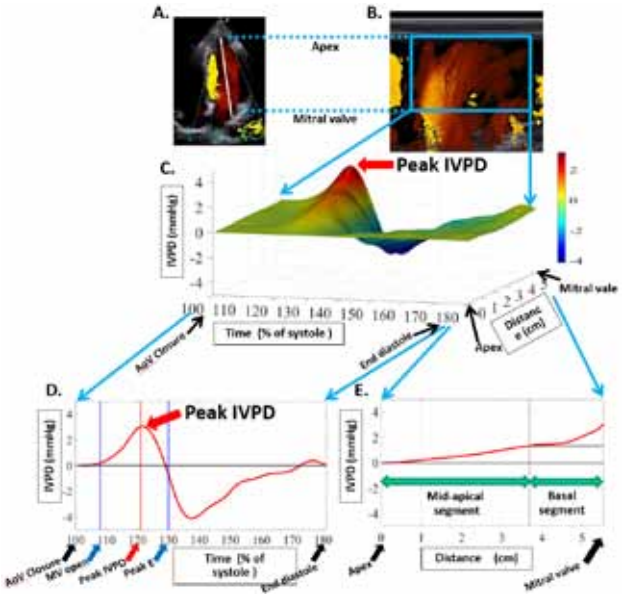
1. **Investigation of the pathogenesis of pediatric inflammatory bowel disease**
2. **Influence of skeletal muscle insulin resistance in a novel fetal growth restriction model**
3. **In-depth insight into the mechanisms of cardiac dysfunction in patients with childhood cancer survivors**

Research Highlights

1. Kudo et al. reported that polarized Th1 cells were involved in the pathogenesis of Crohn's disease in the Peyer's patches, increased expression of IL-17 in the IBD mucosa, and Galectin-9 is up-regulated in IBD. Jimbo et al. reported increased expression of CXCR3 and MMPs in IBD mucosa. Assistant Prof. Ikuse et al. are studying the interaction between IBD epithelium and the intestinal environment using organoid technology.

2. Shoji, et al. established a novel FGR rat model by placing devises to uterine arteries of pregnant rats. The mRNA and protein expression of AKT and GLUT4 in soleus muscle were significantly lower in FGR rats at 12 weeks of age. We will investigate the relationship between dysbiosis and development of metabolic syndrome using this model.

3. Associate Prof. Takahashi and his graduate students have been assessing cardiac function in childhood cancer survivors using layer specific strain and intra-ventricular pressure gradient measurements for cardiac dysfunction, which was newly developed with their own code as described in right figures. These results suggested that those new methods could sensitively detect cardiac dysfunction and play an important role to decide therapeutic plan at early stage.



Department of

Esophageal & Gastroenterological Surgery

Chief Professor

Shinji MINE

STAFF

Professor
Yoshiaki Kajiyama
Masahiko Tsurumaru

Associate Professor
Takashi Hashimoto, Tadanori Hashiguchi, Motomi Nasu, Daisuke Fujiwara

Assistant Professor
Asako Ozaki

Main Research Subjects

1. **Clinicopathological assessment of lymph node metastasis in patients who underwent surgery for esophageal cancer.**
2. **Clinicopathological investigation of patients who underwent endoscopic treatment for superficial esophageal cancer.**
3. **Investigation of cancer microenvironments using a murine esophageal cancer model.**

Research Highlights

◆Most of the patients had undergone 3 fields lymphadenectomy, including cervical lymph nodes, enabling the further analysis of lymph node metastasis and prognosis. In 2019 and 2020, we investigated the optimal procedure for cervical lymph node metastasis positive patients based on preoperative diagnosis and treatment results. The distribution of lymph node metastasis with esophageal adenocarcinoma was also investigated.

◆The patients with superficial esophageal cancer who underwent endoscopic treatment comprehensively analyzed based on tumor depth.

◆The effects of hypoxia and malnutrition on the cancer microenvironment were investigated using the patient-derived xenograft . Using this model, further research into epigenomic treatment was also planned. These researches have been and is to be performed in collaboration with the Chair of Pathological Oncology.

Department of

Coloproctological Surgery

Chief Professor

Kazuhiro SAKAMOTO

STAFF

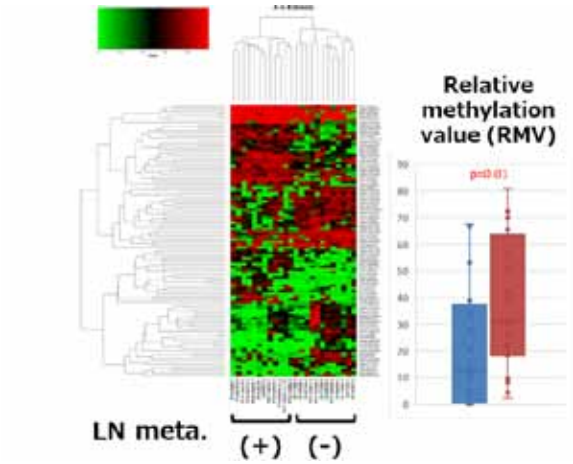
Senior Associate Professor
Yutaka Kojima

Associate Professor
Makoto Takahashi
Kiichi Sugimoto
Shinya Munakata

Main Research Subjects

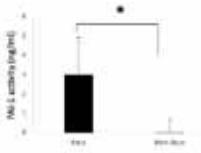
1. **Epigenome in colorectal cancer**
2. **Pathophysiological analysis of postoperative complication such as ileus, anastomotic leakage**
3. **Research of ischemic or adhesive maker**

Research Highlights

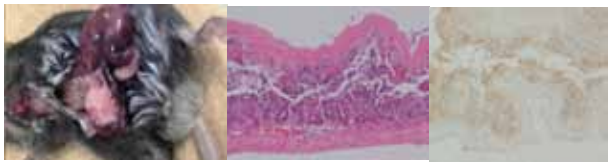


1. Exploration of biomarkers in prediction of long-term outcomes and sensitivity to chemotherapy in colorectal cancer with epigenome

2. Etiology of postoperative complications such as ileus and anastomotic leakage can be linked to preventive drug discovery by analyzing the bacterial flora and using adhesion model of mice.



3. We focused on Receptors for Advanced Glycation End-Products(RAGE) as an intestinal ischemia marker and demonstrated that it induces neutrophil mobilization and suppresses intestinal epithelial regeneration.



Department of

Hepatobiliary-Pancreatic Surgery

Chief Professor

Akio SAIURA

STAFF

Senior Associate Professor
Yoshihiro Mise

Associate Professor
Hiroshi Imamura
Ryuji Yoshioka

Assistant Professor
Tomoya Mizuno
Hirohumi Ichida
Yu Gyoda

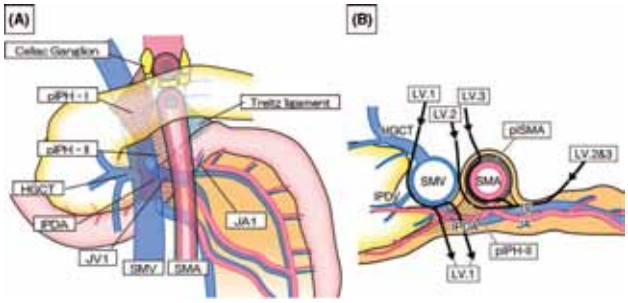
Main Research Subjects

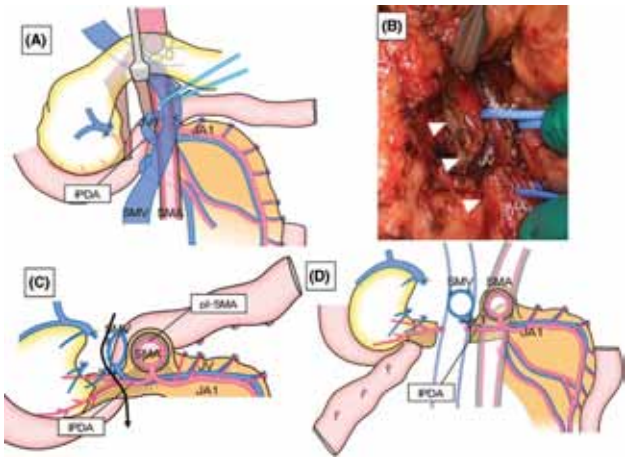
1. **Optimal surgical strategy for pancreatic cancer**
2. **Multidisciplinary treatment of the Hepatobiliary malignancies**
3. **Improvement of QOL after pancreatic surgery**

Research Highlights

We published many reports about surgical approaches to hepatobiliary-pancreatic malignancies, especially focusing on pancreatic cancer.

Our works listed below made a significant contribution to the development of hepatobiliary-pancreatic surgery.





*Supramesocolic anterior artery first approach for PD

*Sinistral portal hypertension after PD with splenic vein resection

*Regional PD for pancreatic caner

Department of

Gastroenterology and Minimally Invasive Surgery

Chief Professor

Tetsu FUKUNAGA

STAFF

Visiting Professor
Malcolm Brock(Adjunct)
Senior Associate Professor
Noriyuki Inaki
Associate Professor
Shinichi Oka, Hajime Orita
Lecturer
Toru Takahashi
Assistant Professor
Sanae Kaji, Yukinori Yube

Main Research Subjects

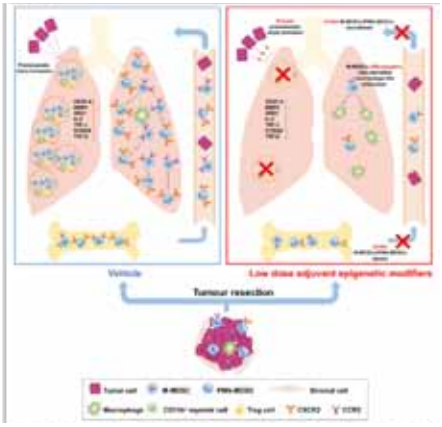
1. **Cancer metabolism (lipid, amino acid etc.)**
2. **Prevention for metastases by Epigenetic therapy**
3. **Predictive Marker for gastric cancer prognosis by In silico**
4. **Development of therapeutic drugs for adiposity (obesity)**

Research Highlights

Epigenetic therapy for lung cancer patients succeeded 20% metastases inhibition by disrupting premetastatic niches

Adjunct professor **Malcolm Brock** reported possibility of epigenetic therapy by MDSCs inductive inhibition and disrupting premetastatic Niches in 2020 Feb, Nature (Fig.1).

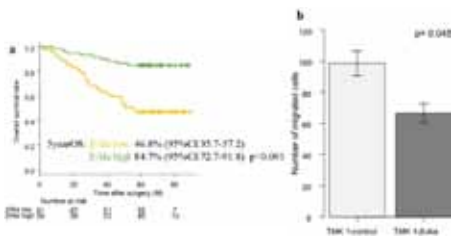
Fig.1



Our Cancer metabolic research team with department of biochemistry and pathology have reported highly express Fatty acid synthase in cancer cells and that inhibition works prevention and treatment.

Recently Dr. Kaji and Dr. Chou reported some amino acids influenced metastasis and recurrences in 2020 March, gastric cancer(Fig. 2).

Fig.2



We are now making international collaboration research team with Prof. Brock. Our goal is the development of epigenetic therapy by inductive inhibition of MDSCs and disrupting metastatic niches.

Department of

Cardiovascular Surgery

Chief Professor

Atsushi AMANO

STAFF

Professor
Tohru Asai

Senior Associate Professor
Shiori Kawasaki
Taira Yamamoto

Associate Professor
Hiroaki Hata, Terumasa Morita, Shizuyuki Dohi, Satoshi Matsushita, Akie Shimada, Keisuke Nakanishi

Assistant Professor
Atsumi Oishi, Daisuke Endo

Main Research Subjects

1. **Relationship between left atrial appendage tissue and occurrence of postoperative atrial fibrillation**
2. **Effect of pericardial fat on cardiac function**
3. **Research of cardiac progenitor cells on cardiac repair**

Research Highlights

Dissemination of clinical data utilizing abundant clinical experience and translational research with advanced basic research

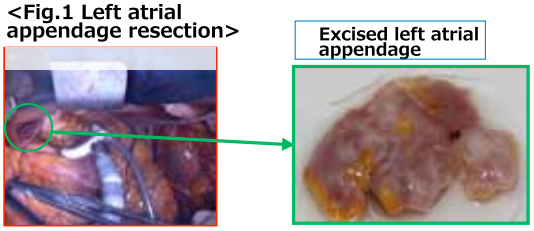
Our department boasts a top-class number of operations and surgical outcomes in Japan. The dissemination of clinical data based on abundant experience is gaining attention from home and abroad.

Simultaneously, we are also conducting analysis using tissue samples obtained during surgery. In our department, we perform resection of the left atrial appendage (tip of the left atrium) to prevent cerebral infarction from atrial fibrillation, an important complication after heart surgery (**Fig. 1**). We are elucidating the mechanism of atrial fibrillation by conducting genetic analysis and histochemical analysis of the resected tissues (**Figs. 2A, 2B**). In addition, we analyze the pericardial adipose tissue to clarify the role it plays in cardiomyocytes and cardiac function, analyze the excised specimen of the hypertrophied left ventricular myocardium, and perform image analysis of the aortic disease and valvular disease using 3-dimensional computed tomography (3D-CT).

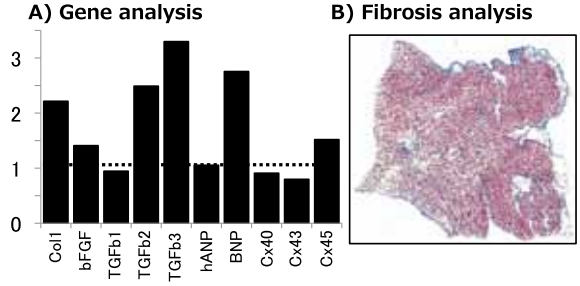
We are also actively engaged in research on regenerative medicine that has been gaining interest in recent years. Our hospital performs autologous skeletal muscle-derived myoblast cell sheets (Heart Sheet®) and is a clinical trial facility for iPS cell sheets. Treatment using regenerative medicine as a new treatment method for severe heart failure is an urgent research topic.

Our department has focused on heart-derived stem cells "cardiac progenitor cells" (**Fig. 3AB**) as a unique cell therapy method. Through gene transfer and physical/electrical stimulation (**Fig. 3C**), we are continuing research with the aim of activating these cells and establishing them as a new treatment for heart diseases.

