JIKEI

Research Activities

The Jikei University School of Medicine
The Jikei University School of Nursing

Founding spirit

Treat the patient, not the disease

Explanation

The founding spirit ‘Treat the patient, not the disease’, is a condensed version of the goal of our founder, Kanehiro Takaki, to ‘train doctors who have medical and human abilities’. This spirit is also incorporated into our nursing education as ‘Care for the patient, not the disease’.

The University’s contributions to society through our research and medical practice are also made with this spirit.

University purpose/mission

The mission of our University, based on the founding spirit of ‘Treat the patient, not the disease’, is to contribute to the health and welfare of humankind through the education of doctors and nurses, the promotion of medical and nursing research, and the practice of medical care.

Preface

The Jikei University School of Medicine was founded in 1881 by Kanehiro Takaki as Sei-I-Kwai Koshujo. After he studied at St. Thomas' Hospital Medical School in London, he started medical and nursing education in Japan modeled after his alma mater. Meanwhile he conducted an epidemiological study of beriberi, a disease that claimed many lives at that time. He published the research results showing the prevention and treatment of the disease by dietary means, and his achievement was recognized internationally, rather than only domestically. We could thus say that our university has been "international" since its founding.

In the 140 years since our university's founding, transportation, information, and communication technology have greatly developed, and cross-border activities have become common in research and medical care. In keeping with the trend of today, to widely disseminate our unique education and research to the world, we have decided to launch a novel digital annual report, Research Activities.

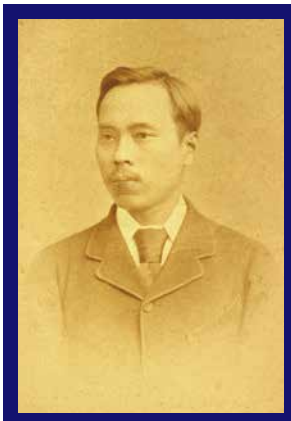
I hope that this report will allow people all over the world to know about our university and more actively exchange students, nurses, scientists, and physicians and collaborate in research. These changes would further promote the global perspective of our people to create a circle of productivity.

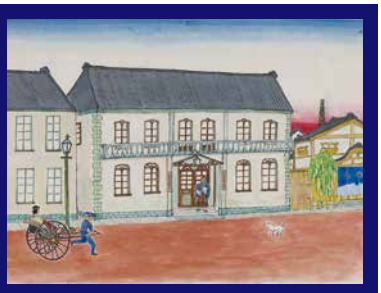
September 30, 2022

Senya Matsufuji, MD, PhD
President

HISTORY of THE

1881	SEI-I-KWAI KOSHUJO (Sei-I-Kwai Medical School) established
1882	YUUSHI KYORITSU TOKYO BYOIN (the Tokyo Hospital Cooperatively Founded by Public-Spirited Persons) opened
1884	Kanehiro Takaki conducted the first large-scale epidemiological research in Japan on the training ship *Tsukuba* as part of the research on beriberi
1885	KANGOFU KYOUIKU-JO (now The Jikei School of Nursing at Shimbashi) established
1887	YUUSHI KYORITSU TOKYO BYOIN was renamed as TOKYO JIKEI IIN (Hospital) by Empress Shoken
1890	SEI-I-KWAI KOSHUJO was renamed as SEI-I GAKKO (School)
1891	SEI-I GAKKO was renamed as TOKYO JIKEI IIN IGAKKO (TOKYO JIKEI HOSPITAL MEDICAL SCHOOL)
1903	TOKYO JIKEI IIN IGAKKO was renamed as TOKYO JIKEI IIN IGAKU SEMMON GAKKO (TOKYO JIKEI HOSPITAL MEDICAL COLLEGE)
1906	*The Lancet* published a lecture by the founder Kanehiro Takaki on the eradication of beriberi
1907	TOKYO JIKEI IIN was renamed as TOKYO JIKEIKAI IIN (TOKYO JIKEIKAI HOSPITAL)
1908	TOKYO JIKEI IIN IGAKU SEMMONGAKKO was renamed as TOKYO JIKEIKAI IIN IGAKU SEMMON GAKKO (TOKYO JIKEIKAI HOSPITAL MEDICAL COLLEGE)
1921	TOKYO JIKEIKAI IKA DAIGAKU (The Jikei University School of Medicine) established
1922	Takaki family donated its privatery owned Tokyo Byoin to the university as its attached hospital
1923	University and hospital burned down in the Great Kanto Earthquake
1930	TOKYO JIKEIKAI IIN main building opened (current building F)
1945	Preparatory school was completely burned down (May 1) and attached hospital was partially burned down (May 25) by air raids
1946	Aoto Hospital opened
1949	Jikei High School opened in April 1949 (closed in 1954)
1950	Daisan Hospital opened
1951	TOKYO JIKEIKAI IKA DAIGAKU (The Jikei University School of Medicine) was renamed as The Jikei University Educational Corporation (transferred to a new university system the following year)
1956	Graduate School of Medicine Doctoral Program established
1971	The Jikei Daisan Higher School of Nursing (now The Jikei Daisan School of Nursing) established
1975	The Jikei Aoto Higher School of Nursing established, closed in 2010
1978	Joint Statement of Affiliation with St. Thomas' Hospital Medical School (now King's College London, Faculty of Life Sciences & Medicine)
1980	Centennial Celebration and Gala Held
1986	President Reiji Natori received the Order of Cultural Merit
1987	The Jikei Kashiwa School of Nursing established
	Kashiwa Hospital opened
1992	School of Nursing established at Kokuryo Campus
2009	Graduate School of Medicine, School of Nursing, Master's Program established
2012	Aoto Hospital was rebuilt and renamed Katsushika Medical Center
2019	Graduate School of Medicine, School of Nursing, Doctoral Program established
2020	New outpatient ward of attached hospital and medical center for mothers and children opened





1881
Sei-I-Kwai Koshujo established

The founder Kanehiro Takaki, with Matsuyama Toan and others, established the Sei-I-Kwai Koshujo, to practice British medicine, in 1881. Takaki also established the Yushi Kyoritsu Tokyo Byoin in 1882 and Japan's first nurses' educational institute, Kangofu Kyoiku-jo, in 1885.

1921
Tokyo Jikeikai Ika Daigaku established

Tokyo Jikeikai Ika Daigaku (Medical University) was established as Japan's first private, single-department medical university in 1921. Eigoro Kanasugi was appointed as the first president of the university.

JIKEI UNIVERSITY


1923
Great Kanto Earthquake

The Great Kanto Earthquake destroyed almost all of the university's facilities, the affiliated hospital, and the nurses' education center in September 1923.


1930
Tokyo Jikei Iin opened

The main building of the Tokyo Jikei Iin (now Building F) opened in November 1930. The attached Tokyo Hospital was also completed in the same year, and the new university building was completed in 1932.



1946
Aoto Hospital opened

Aoto Hospital (now Katsushika Medical Center) opened as an attached hospital of The Jikei University School of Medicine in May 1946. Daisan Hospital opened in November 1950, and the Kashiwa Hospital opened in April 1987.

1956
Graduate School of Medicine established

The establishment of a doctoral program at the Graduate School of Medicine was approved in March 1956, and the school opened in June 1956. The first year 13 students were admitted. The number of M.D. degree recipients in the new graduate school system has been 4,496 as of February 2021.

1980
The 100th Anniversary celebrated

The 100th anniversary of the university's founding was celebrated. A centennial celebration and gala were held. In the presence of Her Imperial Highness Princess Takamatsu, approximately 2,500 people gathered at the Tokyo Prince Hotel.

1992
The School of Nursing established

The School of Nursing was established as the first "Department of Nursing in the Faculty of Medicine" in Japan. A new school building was built at the Kokuryo Campus.

2020
New Outpatient Building opened

The new outpatient building of the attached hospital was opened in 2020. At the same time, a medical center for mothers and children was opened. In December, this center was designated by the Tokyo Metropolitan Government as a comprehensive perinatal maternal and child medical facility.

Anatomy

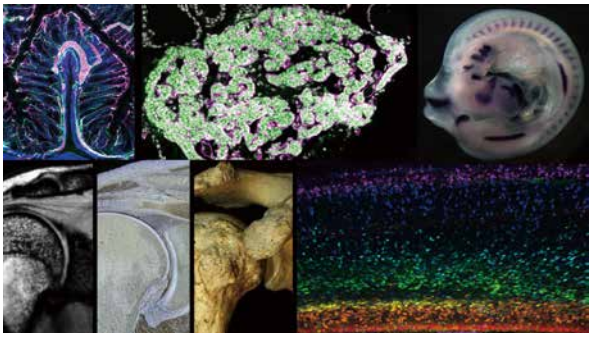
URL : http://www.jikei.ac.jp/academic/course/02_sokaibo.html | E-mail : maokabe@jikei.ac.jp

Overview of 3 groups and ongoing research activities

The Department of Anatomy has 3 research groups: gross anatomy, histology and development, and neuroanatomy.
The gross anatomy group has an extensive collection of human skeletal specimens and has been analyzing the skeletons with their metric and nonmetric data and dissections of cadavers in collaboration with clinical physicians.
The histology and development group studies the ontogeny and phylogeny of the endocrine, respiratory, and digestive systems at the molecular, cellular, and histological levels. For these studies the group uses comparative genomic analyses, molecular biology, and histological and microstructural methods.
The neuroanatomy group has recently been established. This group aims to reveal cellular and molecular mechanisms of normal and pathological development of brains. The group also focuses on pathophysiological mechanisms of psychiatric disorders, which are presumed to develop on the basis of genetic and environmental factors.

Ongoing research projects

1) Evaluations of gender differences in feet using skeletal specimens
   We evaluate gender differences in the talus and calcaneus by analyzing metric and nonmetric data collected from the specimens.
2) Research on the development and regeneration of parathyroid gland and kidney
   We are studying development and regeneration in the parathyroid gland and kidney through analyses of *glial cells missing* (*Gcm*) family genes.
3) Research on the morphological evolution of organs using various fishes and tetrapods
   We are using comparative anatomy and molecular biology to study organ evolution by comparing tetrapods with actinopterygian fishes, including *Polypterus*.
4) Analyses of mechanisms of intestinal inflammations in ulcerative colitis
   We are focusing on blood vessels in the colonic mucosa to investigate how they are involved in the development of enteritis. Specifically, we use confocal laser microscopy to analyze changes in vascular structures in 3 dimensions in mice with experimentally induced colitis.
5) Cellular and molecular mechanisms of the development of the neocortex, hippocampus, and limbic system
   We are focusing on migration profiles of neurons during brain development. We utilize in-utero electroporation and FlashTag techniques to label specific subgroups of neurons.
6) Cellular and molecular mechanisms of pathological brain development
   We produce various mouse models of psychiatric disorders by administering reagents or manipulating genes with the techniques of in-utero electroporation or i-GONAD (improved genome-editing via oviductal nucleic acids delivery) or both and analyze their behaviors.
7) Cellular and molecular mechanisms of the psychiatric disorders using human postmortem brain tissues
   We investigate postmortem brain tissues from patients with psychiatric disorders and healthy control subjects using single-cell RNA sequence and spatial transcriptomics.



Cross-disciplinary approach: molecules, organelles, cells, tissues, organs, gross morphology to evolution

Molecular Physiology

URL : http://www.jikei.ac.jp/academic/course/03_bunsiseiri.html E-mail : maki@jikei.ac.jp

Biophysical approaches to elucidate the structure and function of living skeletal muscle cells

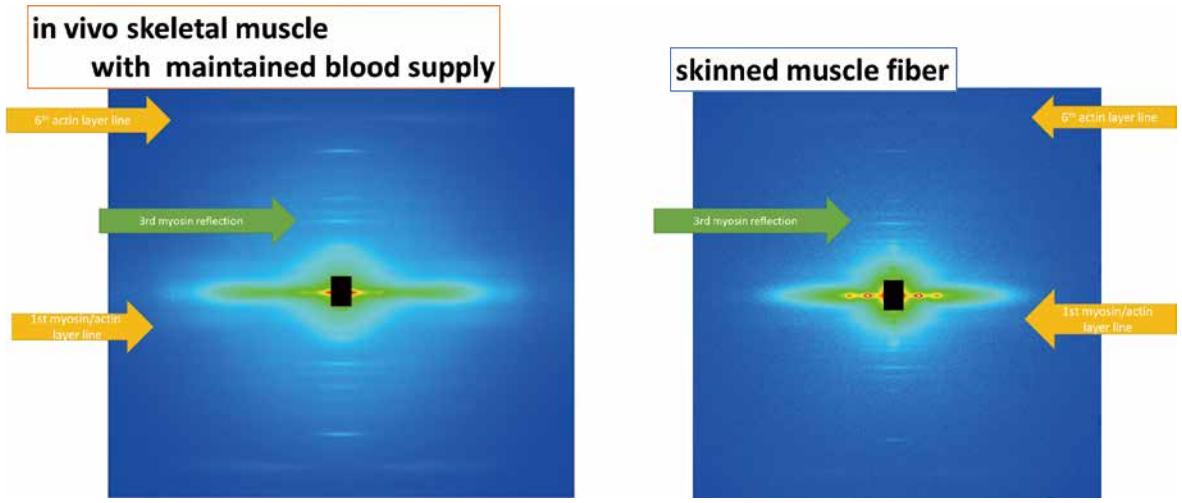
X-ray diffraction study of living skeletal muscle

Repetitive muscle contraction gradually develops so-called muscle fatigue processes that cause muscle function and structure to deteriorate. A potentially suitable technique to monitor the progress of structural deterioration in muscle sarcomeres with repetitive contraction is x-ray diffraction. However, dissection of muscle tissue limits the diffusion of gases and solutes to exacerbate metabolic deterioration, and isolation of a muscle fiber might cause fragility that aggravates structural degradation. To obtain x-ray diffraction patterns of skeletal muscle at a state as physiological as possible, we attempted to obtain x-ray diffraction patterns from in-situ muscle with a maintained blood supply. The X-ray diffraction patterns from the extensor digitorum longus muscle of anesthetized 6-month-old female ICR mice were obtained with the beamline for small angle X-ray scattering (BL-6A) at the High Energy Accelerator Research Organization (KEK), Tsukuba. Diffraction patterns of high quality were obtained and showed high orders of reflections and layer lines.

Analysis of Ca^{2+}-induced Ca^{2+} release control mechanism using molecular dynamics simulation and a mouse model of malignant hyperthermia

Mutations of the ryanodine receptor 1 gene (RyR1) cause severe muscle diseases, such as malignant hyperthermia (MH), which is a disorder of Ca^{2+}-induced Ca^{2+} release via RyR1 in skeletal muscle. We combined functional studies and molecular dynamics simulation of RyR1-bearing disease-associated mutations in the N-terminal region. When expressed in HEK293 cells, the mutant RyR1 caused abnormalities in Ca^{2+} homeostasis. Molecular dynamics simulation of the mutant RyR1 revealed that alterations of hydrogen bonds/salt bridges between N-terminal domains, consisting of A, B, and C domains, strongly correlate with the channel function of RyR1.

Next, we tested the therapeutic effects of a ryanodine receptor 1 (RyR1) inhibitor on MH model mice carrying a mutation of *Ryl1*. The inhibitor suppressed caffeine-induced contraction in skeletal muscle from heterozygous MH mice. The heterozygous mice died with an increased body temperature when they were anesthetized with isoflurane. Pre-administration of the RyR1 inhibitor completely prevented the rise in body temperature and death. In addition, application of the RyR1 inhibitor after the development of MH also successfully protected the mice. These results suggest that RyR1 mutant mice are a promising model for studying the pathogenesis of MH and for screening new drugs.



X-ray diffraction images originated from ordered structures of myofilament proteins

Cell Physiology

URL : http://sminamis.m38.coreserver.jp/Jikei_Cell_Physiology/Welcome.html | E-mail : sminamis@jikei.ac.jp

Regulatory mechanisms of calcium homeostasis and development of the cardiovascular system

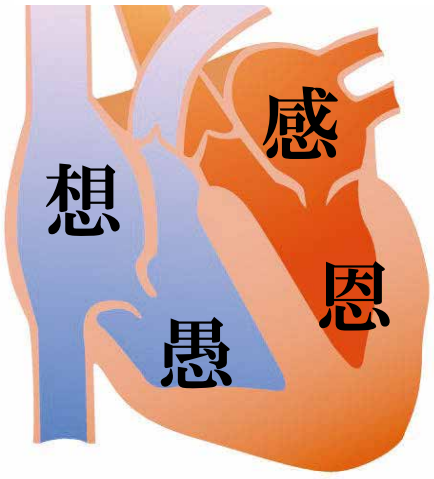
The aim of research in our laboratory is to understand the regulatory mechanism of the cardiovascular system. In particular, we are interested in the molecular mechanisms of development of the cardiovascular system in the fetus, the regulation of calcium-mediated excitation-contraction coupling, metabolomic changes in the diseased heart, and the pathophysiology of cardiac fibrosis and pulmonary hypertension. We established an experimental system to investigate small fetal arteries, such as the ductus arteriosus (DA), and the pulmonary vein. The main current research topics are: 1) analysis of genetic and physiological characteristics of pulmonary veins, 2) the molecular mechanism of closure of the DA, 3) the regulation of cardiac metabolism in the developing heart and vessels, 4) the pathophysiological mechanisms of overstretch-induced cardiac dysfunction, and 5) the mechanism of sarcomere contraction in cardiac muscle.

In detail, the characteristics of pulmonary veins remains a mystery. Using sarcolipin-knockout cre-knock-in mice, we have generated the atrium-specific overexpression or the deletion of paired-like homeodomain transcription factor 2 isoform c (*Pitx2c*), a transcription factor that is specifically expressed in the pulmonary veins and the left atrium. We found that the transgenic mice exhibited sinus node dysfunction and atrial arrhythmia. The DA is an essential artery that connects the main pulmonary artery and the descending aorta in the fetus. The DA closes immediately after birth in accordance with its smooth muscle contraction and vascular remodeling. We have investigated the molecular mechanisms of vascular remodeling of the DA and have found that the vasodilating prostanoid prostaglandin E2 plays a critical role in the structural changes of the DA, such as intimal cushion formation and poor elastogenesis. These studies attracted keen attention in the cardiovascular field.

Selected references:

1. Yokoyama U, et al. Prostaglandin E2 inhibits elastogenesis in the ductus arteriosus via EP4 signaling. Circulation 129: 487-96, 2014.
2. Fujimoto Y, et al. Pulmonary hypertension due to left heart disease causes intrapulmonary venous arterialization in rats. J Thorac Cardiovasc Surgy 154: 1742-1753, 2017.
3. Shigeta A, Nakano A, et al. Endocardially-derived macrophages are essential for valvular remodeling. Dev Cell 48: 617-630, 2019.

Circulation of the spirits (心) in my lab heart



想: imagine a question that you want to know
愚: Just keep moving forward with the question
感: sharpen your sensitivities
恩: appreciate the supports and achievements that you could obtain, and then let's imagine a next question (back to 想)

"Kokoro (心)-no-junkan" **The Four-Chambered Heart I Cherish**

Biochemistry

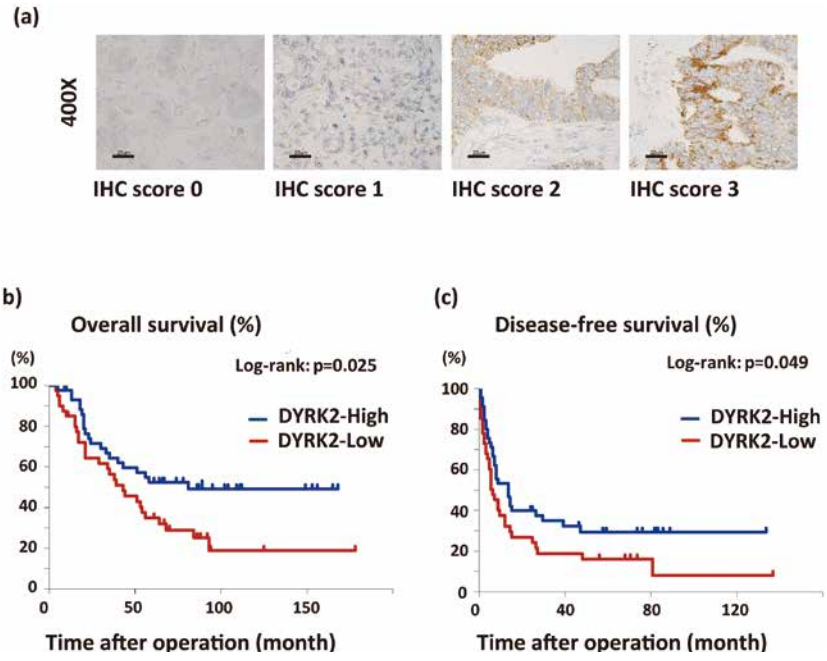
URL : https://jikei-biochem.wixsite.com/yoshidalab | E-mail : kyoshida@jikei.ac.jp

Achievement of a breakthrough by basic medical research in the fight against cancer

Tumors are genetic diseases. The fundamental defect of tumor cells is a deregulated proliferation that results from the progressive accumulation of genetic and epigenetic alterations. These alterations invariably affect the regulatory pathways that govern the proper cellular responses to this myriad of signals. Normal proliferative cells are endowed with the abilities to choose between growth and quiescence, differentiation, and apoptosis. The execution of these alternatives is influenced by physiological factors and stress to achieve a controlled and balanced proliferation. Our research is directed at elucidating signaling pathways that allow normal cells to distinguish between proliferation, differentiation, and apoptosis.

1. The antitumor effect of DYRK2 in colorectal cancer
   We aim to elucidate the function of dual-specificity tyrosine-regulated kinase 2 gene (*Dyrk2*), which is a key regulator of p53 in response to DNA damage. In colorectal cancer cell lines, we recently reported that knockdown of the enzyme dual-specificity tyrosine-(Y)-phosphorylation–regulated kinase 2 (DYRK2) induces proliferation in vitro. To extend this finding, we examined whether forced expression of DYRK2 is a potential novel gene therapy against cancer. We developed a xenograft model of colorectal cancer cell lines and are analyzing the effects of DYRK2-overexpression by adenovirus infection in proliferation and apoptosis.

2. DYRK2-null mouse recapitulates VATER/VACTERL association with lung hypoplasia
   Congenital malformations are a major issue in pediatric healthcare and the leading cause of infant mortality. Most rare congenital malformations, such as vertebral anomalies, anal atresia, tracheoesophageal fistula and/or esophageal atresia, and radial dysplasia (VATER) and VATER with cardiac defects and limb defects (VACTERL) association, have multiple component features, and some are known to involve genetic mutations. Surprisingly, the phenotypes of DYRK2-deficient mice recapitulated those of the human congenital malformations VATER and VACTERL. Transcriptome analysis indicated close similarities between the molecular phenotypes of VATER/VACTERL and DYRK2-deficient mice, particularly with respect to Forkhead box F1 gene (*Foxf1*) reduction. Detailed analyses of primordial lungs at the early developmental stage demonstrated that DYRK2 deficiency leads to altered airway branching and insufficient alveolar development. Taken together, our results confirm the establishment of a novel DYRK2-deficient mouse model that recapitulates the pathological and molecular phenotypes of VATER/VACTERL association with lung hypoplasia.



Immunohistochemical analysis of dual-specificity tyrosine-(Y)-phosphorylation–regulated kinase 2 in human colorectal liver metastases predicts clinical outcome

Molecular Biology

URL : http://www.jikei.ac.jp/mb/index_e.html | E-mail : senya@jikei.ac.jp

The polyamine regulatory system as an intervention target

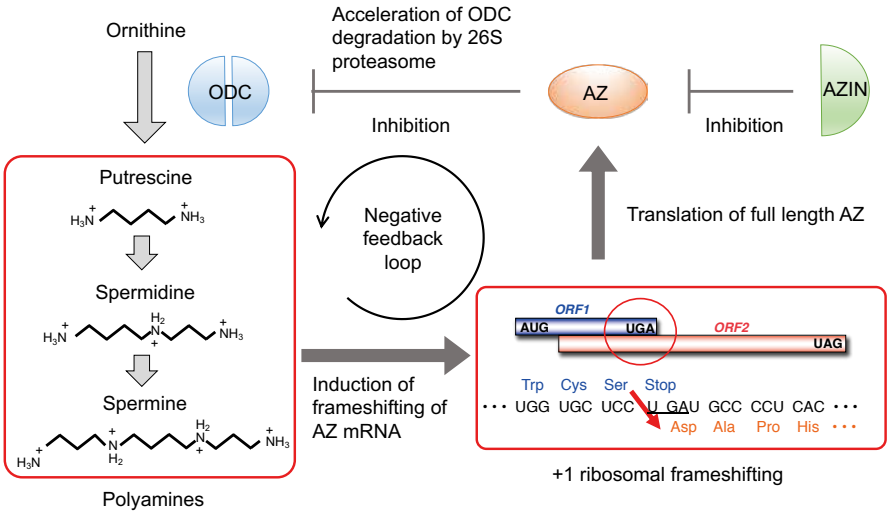
Our goal is to clarify cellular polyamine regulation to develop an intervention strategy that targets this regulatory system.

Polyamines are ubiquitous biogenic amines which are essential for cell proliferation. They are related to various phenomena, such as differentiation, development, cancer, and autophagy. Recent studies have shown that polyamines have effects on the prolongation of life, suppression of age-dependent memory impairment, and prevention of arteriosclerosis. In mammalian cells, the most abundant polyamines are putrescine, spermidine, and spermine. Intracellular polyamine levels are strictly controlled, because an excess of polyamines is toxic for the cells. The key molecule of cellular polyamine regulation is antizyme (AZ). Expression of full-length active AZ is controlled by a unique mechanism called polyamine-induced +1 ribosomal frameshifting on AZ messenger RNA that is induced by a high level of polyamine. In turn, AZ inhibits ornithine decarboxylase (ODC) and recruits it to the 26S proteasome for degradation in a ubiquitin-independent manner. The ODC converts ornithine to putrescine, which is subsequently metabolized to spermidine and spermine. Thus, intracellular polyamine levels are maintained by this negative feedback regulation (Fig. 1). The AZ is further regulated by a protein called AZ inhibitor, which is highly homologous to ODC but has no catalytic activity. Three AZ isoforms—AZ1, AZ2, and AZ3—are present in mammals.

We are currently studying the following topics.

1. Function and medical application of polyamines
   a. Analysis of physiological function of polyamines
   b. Analysis of polyamines on medical diagnosis
   c. Application of polyamines on medical diagnosis
   d. Polyamines and cancer: urinary diacetylspermine as a tumor marker
   e. Analysis of polyamine effects on RNA structure by using RNA aptamer

2. Research for polyamine regulatory protein AZ
   a. Tumor growth and ubiquitin-independent degradation of Myc proteins mediated by AZ2
   b. Identification of AZ1- and AZ2-interaction proteins and their functions
   c. Regulatory mechanism of ATP-citrate lyase by AZ
   d. Mechanism of polyamine-induced +1 ribosomal frameshifting of AZ messenger RNA



Regulation of polyamine levels in mammalian cells

Pharmacology

URL : http://www.jikei-pharm.com/ E-mail : tmomi@jikei.ac.jp

Several functional studies of the central nervous system are independently in progress

Synaptic transmission and its modulation in the central dopaminergic and cholinergic system (Toshihiko Momiyama, Etsuko Suzuki)

Electrophysiological studies using slice patch-clamp recording techniques were performed to analyze synaptic transmission, its modulation, and developmental changes in the central dopaminergic and cholinergic systems. Furthermore, optogenetic activation techniques have been introduced to analyze neuron type-specific synaptic transmission and its modulation by serotonin and muscarinic acetylcholine receptors. These basic analyses can lead to the identification of the mechanisms underlying the related psychological functions and their disorders, such as Parkinson disease and Alzheimer disease, and to the development of novel therapeutic tools.

Functional analysis of cerebrocerebellar interaction (Taro Ishikawa, Misa Shimuta)

Cerebrocerebellar communication is important in a wide range of brain functions, including sensory information processing. We investigated the somatosensory-signaling pathways to the cerebellar cortex in mice whose cerebral cortex can be suppressed by optogenetic methods. We found that direct signals from the trigeminal nuclei and indirect signals via the primary somatosensory cortex are integrated in both Purkinje cells and granule cells in the cerebellar cortex.

Study of exhibition of allergic reactions mediated by P2Y11 receptors in mast cells (Haruhisa Nishi)

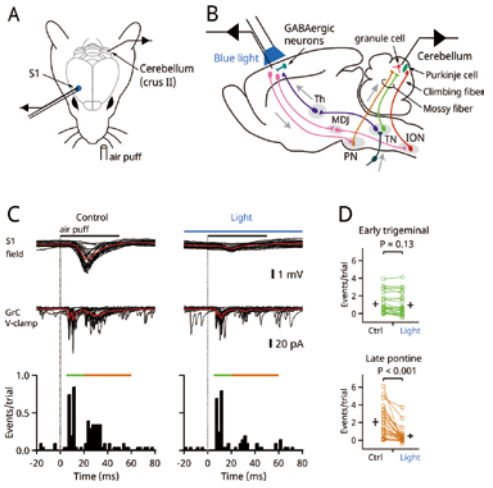
With a human-derived mast cell line, the effect of messenger RNA knockdown expression on the P2Y11 receptor and the degradation of extracellular ATP were investigated. Extracellular ATP enhanced an extremely weak allergic response through stimulation of the P2Y11 receptor. These findings are useful in understanding the many factors underlying the exacerbation of allergic responses.