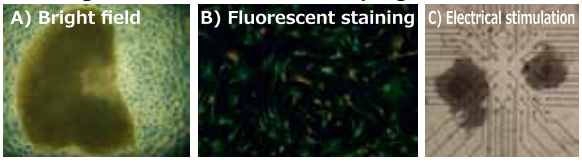
<Fig.1 Left atrial appendage resection>



<Fig.2 Left atrial appendage analysis in atrial fibrillation>



<Fig.3 Cardiac tissue-derived progenitor cells >



Department of

General Thoracic Surgery

STAFF

Senior Associate Professor
Kazuya Takamochi

Associate Professor
Takeshi Matsunaga
Aritoshi Hattori
Mariko Fukui

Assistant Professor
Kota Imashimizu, Hideomi Ichinokawa, Takahiro Tatsumori, Kazuhiro Hata, Mikiko Suzuki, Yukio Watanabe, Yasuhiro Ueno, Takuya Ueda

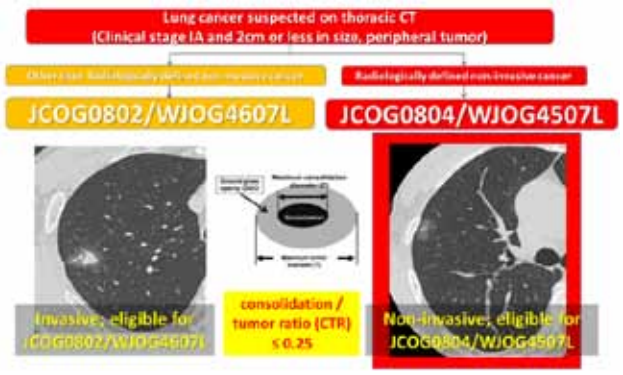
Main Research Subjects

1. **Sublobar resection for lung cancer**
2. **Personalized individual treatment for lung cancer**
3. **Salvage surgery for lung cancer**
4. **Robotic assisted surgery for lung cancer**
5. **Surgery for lung cancer in patients with interstitial pneumonia**

Research Highlights

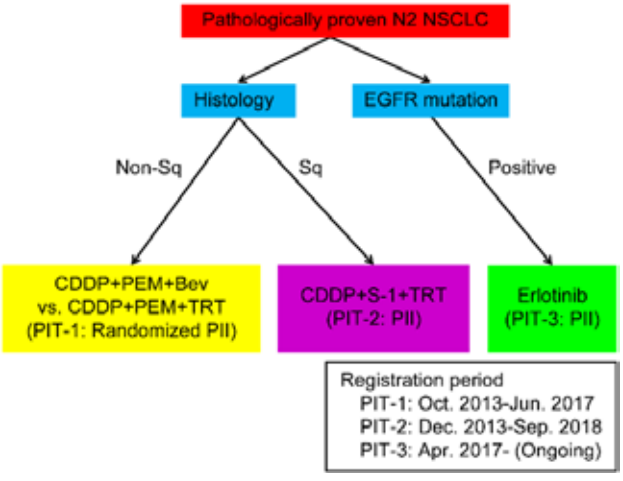
Standard surgical treatment for primary lung cancer may change for the first time in 60 years

In the JCOG Lung Cancer Surgery Group, Professor Kenji Suzuki of the Department of Thoracic Surgery, Juntendo University, examined whether standard surgical treatment for early-stage lung cancer could be converted from conventional lobectomy to segmentectomy, and reported on early postoperative complications after sublobar resection or lobectomy in a randomized trial.



The first personalized individual treatment including surgery for lung cancer

Kazuya Takamochi, senior associate professor of the Department of Thoracic Surgery, Juntendo University, examined the Personalized Induction Treatment (PIT) study, PIT-I, II, or III according to EGFR mutation status and histology. The final report on PIT-I was presented at the European Society for Medical Oncology.



Department of

Pediatric Surgery

Department of

Research and Development for Organoids

STAFF (Department of Pediatric Surgery)

Senior Associate Professor
Hiroyuki Koga

Associate Professor
Naho Fujiwara, Takanori Ochi, Shogo Seo

Assistant Professor
Yuka Matsumoto, Kazuto Suda

Graduate Student
Shusaku Nitta

Main Research Subjects

- **Clinical applications of regenerative medicine research in pediatric surgical diseases**

Research Highlights

Study 1. Functional reconstruction of small intestine in short bowel syndrome by SI organoid transplantation into colonic tissue (Matsumoto & Nakamura)

Short bowel syndrome (SBS) patients suffer from deficient nutrient absorption. We are researching and developing techniques for transplanting organoids derived from the small intestine (SI) into ascending colonic tissue to compensate for diminished SI function in this population. This study is being carried out in collaboration with Professor Tetsuya Nakamura (Department of Research and Development for Organoids), who developed *intestinal epithelial replacement,* a technique involving the transplantation of allogeneic GFP⁺ SI organoids into abraded rectal epithelium (Fig. 1: Fukuda et al., Genes Dev, 2014).

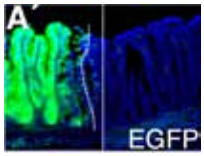
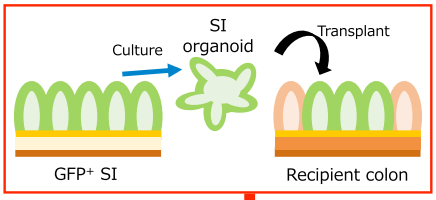
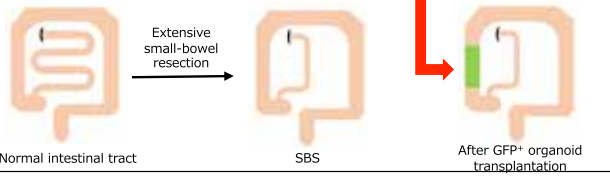


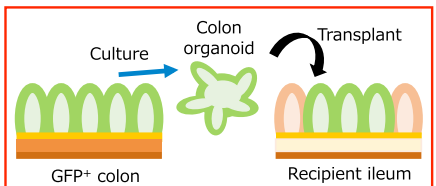
Fig. 1: Intestinal epithelial architecture following GFP⁺ SI organoid transplantation visible in rectal tissue section.

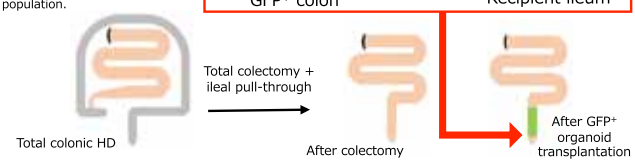




Study 2. Establishing colonic epithelial organoid transplantation into SI tissue as a treatment for total colonic Hirschsprung disease (Suda & Nakamura)

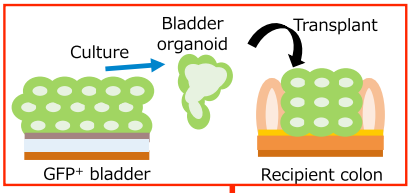
The entire colon is surgically removed in patients with total colonic Hirschsprung disease (HD). We are researching and developing techniques for transplanting colonic organoids into distal SI tissue—the inverse of the procedure explored in Study #1—to improve water and ion absorption in this population.

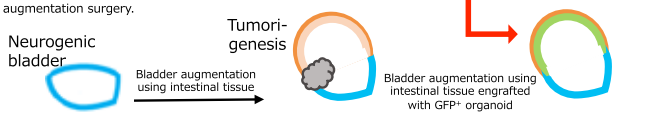




Study 3. Novel enterocystoplasty technique using intestinal tissue engrafted with bladder organoids (Suda & Nakamura)

Spinal bifida patients often suffer from troubling long-term complications, such as malignant tumors, after enterocystoplasty (i.e., bladder augmentation using gastrointestinal tissue). We are researching and developing new cystoplasty techniques that can prevent such complications; specifically, we are applying the technique developed in Study 1 to xenograft bladder organoids onto intestinal tissue for use in augmentation surgery.





Study 4. Experimental restoration of neural function in Hirschsprung disease by neural stem cell transplantation (Fujiwara)

We have previously published findings implicating SEMA3A and other molecules in the development of HD, which show that they inhibit the migration of neural crest-derived cells in HD model mice (Fig. 2: Fujiwara et al., J Pediatr Surg, 2018).
Our current efforts are aimed at reconstructing neural networks in the intestinal tract of HD model mice through the transplantation of enteric neural crest stem cells, in the hopes of establishing new therapies for the disease using this technique.

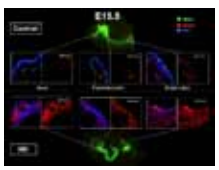
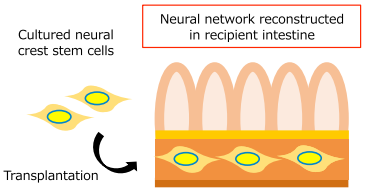


Fig. 2: SEMA3A expression (red) enhanced in intestinal submucosal and muscular layers at E15.5 in HD model mice compared to control.



Study 5. Calretinin expression analysis in Hirschsprung disease (Nitta & Suda)

Calretinin is regarded as a positive marker of intrinsic nerve fibers. We are evaluating this protein's expression in HD model mice over time, starting with the embryonic stage, to determine the mechanisms underlying its appearance in HD pathogenesis along with its utility as a novel diagnostic tool.

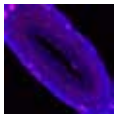


Fig. 3: Nerve fibers within intestinal muscle layer of HD model mice evaluated at E13.5 using calretinin antibody (pink).

Department of

Breast Oncology

Chief Professor

Mitsue SAITO

STAFF

Senior Associate Professor
Kotaro Iijima

Associate Professor
Katsuya Nakai, Yoshiya Horimoto, Toshitaka Uomori

Graduate Student Doctor's Degree Program
Madoka Matsuzawa, Ritsuko Sasaki, May Thinzar Hlaing, Ryoko Semba, Yumiko Ishizuka, Yoshie Shirakami-Takatori, Yuki Saito

Main Research Subjects

1. **Search for predictive factors of systemic treatments for breast cancer**
2. **Elucidation of the immune response to systemic treatments**
3. **Elucidation of mechanisms of invasion in non-invasive breast cancer**

Research Highlights

In relation to estrogen signaling in breast cancer cells, we have shown that increased expression of FOXA1 relates with decrease of chemotherapeutic efficacy[1] and development of later recurrence (Fig. 1)[2]. Furthermore, we revealed that the number of circulating cancer cells with epithelial-mesenchymal transition inversely correlates with chemo-effect[3].

To elucidate the immune response to pharmacotherapy, we are investigating profiling of immunocompetent cells in peripheral blood during treatments. Tumor immunity of primary lesion has also been analyzed and we found that medullary carcinomas have high levels of CD8-positive T-cell infiltration (Fig. 2)[4].

We are also trying to elucidate mechanisms of invasion in noninvasive breast cancer. We showed that at this early-stage, HER2 signaling can be activated without gene amplification[5].

We are collaborating many researchers, both at our university and elsewhere.

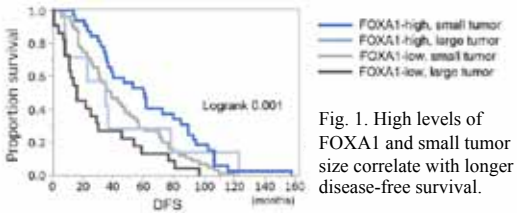


Fig. 1. High levels of FOXA1 and small tumor size correlate with longer disease-free survival.

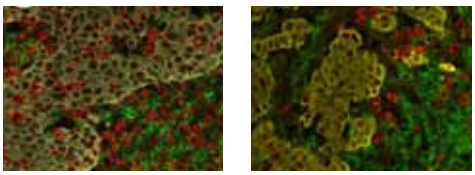


Fig. 2. Medullary carcinoma (left) shows higher level of CD8-positive T-cell infiltration, compared to no special breast cancer (right). Red: CD8; green: CD4; yellow: cytokeratin

Our collaborators:
Cancer Institute Hospital AMD center
National Cancer Center Hospital
Saitama Cancer Center
Hiroshima University Department of Anatomical Pathology
Tokyo Medical University
The Institute of Medical Science, The University of Tokyo
University of Birmingham, Institute of Cancer and Genomic Sciences

1. *Br J Cancer* 112:345-51, 2015
2. *Breast Cancer Res Treat* 183:41-8, 2020
3. *J Transl Med* 16:287, 2018
4. *Hum Pathol* 70:129-38, 2017
5. *Am J Surg Pathol* 43:1221-8, 2019

Department of

Neurosurgery

Chief Professor

Akihide KONDO

STAFF

Professor
Atsushi Umemura, Hidenori Oishi

Senior Associate Professor
Hidenori Sugano

Associate Professor
Yuko Ohara, Yuichi Tange, Kazuaki Shimoji, Madoka Nakajima, Munetaka Yamamoto, Hirokazu Iwamuro, Osamu Akiyama, Mario Suzuki

Assistant Professor
Kosuke Teranishi, Kenji Yatomi, Yasushi Iimura, Yuzaburo Shimizu, Kazumoto Suzuki, Hiroharu Suzuki

Main Research Subjects

1. **Molecular analyses of central nervous system tumors**
2. **Pathophysiology of idiopathic normal pressure hydrocephalus**
3. **Identification and analysis of epilepsy focus with wave studies**

Research Highlights

1. Molecular biology of central nervous system tumors

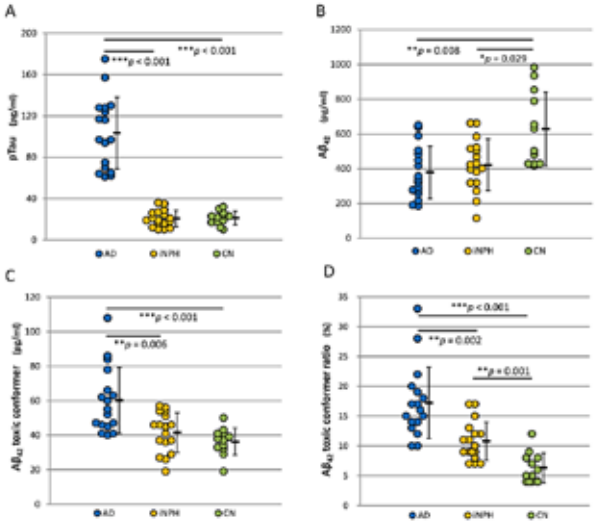
It has become clear the fact molecular backgrounds reflect more correct characters than histopathological appearance. Using comprehensive analysis on excised tumor specimens, we are estimating prognosis of tumors and identifying factors for tumorization. We are promoting researches those lead to treatments.