The basic mechanism underlying the anticonvulsant effects of ketogenic diet (Masahito Kawamura)

A ketogenic diet has been used to treat medically-refractory epilepsy. We fed rats a ketogenic diet, prepared hippocampal specimens, and performed electrophysiology in the seizure-prone CA3 region. Hippocampal specimens from rats fed a ketogenic diet showed reduced excitability, and the effects of the ketogenic diet could be reversed with blockers of adenosine A_1 receptors. These results suggest that the reduction of neuronal activity through activation of adenosine A_1 receptors is a key mechanism underlying anticonvulsant effects of a ketogenic diet.

Short-term presynaptic facilitation at a cerebellar excitatory synapse (Yukihiro Nakamura)

A simple form of residual Ca hypothesis cannot fully account for the synaptic facilitation because decay time of intracellular Ca concentration does not coincide with that of synaptic facilitation. I developed a numerical simulation of intracellular Ca and vesicular transmitter release in the cerebellar parallel fiber-Purkinje cell synapse. The simulations indicated that Ca-dependent vesicular replenishment to empty docking sites is a key determinant of synaptic facilitation.



Highlights from the study of cerebrocerebellar communication. A, Tactile stimulation (air puff) was applied to the upper lip of the mouse during simultaneous recordings from the cerebellum and the primary somatosensory cortex (S1). S1 was optogenetically suppressed in alternating trials. B, The neural circuits involved in this study. Th, thalamus; MDJ, mesodiencephalic junction; PN, pontine nuclei; TN, trigeminal nuclei; ION, inferior olivary nucleus. C, In vivo field potential recording from S1 (top) and whole-cell voltage-clamp recording from granule cell (lower). Detected EPSC events are shown in time histograms (bottom). D, EPSC event numbers were compared for the early phase (green, top) and the late phase (brown, bottom). These results indicate that the individual granule cells receive convergent synaptic inputs from trigeminal and pontine pathways. (Figures modified from Shimuta et al. Commun Biol. 2020)

Pathology

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Human and experimental pathology

The Department of Pathology is a founding department of The Jikei University School of Medicine. It has been focused on human pathology and has recently introduced experimental pathology. Pathology, which is based on morphological diagnosis and research, is entering a major turning point owing to the development of cancer genomics and artificial intelligence technology. On the basis of our abundant knowledge and experiences regarding morphology, we are further incorporating basic research, cancer genomics, and advanced image technologies to create a synergistic effect and to build next-generation pathology together with young people.

Major research topics in our laboratory:

1. Basic research on the tissue microenvironmental biology, especially proteinases and extracellular matrix proteins, under pathophysiological conditions

2. Clinicopathological studies of various tumors, including cancers of the ovary cancer, prostate, lung, liver, and gastrointestinal tract.

Creation of next-generation pathology based on our morphological knowledge/experiences

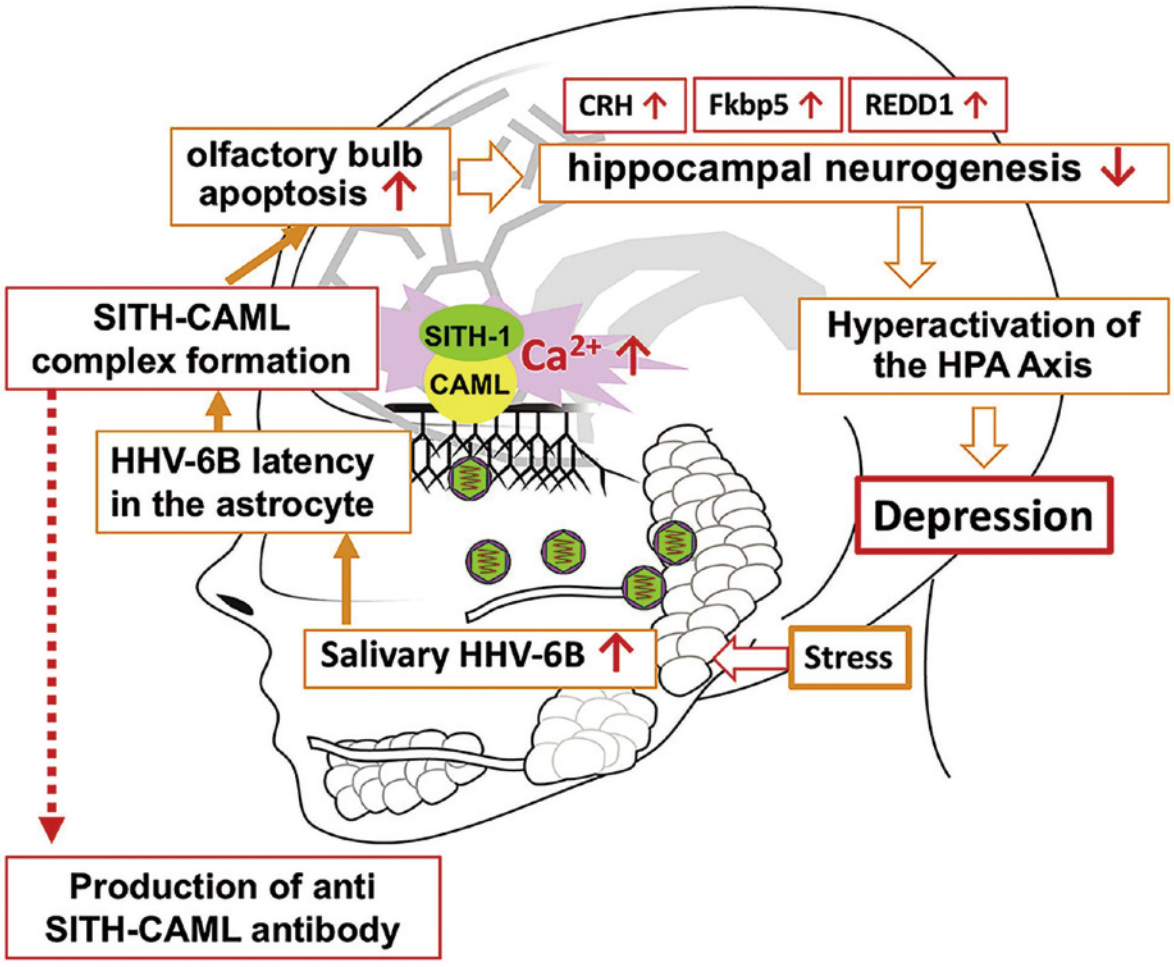
Virology

URL : https://jikeivirus.jp/ E-mail : jikeivirus@jikei.ac.jp

Identification of human herpesviruses 6B latent protein SITH-1 the cause of major depression

Human herpesvirus (HHV) is capable of establishing a lifelong latent infection of its host and is frequently reactivated. We are studying the molecular mechanisms of the latency and pathogenesis of HHV and have found a novel latent protein of HHV-6B which associate with depression. We are also trying to apply HHV-6B and HHV-7 to the tools for studying the mechanism of fatigue. The amounts of salivary HHV-6B and HHV-7 DNA increased with training and decreased with rest, suggesting their usefulness as biomarkers of physiological fatigue and cancer-related fatigue.

Little is known about the effects of latent-phase herpesviruses on their host. The herpesvirus HHV-6B is ubiquitous, and olfactory astrocytes are an important site of its latency. We have identified small protein encoded by the intermediate stage transcript of hhv-6 1 (SITH-1), an HHV-6B latent protein specifically expressed in astrocytes. Mice induced to produce SITH-1 in their olfactory astrocytes exhibited olfactory bulb apoptosis, a hyperactivated hypothalamic-pituitary-adrenal axis, and symptoms of depression. The binding of SITH-1 to the host protein calcium-modulating ligand to form an activated complex promoted the influx of extracellular calcium. The serum antibody titers of patients who had depression, with respect to this activated complex, were significantly higher than those of control participants ($p = 1.78 \times 10–15$), when the antibody positive rates were 79.8% and 24.4%, respectively, and the odds ratio was 12.2. These results suggest that, in the latent phase, HHV-6B is involved in the onset of depression.



Human herpesvirus 6 greatly increases the risk of depression by activating the hypothalamic-pituitary-adrenal axis during the latent phase of infection.

Bacteriology

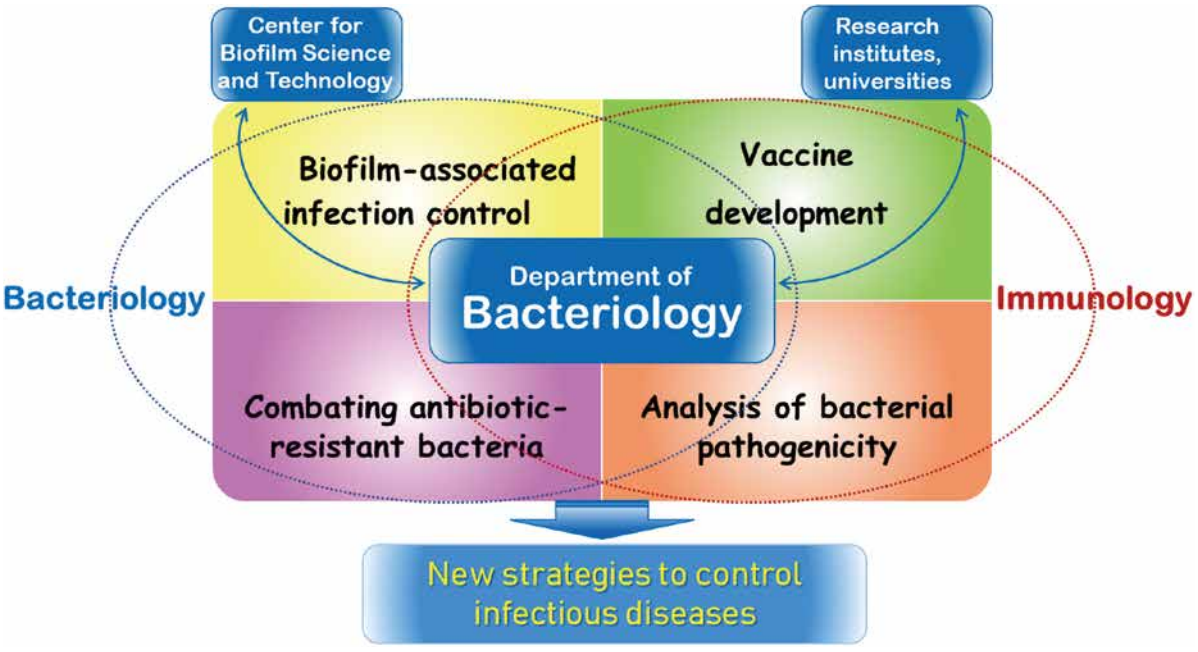
URL : http://www.jikei.ac.jp/academic/course/11_saikin.html E-mail : ykinjo@jikei.ac.jp

Studies of bacteriology and immunology to develop new vaccines and treatments for pneumonia and biofilm infections

Our research goals are to understand the mechanisms of microbial infections and host immune responses and to develop new strategies, such as vaccines and treatments, to control infectious diseases. We have conducted research in both basic science and medical science through our collaboration with researchers in various institutions and universities.

We have recently focused on

1. Development of new pneumococcal vaccines: *Streptococcus pneumoniae* is a major cause of community-acquired pneumonia and occasionally causes invasive pneumococcal diseases, such as bacteremia and meningitis, especially in young children and older adults. Recently, invasive pneumococcal diseases caused by a nonvaccine type of pneumococcus have been increasing, resulting in the insufficient effectiveness of current vaccines. Thus, development of a novel vaccine is desired, and we have generated a novel protein-based vaccine that is expected to provide broad protection against pneumococcal infections.
2. Study of biofilm-associated infections: Bacterial aggregates attaching to surfaces are called biofilms and are a bacterial survival strategy in various environments. However, biofilms can cause serious infectious diseases that are difficult to treat. To develop novel strategies for preventing and treating biofilm-associated infections, we examined the molecular basis of biofilm formation and screened biofilm inhibitors in collaboration with the Center for Biofilm Science and Technology at The Jikei University established as part of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) supported Program for Strategic Research Foundation at Private Universities in 2015.
3. New strategies against antibiotic-resistant bacteria: Antibiotic microbial resistance is a growing global concern, and a new approach is required to overcome this emergency. We have screened compounds effective against antibiotic-resistant bacteria.
4. Analysis of bacterial pathogenicity: Bacteria have many virulence factors that cause diseases in the host. We have examined the role of bacterial factors on their pathogenicity, including *Staphylococcus aureus* and enterohemorrhagic *Escherichia coli* using silkworm models and animal models.



Research projects in the Department of Bacteriology

Tropical Medicine

URL : https://jikei-tropmed2.wixsite.com/english
E-mail : kanuka@jikei.ac.jp

Biology of disease vectors transmitting pathogens via blood-sucking

A variety of arthropods carry and transmit infectious pathogens into other living organisms. An arthropod is considered a vector when it transmits a disease, which is referred to as a vector-borne disease. These hematophagous arthropods form a major group of disease vectors, including mosquitoes, flies, sand flies, lice, fleas, ticks, and mites, that transmit such diseases as malaria and dengue filariasis, Chagas disease, and leishmaniasis. Understanding the molecular mechanisms of how disease-transmitting vectors respond to pathogens is of great importance for current efforts to develop novel strategies for controlling vector-borne diseases. The pathogens, such as viruses, protozoan parasites, and parasitic nematodes, undergo substantial stage-specific losses during their development in vectors which leads in some cases to the vector becoming completely refractory to the pathogen. The underlying genetics of vector competency is complex; however, comparative and functional genomic approaches to the interaction of vectors and pathogens have been allowed by the multifactorial completion of the genome sequences of such major vector species as mosquitoes and ticks, the development of transgenesis in these species, and the extension to vectors of RNA interference and gene-editing techniques (CRISPR/Cas9).
Our department focuses on 4 critical elements for a holistic vector control strategy: (1) development of rapid diagnostic methods for a pathogen and its vector, (2) vector surveillance with systematic monitoring of pathogens, (3) understanding mechanisms related to vector competency and its control by microbe-based paratransgenesis, and (4) neuro-ethological analysis of vector behavior, in particular, host-sensing and blood-feeding.

Insect species that can transmit pathogens to cause infectious diseases

Public Health and Environmental Medicine

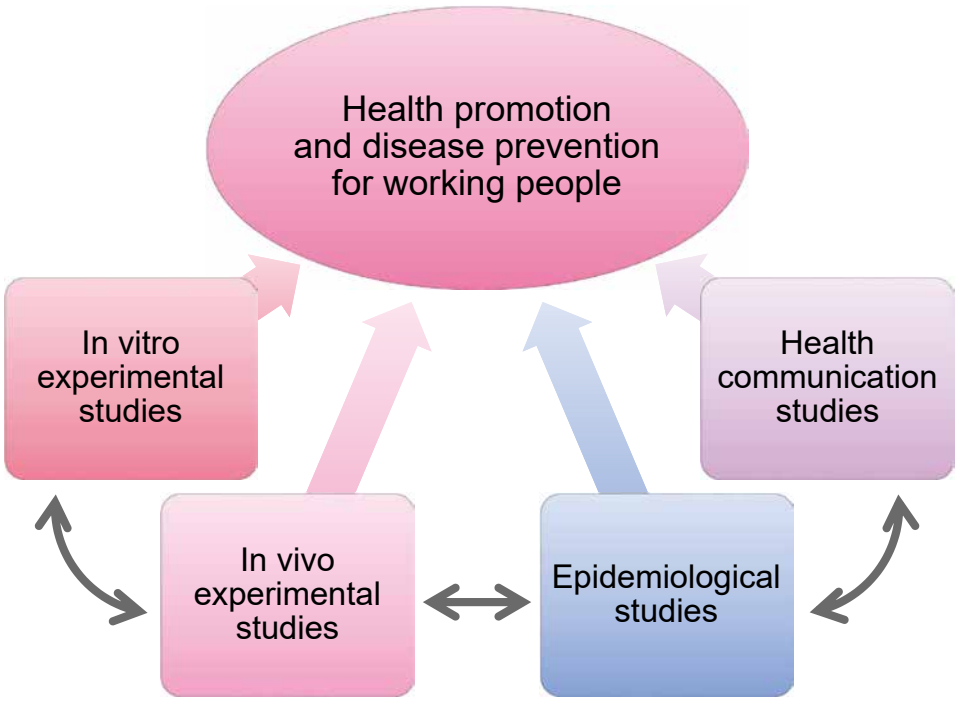
URL : https://plaza.umin.ac.jp/~jikphem/ | E-mail : suka@jikei.ac.jp

Studies of preventive medicine to solve health-related problems among working people

We conduct experimental and epidemiological studies to solve health-related challenges among working people.

Experimental studies:
1. In-vivo function of essential trace elements, especially zinc
2. Toxicological mechanisms of chemicals, especially organic polymers
3. Evaluation of the mutagenicity of chemicals, especially nanomaterials
4. Development of an in-vitro evaluation system for the effects of dermal exposure

Epidemiological studies:
1. Population approach for the prevention of lifestyle-related/noncommunicable diseases
2. Promotion to support the balance between work and medical treatment
3. Overwork-related disorders and accidents/injuries
4. Promotion of help-seeking behavior and suicide prevention
5. Healthcare for menopausal women
6. Prevention of the onset and progression of diabetic complications
7. Quality of life and social independence among patients with rare diseases
8. Public health communication



Research activities of the department

Forensic Medicine

URL : http://www.jikei.ac.jp/academic/course/15_houi.html | E-mail : forensic-med@jikei.ac.jp

A multifaceted investigation, based on forensic autopsy, of the causes of abnormal and sudden deaths

The highlight of the Forensic Medicine Course in Tama, Tokyo, is the performance of more than 800 forensic autopsies per year, garnering the highest number of autopsies performed in a university in Japan. As a result, most studies conducted in this course are based on practical content directly linked to actual forensic autopsies. Interestingly, the approach of this course is multifaceted and varied due to the inclusion of forensic pathology studies based on actual macroscopic and histological diagnoses, radiological postmortem imaging studies using dual-energy computed tomography, drug analysis of specimens obtained at autopsy, studies with various examinations, and statistical analyses based on a large number of autopsy records. Therefore, the purpose of this study was to determine, with forensic autopsy, the causes of abnormal or sudden deaths and to improve the accuracy of this approach.

Concerning the dual-energy computed tomographic scanner introduced in 2019

Gastroenterology and Hepatology

URL : http://www.jikeisyounai.ac.jp/index.html E-mail : m.saruta@jikei.ac.jp

Focus on the elucidation and treatment of diversifying gastrointestinal and liver diseases

Our department consists of approximately 130 physicians belonging to The Jikei University School of Medicine (4 affiliated hospitals) and related branched hospitals. In 2016, our department reorganized into laboratories on the basis of organs and 4 newly established groups: the Gastroenterology group, the Hepatology group, the Biliary–pancreas group, and the Oncology group. We have shifted to a system that enables medical care and research for all diseases in the digestive system. The main research subjects of each group are as follows.

The Gastroenterology group aims to elucidate the pathophysiology of inflammatory bowel diseases, such as ulcerative colitis and Crohn's disease, which are designated as intractable diseases, to establish biomarkers, and to establish therapeutic methods.

Publications

1. J Gastroenterol Hepatol. 2021; 36(9): 2523–2530.
2. J Dig Dis 2020; 21(9): 498–504.
3. PLoS One 2020; 15(11): e0241337.
4. J Vis Exp 2020; 160.
5. J Gastroenterol Hepatol 2021; 36(7): 1744–53.
6. J Gastroenterol Hepatol 2021; 36(4): 864–72.
7. J Gastroenterol Hepatol 2021; 36(2): 329–36.
8. Int J Environ Res Public Health 2020; 17(8): 2926.

The "Gastroenterology group" also focuses on endoscopic evaluation and treatment for gastrointestinal cancer and on mechanisms and the treatment of esophageal reflux disease and gastrointestinal ulcers.

Publications

1. Surg Endosc 2021; 35(5): 2110–8.
2. Dis Colon Rectum 2021; 64(1): 53–9.,
3. Gastroenterology 2021; 160(4): 1075–84.e2,
4. Endoscopy 2021; 53(6): E209–10.,
5. Dis Colon Rectum 2021; 64(1): 53–9.
6. Esophagus 2021; 18(2): 398–406.
7. JGH Open 2020; 5(1): 99–106.

The Hepatology group focuses on the assessment and treatment of viral and alcoholic liver damage and carcinoma and aims to elucidate the pathophysiology of autoimmune hepatitis and primary biliary cholangitis that develop from autoimmune mechanisms.

Publications

1. Cancer Res 2021; 81(2): 414–25.
2. J Gastroenterol Hepatol 2020; 35(4): 663–72.
3. J Breath Res 2021; 15(2): 026010.
4. Intern Med 2020; 59(14): 1695–704.
5. JGH Open 2020; 5(1): 34–40.

The Hepatology group also focuses on frailty, sarcopenia, and osteoporosis in patients with chronic liver disease.

Publications

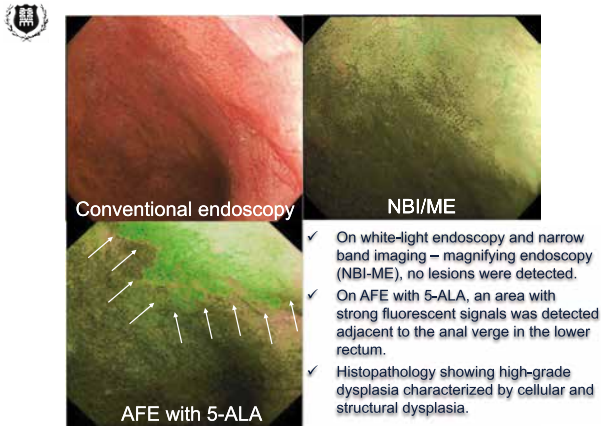
1. Nutrients 2020; 12(12): 3810.,
2. World J Gastroenterol 2020; 26(33): 4960–71.
3. J Clin Med 2020; 9(10): 3239.
4. J Clin Med 2020; 9(8): 2381.

The Biliary–pancreatic group attempts to establish highly specialized diagnostic methods and treatment techniques for the early diagnosis of pancreatic cancer and to clarify the mechanism of pancreatic cancer development.

The Oncology group focuses on the safe use of chemotherapy and tries to elucidate the mechanism of unexpected side effects mediated by an immune mechanism.

Publications

1. Expert Opin Biol Ther 2021; 21(6): 697–703.
2. Support Care Cancer 2020; 28(12): 5861–9.
3. Jpn J Clin Oncol 2021; 51(5): 707–12.



Endoscopic visualization of ulcerative colitis–related cancer and dysplasia with orally administered 5-aminolevulinic acid.

Neurology

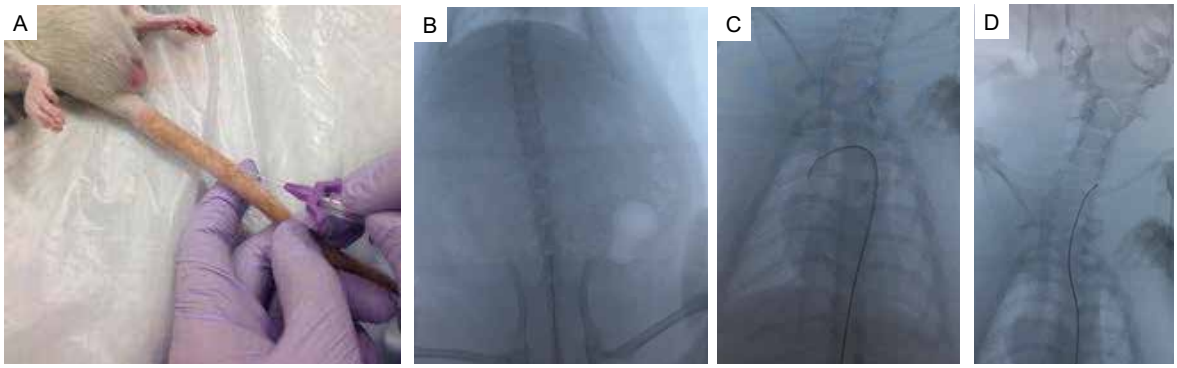
URL : https://jikei-neurology.jp | E-mail : neurology@jikei.ac.jp

Clinical and basic research on stroke and neurodegenerative disease

Our clinical and basic research in 2020 consisted of the following topics:

1. Stroke
- Risk and environmental factors of ischemic stroke in young adults
- Diagnosis of cryptogenic stroke with patent foramen ovale and evaluation of the efficacy of patent foramen ovale closure using a novel ultrasound probe attached to the neck
- Pre-stroke CHADS2 (congestive heart failure, hypertension, age ≥ 75 years, diabetes, and previous stroke or transient ischemic attack) scores should be associated with onset severity and functional outcome in acute stroke patients with atrial fibrillation during oral anticoagulants: A sub-analysis of the prospective analysis of stroke patients taking anticoagulants (PASTA) registry study
- A novel rat model of embolic cerebral ischemia using a cell-implantable radiopaque hydrogel microfiber

2. Neurodegenerative Disease
- Molecular mechanism and clinical application of nuclear medicine in patients with neurodegenerative diseases
- Dopamine transporter single-photon emission computed tomography imaging in the differential diagnosis of progressive supranuclear palsy variants
- Fiberoptic laryngoscopic evaluation of bulbar symptoms in patients with amyotrophic lateral sclerosis
- Multifaceted study of nonmotor symptoms of Parkinson disease
- Risk factors for minor hallucinations in Parkinson disease
- lucidating the association between orthostatic hypotension and nigrostriatal dopaminergic degeneration in Parkinson disease
- Cell biological studies of endosomal dysfunction using induced pluripotent stem cells derived from familial Parkinson disease
- Disease modeling of hereditary motor and sensory neuropathy with proximal dominant involvement using neurons derived from induced pluripotent stem cells
- Dopaminergic dysfunction in de novo Parkinson disease
- Comparison of ^{123}I-metaiodobenzylguanidine myocardial scintigraphy and ^{123}I-N-fluoropropyl-2b-carbomethoxy-3b-(4-iodophenyl)nortropane single-photon emission computed tomography between dementia with Lewy bodies and Parkinson disease



The minimally invasive intra-arterial approach under fluoroscopic guide
A) Puncture of caudal ventral artery in rat. A sheath was inserted through the ventral midline.
B-D) Rat fluoroscopic images of the wire inserted carefully through the sheath inserted into the caudal ventral artery and guided into the abdominal aorta (B), the aortic arch (C) and the left common carotid artery (D).

A new rat model of embolic cerebral ischemia using a microcatheter under fluoroscopic guidance

Nephrology and Hypertension

URL : https://jikei-kidneyht.jp/ E-mail : nephrology@jikei.ac.jp

Nephrology, Hypertension, and Regeneration

Regenerative Medicine Team

We propose "xenogenerative medicine" that has the ability of xeno-organs. A xeno-scaffold (metanephros) with human nephron progenitor cells in its nephrotic zone needed to be transplanted together with an immature ureter and cloaca; however, only nephrons can be generated from induced pluripotent stem cells within the transplant. Therefore, derivatives of the cloaca and ureter remained xenogeneic, and such a "hybrid kidney seed" was transplanted. After urine was produced, the expanded cloaca was connected to the native ureter, so that smaller peristaltic motion in the xeno-ureter and greater peristaltic motion in the native ureter were provided. This system was named the stepwise peristaltic ureter system and can be developed to lead urine from a regenerated kidney to the native bladder.

Renal pathology group

Research projects in the renal pathology study group focus on clinicopathological correlations in glomerular diseases, including immunoglobulin A nephropathy, and a morphometric approach to human nephrons/podocytes.

Renal physiology/metabolism group

We are investigating the association between vascular calcification and chronic kidney disease–mineral and bone disease, especially magnesium, in patients with chronic kidney disease. Our purpose is to prevent and regress vascular calcification.

In our single-center analysis, we reported on the association between donor fibroblasts and posttransplant anemia and are now studying denervation, the effect of tonsillectomy on immunoglobulin A nephropathy, and endoplasmic reticulum stress.

We conduct clinical research on a bicarbonate/lactate-buffered neutral peritoneal dialysis (PD) solution, the clinical efficiency of incremental PD, the management of PD-associated peritonitis, and peritoneal membrane pathology. Additionally, we have started using a newer ultrafine laparoscopy to evaluate peritoneal injury.

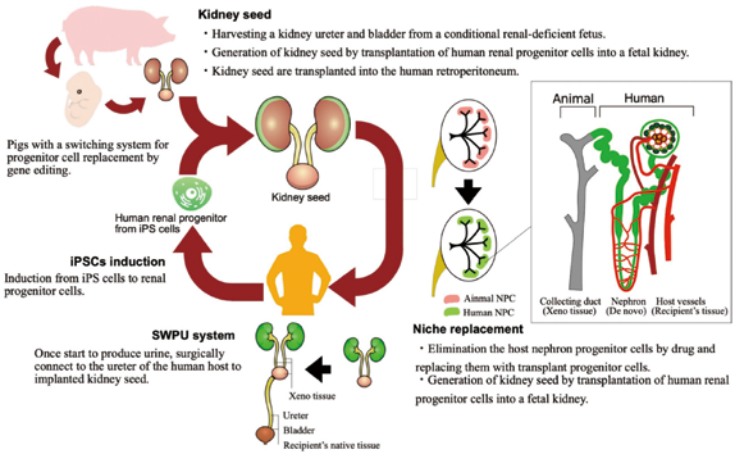
Hypertension group

We are investigating the pathophysiology of hypertension and the metabolism of uric acid.

The renin-angiotensin-aldosterone system is an important mechanism for understanding the pathophysiology of hypertension. In particular, most important is the relationship between salt and aldosterone; therefore, we are investigating with special strengths in their areas by basic and clinical research. We are also investigating the mechanism of the renal protective effect independent of blood pressure, the T-type calcium channel blockade, and the suppression of sympathetic nerve activity.