2. Pathophysiology of idiopathic normal pressure hydrophalus

This disease has been attracted attention as a treatable dementia. We identified biomarkers for diagnosis and the factors of prognosis. We are conducting research directly connected to the treatment by identifying the etiosis. (Figure)

3. Identification and analysis of epilepsy focus with wave studies

The digitization of EEG brought us time frequency analysis. Using this method, we have conducted research to identify epilepsy focus by visualizing high-frequency lesions. This is expected to improve the prognosis of seizures after treatments.



C. Akiba et al. Journal of Alzheimer's Disease, 2018

Some biomarkers for the diagnosis of idiopathic normal pressure hydrocephalus

Department of

Orthopaedic Surgery

Chief Professor

Muneaki ISHIJIMA

STAFF

Senior Associate Professor
TAKAGI Tatsuya

Associate Professor
OKUDA Takatoshi, KAWASAKI Takayuki, NOJIRI Hidetoshi, BABA Tomonori, SUEHARA Yoshiyuki, SAITA Yoshitomo

Lecturer
NAITO Kiyohito, KANEKO Haruka, HONMA Yasuhiro

Assistant Professor
GONDA Yoshinori, WATARI Taiji, KUBOTA Daisuke, NAGURA Nana, YOSHISA Keiichi, SATO Tatsuya

Main Research Subjects

1. **Realization of treatment according to the pathophysiology of knee osteoarthritis**
2. **Locomotive syndrome in cancer patients: Prevention of disability due to bone metastasis**
3. **Elucidation of risk factors and establishment of preventive methods for traumatic shoulder dislocation**
4. **Analysis of influence of aging for the peripheral nerves and tendons**
5. **Establishment of precision medicine in bone and soft tissue tumors**

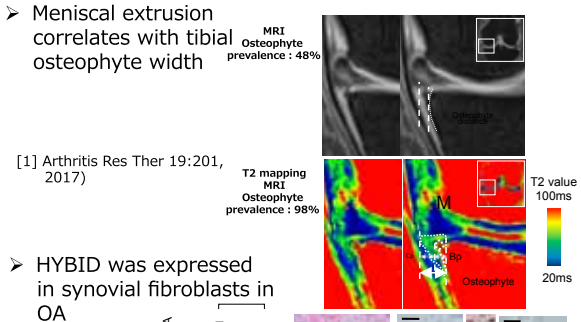
Research Highlights

➢Knee osteoarthritis (OA) is one of the representative diseases of locomotive syndrome that causes mobility dysfunction in elderly people. As knee OA is a slowly but progressive disease, surgical treatment should be necessary when it progresses. The most critical concern of this disease is lack of early diagnosis and treatment. Drs. Ishijima, Okada, and Kaneko and their colleagues are trying to elucidate the pathophysiology of "early stage of knee OA", which has been in great interest worldwide in recent years. Through a series of studies on articular cartilage destruction/regeneration and metabolism of intra-tissue microenvironmental factor, we have previously clarified the mechanism of knee OA by elucidating the articular cartilage extracellular matrix degradation and chondrocyte cloning mechanism[1][2]. We have also reported the importance of osteophytes in the pathology of early stage of knee OA. As the osteophyte has occurred from an early stage in knee OA, it has been speculated that osteophytes may be involved in the onset and progression of knee OA. However, few studies those examining the role of osteophyte in the onset and progression of knee OA have reported. The aim of our study is to develop new treatment of knee OA according to its pathophysiology by focusing on regulation of osteophyte development in knee OA.

➢Cancer locomotive syndrome is a condition in which the mobility is impaired due to cancer including bone metastases. Due to the variety of diseases and pathological conditions of cancer, there are still many unsolved problems in this field. Drs. Takagi and Kubota are examining the current situation and trying to build evidence of cancer locomotive syndrome by conducting the ongoing multicenter joint research project.

➢ Meniscal extrusion correlates with tibial osteophyte width

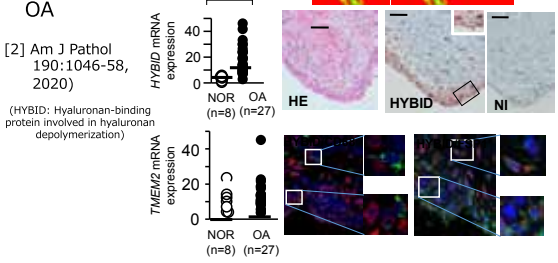
[1] Arthritis Res Ther 19:201, 2017)



➢ HYBID was expressed in synovial fibroblasts in OA

[2] Am J Pathol 190:1046-58, 2020)

(HYBID: Hyaluronan-binding protein involved in hyaluronan depolymerization)



Hypothesis: Whether osteophyte induces medial meniscal extrusion and accelerates articular cartilage destruction in early stage of knee OA

Department of

Dermatology

Chief Professor

Shigaku IKEDA

STAFF

Professor
Yasushi SUGA, Rie UEKI, Toshio HASEGAWA

Associate Professor
Y. HIRASAWA, H. TSUCHIHASHI, T. OGAWA, N. YOSHIHARA, E. KOMIYAMA, T. KANEKO, U. KIMURA, M. KAWAI, T. FUKAI, A. SAKAMOTO

Assistant Professor
A. NOGUCHI, H. YAMASASHI, Y. KOBAYASHI

Main Research Subjects

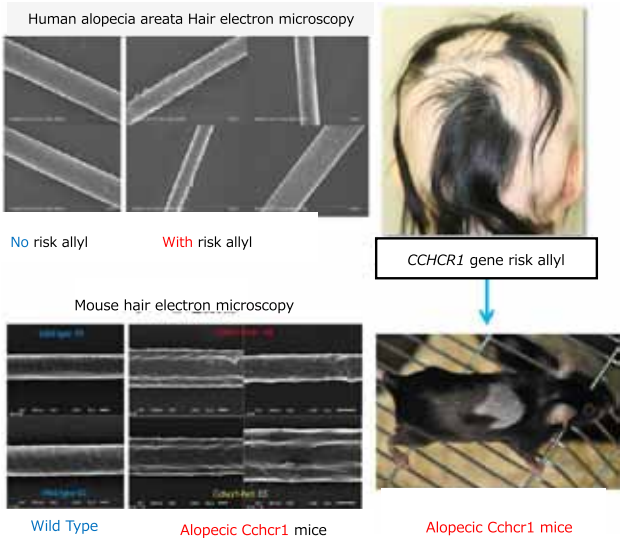
1. **Bullous Diseases**
2. **Keratosis**
3. **Alopecia Areata**
4. **Atopic Dermatitis**

Research Highlights

World's first successful identification of one of the causative genes for alopecia areata

A research group of Prof. Ikeda S. of Juntendo University graduate school of medicine and Prof. Oka A. of Tokai University institute of Medical sciences, as a collaborative research, identified *CCHCR1* as one of the first reported causative genes for alopecia areata.

By introducing risk allyl of the *CCHCR1* gene of human patients with alopecia areata into mice by using genome editing with the CRISPR/Cas9 system, the research group succeeded in reproducing symptoms similar to those of alopecia areata patients. Furthermore, it was confirmed that the presence or absence of risk allele in the *CCHCR1* gene causes a difference in the hair condition of patients with alopecia areata. This result shows the possibility of elucidating the pathogenic mechanism, developing a new diagnostic method and type-specific treatment method based on the presence or absence of risk allele for alopecia areata of unknown cause. In this study, the research group identified one of the causative genes for alopecia areata of unknown cause. Progress in the study regarding elucidation of the pathogenic mechanism of how alopecia areata is caused by the risk allele of the *CCHCR1* gene is expected in the future. Additionally, by clarifying the difference between cases with and without risk allele of the *CCHCR1* gene, it may help develop a type-specific diagnostic method for alopecia areata and a treatment method specialized for each type.



EBioMedicine 2020 Jul;57:102810. doi: 10.1016/j.ebiom.2020.102810. Epub 2020 Jun 21

Department of

Plastic and Reconstructive Surgery

Chief Professor

Hiroshi MIZUNO

STAFF

Professor
Ayato Hayashi, Rica Tanaka
Senior Associate Professor
Kazufumi Sano, Morikuni Tobita
Associate Professor
Yuichi Ichikawa, Miho Tobita
Researcher
Takuma Shimaoka, Misaki Minemura, Miki Minagawa

Main Research Subjects

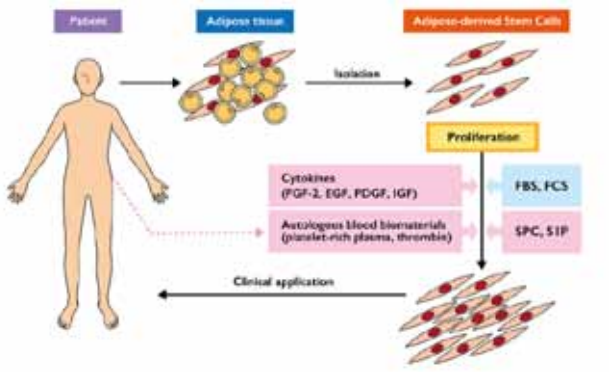
1. **Tissue repair and regeneration using adipose-derived stem cells**
2. **Development of novel therapeutic agents for skin ulcers**
3. **Dynamic analysis of muscular fatigue in surgical care practitioners**

Research Highlights

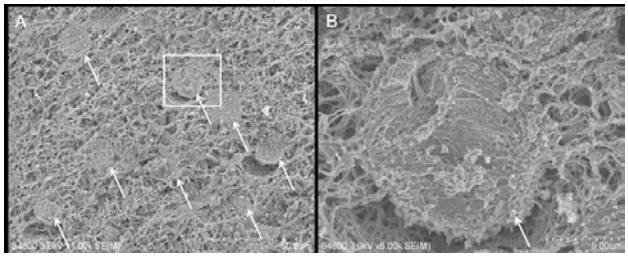
Developing novel cellular therapies for the repair and regeneration of different tissues and health maintenance initiatives to reduce surgeons' physical burden

Our research group—led by Professor Hiroshi Mizuno, Professor Ayato Hayashi, and Professor Rica Tanaka — is conducting research in a variety of different approaches to tissue repair and regeneration, focusing on adipose-derived stem cells (ASCs), Schwann cells, and ex vivo-expanded autologous peripheral blood mononuclear cells (PBMCs), respectively. On a special note, Dr. Tanaka is proceeding to a physician-led clinical trial of ex vivo culutured PBMCs after several studies involving patients with non-healing diabetic ulcers of the lower extremities, while Dr. Mizuno is currently engaged in clinical research in ASC-based periodontal tissue regeneration in collaboration with Senior Associate Professor Morikuni Tobita (Juntendo Medical Technology Innovation Center). Dr. Mizuno is also engaged in drug discovery in the *Advanced Wound Healing Research Chair*, a Joint Research Chair established by Sato Pharmaceutical, looking for new low-molecular-weight compounds that could potentially serve as therapeutic agents for skin ulcers.

In addition, Senior Associate Professor Sano is conducting objective evaluation of excessive physical burden borne by surgeons, especially microsurgeons, during operations and working towards improving surgical techniques to better maintain practitioners' health.



Tissue repair & regeneration using autologous ASCs
(Mizuno H et al. Principle of gender-specific medicine pp459-479, 2017 Elsevier)



Bone regeneration using PRP-supplemented ASCs
(Tajima et al. Histol Histopathol 33:619-627, 2018)

Department of

Urology

Chief Professor

Shigeo HORIE

STAFF

Professor
Satoru Muto

Senior Associate Professor
Yoshiaki Wakumoto
Yuki Nakagawa

Associate Professor
Syuji Isotani, Masayoshi Nagata, Kazuhito Matsushita, Fumitaka Shimizu, Haruna Kawano, Toshiyuki China

Lecturer
Yan Lu

Main Research Subjects

1. **Disease risk analysis associated with Y-chromosome mosaic loss of blood cells**
2. **Prospective study to track leukocyte telomere length in patients with urological diseases**
3. **Prospective study to follow up on the profile of peripheral leukocyte subsets in urological diseases**
4. **Searching for genetic polymorphisms in the risk of developing prostate cancer**
5. **Genetic analysis of the polycystic kidney**
6. **Development of an image-assisted surgical system for robot-assisted partial nephrectomy**

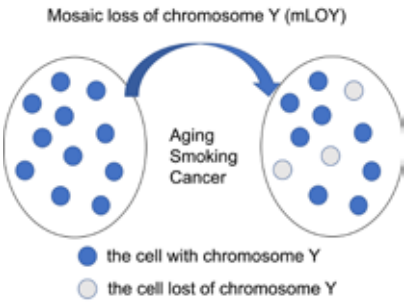
Research Highlights

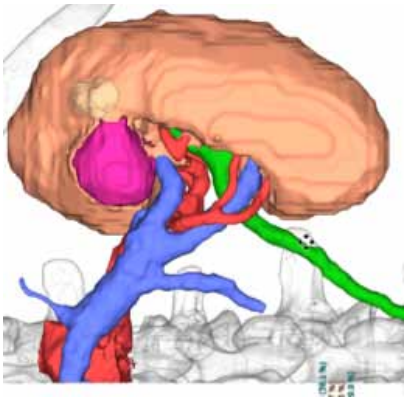
Disease risk analysis associated with Y-chromosome mosaic loss of blood cells

The loss of the Y chromosome from a subclone of the male somatic cell, called mosaic loss of chromosome Y (mLOY), is caused by aging and smoking. Recently, the association of mLOY with age-related diseases (e.g., Alzheimer's disease, heart disease, and cancer) has also been reported. However, the clinical significance of mLOY as a cancer biomarker is not yet clear. We are focusing on the relationship between mLOY and prostate cancer and collaborate with Biobank Japan, which stores DNA and sera donated by the public and Juntendo patients to evaluate the usefulness of mLOY as a biomarker for cancer diagnosis (early detection) and prognosis.

Development of an image-assisted surgical system for robotic-assisted partial nephrectomy

Image support is essential for "robot-assisted partial nephrectomy" for renal cell carcinoma. Therefore, we have been collaborating with FUJIFILM on the development of an image-assisted surgery system. This is an advanced research project that creates a system for simulating partial nephrectomy by computer processing fine detail CT data prior to surgery. It is the most advanced research of its kind in the world, and the results of this research were published by FUJIFILM in 2015 as imaging software. The software has been introduced in about 220 major hospitals, including university hospitals in Japan.