References

Xeno-regenerative medicine: A novel concept for donor kidney fabrication
Takashi Yokoo[1], Shuichiro Yamanaka[1], Eiji Kobayashi[2]
Xenotransplantation. 2020 Sep; 27(5): e12622.
doi: 10.1111/xen.12622. Epub 2020 Aug 6.
PMID: 32761829



Overview of the fetal organ complementation method

Rheumatology

URL : https://www.jikeir.website/ | E-mail : jikei.rheumatology@jikei.ac.jp

Neuro-immune crosstalk in rheumatic diseases

Fasciitis in dermatomyositis

The organs assumed to be most affected by dermatomyositis have been the muscle, skin, and lung. However, our previous study demonstrated that a primary target of dermatomyositis is fascia. Fasciitis usually accompanies dermatomyositis but not polymyositis. Therefore, we are conducting research with RNA sequencing analysis of gene expression in the fascia and muscles of patients with dermatomyositis compared with those of patients with polymyositis and are attempting to detect the localization of the highest gene expression.

Citrullination of peptidylarginine deiminase in rheumatoid arthritis

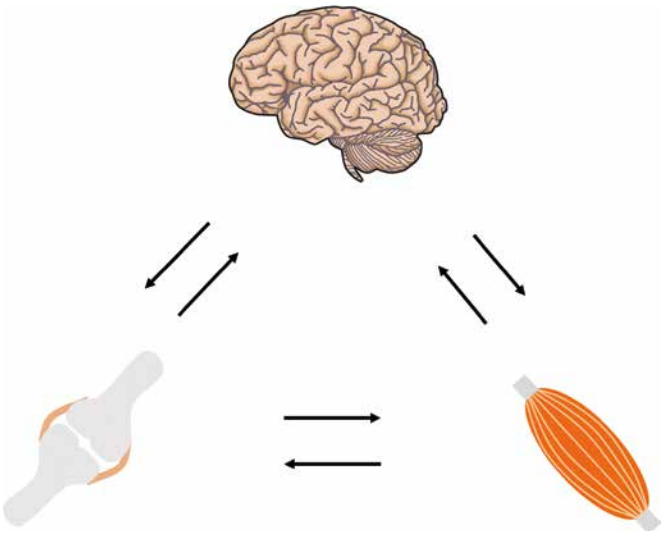
Citrullination, catalyzed by peptidylarginine deiminase (PAD), is a posttranslational modification of arginine to citrulline, which contributes to the pathogenesis of rheumatoid arthritis (RA). Recently, autocitrullination of PAD has also been reported. Although the enzyme activity of PAD is decreased after autocitrullination, the function of citrullinated PAD, other than enzyme activity, remains unclear. However, our study found that citrullinated PAD has monocyte-chemotactic activity in vitro and arthritis-inducible activity in vivo, whereas unmodified PAD does not. We are using a detection system for citrullinated PAD we recently developed to measure the citrullinated PAD concentration in the synovial fluid of patients with RA or osteoarthritis.

Pain in rheumatic diseases

Among patients with rheumatic diseases we have examined symptoms on the basis of various pain-reported outcomes. We have recently shown that neuropathic pain-like symptoms are observed in patients with RA by means of the painDETECT questionnaire and that these symptoms might be due to central sensitization in patients with chronic RA. We have also shown that fasciitis, rather than myositis, is associated with myalgia in patients with dermatomyositis and polymyositis. We examine the association between symptoms and nerve fiber innervation in the muscles and fascia of patients with inflammatory myopathy.

Prokineticin 2 in RA

Prokineticin 2 and its receptors are expressed in various tissues and are involved in diverse physiological functions, such as angiogenesis, neurogenesis, circadian rhythm, and the pain threshold. We previously reported that a prokineticin 2 antagonist suppresses the severity of arthritis in an animal model of RA. Therefore, we established a tissue-specific prokineticin receptor 2 knockout mouse to analyze whether the effect of the antagonist depends on prokineticin receptor 1 or prokineticin receptor 2.



Neuro-immune crosstalk in rheumatic diseases

Cardiology

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Clinical study of cardiology and basic research on cardiovascular disease and cardiac metabolism

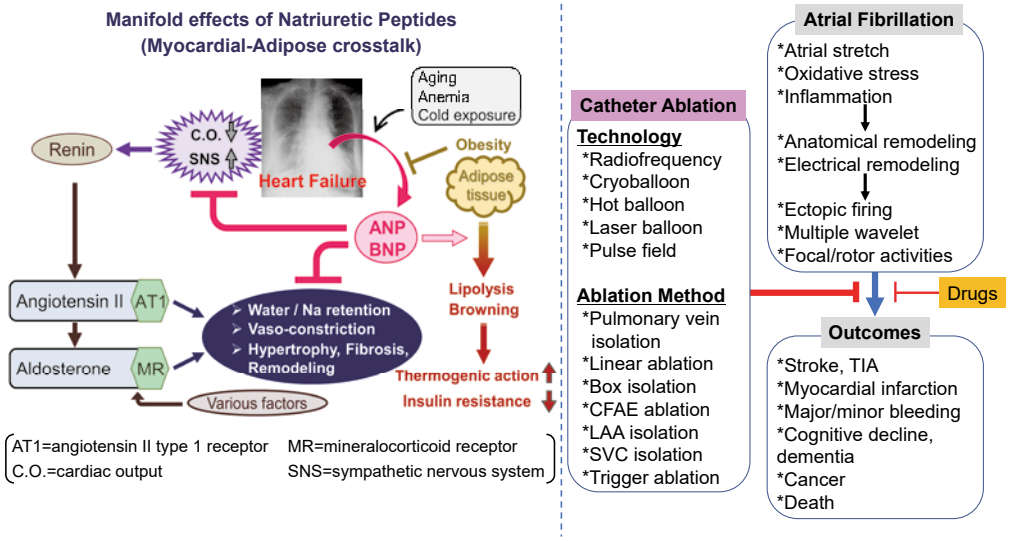
Clinical and basic research on the pathophysiology and treatment of heart failure
We are creating a large clinical database of heart failure caused by various underlying diseases. Considering the heart as a "hormonal organ," we are researching the natriuretic peptide and renin–angiotensin–aldosterone system in heart failure. We also analyze glucose and lipids as energy sources for the heart and conduct research on cardiac metabolism. In addition, we are investigating the relationship of multiple organs in heart failure, such as the kidney, adrenal gland, thyroid gland, and lung.

Clinical research on the pathophysiology and treatment of arrhythmia
We are conducting research on the pathophysiology and treatment of various arrhythmias. In particular, we are focusing on clinical research on catheter ablation for atrial fibrillation. We use the world's latest atrial fibrillation devices and report their effects. We are also working on the treatment of ventricular tachycardia and are reporting new therapeutic strategies and their results.

Clinical research for pathophysiology and treatment of ischemic heart disease
We are creating a clinical database of ischemic heart disease containing hemodynamic data, blood sample data, and treatment strategies to analyze the risk factors, pathophysiology, and therapeutic effects of ischemic heart disease. We are also studying the pathophysiology of coronary artery spasm, which is common in Japanese people. Drug-eluting stents are commonly used in percutaneous coronary intervention, and the long-term effects are analyzed with our database. The effects of coronary artery stenosis on ischemia have also been investigated with various imaging techniques and coronary blood flow assessment.

Imaging of cardiovascular diseases
We are analyzing images of various heart diseases. We are proceeding with the analysis of echocardiography, cardiac computed tomography, and magnetic resonance imaging.

Study of cardiac lesions in Fabry disease
We work with the Department of Pediatrics and other departments to analyze the effects on the heart of Fabry disease.



Outline of research on heart failure (left) and arrhythmia (right)

Diabetes, Metabolism and Endocrinology

URL : http://www.diabendo.jp/ | E-mail : diab-endocrinol@jikei.ac.jp

Various research studies were performed in both the basic and clinical fields of diabetes and endocrinology

General Summary

More than 15,000 patients come to our department each month. Most patients seen by our division have diabetes (including 10% with type 1 diabetes) or endocrinological disorders.

We attempt to provide the best healthcare to our patients on the basis of research evidence, clinical expertise, and patients' preferences. To accomplish this goal, we encourage the members of our division to perform basic and clinical research of high quality. With respect to education, we accept international students from other institutions. Finally, we strongly encourage our investigators to write and publish journal articles.

Epidemiology

1. Clinical trials of the treatment with continuous glucose monitoring of patients with diabetes
2. A nationwide epidemiologic study of mortality in approximately 3500 patients with type 1 diabetes was started in 1986 and has continued to provide important findings about Japanese children with type 1 diabetes.
3. A population-based study of childhood obesity, insulin resistance, diabetes in the elderly, and genetic factors has also continued in Niigata Prefecture.
4. An epidemiological study of data of more than 6000 patients with diabetes from all hospitals affiliated with The Jikei University.

Diabetic vascular complications

We have examined isoforms of Rho-associated coiled-coil-containing protein kinase (ROCK) to elucidate their essential roles in diabetic vascular complications. With regard to renal health, we have shown that ROCKs are required to maintain optimal function of the kidney and that the loss of ROCKs leads to renal protection in the setting of diabetes. Importantly, ROCK levels are elevated in patients with diabetes, suggesting that decreased levels would be therapeutically beneficial.

Molecular biology for pancreatic islets

Type 2 diabetes is known as a "bi-hormonal disorder" due to the dysregulated secretion of insulin and glucagon. Reduced β cell mass is a major cause of dysregulated insulin secretion. Although a combination of high glucose and elevated free fatty acids (glucolipotoxicity) strongly induces β cell dysfunction and cell death, the underlying cause remains unclear. In addition, the precise molecular mechanism of glucagon in α cells remains unclear. We found that serine/threonine kinase protein kinase c (Pkc) δ is involved in β cell death and glucagon secretion from α cells.

Endocrinology

Basic research

1. Effect of aldosterone in macula lutea degeneration
2. Proteogenomic landscape and clinical characterization of growth hormone–producing pituitary adenoma

Clinical research

1. Involvement of growth hormone in patients with diabetes
2. Re-evaluation with chemiluminescent enzyme immunoassay of patients who have primary aldosteronism diagnosed with aldosterone measurement via radioimmunoassay
3. Analysis of the pituitary function progress evaluated with pituitary stimulation test in patients treated for pituitary diseases

Our Members

Clinical Oncology and Hematology

URL : http://jikeishunai.jp/ E-mail : edu.oncolhematol@jikei.ac.jp

Division of Clinical Oncology and Hematology of the Department of Internal Medicine

The immediate goals of our clinical and basic research are to investigate basic and clinical aspects of malignant diseases and to improve outcomes for patients with hematologic malignancies and solid cancers, leading to the ultimate goals of improving the natural history of malignant diseases. Our division consists of 3 clinical parts and has worked in cooperation with other departments.

Research Activities

1. Hematologic malignancies

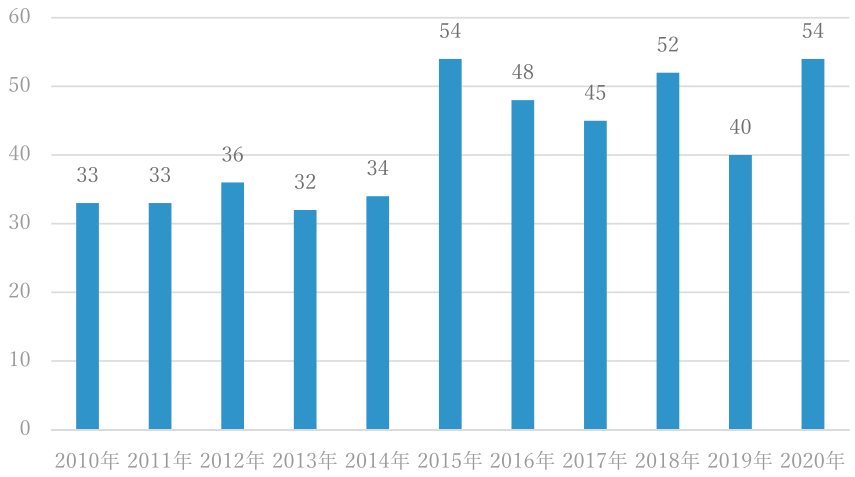
   Many patients with previously untreated hematologic disorders have been referred to our department. We have participated in clinical trials as a member of the Japan Adult Leukemia Study Group and the Lymphoma Study Group of the Japan Clinical Oncology Group. We have analyzed the genes of leukemia cells to understand the biological mechanisms of leukemia. A number of molecularly directed treatment options have recently emerged and have made comprehensive diagnostics an important pillar of clinical decision-making.

2. Cancer center

   Cancer medical care is remarkably progressing and, at the same time, is diversifying and becoming more complicated. Therefore, future cancer medical treatment will be required to respond with comprehensive strength across clinical departments and occupations. Through these practices our oncology center aims to provide cancer medical care with high patient satisfaction. In addition to providing the latest medical care, such as precision medicine, we are also involved in supportive care considering quality of life, fertility preservation, and social support for patients and their families. We will also focus on developing human resources consisting of multiple occupations specializing in cancer medical care, which is still lacking in Japan.

3. Palliative medicine

   For patients who have cancer, the Department of Palliative Care is committed to relieving their physical and spiritual pain, including mental anguish and questions about the meaning of life. The palliative care team is composed of a multidisciplinary group of palliative care physicians, psychiatrists, nurses, and spiritual care workers who intervene at the appropriate time after cancer has been diagnosed to provide seamless palliative care at various stages. In addition, we support patients to make the best choice according to their situation through advanced care planning, as they need to make many decisions, such as a treatment plan and the location of treatment in various situations. In cooperation with oncologists, we do our best to help patients live with peace of mind by relieving their various pains.



Actual achievement of hematopoietic cell transplants

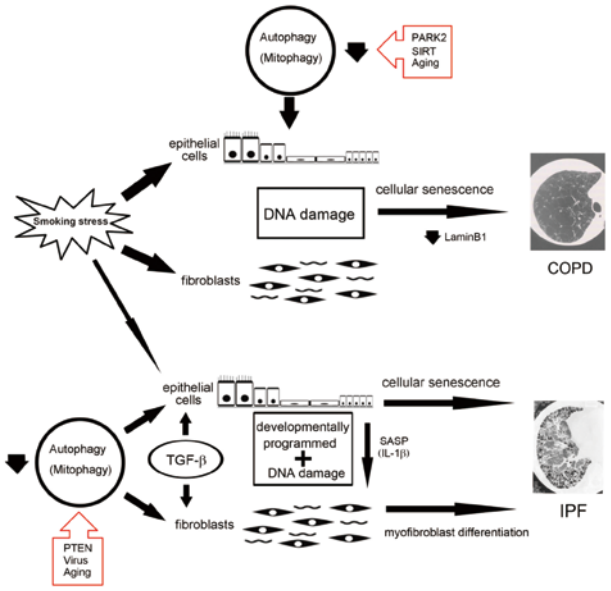
Respiratory Diseases

URL : http://jikei-pulmonology.jp/ E-mail : shunske@jikei.ac.jp

Clinical and basic research to investigate the pathogenesis of lung diseases and to develop novel treatment

We investigate the association between aging and the pathogenesis of lung diseases, especially concerning the loss of homeostasis associated with cell death, cellular senescence, and autophagy.

1. Chronic obstructive pulmonary disease
   a. Cellular senescence and damaged mitochondria (Fujii S et al., Oncoimmunology 2012; Hara H et al., Am J Physiol Lung Cell Mol Physiol 2013)
   b. Autophagy activation by sirtuin 6 (Takasaka N et al., J Immunol 2014)
   c. Regulatory role of PARK2 (Ito S et al., Autophagy 2015; Araya J et al., Autophagy 2019)
   d. Involvement of lamin B1 in mechanistic target of rapamycin kinase signaling (Saito N et al., J Immunol 2019)
   e. Ferroptosis by phospholipid peroxidation (Yoshida M et al., Nat Commun 2019)
   f. Insufficient chaperone–mediated autophagy (Hosaka Y et al., I Immunol 2020)
   g. Deficient lysophagy in epithelial cells (Araya J et al., J Immunol 2021)
2. Idiopathic pulmonary fibrosis
   a. Insufficient autophagy associated with epithelial senescence and myofibroblast differentiation (Minagawa S et al., Am J Physiol Lung Cell Mol Physiol 2011; Araya J et al., Am J Physiol Lung Cell Mol Physiol 2013; Kobayashi K et al., J Immunol 2016)
   b. Metformin–mediated inhibition of fibrogenesis (Sato N et al., Respir Res 2016)
   c. Azithromycin–mediated inhibition of fibrogenesis (Tsubouchi K et al., Autophagy 2017)
   d. Pirfenidone–mediated mitophagy induction (Kurita Y et al., Respir Res 2017)
   e. Receptor–interacting protein 3 kinase–regulated necroptosis (Yoshida M et al., Am J Respir Cell Mol Biol. 2018).
   f. Glutathione peroxidase 4 expression and myofibroblast accumulation (Tsubouchi K, et al. J Immunol 2019).
3. Extracellular vesicles
   a. Airway fibrogenesis induced by senescent epithelial extracellular vesicles (Fujita Y et al. J Extracellular Vesicles 2015)
   b. Epithelial senescence caused by fibroblast extracellular vesicles (Kadota T et al., Am J Respir Cell Mol Biol 2020)
   c. Inhibition of fibrogenesis by normal human bronchial epithelial cell extracellular vesicles (Kadota T et al., J Extracell Vesicles 2021, in press)
4. Bronchial asthma
   a. Perioperative and postoperative pulmonary complications (Numata T et al., BMC Pulm Med 2018)
   b. Treatment of severe asthma by biologics (Numata T et al., BMC Pulm Med 2019; Numata T et al., BMC Pulm Med 2020)
5. Lung cancer
   a. Detection of epidermal growth factor receptor –tyrosine kinase inhibitor mutations using cell-free DNA analysis (Seki Y et al., The Oncologist 2015)
   b. Usefulness of cell-free DNA in patients with epidermal growth factor receptor – tyrosine kinase inhibitor resistance or extrathoracic disease progression (Seki Y et al., ESMO Open 2018)
   c. Plasma soluble programmed cell death ligand 1 levels as a novel biomarker for the efficacy prediction for nivolumab (Wakui H et al., Clin Lung Cancer 2018)
   d. Chaperone–mediated autophagy as a new target against non–small–cell lung cancer (Ichikawa A et al., Cancer Sci 2020)



Cellular senescence and autophagy in pathogenesis of chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis

General Medicine

URL : http://www.jikei.ac.jp/academic/course/46_soushin.html | E-mail : general-med@jikei.ac.jp

The support of continuing professional development with research topics of primary care, clinical ethics, and medical education

We are conducting research activities on the topics of primary care, clinical ethics, and medical education. Each staff member performs research activities in accordance with research questions that arose during clinical practice and undergraduate and postgraduate educational activities in medical school. We hope that the research activities will lead to better continuing professional development for each staff member and contribute to society through primary care. The research topics we are working on are as follows.

- Gas biomarkers exhaled from the lungs of patients with inflammatory diseases and collagen diseases
- Qualitative research on a continuing professional development program for primary care physicians
- Research concerning a Japanese version of the Physician Orders for Life-Sustaining Treatment in a Japanese hospital setting and advance care planning
- Classification of fibromyalgia into several clinical categories and investigation of suitable treatment for each category
- Examination of changes in presepsin, a biomarker for sepsis, in various diseases

A lecture on primary care called *Asunaro-Juku* (Dr. Nobuyuki Furutani)

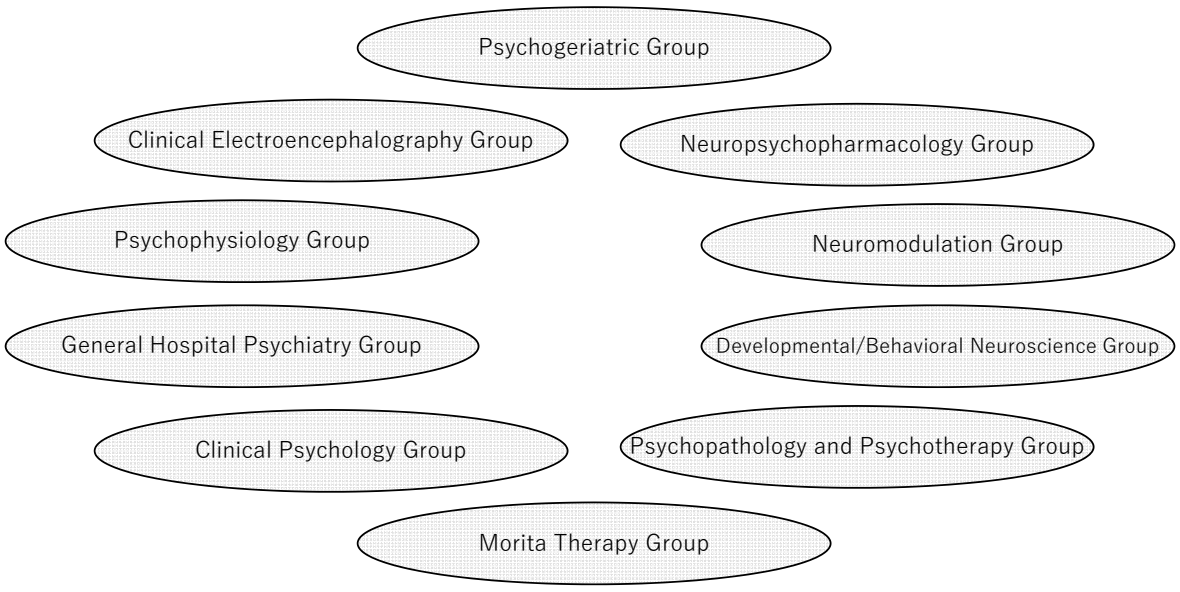
Psychiatry

URL : https://jikei-psy.com/ | E-mail :

Biological and psychosocial approaches based on experience treating patients with various psychiatric disorders

Our department is conducting research using biological and psychosocial approaches based on our previous experience treating patients with various psychiatric disorders. Specifically, we have methodological research groups, such as the psychopathology, pharmacology, psychophysiology, Morita therapy, clinical psychology, and neuromodulation groups, and subject-specific research groups, such as epileptology, child and adolescent psychiatry, geriatric psychiatry, and general hospital psychiatry groups.

- Study of the DNA methylation level as a biomarker for neurodegenerative diseases; now focusing on the effects of DNA methylation on the appearance of neuropsychiatric symptoms
- Research on tau imaging of neurodegenerative diseases and psychiatric symptoms
- Empirical research regarding the efficacy of individual and group cognitive behavioral therapy for primary and comorbid insomnia
- Effect of motivational short-time videos on hypnotics reduction intention
- Research on reading electroencephalographic findings with artificial intelligence
- Study of the clinical significance of comorbidity of psychiatric disorders in gambling addiction
- Research on the pathophysiology, diagnostic markers, and therapeutic interventions for treatment-resistant mental disorders based on "recovery (resilience)" research on psychiatric disorders
- Study of the effect of outpatient Morita therapy in collaboration with other facilities
- Study of confirmatory trial of advanced medicine aiming at the development of a new stimulus condition and expanded adaptation to depressive episodes of bipolar disorder
- Study of elucidation of the antidepressant mechanism of repetitive transcranial magnetic stimulation and identifying biomarkers for therapeutic effects using neuroimaging techniques
- Neurophysiological response of patients with attention deficit hyperactivity disorder measured with near-infrared spectroscopy
- Examination of the characteristics of developmental disorders, higher brain dysfunctions, and cognitive impairment through psychological assessments



Our research groups are multifaceted and multimethodological.

Pediatrics

URL : http://www.jikei-pediatrics.jp/ | E-mail : syounikaikyoku@jikei.ac.jp

Multidisciplinary research of pediatric disease to pursuit child happiness.

Metabolic Disorder Group: We are conducting research and developing gene therapy for mucopolysaccharidosis type II with a view towards practical clinical application. We have used lentiviral vector–mediated ex–vivo gene therapy for mucopolysaccharidosis type II mouse model and reported its effects on important organs, including the central nervous system, and bone involvement.

Endocrinology Group: In a functional study of congenital hypothyroidism due to truncating paired box family protein (PAX) 8 mutations, we clarified that the C–terminal portion of PAX8 is essential for the interaction of PAX8 and NK2 homeobox 1. In addition, as a result of a survey of 26 cases of fetal goitrous hypothyroidism, we recommended treatment with intrauterine injection of levothyroxine.

Hemato–Oncology Group: We conducted a phase I/II clinical trial of a dendritic cell therapy for refractory childhood brain tumors, and further study is planned. We are conducting a long–term follow–up study, including genetic counseling regarding pediatric hereditary tumors.

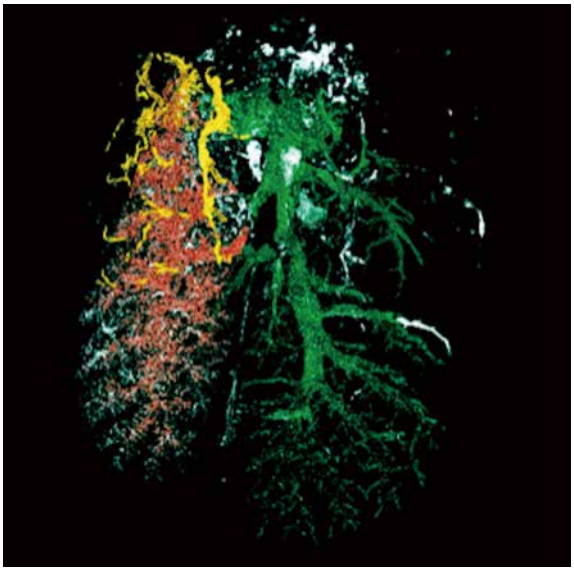
Neurology Group: Our research aims to elucidate the developmental mechanisms of epileptic encephalopathy through the use of rodent models and 9.4–T animal magnetic resonance imaging scanner, specifically focusing on correlations between developmental changes of regional brain activities and clinical characteristics of Dravet syndrome.

Nephrology Group: The research activities of our division cover a wide range of topics in renal physiology and nephrology from the laboratory bench to patient–oriented investigation. Current research topics include the estimated number of nephrons in the whole kidney and the association between chronic kidney disease and low birth weight infants.

Allergy Group: We reported results from a randomized controlled trial (RCT) that the prevalence of Cow's milk allergy was reduced to 10% by avoiding cow's milk formula for the first 3 days of life. The RCT was extended to observe asthma or recurrent wheezing. The findings of this study suggest that asthma and recurrent wheezing can be prevented by avoiding cow's milk formula supplementation at birth.

Neonatal Group: We promote and research high–quality neonatal medicine with the objectives of treating all high–risk newborns, such as premature infants born at the 22nd week of pregnancy, and acute advanced life-saving treatment of newborn with a disease. The main topics of our research are improving the prognosis of preterm infants, hypothermia for hypoxic ischemic encephalopathy (HIE), and suckling exercise.

Cardiology Group: Our topics is to clarify the mechanisms of heart failure and secondary pulmonary hypertension in patients with congenital heart disease. Our topics are pulmonary artery banding, hypoplastic pulmonary artery, and aortopulmonary collateral, which have often been analyzed and reported at meetings and in journals.



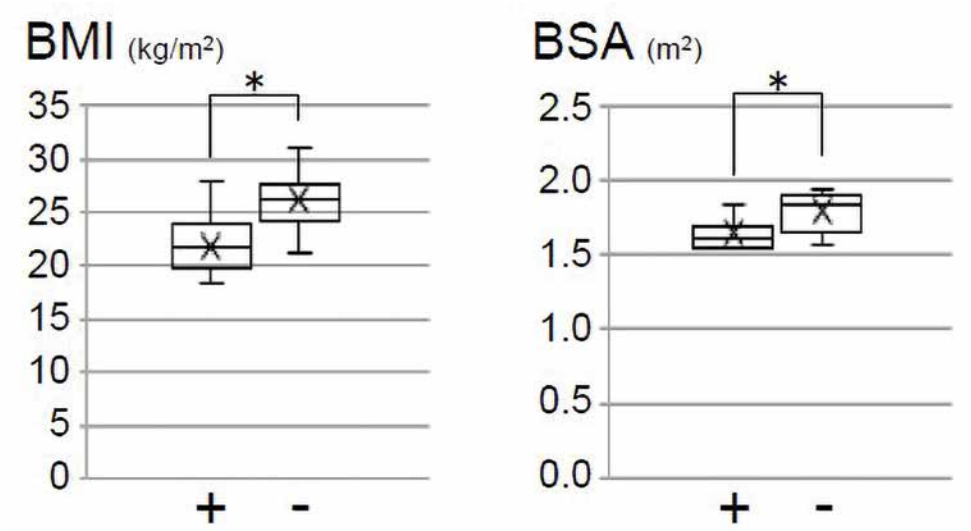
Computer tomographic images of aortopulmonary collateral arteries

Dermatology

URL : https://www.hosp.jikei.ac.jp/diagnosis/department/218.html | E-mail : nobederm@jikei.ac.jp

Clinical and basic research activities in our department

The members of our department endeavor to pursue clinical and basic research for various diseases. We have a large amount of clinical data available on psoriasis and atopic dermatitis from daily clinical practice. We systematically analyzed the data and then widely deliver these achievements to academia and society. For example, we disclosed that apalutamide, a drug administered for treating prostate cancer, induces cutaneous adverse events in a body size–dependent manner. Also, basic data on many subjects, including melanoma, itch mechanisms, and food allergy, have been consistently studied with in-vivo and in-vitro systems.
We believe our research will be beneficial for the well-being of patients who have problems of the skin.



Drug eruption due to apalutamide is dependent on body size
+, presence of eruption; -, absence of eruption; BMI, body mass index; BSA, body surface area

Radiology

URL : https://jikei-rad.jp/ | E-mail : radjikei@jikei.ac.jp

Multidisciplinary approach to all aspect of both diagnostic imaging and radiation oncology

Our department consists of 2 sections: Diagnostic Imaging and Radiation Oncology.

The Diagnostic Imaging section has interests in research related to all aspects of diagnostic imaging and interventional radiology. The section focuses on developing new imaging techniques and assessing imaging findings to assist in determining diagnoses and predicting prognoses, i.e., the predicted responses to treatment.
Texture analysis and radiomics research have also recently been conducted on the basis of data obtained from computed tomography or magnetic resonance imaging or both. Radiomics is an attempt to integrate and analyze the multisystem information of radiological images as data and to link it to pathological diagnosis, molecular and genetic information, and predicting outcomes. Texture analysis is a part of radiomics which attempts to determine the grade of tumors and the prognosis of treatment on the basis of the heterogeneity of pixels in images.
Our section is conducting scientific research with financial assistance from the Grants-in-Aid for Scientific Research. In one project, researchers have developed an animal model of cytokine release syndrome for an experiment using rabbits and are investigating whether chest tube drainage is effective for this model. Other major studies include the followings: a multicenter collaborative study of the construction of an artificial intelligence–based diagnostic imaging support system, a multicenter collaborative study of radiological evaluation of malignant and benign tumors of the head and neck, and a study of optimal dosage and prognostic factors in radioiodine therapy for thyroid cancer.

The Radiation Oncology section aims to improve treatment efficacy and reduce adverse events.
Our section is conducting research on multimodality treatment and prophylactic area irradiation to improve antitumor efficacy, optimal treatment methods to reduce adverse events with intensity modulated radiation therapy (IMRT), and the efficacy of radiotherapy for patients with oligometastases. We have also enrolled in a multicenter study to determine the optimal dose of stereotactic irradiation for lung cancer. Specifically, we are investigating the therapeutic effects of multidisciplinary treatment with brachytherapy and irradiation, including regional lymph nodes for prostate cancer, dose reduction to normal tissues using the 2-step IMRT method for head and neck cancer, the dose setting for radiotherapy of oligometastases, and the use of stereotactic irradiation for this purpose.

Lymphangiography in experimental rabbits (cytokine release model)

Gastrointestinal Surgery

URL : https://jikeisurgery.jp
E-mail : etoken@jikei.ac.jp

Basic research that is returned to the clinical field

General Summary

Our research policy is to conduct basic research, the results of which can be clinically applied.

One surgeon can save only a limited number of patients; however, research can explore different disease mechanisms and discover new treatments that can help patients worldwide. We think it is important to clarify and to verify questions in daily medical care through research and to disseminate the results globally. We aim to train well-balanced academic surgeons who have both a basic perspective and high surgical skills. To that end, we are collaborating with well-known research facilities in Japan and overseas to perform basic research in a variety of fields. We are also conducting many clinical and multicenter joint studies.

Research Activities

Upper gastrointestinal surgery

Our research topics include esophageal cancer, esophageal benign disease, gastric cancer, and morbid obesity. We investigate the efficacy of an intraoperative thermal imaging system and nerve integrity monitoring to prevent complications of esophagectomy performed for esophageal cancer. To treat benign esophageal diseases, we have recently proposed laparoscopic circumferential Heller myotomy as a novel technique to relieve achalasia-associated chest pain (Fig. 1a). For gastric cancer, we assess the usefulness of sentinel lymph node navigation to preserve postoperative quality of life. Regarding bariatric surgery, the first endoscopic operation in Japan to reduce gastric volume was performed at our institution in 2020.

Lower gastrointestinal surgery

We investigate anal function by means of stationary 3-dimensional manometry and aim for the specific treatment of anal disease and the limitation of postoperative complications (Fig. 1b).

In collaboration with the Department of Biochemistry, we analyzed the expression of intracellular signal molecules that are associated with the progression and growth of cancer. We investigated the involvement of dual-specificity tyrosine-(Y)-phosphorylation–regulated kinase 2 (DYRK2) in the induction of apoptosis and the control of the cell cycle. Furthermore, we prepared 3-dimensional cultures with colorectal cancer specimens to form organoids to develop methods to choose the appropriate chemotherapy before treatment.

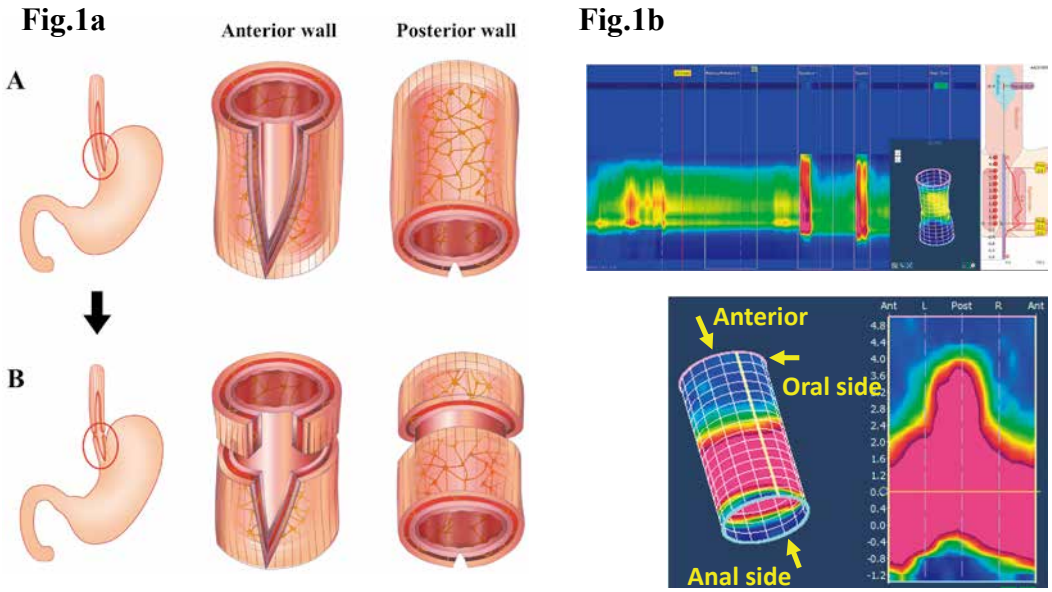


Fig. 1a: Circumference Heller myotomy
Fig. 1b: Stationary 3-dimensional manometry

Hepatobiliary and Pancreatic Surgery

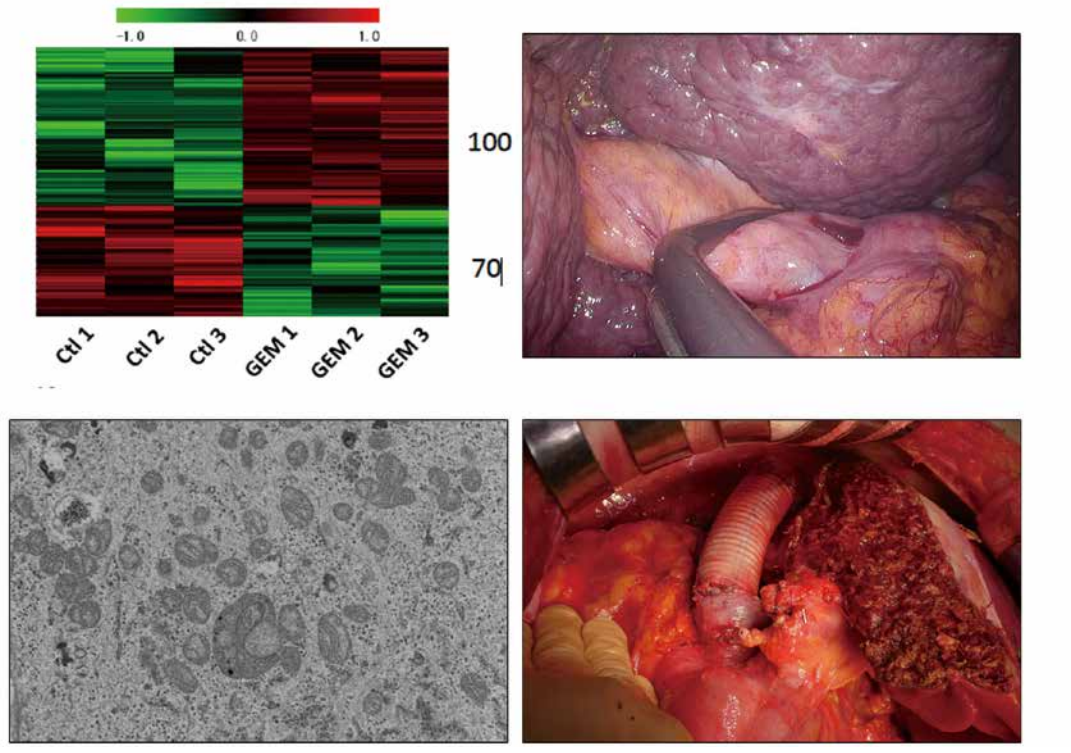
URL : https://jikeisurgery.jp/archives/news_group/group_4 E-mail : toruikegamijikei@jikei.ac.jp

Multidisciplinary approach to overcome hepatobiliary and pancreatic malignancies

We perform more than 80 hepatectomies and 50 pancreatectomies for patients with hepatobiliary and pancreatic malignancies every year. Notably, of all hepatectomies we perform, more than 60% are laparoscopic. Unfortunately, hepatobiliary and pancreatic malignancies have had poor survival rates, even after curative resection, owing to the high rate of tumor recurrence. Our Division of Hepatobiliary and Pancreatic Surgery aims to provide cutting-edge treatment and to improve outcomes for patients with these tumors, and, to this end, we are performing clinical and basic research. We conduct a wide range of research as follows.

- Development of novel techniques for minimally invasive hepatobiliary and pancreatic surgery, including laparoscopic and robotic surgery
- Elucidation of tumor microenvironment in hepatobiliary and pancreatic malignancies and development of novel therapeutic strategies
- Molecular mechanisms associated with tumor evolution and development of hepatocellular carcinoma
- Overcoming therapeutic resistance by focusing on energy dynamics in pancreatic cancer
- Novel strategies to perform safe massive hepatectomy for advanced liver malignancies with or without major vessel reconstruction
- Liver transplantation and strategies of immunosuppression

Our recent publications include our unique approach and techniques in laparoscopic hepatectomy, such as laparoscopic vascular clamp (Surg Endosc 2021), Arantius' approach (Ann Surg Oncol 2021), tumor thrombectomy (Ann Surg Oncol 2021), double cone-unit resection (Surg Today 2021), intercostal port for repeated hepatectomy (Surg Oncol 2021), left ventral hepatectomy (Surg Oncol 2021), and left trisectionectomy (Surg Oncol 2021). We have also proposed our novel strategy for safe massive hepatectomy including dual hepatic vascular embolization (Ann Surg Oncol 2021). Our basic researchers have investigated the role of acid ceramidase (Cancer Sci 2021) and acid alpha-glucosidase (Cancer Sci 2021) in pancreatic cancer metabolism.



Basic and clinical research for hepatobiliary pancreatic malignancies

Thoracic Surgery and Breast and Endocrinology Surgery

URL : https://jikeisurgery.jp/ | E-mail : ohtsuka@jikei.ac.jp

In our divisions, we draw on a legacy of effectiveness and innovation in the treatment of surgical diseases of the chest

General Summary

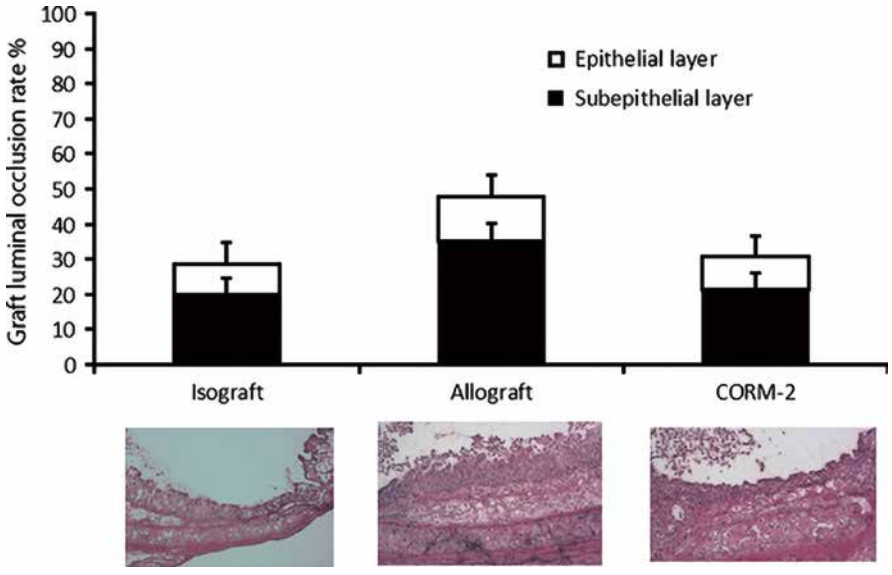
The Divisions of Thoracic Surgery and Breast and Endocrinology Surgery were established in June 2005. Since then, we have provided comprehensive diagnostic and therapeutic services for patients with surgical diseases of the chest, breast, and endocrine systems. We are leaders in our field of surgery, with a focus on minimally invasive surgery.

Research Activities

To improve the lives of patients, thoracic surgeons and breast and endocrinology surgeons of The Jikei University connect biomedical breakthroughs to practical applications. Clinical research is an important part of our program and can provide novel treatment therapies to patients before they are widely available. Our research efforts include: 1) pulmonary function after lung resection, 2) surgery for lung cancer with oligometastatic disease, and 3) the effect of pleural abrasion and covering with polyglycolic acid sheets for pneumothorax. We are also involved in multiple basic research studies to understand, diagnose, and develop new treatments for pulmonary disorders and lung cancer.

Lung transplantation has become a well-established therapy for patients with severe or terminal pulmonary diseases that cannot be cured completely by medical treatments. Bronchiolitis obliterans and a related syndrome are recognized as serious complications of lung transplantation. We have hypothesized that carbon monoxide can improve cases of bronchiolitis obliterans through the inhibition of T-cell infiltration and the downregulation of inflammatory cytokine expressions in the transplanted grafts. To assess this hypothesis, we will examine the effect of carbon monoxide with an artificial gas carrier in a mouse model of orthotopic tracheal transplantation.

We are also starting our basic research in oncology. Tumors are known to exhibit multiple somatic mutations. Neoantigens derived from such tumor-specific mutations are potential targets for antitumor immune responses. The role of neoantigens in naturally occurring and therapeutically induced immune responses to cancer. We are planning to investigate mutation burden, neoantigen load, and the depletion of expected antigenic mutations in lung cancer surgically removed by our division. Our aim is to find new neoantigens derived from tumor-specific mutations which can be targets for antitumor immune responses.



Effect of carbon monoxide-releasing molecule 2 on graft luminal narrowing 1 week after surgery in a model of orthotopic trachea transplant (n = 6 each). Representative Elastin van Gieson staining of airway grafts is shown.

Pediatric Surgery and Vascular Surgery

URL : https://jikeisurgery.jp/ E-mail :

Research activities of pediatric surgery and vascular surgery: clinical studies and basic research

Pediatric Surgery

We have focused on the following clinical studies and basic research.

1. Clinical study

   The Nuss procedure is currently the most common operation for pectus excavatum. We have already performed more than 500 Nuss operations. We have modified the Nuss procedure with a new technique—the mediastinal detachment method using endoscopic surgical instruments with a lifting hook—for better cosmetic results and safer operations.

2. Basic research

   Button battery ingestion causes esophageal ulcers, strictures, and, sometimes, fatal damage, such as a tracheoesophageal fistula. We have been developing a new modified battery with an edge covered by a new material.

Vascular Surgery

Research projects of our department have focused on clinical trials and the development of new endovascular treatment of aortic disease and peripheral arterial disease.

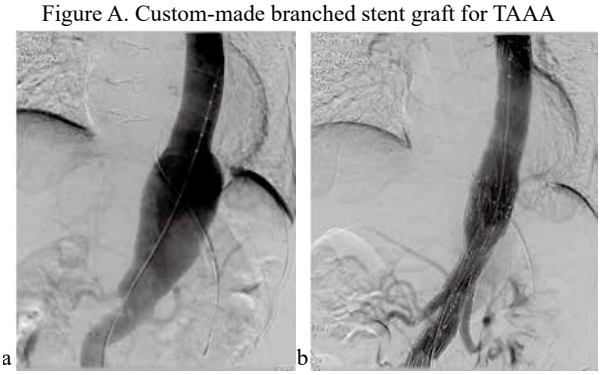
1. Development of endovascular repair of thoracoabdominal aortic aneurysms

   We have used a custom-made fenestrated or branched stent graft for the treatment of thoracoabdominal aortic aneurysms that were considered inoperable because of comorbid conditions. (Figure A, a-b)

2. Development of endovascular repair of aortic arch aneurysms

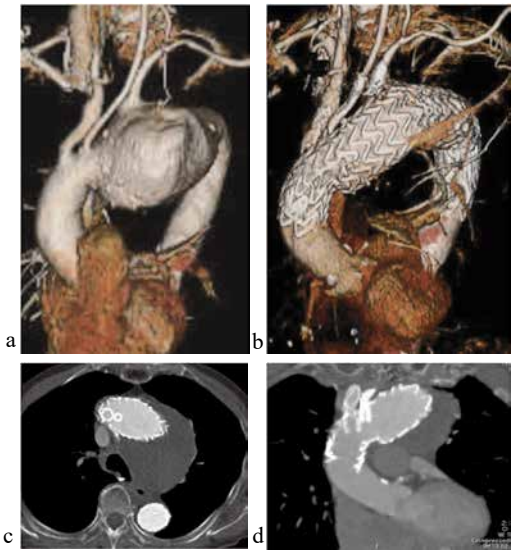
   We have developed a new minimally invasive operation method for aortic arch aneurysms called the "retrograde in-situ branched stent grafting." A needle is used to prick the stent graft through 1 side of a carotid artery, after which a covered stent is inserted as a branch and deployed into the stent graft (in an in-situ retrograde fashion). (Figure B, a-d)

Figure A. Custom-made branched stent graft for TAAA



TAAA; thoracoabdominal aortic aneurysm

Figure B. Retrograde in-situ branched stent graft (RIBS)



Custom-made branched stent graft and retrograde in-situ branched stent graft

Orthopaedic Surgery

URL : http://jikeiseikei.com/about/ | E-mail : seikeigeka@jikei.ac.jp

Translational research in orthopaedics: From basic research to clinical application

The Department of Orthopaedic Surgery at The Jikei University participates in both basic and clinical research. We perform research based on questions raised from our daily clinical practice. We believe that evaluating the clinical uncertainties and publishing our findings to the world will change the way we treat patients.

One example of our research is the concept that the strength of bone is determined by both its mineral density and quality. A series of collagen research studies from The Jikei University have led to publications in international journals. These articles have resulted in worldwide recognition, and a review in *Osteoporosis International* has received awards for being a top 5 most-cited publication in the world for 2 years running. This original concept of The Jikei University has led to changes in the clinical guidelines for osteoporosis treatment.

Other research includes:

Knee
- Computer assisted system in total knee arthroplasty
- Three-dimensional (3D) magnetic resonance imaging (MRI) evaluation of cartilage and the meniscus
- Anterior cruciate ligament reconstruction technique using a rectangular retrodilator for anatomical bone reconstruction

Shoulder
- MRI and elastography analysis in rotator cuff tears

Hand and Elbow
- MRI diagnosis in soft-tissue tumors of the upper limb
- Use of external fixators in distal radius fractures
- Epidemiological analysis of supracondylar humeral fractures in children

Spine
- Mixed reality (virtual and augmented reality) technology in spinal surgery
- Minimally invasive surgery

Hip
- Use of cross laser projection system for MiniHip prosthesis positioning in the anterolateral supine approach for total hip arthroplasty
- Long-term (> 20 years) follow-up of cementless total hip arthroplasty

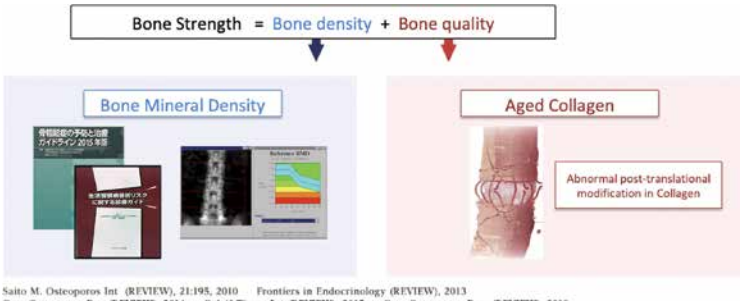
Foot and Ankle
- Pathogenesis of hallux valgus with 3D computed tomography evaluation of metatarsal torsion
- Windlass mechanism analysis with 3D computed tomography evaluation of hallux rigidus

Trauma
- Treatment of unstable fractures with an injectable complex of β tricalcium phosphate, hyaluronic acid, and fibroblast growth factor 2 to promote bone union

Bone metabolism
- Quantitative analysis of advanced glycation end-products in bone and their effects on osteoblasts

Rheumatoid Arthritis
- Evaluation of low molecular weight compounds inhibiting noncanonical Wnt signaling to suppress joint destruction

The Department of Orthopaedic Surgery at The Jikei University also collaborates with other departments and institutions, both domestic and overseas, to increase our understanding of Orthopaedic-related diseases.



Saito M. Osteoporos Int (REVIEW), 21:195, 2010 Frontiers in Endocrinology (REVIEW), 2013
Curr Osteoporos Rep (REVIEW), 2014 Calcif Tissue Int (REVIEW), 2015 Curr Osteoporos Rep, (REVIEW), 2018

The strength of bone is determined by both its mineral density and quality.

Neurosurgery

URL : http://www.neurosurgery.jp/index.html | E-mail : nougeka@jikei.ac.jp

Less-invasive "neurosurgery"

General Summary

The research studies in our department, examining such topics as syringomyelia, endovascular surgery, mechanism of head injury, and pediatric neurosurgery, made good progress in the past year. Research in these areas is performed to international standards. Clinical research has also studied brain tumors, hypothalamic disorders, and spine and spinal cord diseases.

Research Activities

Cerebrovascular diseases Endovascular surgery

1. Analysis of the natural history of unruptured intracranial aneurysms
2. Analysis of biofluid mechanics on human intracranial aneurysms using computational fluid dynamics
3. Newly developed techniques of neuroradiological imaging: intravenous 3-dimensional digital subtraction angiography, Neuro PBV, and metal artifact removal
4. Development of a novel intracranial stent device for the treatment of brain aneurysms
5. Development of a new therapy for ischemic stroke using a small animal model of cerebral infarction
6. Establishment of a telemedicine network utilizing a novel software program for smartphones.

Brain tumor

1. Immunotherapy against malignant glioma

   We have started a clinical trial of immunotherapy with fusions of glioma cells, glioma-initiating cells, and dendritic cells. Although several cell types can induce an antitumor immune response, this function is performed most efficiently by professional antigen-presenting cells, of which dendritic cells are the most potent. We are performing a clinical trial of Poly(I:C)/interleukin 10–short interfering RNA transfected fusion cells as a tumor vaccine.

Spine and Syringomyelia

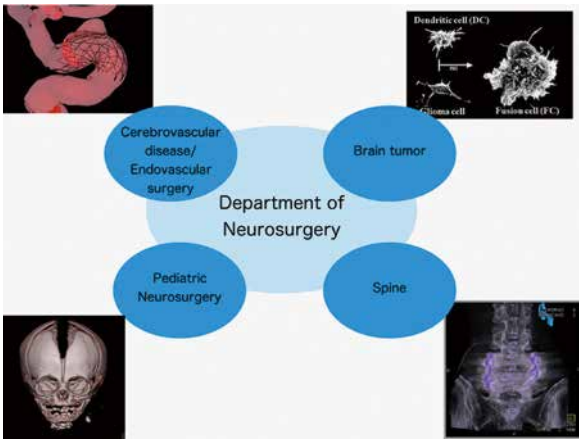
Each year our department performs surgery for approximately 30 patients with syringomyelia. To date, we have treated more than 750 patients with syringomyelia.

We also developed an implant for cervical laminoplasty. This implant can be used for various surgical methods, and its initial fixation power has increased. Furthermore, we have performed spinal surgery in a hybrid operating room as a global pioneer, making the procedure safer and more reliable for patients. We have presented these research results at the Neurospinal Society of Japan, the Japan Neurosurgical Society, and the Global Spine Congress.

Division of Pediatric Neurosurgery

In the Division of Pediatric Neurosurgery, we offer gentle and minimally invasive operations to many patients with spina bifida, hydrocephalus, cranial facial anomaly, and brain tumors. We are also developing operative procedures and instruments for hydrocephalus, intracranial cysts, and brain tumors by neuroendoscopic maneuvering and are proposing the usage of navigation systems.

We have proposed an age-related operative method for craniofacial surgery and have won awards in Japan and international societies of pediatric neurosurgery.



Overview of the Department of Neurosurgery
The picture on the upper right is from *Advanced Medical Series 45:The Latest in Neurosurgery.*

Plastic and Reconstructive Surgery

URL : https://www.plasticsurg.jp
E-mail : prs-resident@jikei.ac.jp

Efforts of the latest research in our department

General Summary

Research in the Department of Plastic and Reconstructive Surgery is focused on 6 basic topics: 1) the causes and treatment of craniofacial anomalies; 2) the causes and treatment of hand and foot anomalies; 3) the mechanism of wound healing and the grafting of skin and bone; 4) microsurgical transplantation; 5) imaging, planning, and computer assisted surgery in plastic surgery; and 6) treatment and rehabilitation of facial palsy. The faculty of our department consists of surgeons representing virtually all areas of plastic surgery and clinicians from related disciplines. This diversity provides the stimulating atmosphere necessary for productive research. The participation of plastic surgery residents and postresidency fellows in research studies provides them with important experience and expands their understanding of anatomical and physiological factors involved in these special areas of surgery.

Our current interests include:

- A computed tomography–based evaluation method of caudal septal deviation
- Effects of septorhinoplasty on nasal obstruction and quality of life
- Minimally invasive techniques in open rhinoplasty using grid projection topography
- Motion analysis to bring objectivity and reproducibility treatment strategies for congenital anomalies
- Analysis of Ilizarov mini-fixator in hand surgery
- Pathological analysis of axillary hyperhidrosis and axillary osmidrosis induced by microwave treatment
- Noninvasive vascular imaging in perforator flap surgery using grid projection topography
- Swallowing and functional outcome after head and neck reconstruction in patients with sarcopenia
- Evaluation of accuracy and functional outcomes of mandibular reconstruction using computer-assisted surgical simulation
- The efficacy and safety of early postoperative botulinum toxin injection for facial nerve reconstruction

The photograph shows Professor Miyawaki with a craniofacial team during cleft palate surgery at The Jikei University Hospital.

Cardiovascular Surgery

URL : https://shinzougeka.com/ | E-mail : kunihara@jikei.ac.jp

Basic and clinical research of the Department of Cardiac Surgery, The Jikei University School of Medicine

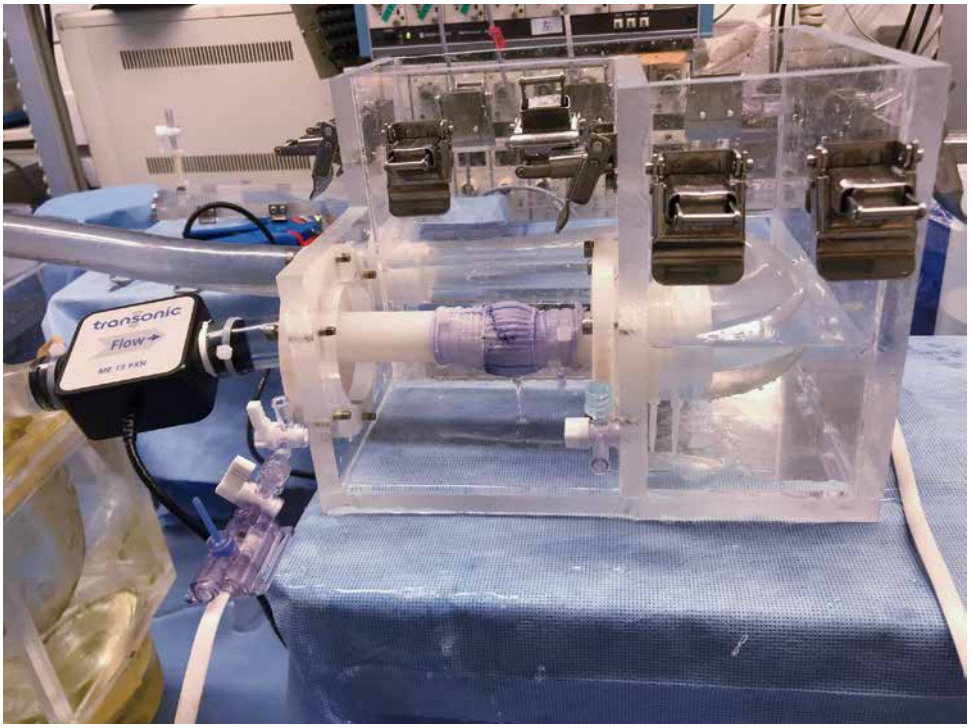
The Department of Cardiac Surgery was established in 1973 and is the oldest such department of a Japanese university hospital. Since June 2018, the department has been supervised by a new team and is involved in a wide range of medical treatments, research topics, and education. In particular, department chairman Professor Kunihara worked for 9 years at Saarland University Medical Center, Homburg, Germany, where he learned from Professor Hans-Joachim Schäfers, a world authority on aortic valve repair surgery. Therefore, in patients with mitral or aortic valve regurgitation, we do our best to repair, rather than to replace, the valve. We also treat all types of congenital and adult cardiac diseases.