Department of

Ophthalmology

Chief Professor

Akira MURAKAMI

STAFF

Professor
Toshiyuki Yokoyama, Nobuyuki Ebihara, Toshihiko Ohta

Senior Associate Professor
Yoshimune Hiratsuka, Hiroshi Toshida, Toshiro Sakuma, Koichi Ono

Associate Professor
Akira Matsuda, Satoru Nakatani, Takashi Negishi, Shutaro Yamamoto, Masahiro Yamaguchi, Takenori Inomata, Yoshihito Sakanishi

Assistant Professor
Daisuke Kudo, Satoshi Iwamoto, Yosuke Asada, Toshiaki Hirakata, Daisuke Shinohara, Asaki Hirai, Kazunori Tamaki, Rei Arai, Atsuhide Takesue, Toshimitsu Kasuga, Yukiko Miyagawa

Main Research Subjects

1. **Pathophysiological analysis of refractory allergic keratoconjunctivitis.**
2. **Social epidemiological studies of visual impairment.**
3. **Pathological analysis and treatment research of inherited retinal diseases.**

Research Highlights

To elucidate the pathophysiological characteristics of refractory atopic keratoconjunctivitis (AKC), we investigated gene expression profiles using tissues of giant papillae obtained from patients with refractory AKC. We found upregulation of 47 immunoglobulin genes and 22 S. *aureus* infection-related genes in refractory atopic keratoconjunctivitis tissue by RNA-seq analysis, suggesting that lymphoid neogenesis and stimuli from infection are essential components of the disorder.
(Matsuda A, Asada Y, Suita N, et al. *J Allergy Clin Immunol*. 2019; 143:1610-1614.)

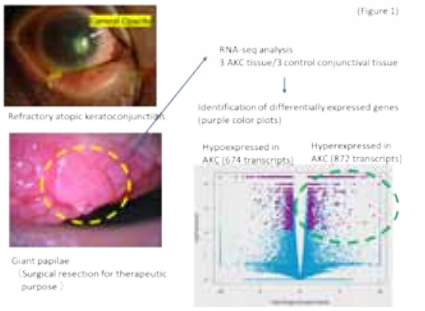


Figure 1. Clinical pictures of refractory AKC patients (left). Volcano plots of differentially expressed genes (FDR<0.05, fold change>2, shown in purple) in RNA-seq analysis

The potential of promoting social participation by improving the visual status of older population.

Vision reported to affect quality of life, independence and mobility, and is associated with many areas, including falls, injuries, mental health, as well as cognitive and social functioning. Social participation by individual older adults has been shown to be effective in maintaining cognitive functioning and preventing care needs. However, the relationship between visual status and social participation has not been studied in detail. We examined the relationship between vision and social participation among 22,291 elderly people living in the community. The results showed that social participation increased by 1.6 times for "excellent" vision, 1.3 times for "good" vision, and decreased by 0.6 times for "fair/poor" vision. Better visual status increases participation in associations and groups, especially spontaneous activities such as involvement in "teaching skills /passing on experiences to others." Poor vision was found to reduce activities that require physical activity, such as involvement in "sports groups." This research has shown that social participation can be improved by improving vision. As the population of developed countries such as Japan is aging at an accelerated rate, the number of people with poor vision will increase. It has been suggested that measures to improve "vision" may help the elderly to participate in society.

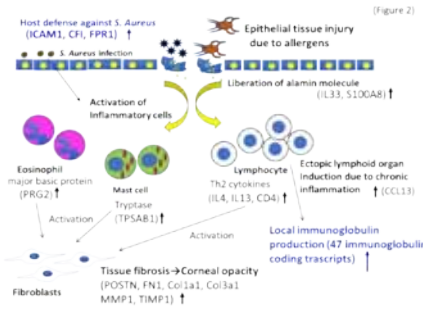
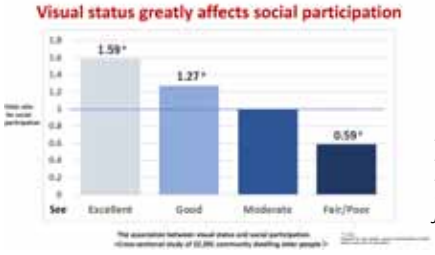


Figure 2. RNA-seq analysis revealed DEGs related to pathophysiology of refractory AKC. In addition to type 2 inflammation related genes (black color), our study suggested local immunoglobulin production and host defense against *S. Aureus* (**blue color**) may be relevant to the pathophysiology of refractory AKC.



The results have been published in "Social Science and Medicine" and reported in many newspapers including the Asahi Shimbun.

(Yoshida Y, Hiratsuka Y, Kawachi I, Murakami A, Kondo K, Aida J. Soc Sci Med. 2020;253:112959. doi:10.1016/ j.socscimed.2020.112959)

Department of

Otorhinolaryngology

Chief Professor

Katsuhisa IKEDA

STAFF

Senior Associate Professor
Fumihiko Matsumoto

Associate Professor
Kazusaku Kamiya, Shinichi Ohba, Yusuke Takata, Ayako Inoshita

Assistant Professor
Mitsuhisa Fujimaki, Takasi Anzai

Main Research Subjects

1. **Study for hearing loss with iPS cell and gene therapy.**
2. **Study for allergy and sinusitis.**
3. **Study for head and neck cancer.**
4. **Study for sleep apnea syndrome.**

Research Highlights

Department of Otorhinolaryngology, Juntendo University Faculty of Medicine

Group for regenerative medicine and gene therapy against hearing loss

Our group aims to discover the molecular mechanisms of hereditary deafness especially for GJB2 associated deafness which is the most typical type in congenital hearing loss. Our goal is to develop novel strategies for inner ear stem cell therapy with multipotent stem cell such as induced pluripotent stem (iPS) cell, gene therapy with virus vector such as adeno associated virus (AAV) and drag screening. These strategies are expected to cure the hearing loss of those patients in near future.

Department of

Diagnostic Radiology (Neuroradiology)

STAFF

Associate Professor
Atsushi Nakanishi, Akihiko Wada, Katsuhiro Sano, Toshiaki Akashi, Koji Kamagata, Nobuo Tomizawa

Assistant Professor
Kanako Sato, Jyunko Kikuta, Yayoi Hayakawa, Yutaka Ikenouchi

Main Research Subjects

1. **diffusion MR imaging (DTI and beyond)**
2. **quantitative MRI (synthetic MR, MRF)**
3. **imaging analysis & artificial intelligence**

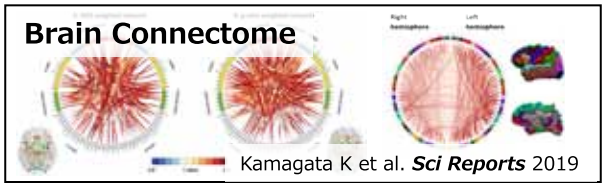
Research Highlights

Shigeki Aoki, M.D., Ph.D., the current chief of the Neuroradiology Division and the previous chairman (from 2014 to 2019) of the Department of Diagnostic and Therapeutic Radiology, is well known for his studies in brain MRI with more than 400 peer-reviewed papers (as a first author or co-author). He also served as the chairman of the Japanese Society of Magnetic Resonance Medicine since 2018, the chairman of the General Assembly of the Japanese Society of Medical Radiology in 2020, and the current chairman of the Japanese Society of Medical Radiology. Currently, in his division, researchers focus on brain MRI cutting-edge technologies, such as diffusion MRI, synthetic MRI and MR Fingerprinting, and AI, with some collaboration with other Japanese or Overseas Universities and research institutes, and various companies.

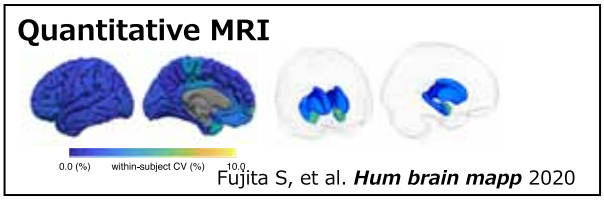
Using diffusion MRI, Prof. Aoki has started the development of tractography methods. Under his supervision, Dr. Koji Kamagata, who graduated from Juntendo University in 2006 and worked as a fellow at the University of Melbourne, is now focusing on brain connectome and statistical imaging analysis with more than 100 publications. Additionally, an international post-doctoral fellow, Christina Andica, is also researching statistical analysis of brain MRI images with more than 50 publications.

Quantitative MRI is a new MRI method for quantitatively evaluating the properties of tissues. At our hospital, we research the standardization of synthetic MRI and MR fingerprint resulting in major papers. Using both methods, it is now possible to detect subtle brain changes and obtain the quantitative values used as objective markers of diseases. Using artificial intelligence (AI), it is also possible to acquire MR angiography from Synthetic MRA data.

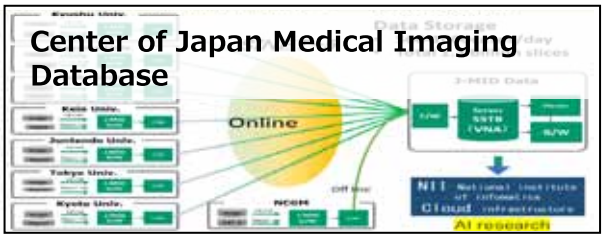
In AI research, as part of the AMED research "Development research for the realization of a national database for diagnostic imaging" led by the Japan Agency for Medical Research and Radiation," CT images and reports were comprehensively collected from eight facilities. In collaboration with the National Institute of Informatics, a database was developed based on the collected data.



Kamagata K et al. ***Sci Reports*** 2019



Fujita S, et al. ***Hum brain mapp*** 2020



Department of

Diagnostic Radiology (General)

Chief Professor

Ryohei KUWATSURU

STAFF

Associate Professor

Shiraishi Akihiko
Suzuki Kazuhiro
Saito Naoko

Assistant Professor

Yamashiro Yuki
Kato Hitomi
Okada Shingo

Main Research Subjects

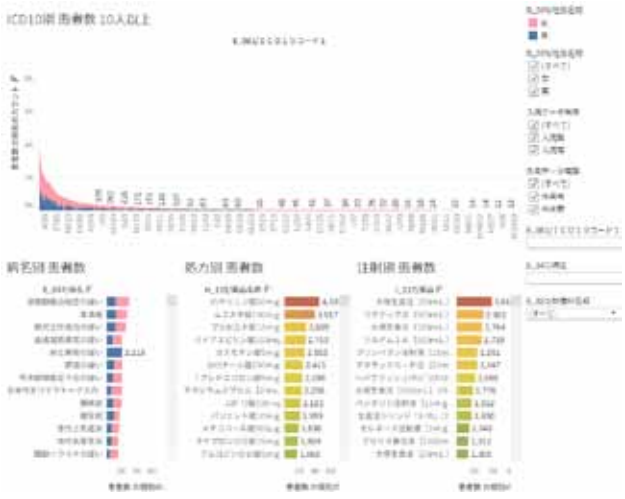
1. **Improvement of minimally invasive treatments.**
2. **Construction of a clinical data warehouse (CDW).**
3. **Clinical research based on CDW.**

Research Highlights

1. Among the various transarterial treatments performed in our department, we are developing new strategies to improve those for renal angiomyolipoma (AML), uterine fibroids and malignant tumors. We take a multifaceted approach to assess the shrinking effect after embolization and to ameliorate the prevention of renal AML rupture. We are also developing a microcatheter that can be quickly and reliably inserted into the main arterial feeders of the tumor.

2. We are constructing a clinical data warehouse (CDW) so that researchers at Juntendo University can efficiently conduct studies based in accurate and actual clinical settings. A CDW is a collection of time-series data organized by purpose for decision making. The basic data of Juntendo Clinic includes disease name, prescription, injection, examination history, surgical history and treatment. In August 2020, such data acquired during the interval of 1 year has been gathered, and its accuracy is currently being evaluated. After this verification, we plan to collect the data of the university hospital and add it on the CDW.

3. One proposal for clinical study using the data collected in CDW is to investigate the changes in renal function over time in patients with different clinical conditions using eGFR rates and creatinine levels. We also intend to prove the validity of imaging inspection for patients presenting dizziness.



Example of data extraction from CDW.
Search for "10 or more patients" by ICD10 disease name.
The software will present the number of patients by disease, prescription and injection type.

Department of

Radiation Oncology

STAFF

Professor
Yutaka Naoi, Naoto Shikama

Associate Professor
Yoshihide Mizutani
Anneyuko I. Saito, Hiroaki Kunogi,
Satoru Sugimoto

Assistant Professor
Yasuo Kosugi, Terufumi Kawamoto,
Jun Takatsu, Tatsuya Inoue

Main Research Subjects

1. **Stereotactic radiotherapy**
2. **Intensity-modulated radiotherapy**
3. **Image-guided radiotherapy**

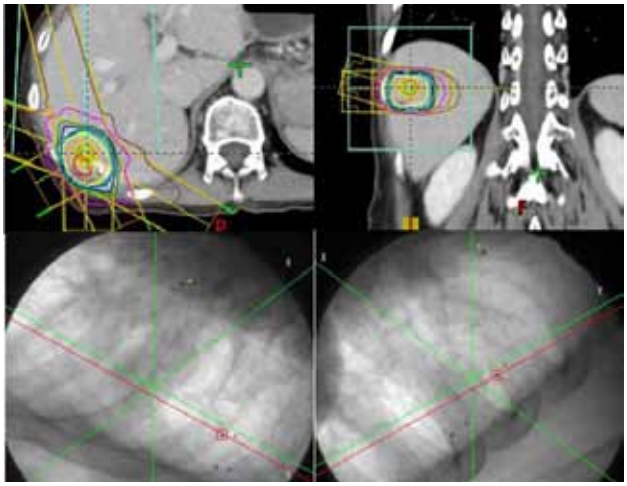
Research Highlights

*Professor Sasai and colleagues perform the less-toxic stereotactic radiotherapy (SRT) for intracranial tumors and extra-cranial tumors in clinical practice. We aim to establish an optimal minimal invasive SRT schedule for multidisciplinary treatments.

*Professor Sasai and assistant professor Kosugi are exploring optimal treatment planning for intensity-modulated radiotherapy for brain tumors and head and neck tumors to decrease the toxicities without compromising oncologic outcomes.

*Associated professor Sugimoto and assistant professor Takatsu, a medical physicist, are evaluating the precision and precise of SRT for extra-cranial tumors with respiratory gated methods and image-guided radiotherapy to apply SRT for various sites. We collaborate on research of adaptive radiotherapy using neural network system with Lecturer Usui in Faculty of Health Science. Assistant professor Inoue is exploring the prediction model of clinical outcomes using the deep-learning methods.

Radiation therapy planning for the liver cancer



Respiratory gating using gold fiducial markers

Department of

Obstetrics and Gynecology

STAFF

Visiting Professor
Kazuhiro Kawamura
Associate Professor
Yuka Yamamoto, Jun Takeda, Keisuke Murakami, Kazunari Fujino
Part-time Lecturer
Keiji Kuroda

Norikazu Ueki, Anna Sato, Shinichiro Ikuma, Rie Ozaki, Asako Ochiai, Yu Kawasaki, Takashi Hirayama, Emiko Yoshida, Hiromi Aoi, Lisa Fujihara, Shiori Takeuchi, Eri Kitamura, Toru Kobayashi, Akemi Matsumoto, Lin Yuling

Main Research Subjects

Obstetrics
- Elucidation of uterine contraction mechanism and identification preterm birth prediction biomarkers
- Evaluation of fetal heart function using ultrasonic Speckle tracking method

Reproduction
- Analysis of implantation disorders and miscarriage mechanism
- Preservation of ovarian tissue and autologous transplantation for postoperative fertility improvement
- Improvement of ovarian function by PRP / exosome

Gynecology
- Validation of clinical efficacy of lymph node metastasis predictive biomarker and development of intraoperative rapid diagnosis method for uterine cancer
- Ovarian cancer enhancer analysis
- Elucidation of epigenetic changes in the development of endometrial cancer

Research Highlights

Diagnosis lymph node metastasis by gene expression patterns

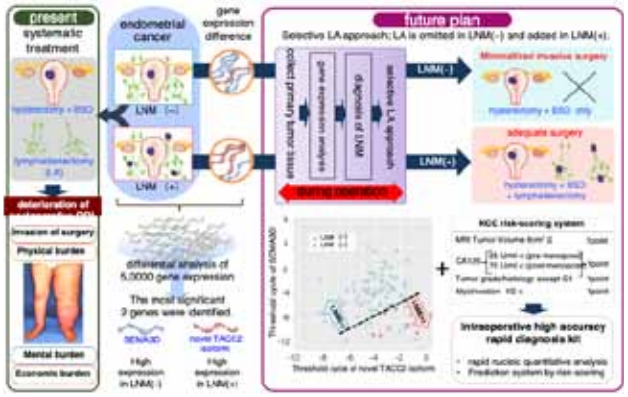
~ for treatment of endometrial cancer with less burden ~

Endometrial cancer is the most common gynecological cancer and has been increasing in recent years.

Standard treatment is surgery, and It is common to resect all lymph nodes which have a possibility of metastasis. If there was no metastasis to the lymph nodes, the result would be that lymphadenectomy was irrelevant.

Excessive lymphadenectomy not only has little therapeutic significance, but also causes intractable lymphedema and significantly impairs daily life after surgery.

If the presence or absence of lymph node metastasis can be identified by gene expression patterns of primary tumor, many women will be able to chose surgical treatment with less burden.



This research was supported by AMED

Department of

Anesthesiology and Pain Medicine

Professor

Kinya NISHIMURA

STAFF

Professor
Masakazu Hayshida
Keisuke Yamaguchi

Associate Professor
Izumi Kawagoe

Assistant Professor
Tsukasa Kochiyama
Masataka Fukuda
Nozomi Ando

Main Research Subjects

1 Analysis of the immunosuppressive mechanisms of action of intraoperative anesthetics in lung cancer patients:
(a) Comparison between propofol and inhaled anesthetics;
(b) additional study of the novel intravenous anesthetic remimazolam.

2 Analysis of the molecular mechanisms underlying the anti-inflammatory effects of intravenous anesthetics.

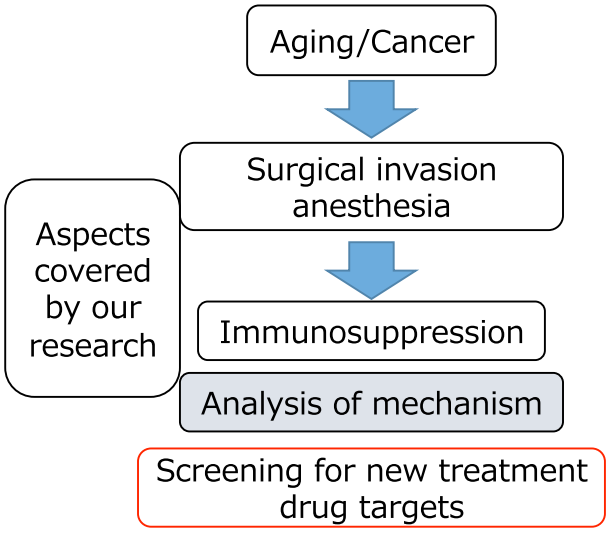
3 Analysis of the mechanisms underlying the effects of combining hydrogen gas with inhaled anesthetics on neurons and glia under ischemic conditions.

Research Highlights

Immunosuppressive mechanisms of different intraoperative anesthetics in lung cancer patients

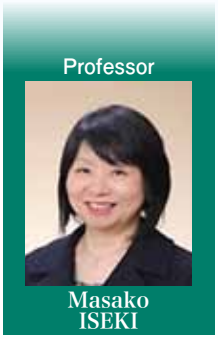
The number of patients undergoing lung cancer surgery in Japan has risen in recent years, and the number of elderly people undergoing this surgery are also increasing. Although the development of techniques such as thoracoscopy has led to lung cancer surgery being less invasive, it remains a highly invasive procedure compared with other types of surgery. Anesthetics are generally believed to have an immunosuppressive effect. Preoperative and postoperative immunosuppression may lead to postoperative complications and increase cancer recurrence.

We have therefore begun investigating the immunosuppressive mechanisms of different intraoperative anesthetics. We have been analyzing the major anesthetics currently in clinical use (the intravenous anesthetic propofol and the inhaled anesthetics sevoflurane and desflurane), and in 2020 we will also begin an investigation of remimazolam, an ultra-short-acting benzodiazepine that has been approved for use in Japan ahead of in other countries.



Department of

Anesthesiology and Pain Medicine



STAFF

Assistant Professor
Keiko YAMADA
Saeko HAMAOKA
Satoko CHIBA

Main Research Subjects

1 Epidemiological study:
Current status and related factors of chronic pains

2 Clinical study:
(1) Treatment responsiveness for neuropathic pain,
(2) Multifaceted evaluation of pain syndromes to define their characteristics and
(3) Risk factors to chronic postsurgical pains

3 Basic/translational research:
(1) Effects of analgesics to the glia cell signal transmission,
(2) Molecular biological clarification of the mechanism of exercise-induced hypoanalgesia,
(3) Relationship between the neuropathic pain and epigenetic modification,
(4) Mechanism of chronic postsurgical pains and
(5) Pharmacological characteristics of opioid analgesics

Research Highlights

1. Epidemiological study:

While many epidemiological studies have been conducted in Japan on musculoskeletal pains, our department has targeted neuropathic pains as well as pains specific to women. Our current focus is the elucidation of factors including the CNS sensitization that are related to chronic pains.

2. Clinical study:

Our pain clinic serves as the clinical arm of our department treating a large number of neuropathic pain patients. Evaluation of novel treatment methods including non-pharmacological therapies such as 3-DVR and analysis of treatment responsiveness are some of our efforts to meet the unmet need in pain treatment. We have also conducted a multicenter joint research for the chronic postsurgical pains, with the results from which we expect to gain further insights into preventive measures to them.

3. Basic/translational research:

We aim to elucidate the mechanism of and to develop novel therapeutic methods for chronic pains by analyzing the effects of analgesics, sedatives and exercise in the glia cell signal transmission. We also have conducted translational research activities in conjunction with Hoshi University, National Cancer Center Japan and Jikei University School of Medicine with the guidance from visiting professors. Our focus is to benefit the clinical practice with the results of research activities.

Department of

Clinical Laboratory Medicine

Chief Professor

Takashi MIIDA

STAFF

Professor
YOKO TABE, MD., PhD.

Senior Associate Professor
SATOSHI HIRAYAMA, MD., PhD.

Assistant Professor
MASAMI SUGIHARA, MD., PhD.
YUKI HORIUCHI, MD., PhD.

Main Research Subjects

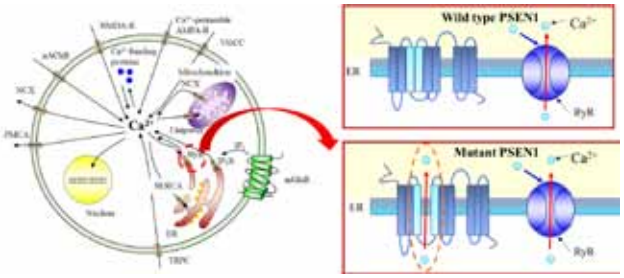
1. **Novel mechanisms of Alzheimer's disease**
2. **Cancer metabolism in microenvironment**
3. **Synthetic lethality in cancer therapeutics**
4. **Voluntary exercise in DCM model mice**

Research Highlights

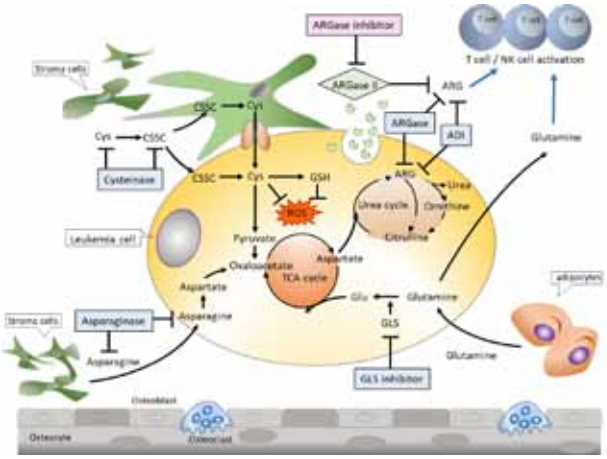
The research team lead by Professor Miida and Associated Professor Hirayama have been studying how lipoprotein, inflammation, and oxysterol in cerebrospinal fluids play roles in pathophysiological mechanisms of Alzheimer's disease. Currently, we are investigating new underlying mechanism(s) of Alzheimer's disease using human iPS cell-derived neuron models. We also found several novel genetic variants in dementia patients using next generation sequencing methods. In addition, we have been collaborating with Dr. Vickers at Vanderbilt University to study a role of HDL-associated small RNA in the pathogenesis of atherosclerosis.

The research group of Professor Yoko Tabe, Assistant Professor Hiroki Horiuchi and Kotoko Yamatani has been working on research of energy / amino acid metabolisms and cell signaling that associate with drug resistance of hematopoietic tumor cells in the bone marrow microenvironment. In addition, we work to establish a novel artificial intelligence (AI) based Deep Neural Network (DNN) system for accurate hematological testing.

Elucidation of new pathopysiological mechanism of Alzheimer's disease: involvement of abnormal ER Ca-release mediated by mutant PSEN1



Therapeutic targeting of amino acids in tumors and the tumor microenvironment.



Tabe Y, et al. Blood. 2019

Department of

Human Pathology

Chief Professor

Takashi YAO

STAFF

Senior Associate Professor
Atsushi Arakawa

Associate Professor
Kazunori Kajino, Yuki Fukumura, Takuo Hayashi, Harumi Saeki, Tsuyoshi Saito

Assistant Professor
Miki Asahina

Main Research Subjects

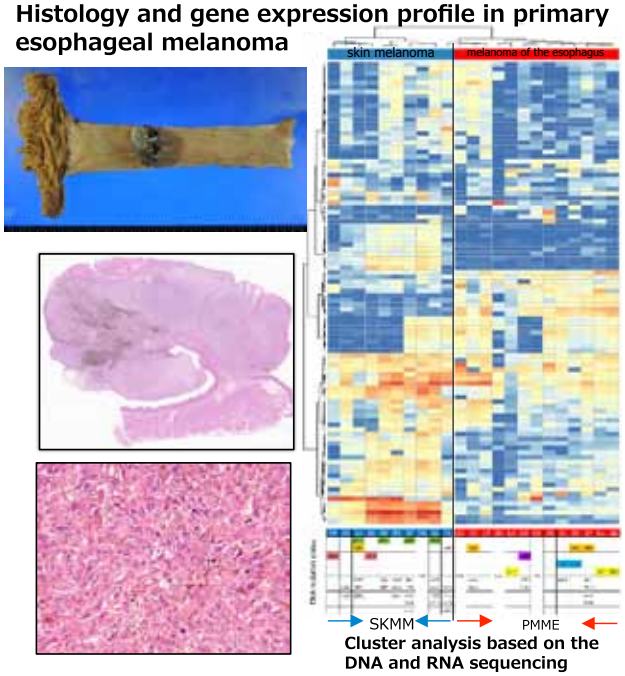
1. **Molecular pathology and molecular pathogenesis of the special type of esophageal and gastrointestinal tract**
2. **Molecular and comprehensive analysis of the association between lung cancer histology and genetic alterations**
3. **Molecular and comprehensive analysis of tumor progression mechanism in panceatobiliary cancer, bone tumor and soft tissue tumor**

Research Highlights

Identification of genetic alterations responsible for the primary esophageal and skin melanomas.

We identified that genetic alterations responsible for the primary malignant melanoma of esophagus (PMME) and skin malignant melanoma (SKMM) are totally different as the collaboration study with Division of Cellular Signaling, National Cancer Center Research Institute. In esophageal malignant melanoma, *NF1* mutations were most frequently detected, whereas BRAF mutations frequently detected in skin malignant melanoma could not be detected. Focal expression of PD-L1 was observed in one PMME. The tumour mutation burden in PMME was significantly lower than that in SKMM. RNA-sequencing revealed a distinctive pattern with respect to RNA expression. T-cell co-stimulation also differed between PMME and SKMM. A subset of PMME may contain actionable mutations such as *KIT*. Immunotherapy seemed to be less effective for most PMMEs in this series. These findings would be useful for the better understating of the tumorigenesis and the therapeutic strategy in esophageal malignant melanoma. (Tsuyama S, et al. Histopathology, 2020)

Histology and gene expression profile in primary esophageal melanoma



Cluster analysis based on the DNA and RNA sequencing

Department of

Hospital Administration Research

Chief Professor

Hiroyuki KOBAYASHI

STAFF

Senior Associate Professor
Shiori Kawasaki

Associate Professor
Takenori Inomata
Munetaka Yamamoto
Yumiko Kurihara

Main Research Subjects

1. **Identifying fall risks and developing preventive strategies**
2. **Evaluating occupational stress and developing improvement strategies**
3. **Preventive, predictive, personalized, and participatory medicine through mobile health-based disease education and behavioral modification**

Research Highlights

1. Identifying fall risk

Falling while being hospitalized can greatly affect a patient's QOL, prolonging lengths of stay, and consequently reducing physical capacity while increasing medical costs. Various initiatives to reduce fall risk have been attempted; however, it still has not been completely eliminated. Focusing on footwear type (one of many factors affecting fall risk identified by previous research), we measured different balance-related variables in subjects as they walked and found that postural/gait balance was disturbed by the use of slippers when compared to shoes in healthy young adults (Figs. 1, 2).