Our basic research team has traditionally studied nondestructive 3-dimensional visualization of the cardiac conduction system by means of phase-difference computed tomography of autopsy specimens of congenital heart disease at the large-scale radiation facility Super Photon Ring – 8 GeV. Another of our main research projects has been cardioplegia, studied with a live porcine myocardial ischemia model that undergoes cardiopulmonary bypass surgery. We have recently been doing research toward the application in Japan of del Nido cardioplegic solution and have achieved promising results.

Since Professor Kunihara becoming chairman in 2018, we have been studying hemodynamics after aortic valvuloplasty using a pulsatile flow model in collaboration with the Center for Advanced Biomedical Sciences (TWIns) of Waseda University (Photo). We have clarified hemodynamic differences between aortic root remodeling operations and aortic valve reimplantation operations. We have recently been engaged in a research project for preventing stenosis after aortic valvuloplasty for a bicuspid aortic valve.

We have also performed several clinical research projects. Professor Kunihara has organized a registry study of valve-sparing root replacement and has just launched a multicenter study of mitral valvuloplasty with papillary muscle procedure for severe ischemic mitral regurgitation. Professor Bando has organized a multicenter prospective registry study of the surgical performance of cardiovascular surgeons.

Please do not hesitate to contact us if you are interested in our research projects.



Hemodynamic study after aortic valvuloplasty using a pulsatile flow model in collaboration with Waseda University

Urology

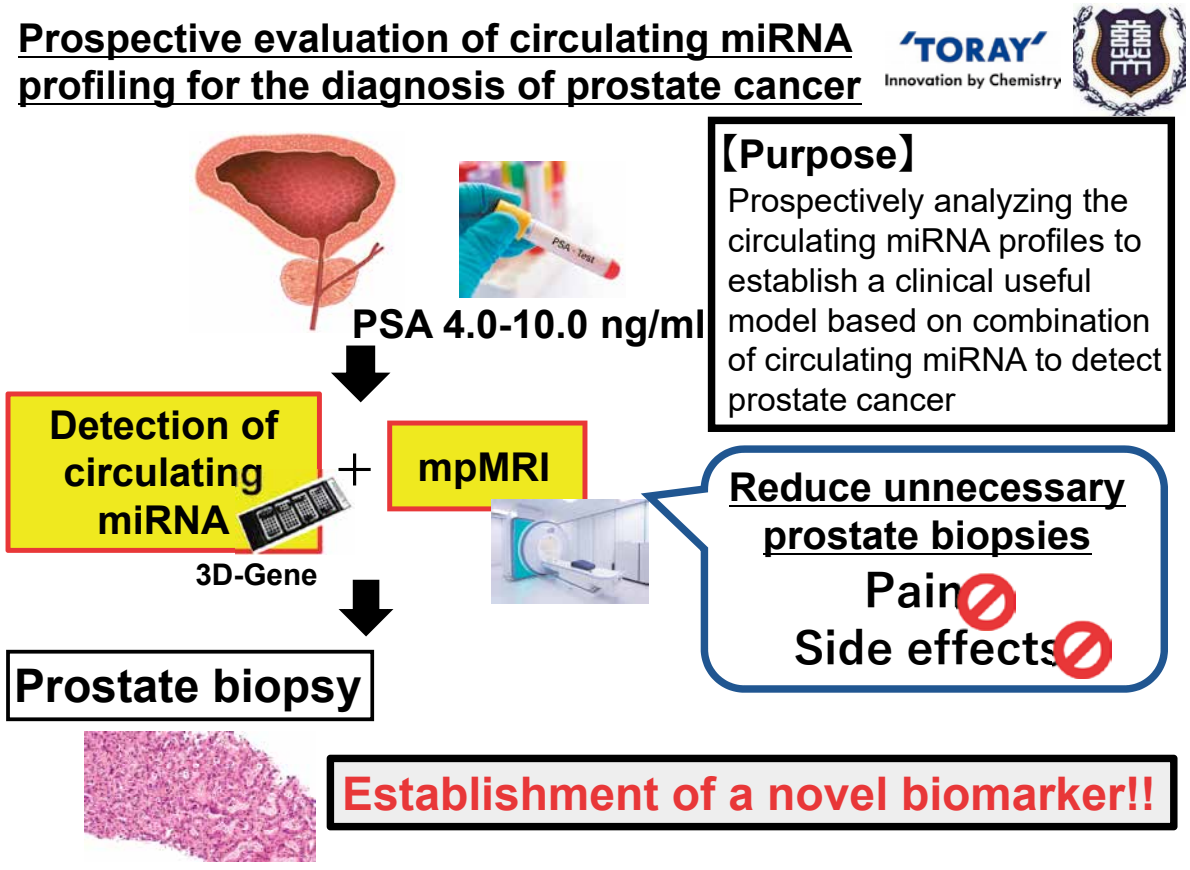
URL : http://jikei-ur.umin.jp/ | E-mail : tkimura@jikei.ac.jp

Research activities for urological diseases

We have performed both basic and clinical research, mainly on genitourinary malignancies and functional urology. In basic research, we are developing new diagnostic tools for prostate cancer using microRNA and exosomes and for both bladder cancer and interstitial cystitis using cystoscopy supported by artificial intelligence. In clinical research, prospective and retrospective studies are conducted of prostate, urothelial, and kidney cancers. Specific information is as follows.

Basic research
- Establishment of new biomarkers using microRNA for prostate cancer (figure)
- Epidemiological study of latent and incidental prostate cancer
- Support system of cryptoscopic diagnosis for both bladder cancer and interstitial cystitis based on artificial intelligence

Clinical research
- Cryoablation for kidney and prostate cancers
- Retrospective study of prostate and urothelial cancers



Prospective evaluation of circulating microRNA profiling for the diagnosis of prostate cancer

Obstetrics and Gynecology

URL : https://jikei-obgyn.jp/index.html | E-mail : surf-side@hotmail.co.jp

Research for the lifelong health of women. Reproductive endocrinology, perinatology, and oncology

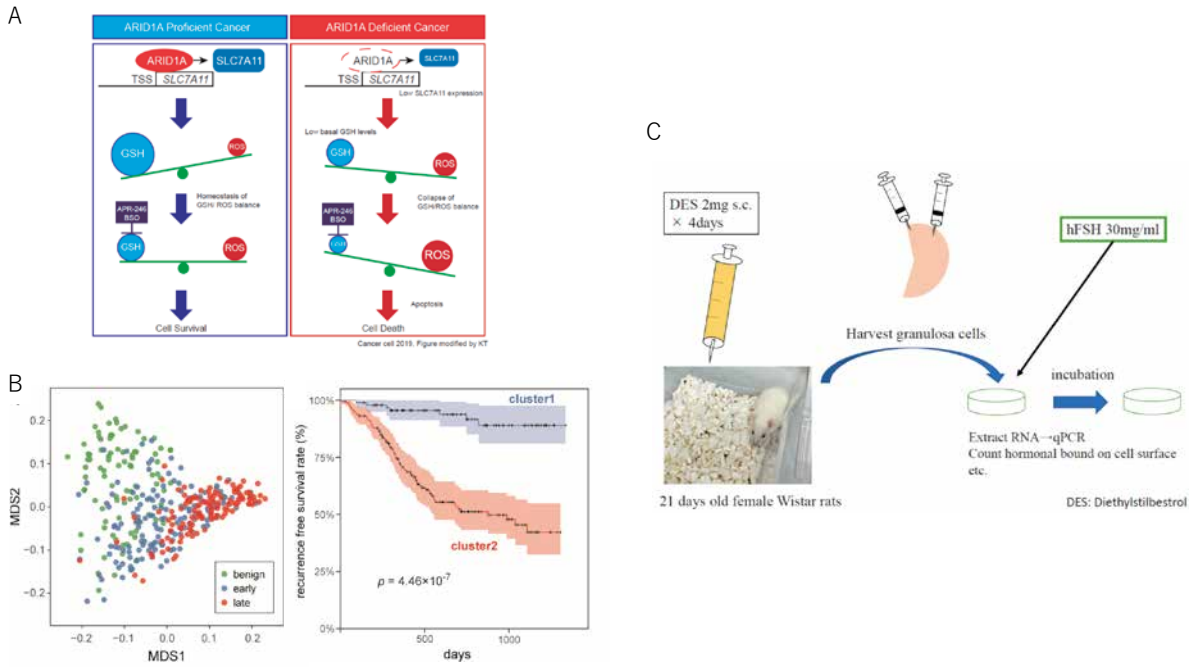
Issues that we encounter in the clinic drive us to basic, translational, and clinical research.
Oncology: We are mainly engaged in ovarian cancer research. Ongoing projects are as follows.

1) Targeting the vulnerability of glutathione metabolism in AT-rich interactive domain-containing protein 1A (ARID1A)–deficient cancers
2) Application of artificial intelligence for preoperative diagnosis in ovarian cancer
3) Identifying common targetable gene alterations among different tumor locations in advanced ovarian clear cell carcinoma

Perinatology: We are engaged in advanced research that might lead to new diagnostic and therapeutic methods in the future.

1) Prenatal fetal genetic testing using free nucleic acids and fetal cells in maternal blood
2) Application to fetal treatment of regenerative medicine technology using induced pluripotent stem cells and embryonic stem cells
3) Elucidation with a molecular genetic analysis method of the pathophysiology of unknown and rare diseases. In addition, we have been conducting clinical research to investigate the effects of COVID-19 on pregnant women and fetuses.

Reproductive endocrinology: Research on follicle development using primary cultures of rat ovarian granulosa cells. Our laboratory has been working on follicle development using a rat ovarian granulosa cell primary culture system to study how the ingredients of some supplements affect follicle development.



(A) Glutathione metabolism in AT-rich interactive domain-containing protein 1A–deficient cancers
(B) Artificial intelligence prognosis of ovarian cancer based on blood biomarkers
(C) Primary cell culture of immature rat granulosa cells

Ophthalmology

URL : http://jikei-eye.com/ | E-mail : tnakano@jikei.ac.jp

Preservation and regeneration of visual function

Glaucoma

- Develop a new program to detect early glaucoma with a head-mounted perimeter (imo®; CREWT Medical Systems, Inc., Tokyo, Japan) and a fundus-oriented perimeter (MP-3; NIDEK CO., LTD., Tokyo, Japan)
- Develop a medical examination for early detection of glaucoma using large-scale health checkup data
- Pharmaceutical treatment for glaucoma with psychological analysis and the evaluation of personality traits
- Develop and establish a normal-tension glaucoma model based on a study of the common marmoset (*Callithrix jacchus*)
- Development of optic nerve regeneration therapy focused on neurotrophic factors in experimental glaucoma
- Develop a new gene therapy vector for recovery of visual function in patients with blindness

We have been developing a new visual field test and a program for its use. In addition, to achieve a comprehensive understanding of the pathologic changes of glaucoma we have conducted multifaceted studies, including higher central nerves utilizing optical coherence tomography and magnetic resonance imaging (MRI).

Cataract

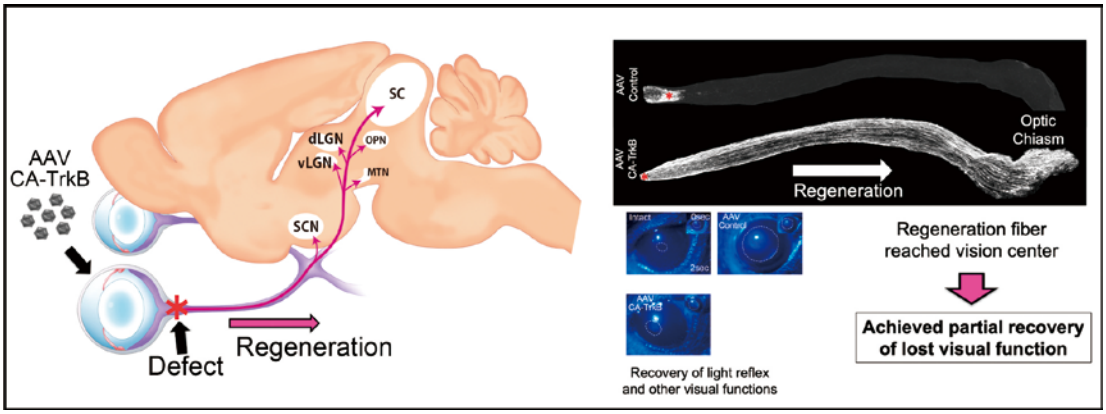
Research and development of minimally invasive techniques for cataract surgery.
We aim to overcome the current issues in cataract surgery by developing surgical techniques that do not place physical stress on ocular tissue: irrigation dynamic pressure-assisted hydrodissection, low-infusion pressure cortical dissection, and femtosecond laser cataract surgery for cases of zonular weakness and acute primary angle closure. We are also developing surgical techniques and intraocular lenses that prevent intraocular lens dislocation.

Visual Neuropsychology

Evaluation and analysis of visual neural circuits using MRI in patients with ocular diseases.
The Visual Neuropsychology Group evaluates and analyzes visual neural circuits using advanced neuroimaging techniques, such as functional MRI, diffusion-weighted MRI + tractography, and qualitative MRI.

Molecular genetics and genetic testing of inherited retinal disorders

The goal of our study group is to characterize genotype-phenotype correlations in patients with inherited retinal disorders (IRDs). The phenotypes of IRDs were determined with ophthalmological examinations, including electroretinography. Genotypes are analyzed with whole-exome sequencing and a next-generation sequencer. To date, we have determined genotype-phenotype correlations in many IRDs and have published several research articles.



Optic nerve regeneration and recovery of visual function using adeno-associated virus type 2-constitutively active tropomyosin receptor kinase B

Otorhinolaryngology

URL : https://jikei-ent.com/ | E-mail : jibika@jikei.ac.jp

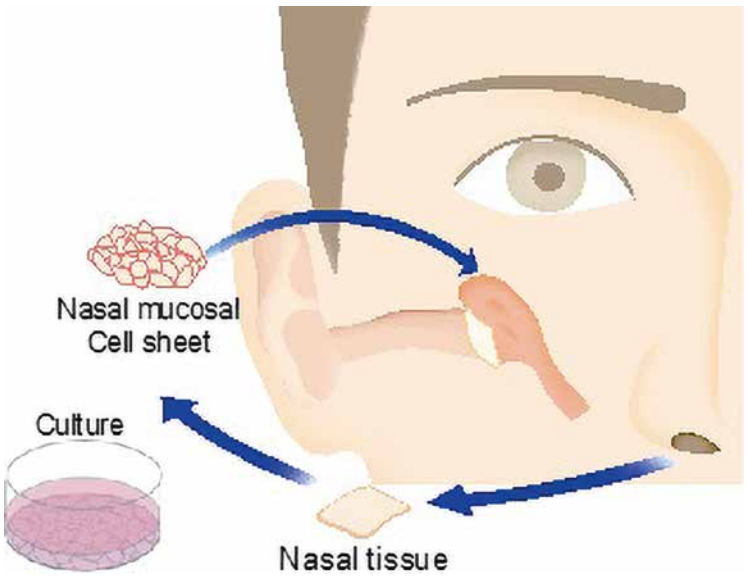
Research activities of the Department of Otorhinolaryngology

Our department members belong to 10 research subgroups and investigate various projects of otorhinolaryngology. In particular, Department Chair Professor Hiromi Kojima and colleagues have been studying regenerative medicine for adhesive otitis media and cholesteatoma, which is one of our main projects supported by large grants.

In the world, there are many patients who suffer from adhesive otitis media and cholesteatoma because no treatments have been established to fundamentally solve the problems of these intractable otitis media. To resolve these problems, many drugs, medical devices, and regenerative medicine products using cultured cells have been developed and are expected to achieve a breakthrough for conventional medicine. In otorhinolaryngology, cholesteatoma is a challenging disease of the middle ear.
Operations for otitis media and middle ear cholesteatoma give rise to mucosal damage in the middle ear which can cause otitis media to recur. To this end, we have developed a novel regenerative medicine approach, combining tympanoplasty and autologous nasal mucosal epithelial cell sheet transplantation to regenerate the middle ear mucosa. We have studied 15 patients treated with this approach. All patients have improved aeration and hearing ability after transplantation with no adverse events or complications and.

Basic research studies of the cell sheet are also ongoing. Because the precise effect and mechanism of the nasal mucosal cell sheet after transplantation are poorly understood, we are investigating the behavior of grafted cell sheets both in vitro and in vivo (animal model study). Combining clinical results, we suggest that a nasal mucosal cell sheet can be engrafted in the middle ear and promote the wound area to heal in the way of epithelial tissue. The ultimate goal of this study is to establish a new regenerative medicine product for clinical application to treat patients with cholesteatoma.

We appreciate that these projects on regenerative medicine for adhesive otitis media and cholesteatoma are supported by the Japan Agency for Medical Research and Development (AMED) [grant numbers 18bk0104051, 19bk0104086, 20bk0104086, 21bk0104086] and Grants-in-Aid for Scientific Research (KAKENHI) [grant number 19H03806].



Regenerative medicine for the middle ear by nasal mucosal cell sheet transplantation

Anesthesiology

URL : http://www.jikei.ac.jp/academic/course/66_masui.html | E-mail : uezono@jikei.ac.jp

Laboratory and clinical research on perioperative medicine, intensive care medicine, and pain management

The functions of the Department of Anesthesiology are to provide quality patient care, to teach, and to perform research in perioperative medicine, intensive care medicine, and comprehensive pain management. In 2020 we made further advances and great achievements with the support of our faculty, institutional administration, and the Dean of The Jikei University. Below we highlight some of our research achievements in 2020.

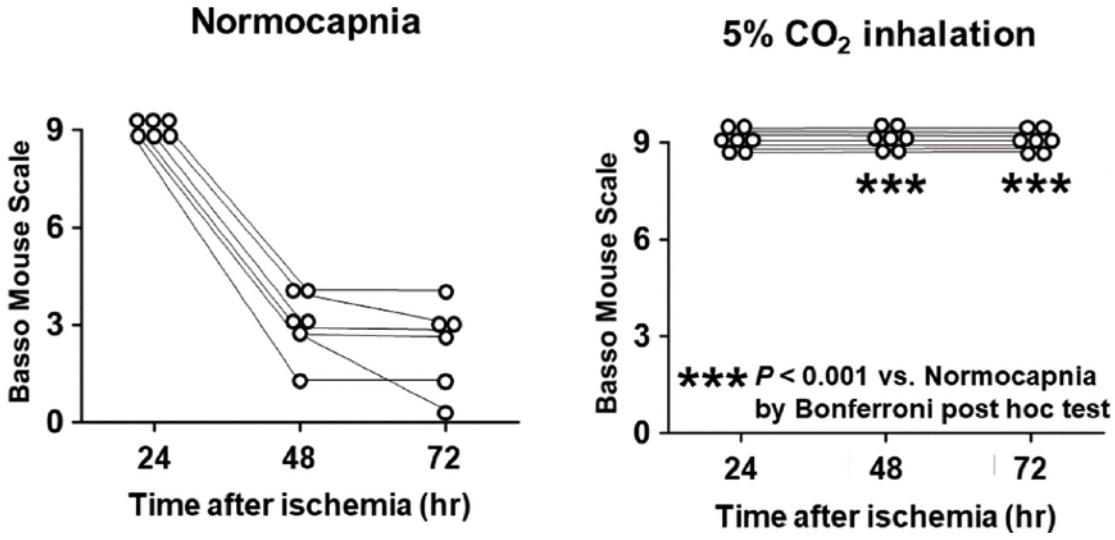
Research activities

Research continues as a growing and important part of the department's activities. The department is committed to enhancing academic productivity and resources by dedicating time to research and granting clinical access to research cases.

Each year the investigators have successfully obtained peer-reviewed research grants. In 2021, Grants-in-Aid for Scientific Research (Kakenhi) have been awarded to 7 members of our faculty. The department continues to build on the strengths of several outstanding programs: cardiovascular anesthesia, thoracic anesthesia, pediatric anesthesia, regional anesthesia, neuroanesthesia, obstetric anesthesia, intensive care medicine, and comprehensive pain management. Listed below are some of the ongoing research projects in which the principal investigators are faculty members of the Department of Anesthesiology.

Doctor Kida, a director of laboratory research, has been investigating the mechanism of spinal cord ischemia during aortic cross clamping, which might lead to new therapeutic interventions, such as inhalational carbon dioxide. Doctor Ikeda's research has been focused on the protective effects of hydrogen nano-bubbles in ischemic encephalopathy.

In clinical medicine, several principal investigators from the Department of Anesthesiology deserve mention. Doctor Kondo has been interested in the postoperative pain treatment service. Doctor Fujii, a new director of our intensive care unit, continues to be active in clinical research in the intensive care unit and has been extremely productive in the field of acute kidney injury. Doctor Abukawa received an award for creating a new model to practice cricothyroidotomy in infants. Doctor Kurata was recruited to establish an outpatient pain clinic in 2019. He has many publications related to neuroimaging techniques for patients with chronic pain.



Inhaled carbon dioxide prevented delayed-onset paraplegia after ischemia spinal cord injury in mice

Rehabilitation Medicine

URL : http://www.jikei-reha.com/Top.cshtml | E-mail : rehabilika@jikei.ac.jp

The department leading the way in Japan's rehabilitation medicine with advanced therapy for the sequelae of stroke

The main research activities of the Department of Rehabilitation Medicine are transcranial magnetic stimulation (TMS) therapy for brain injury and botulinum toxin (BoNT) therapy for spasticity. We are spearheading the promotion of these efforts and supporting rehabilitation medicine in Japan through our clinical research.

In our department, we use TMS to treat brain injury, especially after a stroke, and have made many achievements. On the basis of functional magnetic resonance images, we determined that motor cortex activation on the contralateral hemisphere after brain injury hindered motor function recovery. Thus, in 2008, we started treatment with repetitive TMS (rTMS) to the motor cortex of the contralesional hemisphere and intensive occupational therapy using NEURO® (Novel Intervention Using Repetitive TMS and Intensive One-to-one Training). NEURO® improves upper limb motor function and reduces spasticity. Meanwhile, rTMS minimizes spasticity by decreasing the excitability of anterior horn cells on the affected side. Additionally, rTMS has other effects in the brain, mainly increased blood flow to the ipsilateral hemisphere and heightened expression of neurotrophic factors. In the subacute and chronic phases, improvements in paralysis of both the upper and lower limbs were demonstrated. We have clinically established that, in the recovery from mild-to-moderate paralysis, functional compensation in areas with residual function around the damaged region plays an important role.

Spasticity, a clinical sequela of upper motor neuron lesions, such as brain injury, extensively impairs daily living. In Japan, BoNT therapy has long been used to inhibit muscle contraction. The use of botulinum toxin type A (onabotulinumtoxin A) for the treatment of upper and lower limb spasticity has been covered by insurance in Japan since 2010. Subsequently, our department and affiliated medical institutions have consistently promoted onabotulinumtoxin A, propelling us to the forefront of this treatment. Recently, the dose limit of BoNT therapy for the upper limb has been increased to 400 U, and the interval between injections has been shortened from >3 months to >12 weeks. Moreover, Japan's second botulinum toxin type A (incobotulinumtoxin A) was approved for the treatment of upper limb spasticity in June 2020. Furthermore, in June 2021 medical insurance has allowed up to 400 U of incobotulinumtoxin A to be administered to each of the upper and lower limbs (total of 800 U). Although BoNT therapy is already widely recognized today, we perceived from the beginning that it needs to be combined with rehabilitation evaluation and therapy. Therefore, we have performed several clinical studies in collaboration with occupational therapists and other co-medical staff and have achieved favorable results.

Transcranial magnetic stimulation therapy

Emergency Medicine

URL : http://jikeier.com/ | E-mail : jikeidem@jikei.ac.jp

Emergency Medicine Research in Clinical and Education for Patient Safety

Research in Clinical

An important task of emergency medicine is to prevent the critical condition of patients.Because diagnosing the cause of all symptoms is impossible in the emergency room, prognosis in performing diagnostic and therapeutic interventions are extremely important elements. Our department is focused on patients with chest pain and elderly patients.

An ageing population is a major topic in public health worldwide, and increasing in parallel is the number of patients older than 65 years coming to emergency departments (EDs). A serious problem due to the high proportion of elderly patients is the overcrowding of hospital EDs.

On the other hand, for patients visiting EDs a common symptom of life-threatening illnesses is chest pain, and most ED physicians struggle with intervention.

Research studies of our department are as follows.

1. Comparison of the Early Warning Scores (National Early Warning Score, NEWS; Modified Early Warning Score,MEWS) for predicting admission or in-hospital mortality in elderly patients presenting to EDs
2. The triage ability of the soluble urokinase plasminogen activator receptor in elderly patients.
3. Validation study of the modified history, electrocardiogram, age, risk factors, and troponin (HEART) score and the history, electrocardiogram, age, and risk factors (HEAR) scores in patients with chest pain who visit the ED

Research in Education

Our other important research topic is research in education including simulation trainings for patient safety. We began training for basic life support and advanced life support from 2003, for rapid response teams from 2011, and for airway management,including difficult airway management from 2014.

The topics of research are as follows.

1. Basic Life Support and Advanced Life Support trainings
2. Rapid Response Team training
3. Airway Management training
4. The other Patient Safety Simulation trainings
5. New technology in Education including Virtual Reality and Virtual Patient Simulators

Our research topics are clinical medicine and education that includes simulation training.

Laboratory Medicine

URL : http://www.jikei.ac.jp/academic/course/13_rinshokensa.html | E-mail : rinken@jikei.ac.jp

Laboratory Medicine: conventional and novel field of research

Our department was established in 1977 as the first department in Japan that bears the Japanese name of "臨床検査" (Clinical Laboratory Medicine). Since then, our unchanging aim has been to bridge basic science and clinical medicine.
Laboratory medicine is now embarking on a new era of multiplex assays: single tests that generate a huge amount of information. As many other types of laboratory data have also been digitalized, sharing and utilizing this rapidly accumulating laboratory data for the benefit of patients is becoming a major task of our department.
We must also play a key role in the management of newly emerging infectious diseases, such as COVID-19, by providing appropriate and accurate diagnostic testing in a standardized manner.

Given these backgrounds, our research activities are centered on the following 5 topics.

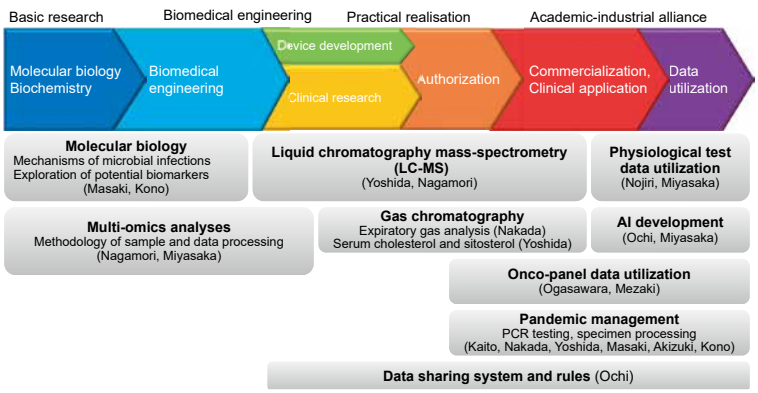
1. Clinical application of multiplex assays
   We promote clinical application of liquid chromatography-mass spectrometry in close collaboration with Shimadzu Corporation. Research is also underway on liquid chromatography-mass spectrometry for high-density lipoprotein-efflux cholesterol, gas chromatography assay for stable isotope analysis using, and high-quality gas chromatography that detects sitosterolemia.

2. Practical realization of genomic medicine
   Genomic medicine requires standardization of genetic test procedures and secure storage of patients' data and specimens, for which our department plays pivotal roles. In collaboration with the the Clinical Genetics, we seek the best way to utilize OncoPanel data in a secure and effective manner.

3. Translational research on microbial infections
   Our department covers a variety of research topics on microbial infections from bench to bedside: molecular mechanisms of transmission, biomarkers that predict susceptibility to infection or disease severity, and diagnostic tests for emerging infectious diseases.

4. Development of artificial intelligence
   Some laboratory tests, such as electroencephalography, are affected by a lack of skilled staff who can analyze images. To solve this problem, research on artificial intelligence that supports these skilled staff are now under way in collaboration with Meiji University.

5. Making rules for data sharing
   The academic use of patients' data and specimens often raises concern about ethics, data security, and biosecurity. We assume a proactive role in establishing an ethically acceptable and researcher-friendly system of data sharing.



Laboratory medicine as a hub of translational research

Endoscopy

URL : http://www.jikei-endoscopy.com/ | E-mail : j.endoscopy@jikei.ac.jp

Illuminate the body within and pave the way for the future of medicine

Endoscopic sleeve gastroplasty (ESG) for Japanese patients with obesity: We successfully introduced ESG to Japan for the treatment of obesity. We are conducting a prospective trial to show the safety and effectiveness of ESG for Japanese patients.

Usability of an ultrathin endoscope for diagnosing pharyngeal and esophageal cancer: This study will show the advantageous diagnostic performance of an ultrathin endoscope for cases of pharyngeal and esophageal cancer.