Fig. 1 Body tilt at rest: Change after walking

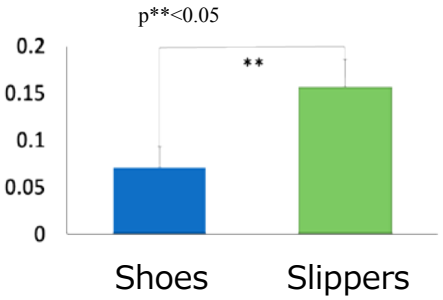
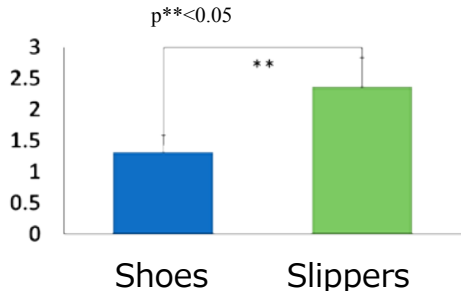


Fig. 2 Stride length while walking: Left-right difference



2. Preventive, predictive, personalized, and participatory medicine via mobile health-based disease education and behavioral modification

We are conducting integrated analyses of dry eye and pollinosis based on comprehensive user data collected from two smartphone apps: DryEyeRhythm® and AllerSearch®, respectively. Using artificial intelligence, we analyzed big data collected by these apps to identify risk factors for these conditions, as well as stratified and personalized profiles of their pathologies. (*Ophthalmology* 2019, *Ocular Surface* 2020)

Department of

Emergency and Disaster Medicine

Professor

Toshiaki IBA

STAFF

Professor
Naoyuki Hashiguchi
Senior Associate Professor
Shin Watanbe
Associate Professor
Koichiro Aihara, Makoto Hiki
Lecturer
Katsuhiko Kadota
Assistant Professor
Atsushi Yamada, Kenta Kondo

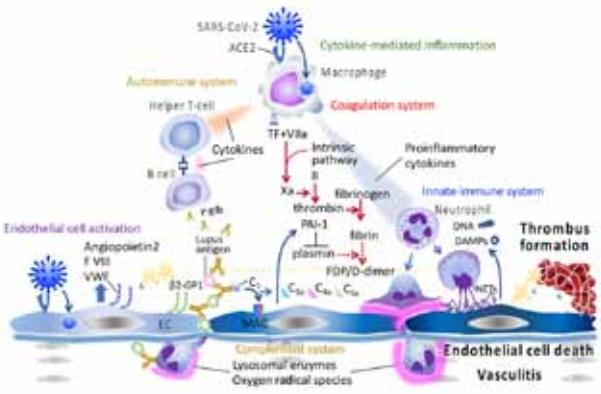
Main Research Subjects

1. **Pathophysiology of sepsis**
2. **Management of DIC (disseminated intravascular coagulation)**
3. **COVID-19-associated coagulopathy**

Research Highlights

The tight connection between inflammation and coagulation in sepsis has been studied and the important role of anticoagulation was revealed.

The connection between inflammation and coagulation has been the research focus of the Department of Emergency and Disaster Medicine. Prof. Toshiaki Iba is a committee member of the Japanese Guidelines for Sepsis Management 2016 and 2020 (J-SSCG2016&2020) and is currently working on the update. He has established the diagnostic criteria for the sepsis-induced coagulopathy (SIC) as a chairman of the Scientific Standardization Committee of the International Society on Thrombosis and Haemostasis (ISTH/SSC). In addition, he and ISTH/SSC released the international guidance for the COVID-19-associated coagulopathy (CAC). The above achievements are published in the J Thrombosis and Haemostasis (April 2020), Lancet Haematology (May 2020), and other major journals. Prof. Iba is currently working as a member of the WHO advisory group on therapeutic prioritization for COVID-19.



Department of

Medical Oncology

Chief Professor

Shunsuke KATO

STAFF

Assistant Professor

Shigeo Yamaguchi

Hidenori Kido

Main Research Subjects

1. **Functional analysis of cancer-related genes using comprehensive expression analysis**
2. **Non-coding RNA analysis as a biomarker that contributes to the tumor biology**
3. **Research on cancer genome profiling that affects FDG accumulated data**

Research Highlights

Research for cancer biomarkers using omics data

In order to establish biomarkers that will lead to precision medical treatment of cancer, we are investigating the correlation between gene expression profiles of tumor tissues and clinical data (Assistant Professor Shigeo Yamaguchi).

1. TP53 signature

TP53 signature is the gene expression profile set that predicts structural abnormalities of the tumor suppressor TP53.

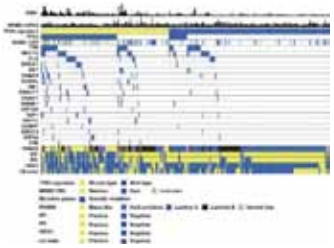
Using TCGA data and our cohort data, we reported that TP53 signature can also predicts the prognosis of early breast cancer patients more accurately than Oncotype Dx and Mammaprint.

In addition, we revealed that tumor tissues with a TP53 signature mutant expression profile have molecular biological characteristics of high PD-L1 and high TMB levels, which may be an index for predicting the effects of immune checkpoint inhibitors (Oncotarget. 2018 Feb 8;9(18):14193-14206).

2. EGFR impact score

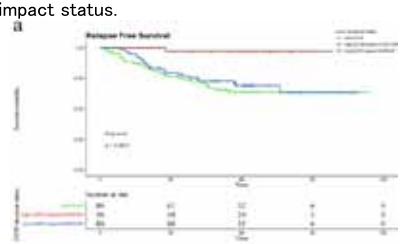
Using cohort data from a comprehensive expression analysis of early-stage lung adenocarcinoma, we extracted the expression profile characteristic of EGFR mutations and named it the EGFR impact score. The EGFR impact score indicates dependence on EGFR pahway, and at the same time, is useful for predicting the prognosis of early-stage lung cancer, and may be useful for predicting the susceptibility of EGFR TKIs to lung adenocarcinoma with EGFR gene mutation (Sci Rep. 2020 Apr 10; 10 (1): 6214).

TP53 signature: Molecular back ground of TP53 signature in TCGA data.



Oncotarget. 2018 Feb 8;9(18):14193-14206.

EGFR impact score: RFS curves according to the EGFR structural status and EGFR impact status.



Red：EGFR structural mt、EGFR Impact Score High
Blue：EGFR structural mt、EGFR Impact Score Low
Green：EGFR structural wt

Sci Rep. 2020 Apr 10;10(1):6214

Department of

Palliative Medicine

STAFF

Visiting Associate Professor
Shigeko Okuno
Lecturer (part-time)
Takuji Yamaguchi, Takaaki Ito, Yoshihisa Matsumoto
Teaching Staff
Suzu Yae, Teruya Asahina, Mutsuhito Ui

Graduate Student
Daisuke Watanabe, Yuko Uehara, Kazumi Hasebe, Naoko Hikima, Amaka Watanabe, Meilin Zhu
Cooperative Researcher
Atsufumi Nishio, Yoshibumi Chiba, Kiyoko Moriya, Tetsuro Toyoda, Mieko Abe, Yang Zhao, Masahiko Kuribayashi, Ailing Hu, Shilin Xia, Yuji Kuwashima, Keiji Takahashi, Yan Yan, Masahiro Tabuchi, Hiroaki Yamakawa

Main Research Subjects

1 Collaboration between medicine, well-being, and agriculture integrated through "agri-healing"
Juntendo CO-CORE, February 13, 2020: https://www.juntendo.ac.jp/co-core/research/agrihealing.html

2 Making stress levels visible
The Japan Society for the Promotion of Science, Foundation Research (C) 19K07924

3 Frailty prevention and nutrition management for cancer patients
Excellent Presentation Award, the 31st Academic Conference of the Japan Society for Geriatric Anesthesia (2019)
2020 Excellent Paper Award, Journal of Japan Surgical Association (2020)

Research Highlights

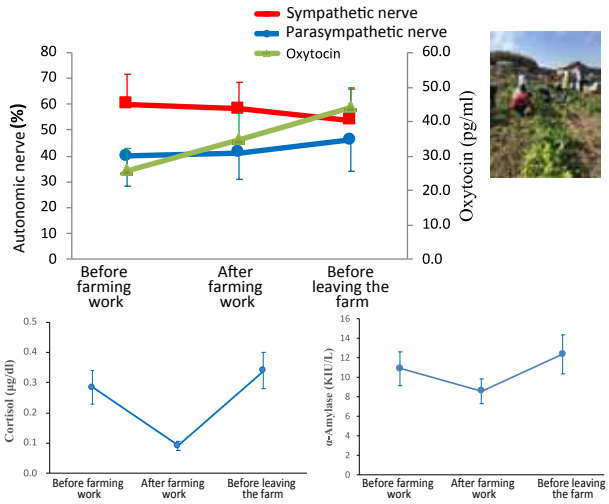
The potential of agri-healing: Achieving collaboration between medicine, well-being, and agriculture when the three areas are integrated

When a patient is fighting a serious disease, both the patient and their family members bear significant physical and psychological burdens. Palliative care (palliative medicine) aims to alleviate various kinds of suffering that the patient and their family are experiencing so that they can spend more meaningful time together.

Palliative care is increasingly expected to provide stress alleviation and whole person care while being deeply embedded in people's everyday lives. As people know from experience, being amidst nature helps reduce stress. We work on "agri-healing," which transcends existing horticultural therapy and which incorporates agriculture, horticulture, farming, and harvesting experience, in the context of the natural environment. Studies have verified that the experience of farming and being in nature decrease cortisol and α -amylase levels and increases oxytocin levels. We, therefore, reported at an academic conference of the Japanese Association of Stress Science that such experiences are effective in alleviating stress.

As the COVID-19 pandemic continues to persist, an increasing number of people are feeling anxious and stressed. It is of utmost importance for health professionals to help people stay healthy – both physically and mentally. We are committed to contributing to people's physical and mental health through "agri-healing."

*Joint press release with NTT Com. (https://www.juntendo.ac.jp/news/20181107-01.html)



The 33rd National Conference of the Japanese Association of Stress Science (2017)

* Ongoing commissioned/joint research projects with Yanmar, NTT, and JA-Zenchu

Department of

Oral and Maxillofacial Surgery

STAFF

Senior Associate Professor
Morikuni Tobita

Associate Professor
Mariko Hide

Teaching Associate
Umeyama Ryo

Main Research Subjects

1. **The retrospective study of risk factors of Medication related osteonecrosis of the jaw (MRONJ)**
2. **A study of oral care interventions during the perioperative period**
3. **Periodontal tissue regeneration with Adipose-derived stem cells**
4. **Search for the mechanism of action of Platelet-Rich Plasma**
5. **Practical research using Embryonic Stem cells**
6. **Research on bone regeneration using plant alkaloids**

Research Highlights

The retrospective study of risk factors of Medication related osteonecrosis of the jaw (MRONJ)

Our laboratory collects information on the daily practice of patients receiving denosumab who have undergone surgical procedures at Juntendo University Hospital and Joint Research Facility.

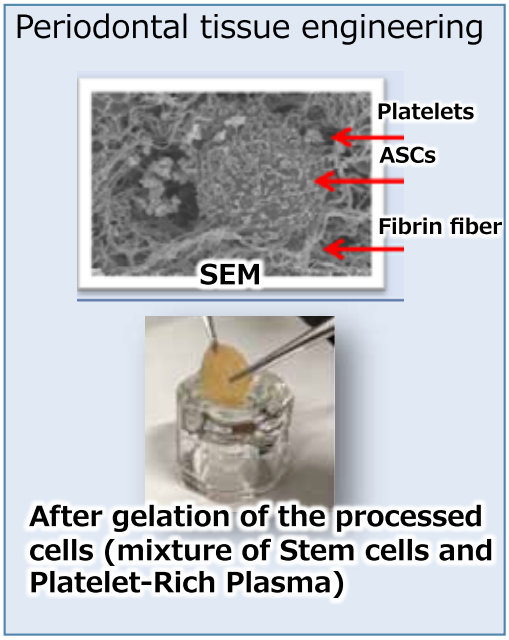
From the collected information, we are conducting research to investigate factors that may affect side effects, safety, efficacy, etc.

A study of oral care interventions during the perioperative period

In our laboratory, we are researching the clinical outcome of "perioperative oral management", which is a comprehensive oral care for the perioperative period, which is being undertaken at Juntendo University Hospital and the mechanism of cooperation between medical department and dental department.

Periodontal tissue regeneration with Adipose-derived stem cells

Our laboratory aims to establish a treatment method that regenerates periodontal tissue destroyed by periodontal disease using adipose-derived stem cells. The processed cells to be transplanted into the periodontal tissue defect is a mixture of Adipose-derived stem cells and platelet-rich plasma.



Department of

Rehabilitation Medicine

Chief Professor

Toshiyuki FUJIWARA

STAFF

Professor
Akito Hayashi

Senior Associate Professor
Kozo Hatori
Tatsuya Takagi

Associate Professor
Akihiro Kurosu, Akira Tanuma, Tomokazu Takakura, Kaoru Honaga

Lecturer
Nana Izawa

Assistant Professor
Yasuko Hayashi, Ayako Aiba, Yuto Furukawa

Main Research Subjects

1. **Non-Invasive Brain and Spinal stimulation for functional recovery**
2. **Robotics and VR for Rehabilitation**
3. **Neurophysiological study for functional bio-marker of Rehabilitation Medicine**

Research Highlights

- Transcutaneous spinal stimulation for gait among patients with stroke
- VR home-based training for upper extremity motor function among chronic stroke
- Robotic rehabilitation for upper extremity motor function among patients with chronic stroke
- Transcutaneous spinal stimulation and splint therapy for upper extremity motor function among patients with chronic stroke
- EMG-triggerd rTMS (iTBS) for upper extremity motor function among patients with stroke
- Gait analysis of Parkinson's disease
- ADL structure of Parkinson's disease
- Trunk impairment and balance function of Parkinson's disease
- Gait rehabilitation and functional prediction of acute stroke
- Trunk impairment scale for acute stroke
- rTMS and cognitive rehabilitation for cognitive impairment
- Physical, mental and social activity of community living elder persons

Department of

Transfusion Medicine

Our laboratory is currently developing diagnostic techniques
for hematopoietic tumors and researching the onset mechanism.
For more information, please visit our laboratory website.