Long-term outcomes of endoscopic resection for esophageal squamous cell carcinoma: We started performing endoscopic resection of esophageal cancer more than 20 years ago. We showed that endoscopic treatment was effective even for an esophageal cancer that had invaded the muscularis mucosa.

Characteristics of superficial esophageal squamous cell carcinomas undetectable with narrow-band imaging endoscopy: We showed a disadvantage for detecting esophageal cancer with narrow-band imaging endoscopy.

The usability of texture and color enhancement imaging (TXI) for detecting neoplasms in the pharynx and esophagus: We showed that endoscopy with TXI improves the visibility of neoplasms in the pharynx and esophagus.

The usability of TXI for detecting gastric cancer: We are performing a prospective trial.
Pilot study for predicting gastric cancer in patients with gastric intestinal metaplasia: We are developing an algorithm for predicting gastric cancer with specimens obtained with biopsy.

A development of multiloop traction device (MLTD) for endoscopic submucosal dissection (ESD): We developed a new device for ESD and MLTD that enables ESD to be performed with increased safety and speed.

A prospective study of pancreatitis after endoscopic retrograde cholangiopancreatography using a simplified predictive scoring system

A validity study of inserting two 10-Fr plastic stents through the obstructive bile duct cancer

An evaluation of the bacteria profile of the biliary sludge formation that might be due to the stent being occluded by 16S ribosomal RNA sequencing

The prognostic implication of pancreatic cancer using the fine needle aspiration material in the excised specimen of the pancreatic cancer.

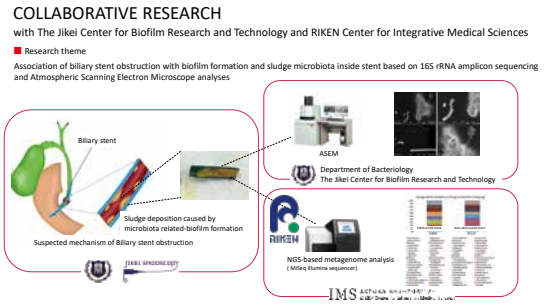
Establishment of a training program for interventional endoscopy using a competency assessment tool.
Single-center prospective study supported by Grants-in-Aid for Scientific Research is ongoing.

Long-term outcome evaluation of aspirin for reducing the incidence of colorectal neoplasia.
A multicenter study is ongoing.

Long-term outcomes evaluation of T1 colorectal cancer after treatment.
A multicenter study is ongoing.

Effectiveness evaluation of TXI for detecting colorectal neoplasia.
A multicenter study is ongoing.

Effectiveness evaluation of extended depth of field function for the differential diagnosis of colorectal lesion.
A single-center prospective study is ongoing.



Collaborative research with The Jikei Center for Biofilm Research and Technology and the RIKEN Center for Integrative Medical Sciences

Clinical Pharmacology and Therapeutics

URL : http://www.jikei.ac.jp/academic/course/81_rinsho-yakuri.html E-mail : shiga@jikei.ac.jp

Clinical pharmacology explores the relationship between drugs and humans from multiple perspectives

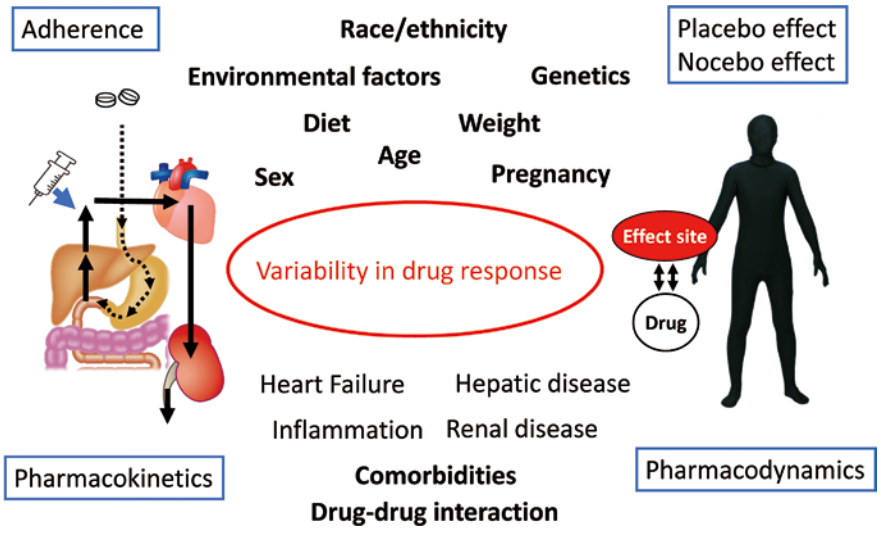
The principle of drug treatment is to maximize the pharmacological effect while preventing adverse events. Clinical pharmacology is a scientific discipline that involves all aspects of the relationship between drugs and humans. Research in clinical pharmacology is usually interdisciplinary and is often conducted in collaboration with other professionals and with clinical researchers from other medical specialties. Clinical pharmacokinetics is the basis for personalized medicine, in which the dose of a drug is individualized and the results achieved are optimized for each patient. Clinical pharmacology has important roles in the development of new drugs, in repositioning drugs, and reevaluating drug efficacy in prospectively conducted clinical trials on the basis of exploratory hypotheses from cohort studies.

Research topics

- Cardiotoxicity of anticancer drugs
- Pharmacokinetic/pharmacodynamic studies in disease states
- Clinical pharmacology of cardiovascular drugs
- Clinical outcome of patients with heart failure
- Studies of medication adherence

Selected Publications

- Shiga T, Kimura T, Fukushima N, Yoshiyama Y, Iwade K, Mori F, Ajiro Y, Haruta S, Yamada Y, Sawada E, Hagiwara N; SMAAP-AF investigators. Electronic monitoring of adherence to once-daily and twice-daily direct oral anticoagulants in patients with atrial fibrillation: Baseline data from the SMAAP-AF trial. J Arrhythm 2021; 37: 616-625.
- Kido K, Shimizu M, Shiga T, Hashiguchi M. Meta-Analysis Comparing Direct Oral Anticoagulants Versus Warfarin in Morbidly Obese Patients With Atrial Fibrillation. Am J Cardiol 2020; 126: 23-28.
- Hirai T, Naganuma M, Shiga T, Echizen H, Itoh T, Hagiwara N. Serum digoxin concentrations and outcomes in patients with heart failure and atrial fibrillation: a single-center observational study. Jpn J Clin Pharmacol Ther 2020; 51: 57-64.
- Shiga T, Suzuki A, Haruta S, Mori F, Ota Y, Yagi M, Oka T, Tanaka H, Murasaki S, Yamauchi T, Katoh J, Hattori H, Kikuchi N, Watanabe E, Yamada Y, Haruki S, Kogure T, Suzuki T, Uetsuka Y, Hagiwara N; HIJ-HF II Investigators. Clinical characteristics of hospitalized heart failure patients with preserved, mid-range, and reduced ejection fractions in Japan. ESC Heart Fail 2019; 6: 475-486.



Several factors contribute to the variability of drug responses

Dentistry

URL : https://www.hosp.jikei.ac.jp/diagnosis/department/221.html E-mail : dental@jikei.ac.jp

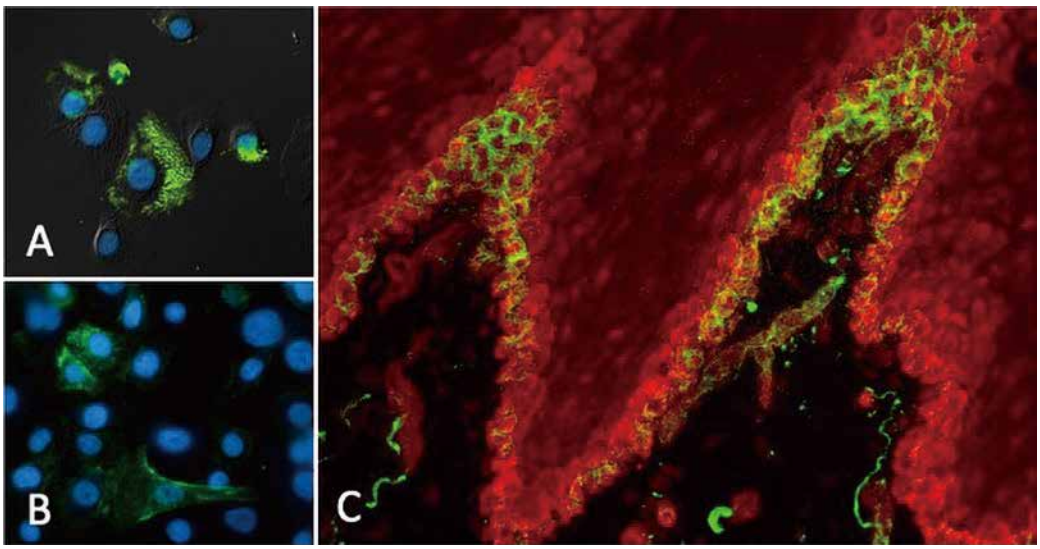
We promote research activities focus on translational research that are useful for clinical practice

1. Study of the treatment of odontogenic maxillary sinusitis
   The availability of multiple treatment methods makes the optimal treatment of odontogenic maxillary sinusitis unclear. The present study aims to determine the factors contributing to the cure of odontogenic maxillary sinusitis. The identification of intractable factors would help provide an optimal treatment.

2. Validation of periodontal disease management to improve outcome of strokes
   Cerebrovascular disease is the fourth most common cause of death and the leading cause of patients being bedridden. To prevent cerebral infarction from recurring, it is important to control arteriosclerosis-related diseases (hypertension, dyslipidemia, diabetes) and improve lifestyle (such as diet, exercise, and smoking). Periodontal disease, which affects about half of the Japanese population, has recently attracted attention as a factor that increases the risk of developing cardiovascular diseases, such as myocardial infarction and cerebral infarction. However, what remains unclear is whether active intervention for periodontal disease can inhibit the onset of cerebral infarction. Furthermore, no studies have evaluated whether periodontal disease management can prevent recurrence, complications, and atherosclerosis after acute cerebral infarction. This study examines whether controlling periodontal disease is useful in improving the outcome of strokes.

3. Investigating receptor alteration in the trigeminal ganglion in persistent orofacial pain
   Trigeminal neuralgia is a characteristic disease that manifests as orofacial phasic or continuous severe pain triggered by innocuous orofacial stimulation; its mechanisms are not fully understood. In this study, we established a new animal model of trigeminal neuralgia and investigated the role of receptor alteration of the trigeminal ganglion in cases of persistent orofacial pain.

4. Nerve growth factor beta/pro-nerve growth factor and their receptors in normal human oral mucosa.
   The aim of this study was to determine the role that nerve growth factor (NGF) might play in the differentiation and wound healing of oral mucosa. Differential expression of NGF and NGF receptors (tropomyosin-related kinase A and p75 neurotrophin receptor) throughout the epithelium suggests a role in epithelial differentiation. This in-vitro study indicates that NGF-β/proNGF have mitogenic and motogenic effects on oral mucosal keratinocytes and, therefore, may help oral wounds to heal.



Immunofluorescent staining for tropomyosin-related kinase A (A) and p75 neurotrophin receptor (B) in cultured keratinocytes and normal oral mucosa (C).

Infection Control

URL : https://www.hosp.jikei.ac.jp/diagnosis/department/110.html E-mail : tohoshina@jikei.ac.jp

Tackling tasks in various research fields of infectious disease

Our department is part of the group of clinical medicine departments of The Jikei University. Specialists in infectious diseases serve patients in The Jikei University hospital and work as a scientist that conducts clinical research. As our interests vary from virus to parasites, our department has recently reported several unique research findings.

Horino, et al. revealed predictive factors for metastatic infection in patients with staphylococcal bacteremia. The study demonstrated that additional diagnostic tests should be performed to identify metastatic infection, particularly in patients with delayed antimicrobial treatment, persistent fever, and persistently high C-reactive protein levels (Am J Med Sci 2015; 349: 24–8).

Nakaharai, et al. reported that routine, early use of a prophylactic antibiotic has no significant clinical benefit in patients with severe acute pancreatitis but might increase the risk of hospital-acquired infections (J Infect Chemother 2018; 24: 753–758). The effect of the study is highly engaged in antimicrobial stewardship to facilitate an appropriate usage of broad-spectrum antibiotics.

Hoshina, et al. reported the seroprevalence of *Toxoplasma gondii* in the Yezo sika deer, which people consume as game meat, and suggested that both appropriate handling and treatment of bushmeat are required to prevent food-borne toxoplasmosis in Japan (Parasitol Int 2019; 71: 76–79). The authors also published research about the seroprevalence of *T. gondii* among people living with human immunodeficiency virus (HIV) in Tokyo and found that the HIV-positive population has been maintained at a similar level as that of the HIV-negative population in Japan (Infect Chemother 2020; 26: 33–37). This study was the largest survey of toxoplasma prevalence in people living with HIV in Japanese society.

After the coronavirus infection 2019 (COVID-19) pandemic was declared by WHO in March 2020, we focused on this novel infection and conducted our research in 2020. From February 2020 through August 2021, approximately 1000 patients with COVID-19 have been admitted to our hospital. After analyzing clinical specimens, we have reported, in collaboration with the Department of Respiratory Disease, novel biomarkers to predict severe COVID-19 (J Extracell Vesicles 2021; 10: e12092). While our department contributed to the establishment of the clinical polymerase chain reaction (PCR) center for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with the Department of Tropical Medicine and others, we reported a review of the management of diagnostic issues of COVID-19 in collaboration with the members of the Team COVID-19 PCR center (Inflamm Regen. 2020; 40: 38).

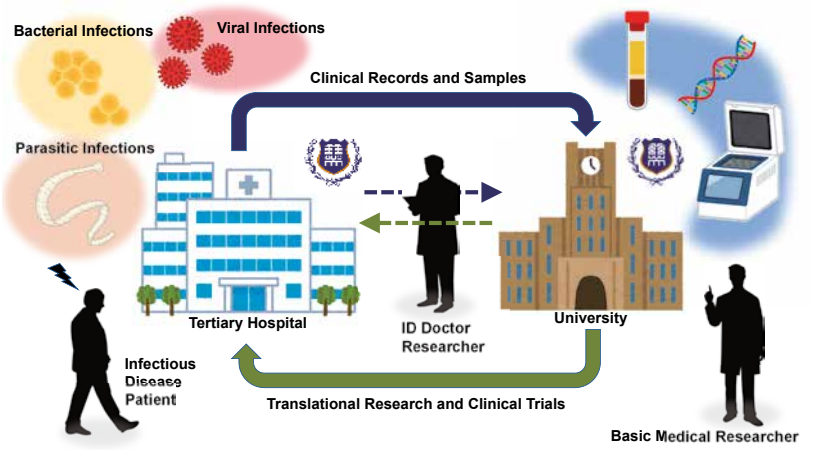


Diagram of clinical trials and translational research between a tertiary hospital and academia.
Department of Infection Control

Transfusion Medicine and Cell Therapy

URL : https://www.hosp.jikei.ac.jp/diagnosis/department/505.html E-mail : ttasaki@jikei.ac.jp

An attempt to establish a diagnostic algorithm of transfusion-associated circulatory overload

Among various adverse reactions to blood transfusion, dyspnea has now become of greatest concern worldwide. Well-known causes of this adverse reaction include transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), anaphylaxis, and transfusion of bacterially-contaminated or ABO-incompatible blood. Differentiating between TRALI and TACO is extremely important and difficult, because the treatment of each condition is quite different, although patients present with similar signs and symptoms.

Diagnostic criteria for TRALI were established in 2004 at a consensus conference held in Toronto, Canada, and were revised in 2019. However, no such criteria exist for diagnosing TACO. Therefore, to establish clinically significant and useful diagnostic criteria for TACO, the principal investigator Tasaki and his colleagues formed a study group supported by a Health and Labour Science Research Grant.

The new proposed criteria for TACO are composed of 6 primary features and 5 items to support diagnosis, and the algorithm is shown in Figure 1. Unfortunately, the criteria have not achieved worldwide acceptance because of its complexity and the need for a large amount of data to perform an accurate diagnosis. In particular, proper evaluation of the patient's clinical signs and symptoms by a physician was the most important factor for the final diagnosis, although detailed laboratory data would be desirable. To enhance both the utility of the guidelines and the differential diagnosis of TRALI and TACO, we have tried to simplify the algorithm by modifying the guidelines considering data from patients with dyspnea associated with blood transfusion.

In any case, safe blood transfusions depend on lowering the risks from allogeneic blood units and on the appropriate use of transfusions, especially in the prevention of TACO sometimes observed in cases of cardiac pulmonary edema due to massive or rapid transfusion of blood products. Educating medical and nursing students and practicing physicians and nurses about transfusion medicine is, therefore, extremely important for improving the safety of blood transfusions.

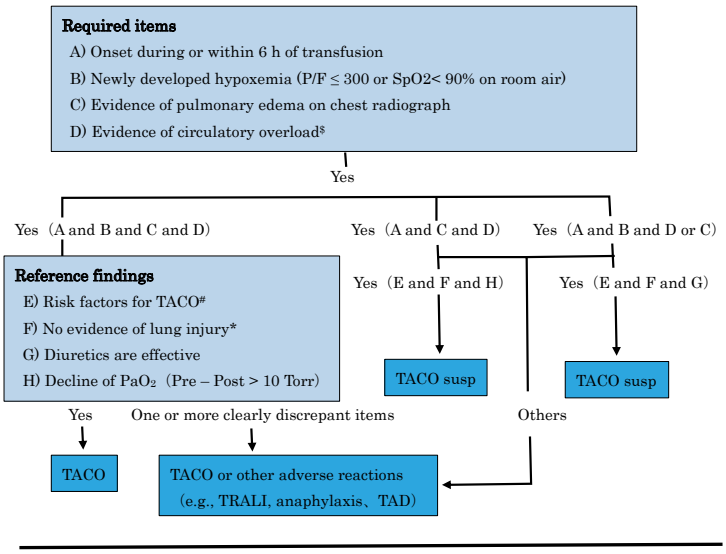


Figure 1. Diagnostic algorithm of TACO

Abbreviations: TRALI= transfusion-related acute lung injury; TACO= transfusion-associated circulatory overload; TAD= transfusion-associated dyspnea; P/F= arterial oxygen partial pressure / fractional inspired oxygen; TACO susp= TACO is suspected

$ Evidence of circulatory overload

1. Elevated blood pressure
2. Tachycardia
3. Neck-vein distention
4. Rales and/or a third heart sound on auscultation
5. Acute respiratory distress
6. Laboratory findings
   - BNP ＞200 pg/mL、NT-proBNP ＞900pg/dL
   - CVP ＞12 cmH_2O
   - Enlarged cardiac shadow on chest radiograph

 # Risk factors for TACO

1. Age (< 3 yo, >80 yo)
2. Pre-transfusion fluid balance (> 2L)
3. Cardiac dysfunction
4. Renal dysfunction (eGFR <29)
5. Rapid transfusion (＞5ml/kg/h)

*** No evidence of lung injury**

1. No elevation of temperature or CRP or WBC
2. No elevation of SP-D or KL-6

Diagnostic algorithm of transfusion-associated circulatory overload

Clinical Genetics

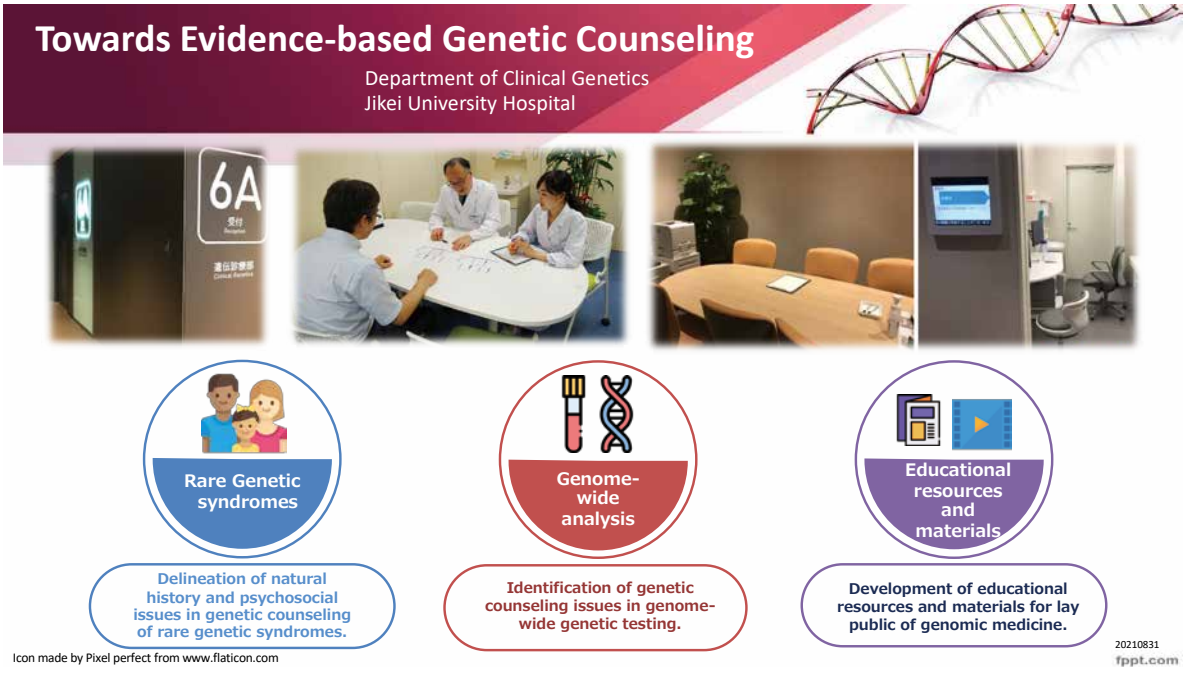
URL : https://www.hosp.jikei.ac.jp/diagnosis/department/512.html | E-mail : jikei.clingenet@gmail.com

Towards evidence-based genetic counseling

To provide cutting edge clinical genetic services, the Department of Clinical Genetics was established in The Jikei University Hospital in April 2018. As well as providing clinical services, our department conducts research, trains medical fellows who specialize in clinical genetics, and provide educational seminars regarding clinical genetics to all professionals of The Jikei University. The goal of our research is to elucidate multiple aspects of genetic counseling. The research questions will be found in the varieties of ordinary genetic clinics. Our certified genetic counselors and clinical geneticists submit research abstracts to relevant genetic national meetings and turn in an article written in the format for submission to a journal. Our research activities are partly incorporated by a Health and Labor Sciences Research Grant and the grant program of the Japan Agency of Medical Research and Development.

Main research topics:

- Delineation of natural history and psychosocial issues in genetic counseling for rare genetic syndromes.
- Identification of genetic counseling issues in genome-wide genetic testing.
- Development of educational resources, methods, and materials for the lay public of genomic medicine, genetic counseling, and genomic literacy.



Towards evidence-based genetic counseling

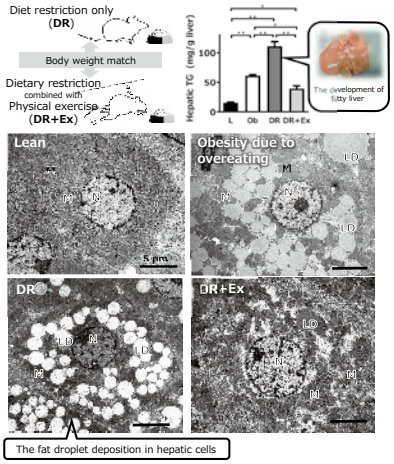
Physical Fitness

URL : http://www.jikei.ac.jp/academic/course/68_tairyoku.html | E-mail : sml@jikei.ac.jp

Exercise benefits functional preservation and improves the musculoskeletal system and metabolism

Research activities in our division have focused on preventive medicine against locomotive and metabolic syndromes in terms of exercise physiology based on animal studies.

1. We have reported that unloading disrupted myofibrils with a decrease in sarcomeric proteins, formed inclusion bodies, and accumulated abnormal mitochondria in type I fibers of aged rats. Our results suggest that autophagic adaptation and myogenic responses account for age-related muscle responsiveness to unloading, which is ameliorated by exercise.
2. We have been studying the effects of eccentric contraction on contractile properties, protein signals, and the intramuscular microstructure to find the optimal intensity of eccentric contraction for rehabilitation to induce muscle protein synthesis while suppressing deteriorative damage. Limiting the intensity of eccentric contraction at a lower level appears to be safe for general rehabilitation.
3. Weight control depending on dietary restriction alone might cause the failure in lipid metabolism to induce fatty liver. Our results suggest that habitual exercise with dietary restriction enhances the expression of hepatic fatty acid binding protein 1 and ameliorates fatty liver in hyperphagic Zucker fatty rats.



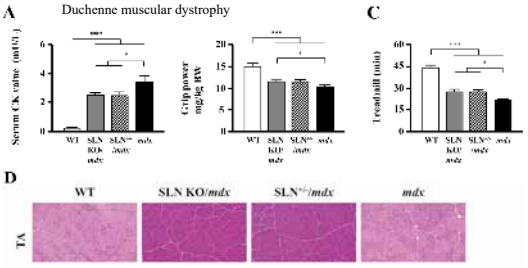
Habitual exercise with dietary restriction effectively ameliorates hepatic fat accumulation.

Aerospace Medicine

URL : http://www.jikei.ac.jp/academic/course/05_uchu.html | E-mail : sminamis@jikei.ac.jp

Regulatory mechanisms of the effect of gravity on cell and organ homeostasis

The time has come for humankind to dramatically advance into space. However, space is extremely harsh for human beings because of such factors as microgravity, radiation, and the closed environment. Our main research interests are to understand how human beings can adapt to the harsh environment and maintain homeostasis in the body. From the viewpoints of gravitational physiology and aerospace medicine, the main current research topics are: 1) phenotypic analysis and gene therapy of a mouse model (troponin T amino acid mutation [ΔK210] knock-in mouse) of juvenile onset dilated cardiomyopathy, 2) molecular mechanisms of intracellular Ca^{2+}-mediated muscle atrophy using sarcolipin knockout mice, 3) the effect of microgravity on the morphology of the stomach and liver tissues of mice aboard the International Space Station, and 4) morphological analysis in the transplantation strategy of machine perfusion preservation of the liver.



Reducing sarcolipin expression ameliorates muscle dysfunction and the pathology of the mdx strain, a mouse model of Duchenne muscular dystrophy.

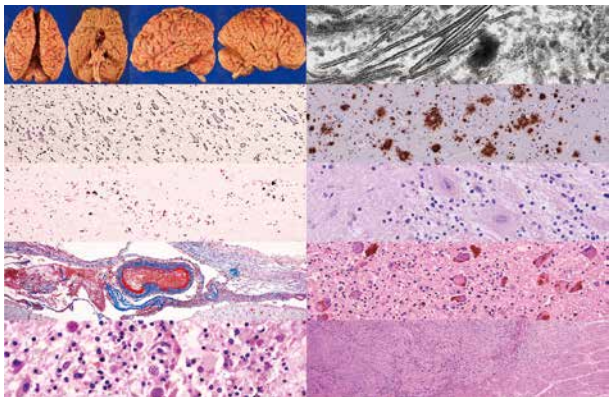
Selected references:

1. Tanihata J, et al. Truncated dystrophin ameliorates the dystrophic phenotype of mdx mice by reducing sarcolipin-mediated SERCA inhibition. Biochem Biophys Res Commun 505: 51-59, 2018.
2. Bochimoto H, et al. Ultrastructural changes in colonic epithelial cells in a rat model of inflammatory bowel disease. Microsc Res Tech 82: 1339-1344, 2019.

Neuropathology

URL : https://plaza.umin.ac.jp/jikei-np/ | E-mail : neuropathology@jikei.ac.jp

Neuropathology



Neuropathology

Neuropathology is the study of diseases of the nervous system and typically includes the laboratory analysis of tissue samples for pathological diagnosis or investigation. Neuropathologists are the physicians and scientists who make these diagnoses and conduct research in this field. Common topics of study are brain tumors, neurodegenerative disorders, cerebrovascular disorders, developmental disorders of the brain, traumatic brain and spinal injuries, infectious diseases, nutritional and metabolic disorders, demyelinating disorders, toxic injuries, and the pathobiology of nerve and muscle diseases, such as the muscular dystrophies and neuropathies. Our purpose is to advance the science, teaching, and training regarding diseases of the nervous system and the practice of neuropathology. Our missions are to advance the study of diseases that affect the nervous system and to minimize suffering through discovery, education, and the delivery of patient-centered clinical care. Our research projects have concerned neurodegenerative disorders caused by the intracellular accumulation of abnormal proteins and metabolic disorders. We are also studying mouse models of neurodegenerative disorders and autopsy cases by means of standard morphologic analysis and molecular biological analysis.

Sports Medicine

URL : http://jikeiseikei.com/orthopedics/sports/ | E-mail : funasaki@jikei.ac.jp

Clinical research on sport injuries in professional and amateur athletes

Sport activities in soccer, rugby, and baseball fields

We have conducted several studies based on daily clinical examinations and analyses of sport activities performed by physicians of professional soccer teams and female rugby teams and on off-season medical check-up data collected from athletes of junior/youth soccer and baseball teams. We have recently focused our research on pathological changes underlying throwing-shoulder disability in baseball players; risk factors for epiphysitis, including Osgood-Schlatter disease in junior soccer players; the diagnosis and treatment of muscle strains; magnetic resonance imaging–based diagnosis of fatigue fractures; and arthroscopic surgery in athletes. In addition, we have reported many cases of rare clinical illnesses often encountered in athletes.