Department of

Clinical Genetics

Our laboratory was established in October 2019.
We aim to contribute to the development of human resources
for new medical professionals who will be responsible
for genomic medicine in the future, and to lay the foundation
for future genomic medicine.
For more information, please visit our laboratory website.

Clinical Pharmacology

Chief Professor

Kazuhiro SASE

STAFF

Senior Associate Professor

Associate Professor

Lecturer

Assistant Professor

Main Research Subjects

1. **Global Regulatory Harmonization**
2. **Real-World Evidence**
3. **Cardio-Oncology**

Research Highlights

The Department of Clinical Pharmacology provides education and research in regulatory science to promote medical innovation and safety.

Our contributions to regulatory harmonization include guidance documents for the Global Harmonization Task Force (GHTF/SG5) and the International Medical Device Regulators Forum (IMDRF/RWG).

We have also pioneered through the US-Japan Harmonization by Doing (HBD) and international collaboration of registries for artificial hearts (Intermacs/JMACs).

As we enter the precision medicine era, the need for a sustainable ecosystem for risk/benefit assessment is increasing. Therefore, we are working on a new methodology called Real World Evidence, starting with unmet medical needs in novel inter-disciplinary fields including the Cardio-Oncology as well as the Cardio-Obstetrics.

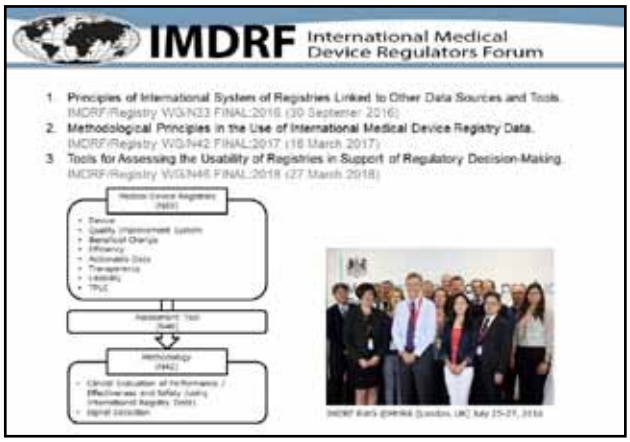
(1) Miyazaki Y, Sase K, Hasegawa K, et al. VTE and anti-coagulation therapy in cancer patients. Eur Heart J Cardiovasc Pharmacother. 2019 Oct 1;5(4):189-191.

(2) Nakatani T, Sase K, Oshiyama H, et al. Japanese registry for Mechanically Assisted Circulatory Support: First report. J Heart Lung Transplant. 2017 Oct;36(10):1087-1096.

(3) Sase K, Kida K, Furukawa Y. Cardio-Oncology rehabilitation- challenges and opportunities to improve cardiovascular outcomes in cancer patients and survivors. J Cardiol. 2020 Dec;76(6):559-567.

(4) Ohta Y, Kamide K, Hanada H, Sase K, et al. Genetic factors associated with elevation of uric acid after treatment with thiazide-like diuretic in patients with essential hypertension. Hypertens Res. 2020 Mar;43(3):220-226.

(5) Sase K. [Clinical pharmacology of cardio-oncology: a novel interdisciplinary platform for basic and translational research]. Nihon Yakurigaku Zasshi. 2020;155(3):179-184. Japanese.



Guidance Documents for Patient Registries
(N33, N42, N46),
International Medical Device Regulators Forum
www.imdrf.org

Infection Control Science

Professor

Satoshi HORI

STAFF

Senior Associate Professor

Associate Professor

Lecturer

Assistant Professor

Main Research Subjects

1. **Development of safety facility design and management for preventing healthcare associated infections**
2. **Development of "Pandemic Ready" constructions.**
3. **Analysis of aerosol dynamics in the healthcare settings.**

Research Highlights

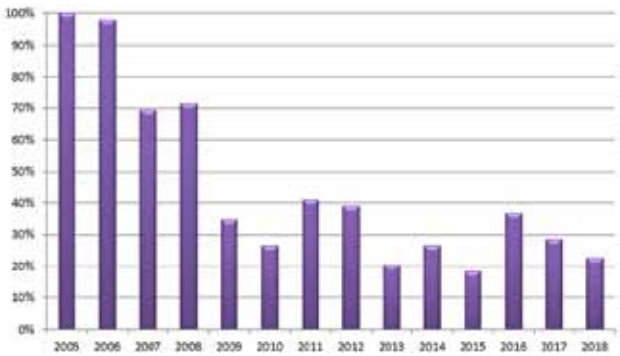
Development of the comprehensive infection prevention programme and investigation of optimal healthcare facility design & management though real hospital settings.

Over the last decade, the isolation rates of hospital-portioned MRSA as well as multidrug resistant Gram negative bacilli in the Juntendo University Hospital were dramatically reduced by 70% and 82%, respectively.

The infection prevention and control programme was comprehensive strategy including good hand hygiene, clean environment, antimicrobial stewardship and ideal healthcare facility construction.

Since 2019, the novel corona virus infections, named COVID-19 which is caused by SARS-CoV-2 virus has emerged. The aftermath of this pandemic will change the infection control common sense permanently and profoundly. Analysis of aerosol dynamics has been performed to elucidate mechanism of transmission and develop preventive measures.

Reduction of MDR-GNB isolates in the Juntendo University Hospital.



Aging Biology in Health and Disease

Professor

Eri ARIKAWA-HIRASAWA

STAFF

Assistant Professor

Aurelien Kerever

Yuri Yamashita

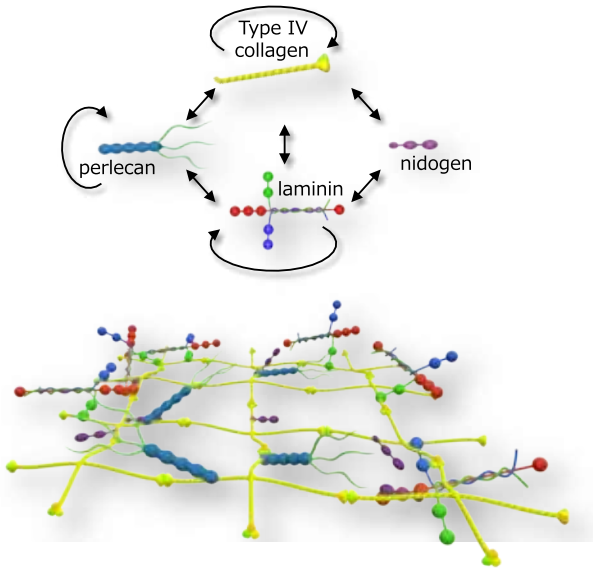
Main Research Subjects

1. **Extracellular matrix biology in brain function and aging**
2. **Research on locomotor disorders in disase and aging**
3. **Using iPS cells to create disease models**

Research Highlights

With the advent of a super-aging society, there is an urgent need to understand the pathophysiology of diseases in the elderly. The interaction between cells and the extracellular environment is critical to maintain the organ function.

In our laboratory, we use molecular biology, cell biology, and morphological analysis to analyze the physiological characteristics of the elderly. We use animal models and develop 3 dimensional cell/ extracellular matrix culture models for the development of diagnostic and therapeutic methods. We are accepting graduate students with the aim of developing human resources who can carry out cutting-edge medical science aiming for healthy longevity by taking courses in brain cognitive function and musculoskeletal science.



Sports Medicine and Sportology

Senior Associate Professor

Yuji TAKAZAWA

STAFF

Associate Professor
Atsushi Kubota
Masashi Nagao

Lecturer
Yuka Murofushi

Assistant Professor
Hirohumi Nishio

Main Research Subjects

1. **Prevention for sports injury (Pre-hospital care support)**
2. **Conditioning**
3. **Sports and anti-doping**

Research Highlights

Our team at the department of sports medicine consists of members who specialize various aspects of sports medicine. Investigators, physiotherapists, athletic trainers, graduated students, coaches, part-time staffs are cooperatively working on the projects. Especially we are focusing on epidemiology, strategy for preventing sports injuries, how to improve performance after return to play.

In addition, we are conducting a study on conditioning using the recent instruments such as ultrasound, MRI and muscle strength dynamometer to verify muscle strength and tissue hardness.
We are focusing on throwing performance enhancement for baseball pitchers with cooperation from the professional baseball team players. Other research topics are prevention of muscle stain of the hamstring and rectus femoris muscles.

Also, we are conducting research to promote anti-doping education on doping as a threat to sports integrity. We are conducting basic research on the status of athletes' anti-doping knowledge, their perceptions and behaviors towards prohibited substances and methods, and developing measures to prevent them from falling into a pitfall of intentional or unintentional doping.

Department of

Personalized Kampo Medicine

Professor

Hiroyuki KOBAYASHI

STAFF

Associate Professor
Kurihara Yumiko Md. PhD.

Lecturer
Yamaguchi Takuji PhD.

Assistant Professor
Harada Yoshinao MO. PhD.

Main Research Subjects

1. **Elucidation of action mechanism of the Kampo medicine based on the advanced medical**
2. **Stress control by the mind-body unity**
3. **'Eat healthy, live healthy' and Health Science**

Research Highlights

Effects of the Kampo medicine on the stress-induced emotional disorder

At the moment, there is more feeling anxiety and stress induced by the new coronavirus infection. Maintenance of the psychosomatic health becomes the important and urgent problem. The continued stress causes sleep disorders, depression, anxiety, obesity, pains, and many divergences including the malaise as well as various kinds of somatic diseases.

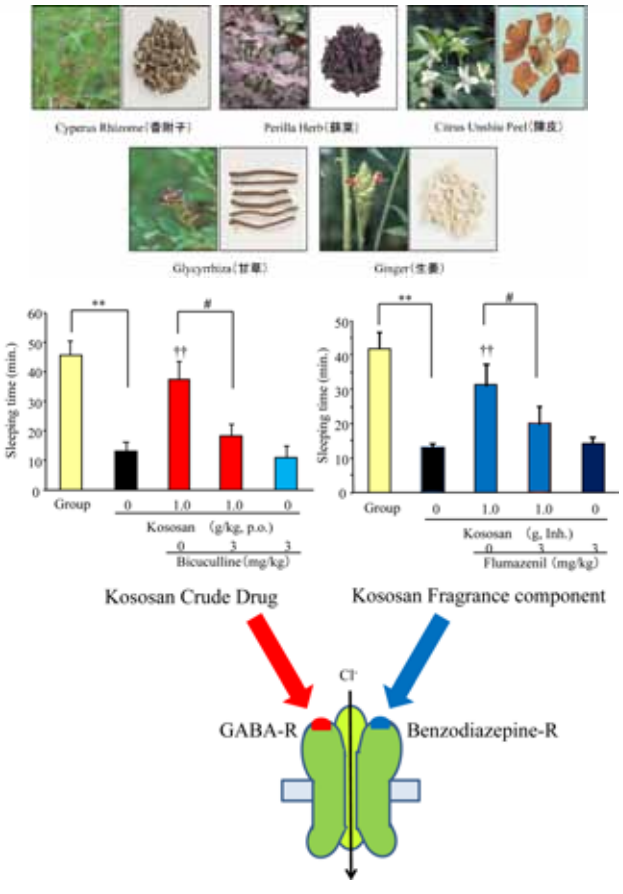
We examined effects of the Kampo medicine using a stress model.

Kososan(TJ-70) reversed sleep disturbance in socially isolated mice. It has also remedial effects on the depression, in which mechanism is different from the extract of crude drug and the fragrance ingredient of the TJ-70.

Hangekobokuto (TJ-16) has remedial effects on the aggressive behavior in the isolated mice. And the effects suggested to be mediated via the serotonin system.

Kamikihito (TJ-137) improved the agitation of patients with chronic constipation of women, and the quality of life of the digestive symptom.

We hope to contribute to the stressful modern society through the research of the Kampo medicine.



Effects of Kososan on pentobarbital-induced sleep in socially isolated mice

Phytomedicine. 21,697-703(2014)

Diagnostics and Therapeutics of Intractable Diseases

Chief Professor

Yasushi OKAZAKI

STAFF

Associate Professor
Masami Arai
Hidetaka Eguchi
Atsuko Okazaki

Lecturer
Kazuhiro Nitta
Ayumu Sugiura

Assistant
Yukiko Yatsuka

Main Research Subjects

1. **Genomic and functional analysis of mitochondrial diseases**
2. **Development of treatment methods for mitochondrial diseases**
3. **Genomic analysis of other human genetic disorders**
4. **Cell transdifferentiation into different cell types (“direct reprogramming”)**

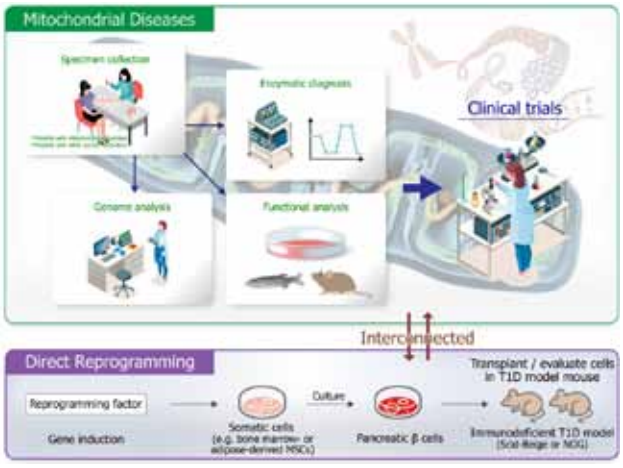
Research Highlights

Department of Diagnostics and Therapeutics of Intractable Diseases was established in 2016. We are engaged in a wide range of research on intractable diseases, from diagnosis to treatment. Our primary research interests are genomic analyses of congenital metabolic disorders (mainly mitochondrial disease), other inherited diseases* and regenerative medicine for type 1 diabetes. In collaboration with Intractable Disease Research Center of Juntendo University, our mission involves identifying novel causative genes underlying diseases and performing functional analyses, with the aim to clarify their pathologies and pave the way for treatments.