Environmental Allergy

URL : http://www.jikei.ac.jp/academic/course/82_kankyo_allergies.html E-mail : misaburo@jikei.ac.jp

Rice-based oral peptide vaccine for Japanese cedar pollinosis antigen and recognition mechanism of paraphenylenediamine-specific T-cells

This department was established in April 2019 with the following aims: disseminating cedar pollen rice, which has few side effects and can be an effective immunotherapy against cedar pollinosis; elucidating the antigen recognition mechanism of T-cells for contact dermatitis caused by small molecules, such as drugs and metals; and further evaluating the usefulness of plaster as a building material from the viewpoint of antiallergic effects.

Recent clinical studies have shown that oral administration of transgenic rice seeds significantly suppresses specific T-cell responses without side effects (Int Arch Allergy Immunol 2021; 182(2): 109-119) and that the administration of transgenic rice seeds will clinically improve pollen symptoms (Allergy Asthma Proc 2021; 42(4): 293-300).

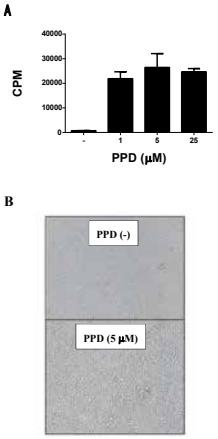


Figure 1. Evaluation of proliferative response of paraphenylenediamine-specific T-cells by uptake of ^{3}H-thymidine (A) and under a microscope (B)

Allergic contact dermatitis due to paraphenylenediamine (PPD) has recently increased in both hairdressers who dye hair and in people whose hair is dyed. Exposure to PPD, a central component of most permanent hair dye formulations, is associated with the development of T-cell–mediated allergic contact dermatitis. Therefore, a PPD-specific T-cell line was established to analyze how PPD is presented to T-cells as an antigen (Figure 1).

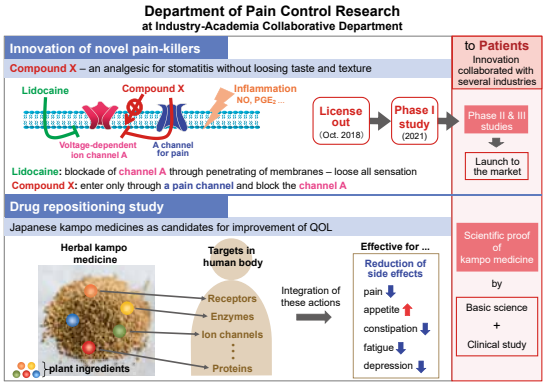
Pain Control Research

URL : http://www.jikei.ac.jp/academic/course/85_toutsuu.html | E-mail : yuezono@jikei.ac.jp

We develop novel pain-killers as a member of the Industry-Academia Collaborative Department

In 2020, the Department of Pain Control Research was established in the Industry-Academia Collaborative Department of The Jikei University School of Medicine. For more than 10 years, our research group was based at the Division of Cancer Pathophysiology of the National Cancer Center Research Institute and studied supportive and palliative care therapy to improve the quality of life of cancer patients. At The Jikei University School of Medicine we develop novel analgesics through joint research with several pharmaceutical companies.

In the laboratory, we also conduct drug repositioning research aimed at expanding the indications of drugs, such as Japanese *kampo* medicine for cancer pain, and conduct research to develop novel, first-in-class drugs for unmet medical needs. For example, our 2 goals are to develop an analgesic that does not change the texture and taste of patients with intractable pain due to mucositis, and to develop analgesics for patients suffering from chronic neuropathic pain.



Our 2 projects: the development of novel analgesic agents and drug repositioning research on *kampo* medicine

In the laboratory, we strongly hope that the drugs we develop while doing research at The Jikei University School of Medicine will advance through phase I to III clinical trials and will eventually be used clinically as novel analgesic agents.

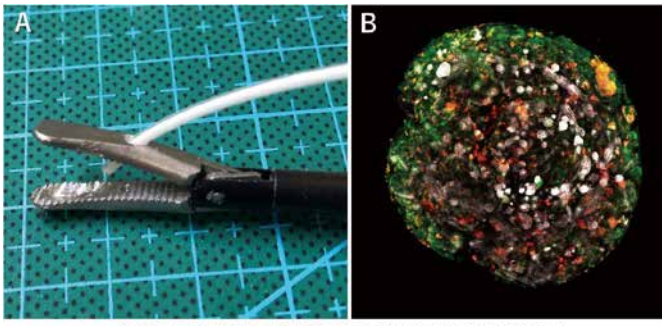
Kidney Regenerative Medicine

URL : https://jikei-kidney-regeneration.com/ja/lab/ | E-mail : eijikoba@jikei.ac.jp

Novel transplantation methods of vulnerable renal organoids in mice and pigs

We aim to develop surgical methods to transplant in vivo extremely fragile renal organoids, created by in vitro reaggregation of metanephros from fetal mice, and have performed the first laparoscopic cloaca transplantations using the novel devise (A) in pigs.

Initially, metanephros from fetal mice (E13) were enzymatically treated to form single cells, and spheroids were generated in vitro (B). Under a microscope, the renal capsule was detached to avoid bleeding, and the outer cylinder of the indwelling needle was inserted to detach the renal parenchyma from the renal capsule by means of water pressure. A simple and easy method to transplant fragile spheroids and renal parenchyma under the renal capsule without damaging them was developed.



A: A prototype devise of fragile tissue by water-jet for clinical use
B: A re-agglutinated spheroid made from fetal mouse metanephrons

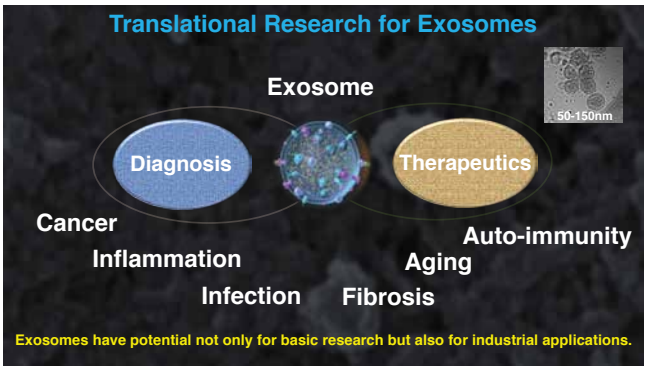
A novel laparoscopic device for the transplantation of renal organoids

To provide a preclinical point of view, allogenic fetal cloacae were laparoscopically transplanted into mature microminiature pigs. No postoperative adverse events were observed, and histopathological assessments confirmed that the allogenic fetal cloacae had grown under adequate immunosuppression. We succeed in performing the first laparoscopic transplantation of vulnerable renal organoids in pigs.

Translational Research for Exosomes

URL : https://jikeiexosome.wordpress.com | E-mail : yuugot@jikei.ac.jp

Development of exosome-based liquid biopsy and therapeutics for clinical applications



Translational research on exosomes for biomarker analysis and therapeutic development

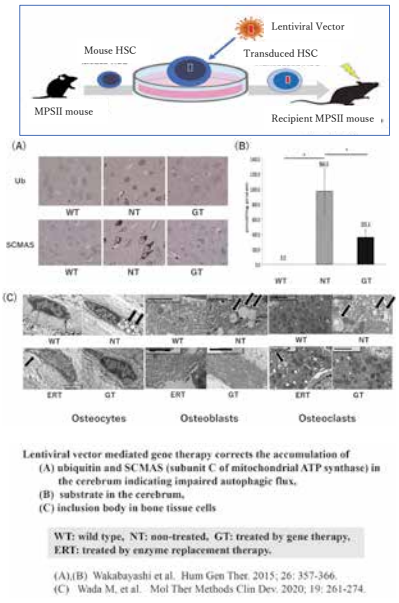
Exosomes are small particles with a diameter of 50 to 150 nm which are secreted by all cell types. They carry many cell-specific signaling substances, such as messenger RNA, microRNA, and proteins. Due to these properties, the potential of exosomes serving as disease biomarkers has grown over the past decade. In collaboration with many clinical departments in The Jikei University and with pharmaceutical companies, we investigate the potential of exosomal biomarkers for cancer diagnosis, treatment responses of immune checkpoint inhibitors, and various types of diseases, including COVID-19 severity (Fujita et al., *J Extracell Vesicles*, 2021),
Exosomes have important clinical significance and application potential in the treatment of disease. Our team reported on human bronchial epithelial cell-derived exosome therapy for pulmonary fibrosis via inhibition of transforming growth factor (TGF)-β-Wingless/Int (WNT) crosstalk (Kadota et al., *J Extracell Vesicles*, 2021). We will conduct an investigator-initiated clinical trial of inhaled exosomal therapeutics for idiopathic pulmonary fibrosis. Our goal is to obtain commercialization and pharmaceutical approval of the first exosome medicine in Japan.

Gene Therapy

URL : http://www.jikei-gene.com/index.html | E-mail : hrkb@jikei.ac.jp

Research and development of gene therapy for inborn errors of metabolism

Our laboratory has been researching and developing gene therapy for lysosomal diseases caused by the insufficiency of enzymes in lysosomes, and has been using such viral vectors as retrovirus, adenovirus, adeno-associated virus, and lentivirus. Our main theme now is mucopolysaccharidosis type II, caused by dysfunction of the enzyme isuronate-2-sulfatase (IDS). We constructed a lentiviral vector containing IDS, a gene encoding this enzyme, and performed gene therapy targeting hematopoietic stem cells in a mouse model. As a result, the mice maintained significantly high enzyme activity in the peripheral blood and showed biochemical and pathological improvements in organs, including the central nervous system and bone tissue, and improvements in behavioral tests. Furthermore, when IDS-transduced human hematopoietic stem cells were transplanted into immunodeficient model mice, were observed differentiation into various cell lineages and biochemical improvement in major organs. On the basis of these results, we determined that we had obtained proof of concept and applied for a patent. We have started studying the conditions for the stable production of transgenic cell products using cell processing equipment for clinical development and are working on the application of this technology to the treatment of other lysosomal diseases, such as GM1 gangliosidosis.



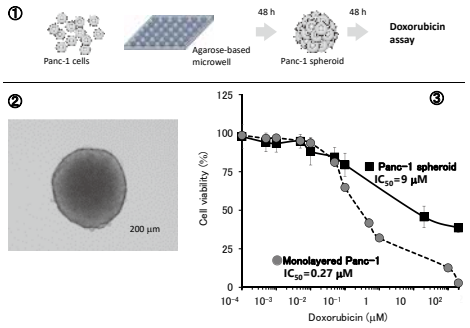
Lentiviral mediated gene therapy for MPS II

Oncology

URL : http://www.jikei.ac.jp/academic/course/17_akuseisyuyo.html | E-mail : murahashi@jikei.ac.jp

Basic and clinical research aimed at developing new cancer therapies

Cancer immunotherapy has recently been established as a field. However, Dr. Sadamu Homma, the former professor of our research department, and his collaborators conducted a clinical trial of immunotherapy using dendritic cells for intractable cancers, such as glioblastoma, when host immunity was not yet believed able to control cancer. With this study they provided good clinical results to the world. We have inherited their spirits and will proceed with cancer treatment research. Below, we describe the basic and clinical research that we are currently working on.



In vitro immunotherapy evaluation system using cancer spheroids

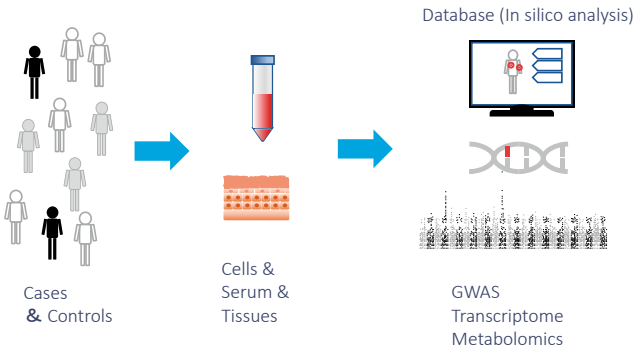
1) Basic research on new immunotherapy for pancreatic cancer
We have demonstrated the effectiveness of multidrug immunotherapy for pancreatic cancer in a tumor-bearing mouse model with a fibrosis-inhibiting peptide (Oyama Y, J Immunother. 2020). To utilize the evaluation of 3-dimensional structures in the analysis of the antitumor effect of immune cells, we are working on the development of new pancreatic cancer cell spheroids by applying our unique cell spheroid production technology.
2) Search for mutant antigens that are targets of dendritic cell therapy for malignant glioma
We have been conducting dendritic cell–tumor cell fusion vaccine therapy for malignant glioma in collaboration with the Department of Neurosurgery. We are searching for tumor mutant antigens in tumor cells of malignant glioma with gene mutation analysis via next-generation sequencing.

Molecular Genetics

URL : http://square.umin.ac.jp/jikeimolgen/ | E-mail : mayumitamari@jikei.ac.jp, thirota@jikei.ac.jp

Research on genetic factors related to allergic and immunological diseases

The aim of our project is to explore genetic factors of allergic and immunological diseases to improve our understanding of the pathophysiology. We conducted genome-wide association studies (GWASs) in the Japanese population of bronchial asthma (Nat Genet. 2011; 43: 893-6), atopic dermatitis (Nat Genet. 2012; 44: 1222-6), wheat-dependent exercise-induced anaphylaxis (J Allergy Clin Immunol. 2019; 122: 1354-63), and autoimmune pulmonary alveolar proteinosis (Nat Commun. 2021; 12: 1032). We perform collaborative research with other institutions and perform GWASs, next-generation sequencing analysis, and metabolome analysis of psoriasis and food allergies. Professor Tamari is working in a research group established to make plans for the next 10 years of allergy and clinical immunology research. This work is supported by Health Science Research Grants from the Ministry of Health, Welfare and Labour of Japan. The group has published an article on an effective strategy for research on allergic and immunological diseases (Allergol Int. 2020; 69: 561-570) and launched a website for the research plans: Empowering Next Generation Allergist/immunologist toward Global Excellence Task Force toward 2030 (ENGAGE-TF toward 2030) [https://www.engage-tf.jp]).



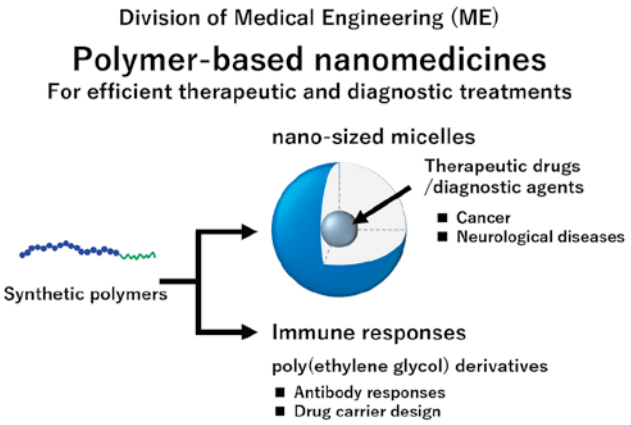
Research flow of genetic analyses of allergic and immunological diseases

Medical Engineering

URL : http://www.jikei.ac.jp/academic/course/24_gazou.html | E-mail : kshiraishi@jikei.ac.jp

Development of nanosized formulations for novel therapeutic and diagnostic systems

The Division of Medical Engineering aims to provide new and essential techniques, which are based on polymer nanomedicines, for efficient therapeutic and diagnostic treatments. A current project aims to evaluate relationships between neurological disease states and cerebral circulation by the use of magnetic resonance imaging (MRI). We have used, in particular, gadolinium-based polymer MRI contrast agents, which provide positive contrast for MRI. Polymer MRI contrast agents are high molecular weight polymers or polymer nanosized aggregates and have a long blood half-life. These characteristics are helpful for visualizing neurological disease states. Another project aims to understand immune responses related to the synthetic polymer poly(ethylene glycol) (PEG). Although PEG has been widely used for biopharmaceutics, the generation of antibodies against PEG is an issue that remains to be fully understood and solved. We have studied PEG-related antibody responses and know that PEG plays a unique role in PEG-specific antibody responses. Based on our results regarding PEGs' binding behaviors, we have developed new PEG technology for biopharmaceutics.



Polymer-based nanomedicines developed in the Division of Medical Engineering

Artificial Intelligence in Medicine

URL : http://www.jikei.ac.jp/academic/course/75_ultrasonic.html | E-mail : nakata@jikei.ac.jp

Research and development of a diagnostic support system that applies artificial intelligence using deep learning in medicine

1. Research on the development of a diagnostic support system for ultrasonography of the breast using deep learning
   To develop a diagnostic support system that uses artificial intelligence (AI) to make benign and malignant judgments of B-mode mammary ultrasonographic images using deep learning
2. Preparation of computer hardware and software environment for AI development
   We developed and verified the accuracy of an AI system for disease classification of ultrasonographic images of liver masses and for the judgment of benign and malignant tissue using image groups of ultrasonographic images of breast masses.

Computers for deep learning calculations

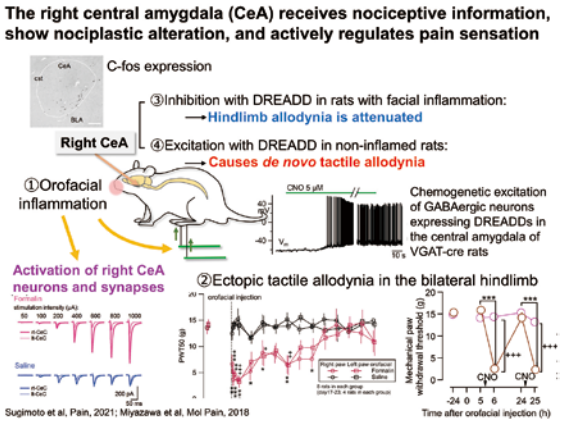
3. Research on AI for COVID-19 pneumonia detection with computed tomography of the chest
   We are developing an AI system to detect COVID-19 pneumonia using computed tomographic (CT) images of COVID-19 pneumonia and more than 40,000 CT images of healthy chests collected from data archives in China, Italy, the United States, Iran, and other countries. We are verifying the accuracy of the system.
4. Educational activities to promote the use of AI in diagnostic imaging
   We are conducing education and awareness-raising activities to explain the future prospects and principles of using AI to support diagnostic imaging.

Neuroscience

URL : http://www.jikei-neuroscience.com/website/ | E-mail : fusao@jikei.ac.jp

From synaptic transmission to behaviors – to understand why pain is aversive and unpleasant

Historical overview: The Department of Neuroscience was established in 2001 as the Laboratory of Neurophysiology of the Department of Neuroscience, with Fusao Kato as its director. In 2014 its name was changed to the Department of Neuroscience owing institutional reorganization (we still continue to use "Department of Neuroscience" for the bibliographical consistency of external publications, despite administrative affiliation as "Division of Neuroscience" according to the intraorganizational policy). This laboratory also functions as the headquarters of the Jikei Center for Neuroscience of Pain, which was created in 2014 with support from the Ministry of Education, Culture, Sports, Science and Technology.



The right central amygdala neurons play critical roles in widespread latent sensitization

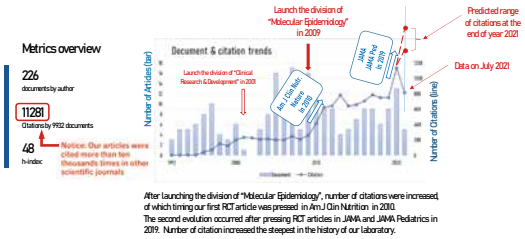
Ongoing activities: The topics of the research activities of the laboratory include brain plasticity in pain and emotion networks, particularly the parabrachio-amygdala system, the inflammation-pain link in the brain network, and the role of astrocytes in the maintenance of synaptic functions. Powerful tools to achieve these goals include electrophysiology, functional imaging, and behavioral analyses combined with interventional manipulation of neuronal activities.

Molecular Epidemiology

URL : http://docrd.jp/ | E-mail : urashima@jikei.ac.jp

Two randomized clinical trials: AMATERASU to prevent cancer relapse and Atopy Induced by Breastfeeding or Cow's Milk Formula to prevent allergies in children

In the AMATERASU trial, a randomized clinical trial of secondary prevention which included 417 patients with digestive tract cancers from the esophagus to the rectum, the 5-year relapse-free survival rate was 77% for patients who received vitamin D and 69% for patients who received a placebo and did not differ significantly[1] However, post hoc analysis of the AMATERASU trial showed that vitamin D supplementation, compared with a placebo, reduced the risk of relapse/death in the subgroup of patients with p53 protein-positive cancer.[2] We are going to start the AMATERASU2 trial to confirm the effect of vitamin D supplementation on cancer relapse and death.



Document and citation trends before and after the launch of the Division of Molecular Epidemiology

The Atopy Induced by Breastfeeding or Cow's Milk Formula (ABC) trial
Immediately after birth, newborns were randomly assigned to undergo breastfeeding with or without an amino acid–based elemental formula for at least the first 3 days of life or to undergo breastfeeding supplemented with cow's milk formula from the first day of life. The evidence suggests that food allergy, including cow's milk allergy and anaphylaxis, are primarily preventable by avoiding cow's milk formula supplementation for at least the first 3 days of life.[3] We have already launched the ABC2 trial: the title is "Primary prevention of food allergy by restricting maternal intake of processed food during the first month after birth."

References
1. JAMA. 2019; 321: 1361-1369
2. Cancer Epidemiol Biomarkers Prev 2020; 29: 406-413
3. JAMA Pediatr 2019; 173: 1137-1145

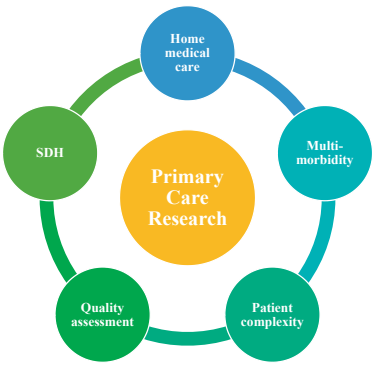
Clinical Epidemiology

URL : https://www.jikei-clinicalepi.com/ | E-mail : clinicalepi@jikei.ac.jp

Clinical research for general practice and primary care

The research topics of our division include home medical care, multimorbidity, patient complexity, quality assessment of medical care, and social determinants of health in the field of primary care research.

1) Little is known concerning the prognosis of patients receiving home medical care in Japan. The Elderly Mortality Patients Observed Within the Existing Residence (EMPOWER-JAPAN) study was a multicenter prospective cohort study. The study found a rapid decrease in the overall survival curve for the first 6 months of follow-up. In addition, the risk for overall mortality was increased for patients that were male (vs. female); had a high Charlson Comorbidity Index score, a low serum albumin level, a low Barthel Index score, a high Cornell Scale for Depression in Dementia score; were receiving oxygen therapy; were not receiving public assistance. (Kaneko M, et al, https://doi.org/10.1093/fampra/cmaa141)



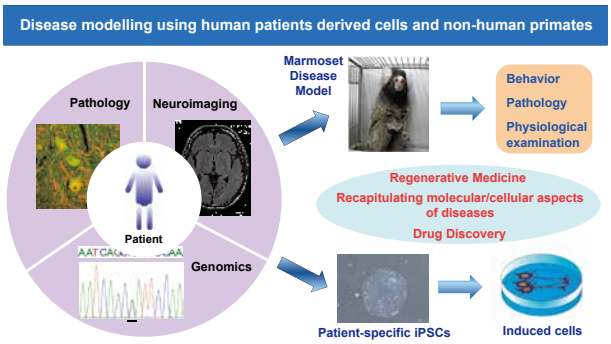
Clinical research for general practice and primary care

2) Patient experience has recently gained international popularity as a new measure of patient-centeredness. To investigate the roles of patient experience in various settings, our division has been performing health service research and developmental studies of patient experience measures. For example, the Japanese Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) scale, which is the first validated scale measuring patient experience with hospital inpatient care in Japan, was developed and has been used in a nationwide survey. (Aoki T, et al, http://dx.doi.org/10.1136/bmjopen-2020-040240)

Regenerative Medicine

URL : http://www.jikei.ac.jp/academic/course/71_saisei.html | E-mail : hjokano@jikei.ac.jp

Disease modelling and regenerative medicine utilizing human induced pluripotent stem cells and nonhuman primates



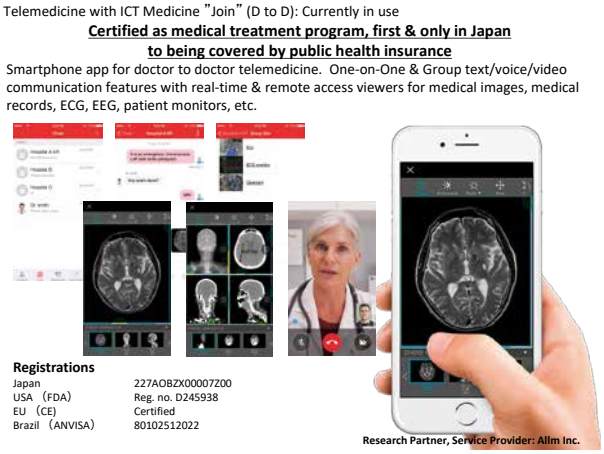
Disease modelling using cells derived from human patients and nonhuman primates

Advances in in-vitro/in-vivo disease modelling using cells derived from human patients and non-human primates will have great effects on the future opportunities and progress of biomedical research. To study the mechanisms of disease in human cells, differentiated cells of various types can be generated and expanded from patient-derived cells via induced pluripotent stem cell (iPSC) technology; these differentiated cells can also be applied to cell therapy. We have recently generated patient iPSCs to recapitulate molecular and cellular aspects of neurodegenerative diseases, including amyotrophic lateral sclerosis, Parkinson disease, and hereditary motor and sensory neuropathy. An investigation of the iPSC-derived neurons is underway and is expected to uncover the relationship between the genomic variant and the neuronal phenotype. Magnetic resonance imaging (MRI) is a powerful and flexible imaging tool for diagnosis in clinical practice but also for basic research. We use structural MRI, diffusion tensor imaging, and MR spectroscopy to investigate the structure and functions of the brain in animal models. Sophisticated MRI hardware enables image assessment from small experimental animals, such as rodents and marmosets, at a resolution of several tens of micrometers.

Innovation for Medical Information Technology

URL : http://dimitjikei.jp/ | E-mail : dimit@jikei.ac.jp

Medical use of information and communication technology from basic research to clinical applications



A program for a general image diagnosis "Join" (Image courtesy of Allm Inc.)

Remarkable advances have recently been made in information and communication technology.
The division investigates, plans, and verifies applications for healthcare professionals, personal health records, telemedicine systems, diagnostic support systems, and other tools for digital medicine overall, with the goal of improving the quality of healthcare in Japan through the utilization and application of information and communication technology. Our division's philosophy is based on healthcare services that provide a high level of patient satisfaction while decreasing the burden on healthcare professionals and, ultimately, on saving as many lives as possible and helping all people to live a long healthy life.

Summary of major research
1. Research and development to enhance the functions of the medical device software, "Join"
2. Research to optimize social welfare spending
3. Research and other efforts for medical information and communication technology

Core Research Facilities

URL : http://www.jikei.ac.jp/academic/course/19_bunsisaibo.html | E-mail : mcb@jikei.ac.jp

Annual activities of Core Research Facilities (2020)

1. Support for medical research at The Jikei University School of Medicine
   - Support for histopathological and biochemical studies
   - Open access of laboratory instruments for registered researchers
2. Research activities
   - Cancer biochemistry and biophysiology, e.g., Fushimi A, Takeyama H, Tachibana T, Manome Y. Sci Rep. 2020; 10: 12669.
   - Mass spectrometry, e.g., Akizuki S, Kawano K, Iwamoto T, Nakata K, et al. Ther Apher Dial. 2021; 25: 197.
   - Adenoviral vector construction, e.g., Mostafa D, Takahashi A, Yanagiya A, Kanegae Y, et al. RNA Biol; 2020, 17: 403.
   - Hepatology, e.g., Ishida J, Oikawa T, Fujioka K, Tsubota A, et al. J Breath Res 2021; 15: 026010.
   - Microbiology (Pathogenicity and Ecology)
   - Endocrinology (Stress responsive peptides, etc.)
   - Intellectual properties
3. University educations
   - Undergraduate students
     Immunology, Histology, Virology, Bacteriology, etc.
   - Graduate students
     Bioinformatics, Fine morphology, Immunology, Molecular Diagnosis and Therapeutics, Liver Disease Control Science, and Molecular Oncology
4. Collaboration with other facilities
   - The Tokyo University of Science, the National Cancer Center, and others

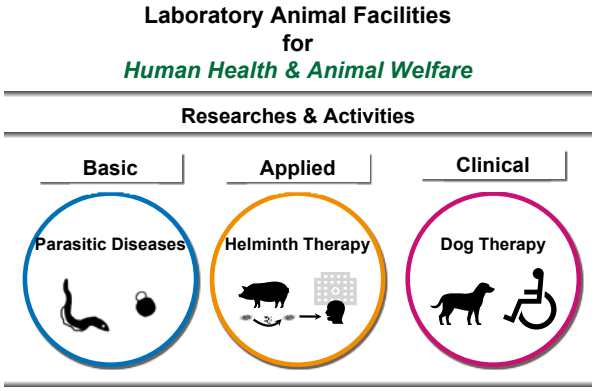
Our staff and activities

Laboratory Animal Facilities

URL : http://www.jikei.ac.jp/academic/course/28_dobutu.html | E-mail : tsakurai@jikei.ac.jp

Making contributions to medical science, human health, and animal welfare

The Laboratory Animal Facilities (LAF) is equipped with highly sophisticated facilities and high-performance devices for breeding and analyzing various animal species. The LAF is conducting multiple research studies and activities by taking full advantage of its capacities. Specifically, the basic research of the LAF is focused on protozoan diseases, such as malaria and African sleeping sickness. The LAF is studying the molecular mechanisms of host-pathogen interactions of parasites for developing the novel control measures against the deadly protozoan diseases. In addition, the LAF is conducting applied research on helminth therapy that effectively improves the symptoms of autoimmune diseases, such as inflammatory bowel disease. The LAF is developing effective techniques for preparing ova of the pig whipworm (*Trichuris suis*) for therapeutic use. Besides scientific research, the LAF is engaged in activities related to animal assisted therapy. The LAF adopts rescued dogs and trains them as therapy dogs for animal-assisted therapy to be conducted at The Jikei University Hospital. The LAF is tackling various issues for contributing to the improvement in human health and animal welfare.