Although standard approaches to genomic analysis can identify pathogenic variants in 30–40% of genetic disorders, in the remainder of cases, they cannot identify any candidate or can identify variants of uncertain significance (VUSs) to pathology. To address these issues, we employ a variety of omics tools and approaches, as well as functional verification, i.e., examining whether the gene can rescue the damaged function in patient-derived fibroblasts or loss-of-function cells by the gene overexpression.

Lynch syndrome, polycystic kidney disease, childhood-onset inflammatory bowel disease, familial hypercholesterolemia, etc.

We are also interested in diabetes therapeutics, engaging in applied clinical research on transdifferentiation (“direct reprogramming”) of somatic cells to pancreatic β cells using patented innovative technology, as well as R&D for drug therapies using cardiomyocytes induced from induced pluripotent stem cells (iPS cells) of patients.



Funded research topics (AMED):
- Comprehensive functional annotation of VUSs specific to mitochondrial diseases in Japanese children
- Development of innovative technology to create artificial pancreatic islets by the direct conversion of somatic stem cells

Regenerative Therapy

STAFF

Project Assistant Professor
Satoshi Fujimura
Postdoctoral Researcher
Tsubame Nishikai
Satomi Furukawa
Researcher
Kayo Arita, Rie Hirano, Ai Sugawara, Ikuko Takamaeda, Yukiho Hirayama
Graduate Student
Taro Fukuda, Jiang sen

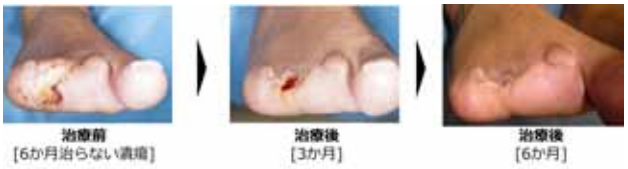
Main Research Subjects

1. **Developing vascular and tissue regeneration therapies based on the transplantation of autologous peripheral blood mononuclear cells expanded in vitro (MNC-QQ, Repri)**
2. **Identifying the mechanisms governing angiogenesis and wound healing, and developing tissue regeneration therapies using part of a novel macrophage (ReMa cells)**
3. **Identifying the mechanisms governing tissue regeneration and breakdown using diabetic skin and vascular stem cells**
4. **Developing MASQ cell mixtures (adipose-derived stem cells + Repri cells)**

Research Highlights

Blood vessels are absolutely essential for tissue regeneration. We have independently developed a culture technique to expand the quantity and improve the quality of vascular stem cells and M2 macrophages present in patients' peripheral blood. Our protocol can produce highly angiogenic cells (MNC-QQ cells) from a small amount of blood just after one week of suspension culture, which can have high tissue regenerative potential. We have started clinical trial of MNC-QQ cell transplantation in patients with non-healing leg ulcers. In an AMED Research Project for Practical Application of Regenerative Medicine, we treated a total of 10 patients between 2015 and 2017, confirming the therapy's safety and efficacy. Company- and physician-led clinical trials are planned to start in 2021, aiming to enhance the effectiveness of MNC-QQ cells, improve our culture technology, and obtain regulatory approval for Repri cells as a new regenerative medical product. Our technology will become the world's first vascular tissue regeneration therapy requiring only blood collection.

MNC-QQ Cell Therapy - Example



Department of General Education

Division of Foreign Language

Professor

Keiko ASANO

STAFF

Associate Professor
Rie Koizumi
Marcellus Nealy
Ryoko Fujita

Assistant Professor
Andrew Mason

Main Research Subjects

1. **Process of speech language perception and generation in L2learners**
2. **Assessment of speaking ability in English classroom in Japan**
3. **Practical applications of adult education theory in language learning**
4. **Effects of background noise on learners' listening comprehension**
5. **Effect of healthcare situation on consumer purchasing behaviors**

Research Highlights

In a collaborative research group of Professor Asano, Senior Associate Professor Sugano of the Graduate School of Medicine, Juntendo University, and Dr. Mitsuashi, we focused on brain plasticity in language function and performed functional MRI (fMRI) of the brain activation site during language learning as well as preformed by diffusion MRI (dMRI), which is a comprehensive mechanism elucidation that combines function and structure. We also targeted Japanese-English bilingual and early and late language learners in the critical period to identify sites that affect language function plasticity. The results contributed to the reacquisition of language function after surgery and the progress of subsequent treatment. This result was published in journal, *Neuroscience* (2020).

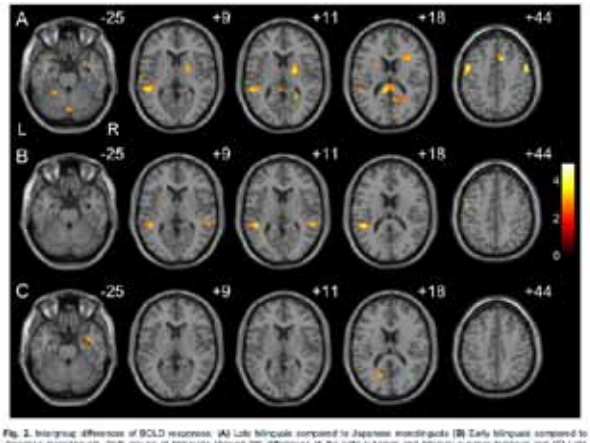
Associate Professor Koizumi primarily investigates key factors in the effective implementation of speaking tests at senior high schools in Japan. For example, she has shown that holding discussions at the beginning of the test enhances interrater reliability and that regular administration of the tests and test result feedback improve speaking ability.

Associate Professor Nealy is studying practical ways to apply adult education theories to the English language classroom to better understand the language learning process and improve learning outcomes.

Associate Professor Fujita focuses on second language acquisition, with special emphasis on listening skills and authentic materials, previously investigated the effects of noise pollution on listening comprehension and found that the presence affected the learners' ability to use contextual information in their listening comprehension process.

Assistant Professor Mason's research interests are in the merged disciplines of health care and business. His current ongoing research is on the impact of the COVID-19 pandemic and government mitigation strategies on consumer purchasing behaviors.

Identification of activated brain areas that affect language function plasticity of language learners



Department of General Education

Division of Mathematics

STAFF

Associate Professor
Hiroyuki Kawamura

Main Research Subjects

1. **Representation theory of algebras**
2. **Perturbative Quantum Chromodynamics**

Research Highlights

Dr. Okuno specializes in representation theory of algebras.

Dr. Kawamura performed a global analysis of the fragmentation function of pi and K mesons (Fig.1) and showed the impacts of the B factory measurements on the fragmentation function determination, specifically, for the components of sea quarks and gluon. He has also been working on the light-cone distribution amplitude of the B meson which appears in the factorization formula of exclusive B meson decays (Fig.2) and examined the various features of the B-meson light-cone distribution amplitudes including its scale dependence, radiative corrections, its relation to the static correlation in the heavy quark limit, which are eventually relevant to the accurate prediction of the exclusive B-meson decays.

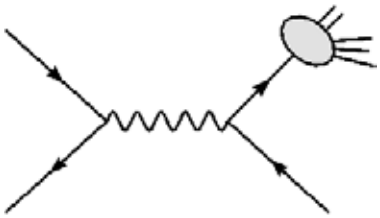


Fig.1: meson production in e^+e^- collision

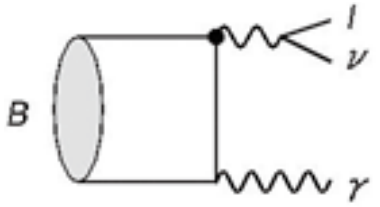


Fig.2 : radiative decay of B meson

Department of General Education

Division of Physics

Professor

Kazuhiro TANAKA

STAFF

Associate Professor
Yuichiro Kiyo

Assistant Professor
Masaya Yata

Main Research Subjects

1. **Tomography of nucleons/mesons from hard processes**
2. **Computation of QCD heavy quark boundstates**
3. **Study of extended objects in string theory**

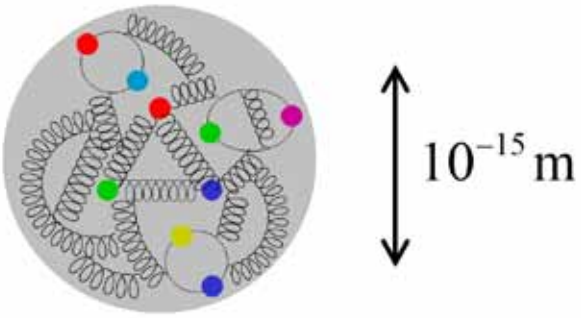
Research Highlights

Formula for origin of proton mass・Precise quark-gluon coupling・String theory approach

Prof. Tanaka derived a formula for the proton mass as the sum of the contributions due to the quarks and gluons constituting a proton. He proved the formula using the "trace anomaly" in QCD, the theory for quarks and gluons. He also applied the formula to the pion mass and found the quite different result.

Associate Prof. Kiyo determined the precise value of QCD coupling constant from heavy quark boundstate informations by computing the wave function and energy levels of heavy quarkonium. He also studied the application of these results to collider physics to search for new physics model beyond standard model of particle physics.

Assistant Prof. Yata studied extended objects, "branes", in superstring theory. He examined the properties of exotic branes — branes that have unique geometrical structures, by using a technique in superstring theory called T-duality transformation.



This represents an intuitive picture of the quarks (colored dots) and gluons (curly lines) constituting a proton, implied by the results based on Quantum Chromodynamics (QCD).

Department of General Education

Division of Chemistry

STAFF

Associate Professor
Eri TOBA (SHIMURA)

Assistant Professor
Ryo ISHIHARA

Main Research Subjects

1. **Regulation of signal transduction networks by post-translational modifications**
2. **Functional analysis of immune cells in the skin tissue**
3. **Development of novel functional materials**

Research Highlights

1. The role of GAPDH nitration in insulin signaling

GAPDH is a catalytic enzyme commonly known to be involved in glycolysis. Increase in GAPDH nitration as well as phosphorylation was observed after insulin stimulation in the H9c2 cell line. After glucose intraperitoneal injection, the nitration level of GAPDH was weak in cardiac muscle of type2 diabetic rat compared with normal rat. These results demonstrated the possibility that insulin signaling mediated by GAPDH was impaired in the heart of type2 diabetic rat. We suggest that the nitration of GAPDH may play a role in the insulin signal transduction in cardiac muscle.

2. Functional analysis of Dendritic epidermal T cells (DETCs)

Dendritic epidermal T cells (DETCs) reside in the primary barrier that protects against diverse environmental insults. Migrated DETCs was observed in the cutaneous draining lymph nodes where they helped initiation process of epidermal antigen-specific humoral immune responses, genetic screening of DETCs have been undertaking to determine DETCs-specific genes. It is anticipated that identification of DETCs-specific genes will be valuable for detection of DETCs and contribute to understanding of novel cutaneous immune responses.

3. Development of SF-PF microchips toward cancer point-of-care testing

To establish a cancer point-of-care testing (POCT), portable surface-functionalized power-free microfluidic chips (SF-PF microchips) have been developed (*Ana. Sci*., 2017, *React. Funct. Polym*., 2019). The SF-PF microchips rapidly and highly sensitively detect promising cancer biomarkers, microRNAs and extracellular vesicles. Liver cancer biomarker, miR-500a-3p, was detected on the SF-PF microchip with 41fmol/L (= 21 zeptomole = 1.2×10^5 copies) sensitivity from 0.5 μL sample for 18 min (*I&EC Res*., 2020). The SF-PF microchip will contribute to establish the cancer POCT.

Department of General Education

Division of Biology

Professor

Akira MATSUMOTO

STAFF

Associate Professor
Mari Wada
Hironori Edamatsu

Main Research Subjects

1. **Age-related changes in circadian gene expression (Matsumoto)**
2. **Oncogenic-RAS-induced cellular stress and ER homeostasis (Edamatsu)**
3. **Development of a new ICT-directed teaching method in Basic Biology for medical students (Wada, Matsumoto, Edamatsu)**

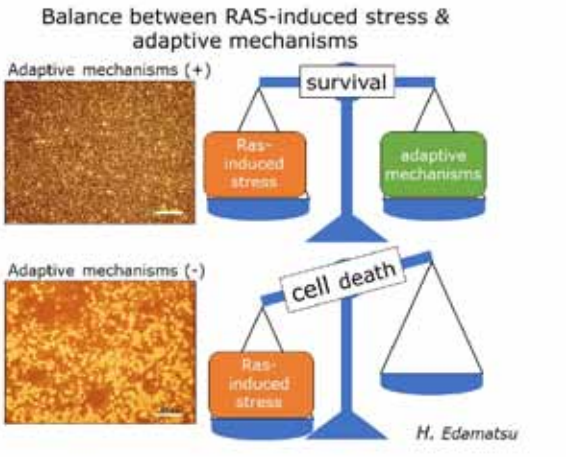
Research Highlights

Age-related changes in circadian gene expression in *Drosophila* (Matsumoto)

Circadian clock is driven by daily rhythmic expression of clock-related genes, and governs many physiological functions in organisms. Recently Prof. Matsumoto and his collaborator, Taichi Itoh in Kyushu Univ, identified a new group of clock-related genes namely "late-life cycler", whose rhythmic expression is strongly induced by age. The molecular mechanism of its expression and physiological functions are now analyzed using transgenic flies.

RAS-induced ER stress (Edamatsu)

Mutational activation of RAS oncogenes leads to excessive cell growth, which is often accompanied by cellular stress to which cells need to adapt. Assoc. Prof. Hironori Edamatsu is studying the mechanisms by which oncogenic RAS induces cellular stress, especially ER stress induced by disruption of the homeostasis of the endoplasmic reticulum (ER). Elucidation of the mechanisms of ER stress induced by oncogenic RAS may provide a hint for therapeutic strategies for cancers harboring oncogenic RAS.



Juntendo University Research Highlights

《 Graduate School of Medicine, Faculty of Medicine 》

Date of Issue：March 1st, 2021

Information Strategy and Institutional Research Office, Juntendo University

2-1-1, Hongo, Bunkyo-ku, Tokyo, 113-8421, Japan　Tel +81-3-3813-3111
https://www.juntendo.ac.jp/english/

Information Strategy and Institutional Research Office, Juntendo University

2-1-1, Hongo, Bunkyo-ku, Tokyo, 113-8421, Japan　Tel +81-3-3813-3111
https://www.juntendo.ac.jp/english/