Research and activities of the Laboratory Animal Facilities

Radioisotope Research Facilities

URL : http://www.jikei.ac.jp/academic/course/29_aisoto.html | E-mail : ric@jikei.ac.jp

Support for research using radioisotopes

Radioactivity is an interesting natural phenomenon that exists around us every day. In life science research, radioisotopes are used as a sensitive tracer of in-vivo chemical reactions. The Radioisotope Research Facility supports studies using radioisotopes in basic medical research.

The radioisotopes that can be used at this facility are 20 nuclides, such as ^{3}H, ^{14}C, ^{32}P, ^{35}S, ^{51}Cr, and ^{125}I. Our facility has a laboratory for pathogens of protection level 3. Instruments in our laboratory that can be shared are as follows: liquid scintillation counter, radioimmunoassay counter, bio-image analyzer, fluorometer, nanodrop, polymerase chain reaction equipment, gel imaging system, automatic film processor, ultracentrifuge, CO_2 incubator, and microplate reader.

Laboratory of radioisotope research

The following topics are studied at this facility: (1) development of methods of measuring radiation. (2) research on environmental radioactivities and radioactive materials released by the nuclear accident of 2011, (3) research on the mechanism of radiation resistance in radiation-resistant organisms, (4) analysis of the mechanism by which cancers acquire drug resistance and (5) development of medicines for overcoming resistance.

Cell Processing Facilities JIKEI-CPF

URL : http://www.jikei.ac.jp/academic/course/83_jikei-cpf.html | E-mail : murahashi@jikei.ac.jp

The JIKEI-CPF evolving into a development base for Human Cell Therapy and Gene Therapy Products

Practice of cell preparation in JIKEI-CPF

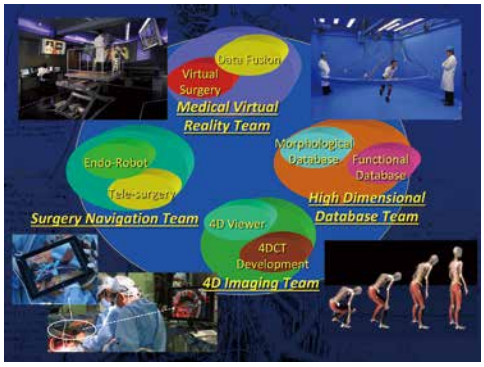
The JIKEI-CPF has been renewed as a new cell processing facility that applies the concept of manufacturing control and the quality control standards of the GMP/GCTP Ministerial Ordinance in 2020. "GMP" is an abbreviation for "Good Manufacturing Practice," which is called "Manufacturing Control and Quality Control Standards." It sets the requirements that pharmaceutical manufacturers must comply with throughout. "GCTP" is an abbreviation for "Good Gene Cellular and Tissue-based Products Manufacturing Practice" and is regarded as the standard for manufacturing control and quality control of "Human Cell Therapy and Gene Therapy Products." Because "Human Cell Therapy and Gene Therapy Products" use human-derived cells and tissues, they exhibit diverse and complex quality characteristics and have high nonuniformity. Therefore, quality is difficult to control with standards, and building a quality control system that guarantees quality by controlling the manufacturing process is important. We believe that our primary mission is to conduct the first clinical trial in humans for academia seeds. Our goal is to optimize the protocols with the findings and problems observed during the exploratory period and to connect them to the next development step. We also aim to support and activate cancer immunotherapy and regenerative medicine research through industry-academia collaboration.

Institute for High Dimensional Medical Imaging

URL : http://www.jikei.ac.jp/ihdmi | E-mail : hat@jikei.ac.jp

Realizing the future of medicine expected a decade from now by utilizing high-dimensional medical imaging engineering technology

With the development of X-ray computed tomography and magnetic resonance imaging, the detailed internal structure of the human body can now be measured as a 3-dimensional (3D) image without causing damage. In addition, The 3D image can now be converted into a (4D) image adding dynamic changes, such as functions. By applying these technologies in other sectors, new technologies, such as surgical simulation, surgical navigation, and 4D motion analysis, have been developed and offer new possibilities in diagnosis, treatment, and education in modern medicine. However, many problems must still be solved to utilize these high-dimensional (3D and 4D) medical imaging technologies in clinical practice. The institute is a research institute that can research and develop advanced medical technology in a clinical environment.



Various advanced medical technologies being researched at the Institute for High Dimensional Medical Imaging

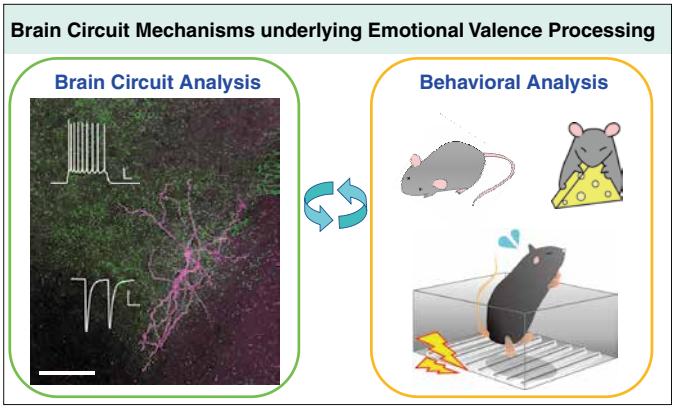
In particular, we believe that new medical technologies—3D imaging technology that can display the 3D structure of living organisms and 4D imaging technology that can recognize the dynamics of the 3D structure—can greatly contribute to the field of medicine. Our top priority is to realize as soon as possible the future of medicine that we envision 10 years from now. We aim to realize advanced medical technology needed in the clinical field by conducting research and development next to the clinical site from an academic standpoint.

Institute of Clinical Medicine and Research

URL : http://watabe-lab.jp/en/index.html | E-mail : awatabe@jikei.ac.jp

Cellular and Behavioral Neurobiology

Our research group aims to elucidate the brain circuit mechanisms underlying the emotional valence processing of sensory information, which drives various adaptive behaviors. Avoiding harm and gaining rewards are fundamental for our survival, and thus aversive and affective sensory information potently induce adaptive behaviors and memory formation. Elucidating the neuronal circuits of such valence processing is fundamental to understanding our brain functions, and dysregulation of these circuits can lead to various anxiety disorders, such as posttraumatic stress disorders and other psychiatric diseases. To address these issues, we take an interdisciplinary approach that combines electrophysiology, behavioral paradigms, and advanced technologies, including engineered optogenetics and chemogenetics.



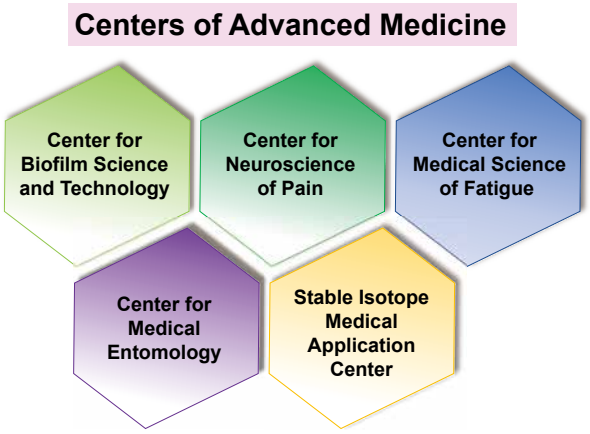
Brain circuit mechanisms underlying emotional valence processing

In addition to our research activities, we provide research support services to enable registered researchers at The Jikei University Kashiwa Campus to achieve their best results as physician-scientists.

Centers of Advanced Medicine

URL :
E-mail : hjokano@jikei.ac.jp

Organized collaboration, investment, and innovation among physicians and scientists



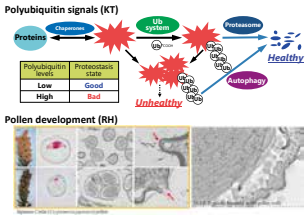
Bridging basic research and clinical investigation

The core mission of the Centers of Advanced Medicine is to lay the foundation for a focal point of translational research by exchanging the ideas between basic research and clinical investigation and to provide practical solutions to improve clinical questions. Several networks have been organized to address the bridging of basic and clinical science at The Jikei University by sharing and rationing limited resources to implement joint and collaborative research in medical sciences. However, to address the emerging clinical questions effectively and efficiently, what are greatly needed are more organized collaboration, investment, and innovation among physicians and scientists. Currently, the Centers of Advanced Medicine include 5 specialty centers for collaborative research among Jikei laboratories: the Center for Neuroscience of Pain, the Center for Medical Entomology, the Center for Medical Science of Fatigue, the Stable Isotope Medical Application Center, and the Center for Biofilm Science and Technology. Each center performs unique research based on the ideas elucidating clinical questions and the concept of bed to bench and translates research outcomes into medical practice from bench to bed.

Biology

URL : http://www.jikei.ac.jp/academic/course/35_sizenkagaku.html | E-mail : takada@jikei.ac.jp (KT), hiratsuka@jikei.ac.jp (RH)

Research on polyubiquitin signals in eukaryotes and pollen development in plants for the biomedical applications



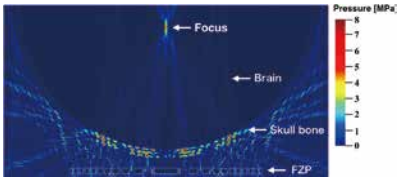
Schematic diagram of research in the biology laboratory.

Polyubiquitin signals (KT): Protein homeostasis (proteostasis) is essential for living eukaryotic cells to maintain a variety of cellular functions. Polyubiquitination induces the degradation, which is proteasomal or autophagic or both, of tagged proteins; thus, polyubiquitin signals play a fundamental role in proteostasis. We have developed a method to quantitate polyubiquitin chains in biological samples containing sodium dodecylsulfate–solubilized proteins and have attempted to establish a protocol to estimate the proteostasis state in organisms.
Pollen development (RH): The pollen development process is highly controlled by the interaction between pollen and the cells around it. To elucidate the mechanism of pollen development, we are studying the micromorphology of pollen during development by using wild-type pollen and mutant pollen with abnormal pollen growth and are analyzing the subcellular localization of proteins that function in pollen.

Physics

URL : http://www.jikei.ac.jp/academic/course/35_sizenkagaku.html | E-mail : tsuyoshi_ueta@jikei.ac.jp

Inquiry on vibrating photonic crystals and structural optimization of an ultrasonic Fresnel lens



Sound pressure distribution around and within a head for the incident plane wave focusing by an ultrasonic Fresnel lens

We have 2 major projects. One project is to investigate the properties of vibrating photonic crystals. We have found that an incident electromagnetic wave is amplified resonantly within an artificially vibrating or modulating 1-dimensional photonic crystal. We are investigating the relation between the conditions of the amplification and the virtual bound states. The other project is to investigate the structural optimization of an ultrasonic Fresnel lens. We are investigating an ultrasonic lens as an adaptively deformable phononic structure constructed by controlled micro air bubbles. In this research, we are attempting to stimulate a cerebral deep part by designing a phononic lens in which a brain and the cranial bones are also taken into account as metamaterials.

Chemistry

URL : http://www.jikei.ac.jp/academic/course/35_sizenkagaku.html | E-mail : komiya@jikei.ac.jp

Exploitation of organic and organometallic functional molecules

Synthesis-oriented organic chemistry

The research of this laboratory is focused on synthesis-oriented organic chemistry, including the synthesis of bioactive compounds and fluorine-containing materials, and, particularly, on difluoromethylene functionality. The research is also focused on the development of novel functional organometallic compounds, including highly emissive phosphorescent materials in the solid state and kinetic probes for dynamic behavior in the solution state.

Social Science (Law)

URL : http://www.jikei.ac.jp/academic/course/36_ningen.html | E-mail : jrozawa@jikei.ac.jp

Problems of constitutional law in present-day Japan and social science education

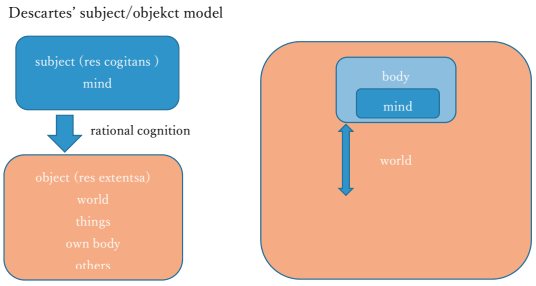
Professor Ryuichi Ozawa belongs to this laboratory and is conducting research on constitutional issues in present-day Japan.
The Social Science Laboratory is in charge of the social science education part of liberal arts education. We are conducting research for this education. The role of social science in medical education is increasing.

Human Science

URL : http://www.jikei.ac.jp/academic/course/36_ningen.html | E-mail : misakik@jikei.ac.jp

Interactive approach to the human "subject"

The subject-object scheme of René Descartes, which was dominant in modern philosophy, has been radically modified since the philosophy of the 20th century. What makes human beings "subjects" are interactions with things and others in the world. From this perspective, human perception and self-understanding have been interpreted in a new way. Out of action arises perception, which is inseparable from the consciousness of value. That sense of value also influences perception. The human perception of the world is framed by these values.



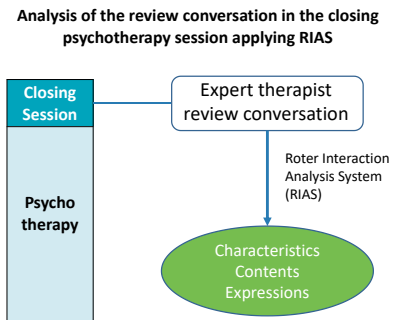
Descartes' subject/object model

Japanese

URL : http://www.jikei.ac.jp/academic/course/36_ningen.html | E-mail : inoro@jikei.ac.jp

Analysis of the review conversation in the closing psychotherapy session by applying the Roter Interaction Analysis System

The characteristics, contents, and expressions of the review conversation in the closing psychotherapy session by an expert therapist was examined by applying the Roter Interaction Analysis System, a quantitative method to analyze medical communication.
The study was published in the journal of the Japanese Federation for Psychotherapy 20(1).



Analysis of the review conversation in the closing psychotherapy session by applying the Roter Interaction Analysis System

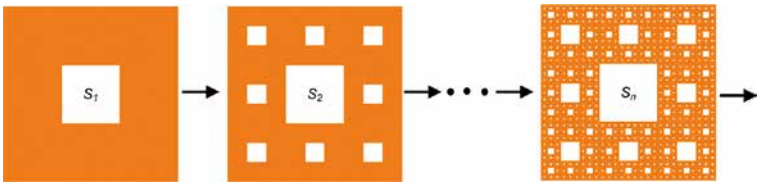
Mathematics

URL : http://www.jikei.ac.jp/academic/course/36_ningen.html | E-mail :

Pure mathematics

Our mission is the creation and discovery of mathematics on a broad front. We focus on topology and number theory. The following are recent major subjects of our research.

- Dimension and cohomological dimension theory
- Geometric topology
- Topological dynamical system
- Applications of automorphic forms to number theory



$S = \bigcap_{n=1}^{\infty} S_n$: Sierpinski carpet

English

URL : http://www.jikei.ac.jp/academic/course/37_gaikokugo.html | E-mail : alan@jikei.ac.jp

English education and medical English education

Our research focuses on the practical application of language and education theory. The goal is to provide English education that fits our students' needs in a global medical environment. We study the authentic language used in overseas medical textbooks to develop teaching materials that use the same terms with the content reduced to fundamental concepts. We coordinate our lesson topics with other departments to make our classes more relevant. We also research how to help our students improve their understanding and retention of study materials and develop higher-level thinking skills. Our lesson materials promote self-learning based on current teaching theories by having our students summarize texts and formulate questions that identify key issues. Finally, we are authoring high school and university textbooks and serving as an editor of the *Journal of Medical English Education*.

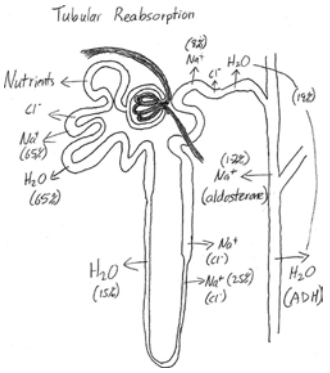


Image from the English for Anatomy class showing the main elements reabsorbed from the nephron into the blood.

First Foreign Languages

URL : http://www.jikei.ac.jp/academic/course/37_gaikokugo.html | E-mail : suzuki.katsumi@jikei.ac.jp

German contemporary literature

The research topic of this department is modern German literature by writers who have a background of being an immigrant. These include works by Şinasi Dikmen, Ilija Trojanow, Rafik Schami, Aras Ören and Sherko Fatah. Through their works, the following themes emerge: how to free oneself from prejudice, what should "homeland" mean, and how we can understand each other.

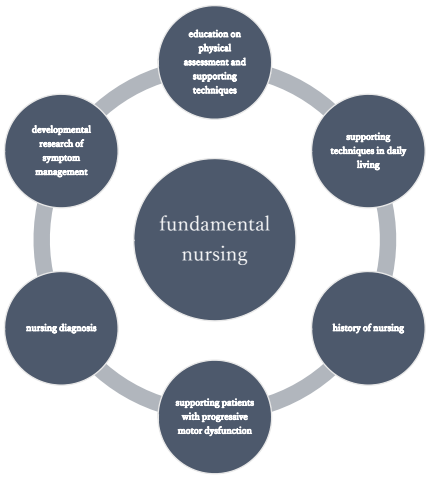
The wall will come down someday (The site of the Berlin Wall)

Fundamental Nursing

URL : http://www.jikei.ac.jp/univ/nurse/edu/e_basic01.html | E-mail :

Research activities by fundamental nursing teachers

Sachiko Tanaka: Tanaka studied the development of oral history archives of nursing. She gave a poster presentation about the ethical consideration of oral history in nursing research at the conference of the Japan Society of Nursing History.
Hiroko Yatsu: Yatsu published with 2 supervisors a revised edition book about maternity nursing skill. She gave a poster presentation about global nursing using an integrative literature review at an international conference held in Chang Mai, Thailand. The two manuscripts she wrote in 2019 about nursing theory and animal rights will be published in 2021.
Chieko Hanyu: Hanyu studies the topic of "Clinical Judgment in Nursing." She has conducted a pilot test of a clinical judgment program for nurses who have 1 year's experience.
Sumiko Satake: Satake studies the topic of "a reply of autonomic nerve activity to hearing stimulation in patients who have chronically lain in bed." In addition, she has worked as a research member of "Neuroscience Nursing" and "Positioning in Nursing."
Noriko Aoki: Aoki studies the easing of intra-abdominal pressure by changing the head elevation angle while the patient uses a bedpan.
Kiyoko Fukai: Fukai is currently the president of 2 nursing academic societies. She is conducting an interventional study of pain management while preparing papers with graduate students of her former university. In addition, 2 books on basic nursing written by her have been published.



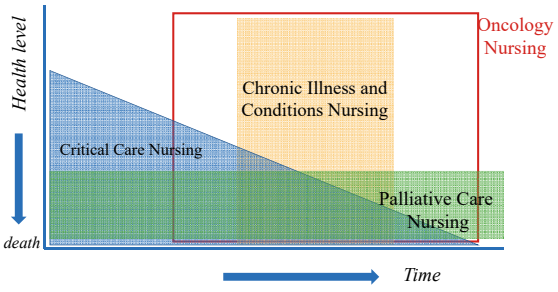
Fundametal Nursing

Adult Nursing

URL : http://www.jikei.ac.jp/univ/nurse/edu/e_adult.html | E-mail : masami.sato@jikei.ac.jp

A study of nursing practices for patients at various health levels and receiving treatment

- Critical care nursing
  A study of patients with life-threatening illnesses and their families in units for intensive care, coronary care, emergency care, and critical care. Research on support for family proxy decision-making, pain relief, and perioperative nursing.
- Oncology nursing
  Research on nursing care so that patients who have cancer, postoperative disorders due to surgical therapy, or side effects due to chemotherapy can self-care. Research on nursing care for patients with cancer who have children and are receiving treatment while returning to work.



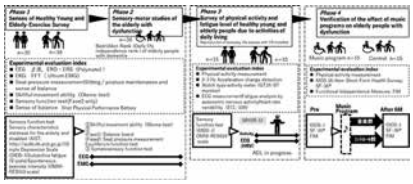
Field of study in adult nursing

- Wound care and stoma care
  Development of skin care methods to prevent skin problems and injuries in patients undergoing treatment or to maintain healthy skin. Also, research on the development of nursing care for the early healing of wounded skin and a system that guarantees the quality of nursing care.
- Continuing education for clinical nurses
  A study of the method and evaluation of continuing education for nurses engaged in critical care

Gerontological Nursing

URL : http://www.jikei.ac.jp/univ/nurse/edu/r_oldage.html | E-mail : 1.kajii@jikei.ac.jp, 2.ynakaji@jikei.ac.jp

A community system for people with dementia and their families and music rehabilitation for people who have had a stroke



Outline of research on establishing a community-based rehabilitation program with music for patients who have had a stroke

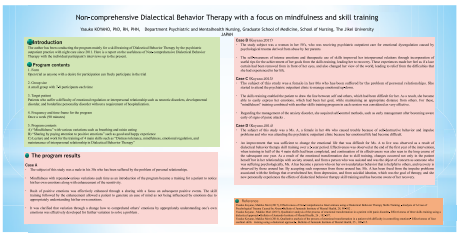
1. Community system for people with dementia and their families
   This study aims to create a community system for unemployed nurses to provide continuous support for people with dementia and their families affected by the COVID-19 pandemic. The aims of the study are to (1) clarify support needs for people with dementia and their families living in the community after the COVID-19 pandemic, (2) develop a re-education program for nurses who support them, and (3) clarify an operational system that enables unemployed nurses to perform continuous nursing support activities in the community. This research is a collaboration of The Jikei University School of Nursing, The Jikei Daisan Hospital, and surrounding areas undertaken through basic research (C) of the Grant-in-Aid for Scientific Research.
2. Music rehabilitation for people after a stroke
   The purpose of this study is to develop a long-term care support program with a comprehensive community-based care system for people after a stroke. Health professionals can assess the effectiveness of music rehabilitation, which is a combination of music and musical activities based on safety, relevance, and reliability, to meet the needs and objectives of patients of hospitals and communities. People who have had a stroke can choose to achieve their life goals through self-training in music rehabilitation, to live a better life in their immediate area, and to coexist with illness and various types of dysfunction. This research was supported by the Grant-in-Aid for Scientific Research 17K12266 and 20K11033 of the Japan Society for the Promotion of Science.

Mental Health/Psychiatric Nursing

URL : http://www.jikei.ac.jp/univ/nurse/edu/e_moral.html | E-mail : ykoyano@jikei.ac.jp

Research on the usefulness of psychological programs and research on mental health promotion

Our laboratory is engaged in research on mental health and mental health problems. This research is directed at the maintenance and improvement of mental health in healthy people and at the support for people with mental illnesses. However, the research also includes social contribution activities, such as open seminars on “Mental Health Promotion,” held with the Academic Nursing Practice Center for the Community, and aimed at providing mental health support for local residents.



Noncomprehensive dialectical behavior therapy with a focus on mindfulness and skill training

Research on the usefulness of psychological programs
Usefulness of noncomprehensive dialectical behavioral therapy with interviews of individual participants
Research on mental health promotion

- Development of a program to construct a model to support the mental health of residents by an interdisciplinary team and verification of its effects
- Research on community-based life support for people with mental disorders
- Development of a self-management program based on the well-being theory of people with mental illnesses living in the community
- Development of a self-management evaluation scale for people with mental illnesses living in the community
- Development of a remote nursing support system for people with mental illnesses living in the community
- Research on approaches to involuntary hospitalization in the department of psychiatry for emergency medical care

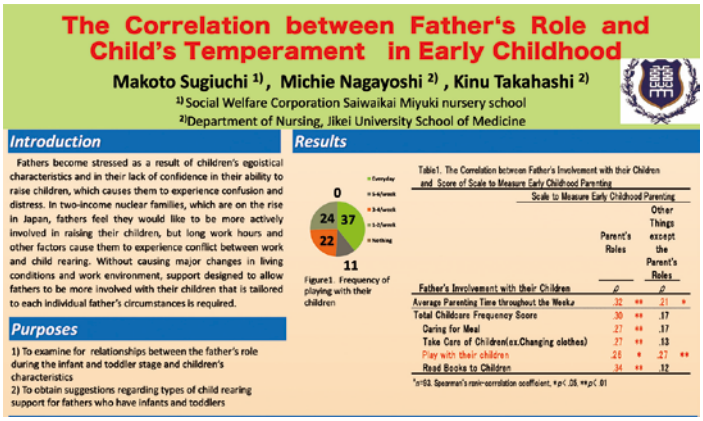
Child Nursing

URL : htt://www.jikei.ac.jp/univ/nurse/edu/e_child.html | E-mail : takahashikinu@jikei.ac.jp / mnaga1@jikei.ac.jp

Child Nursing

The purpose of child nursing research is to create nursing care for children who have chronic diseases or disabilities and live in a variety of different environments in communities or hospitals. We will explore child nursing and discuss it from a broad perspective of social problems related to children, the child and family, childhood development, and child advocacy.

- Child advocacy
- Education to enhance children's advocacy practices
- Nursing ethics education in basic nursing education
- Psychosocial development of children with cancer
- Process of self-development and long-term follow-up in survivors of childhood cancer
- Infant mental health and the parent-child relationship



The poster presentation at the 16th congress of the World Association for Infant Mental Health in Rome

Maternity Nursing

URL : http://www.jikei.ac.jp/univ/nurse/edu/e_motherhood.html | E-mail :

We make maternal health better by producing nursing knowledge to improve the health of women during pregnancy, childbirth, and the postnatal period

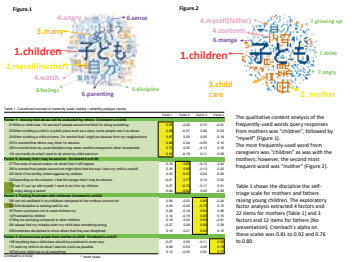
Our departments conduct research on parenting, child abuse, breastfeeding support, and nursing research. We aim to promote the parent-child relationship and make child-rearing a positive experience. Our research projects are as follows.

Perceived paternal incompetence and maltreatment

- Participants' parenting ideals were compromised in stressful or anxiety-provoking situations
- Fathers may face specific vulnerability to maladaptive parenting behavior

Development of Self-Triage Scales for Maternal and Paternal Discipline

- The exploratory factor analysis extracted 4 factors and 22 items for mothers and 3 factors and 12 items for fathers.



Figures 1 and 2 are diagrams of how mothers and fathers view childcare. Table 1 shows the self-triage scales for maternal discipline.

Empower breastfeeding mothers or bottle-feeding mothers

- Experiences of midwives who support breastfeeding mothers
- Mothers' experiences of feeding their babies: A meta-summary of qualitative research
- Social norms affecting first-time mother's intention of infant feeding
- Discourse on breastfeeding in nursing journals in Japan
- The mother's experience throughout the lactation period

Improvement of qualitative research in nursing

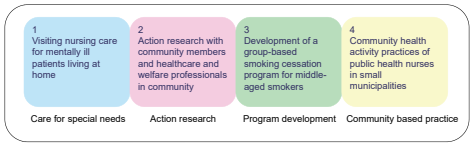
- Beth L. Rodgers' concept analysis: Re-examining research purpose, results to follow her philosophical underpinnings

Community Health Nursing

URL : http://www.jikei.ac.jp/univ/nurse/edu/e_area.html | E-mail :

Health promotion and improvement of quality of life with the community

1. Visiting nursing care for mentally ill patients living at home
   The purpose of this study is to clarify the features of assistance provided by visiting nursing care to promote continued community life by mentally ill patients living at home.



Specificity of the study viewpoints of the Department of Community Health Nursing

2. Action research with community members and healthcare and welfare professionals in the community
   The purpose of this study is to promote mutual aid in the community and to clarify the system of community cooperation.

3. Development of a group-based smoking cessation program for middle-aged smokers
   The current study aims to develop a group-based smoking cessation program based on the smoker's needs evaluated with a literature review, informant interviews, and a questionnaire survey.

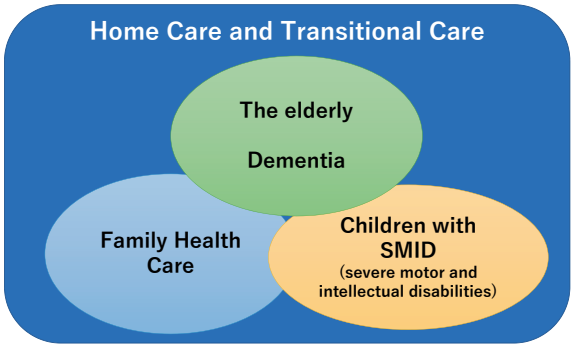
4. Community health activity practices of public health nurses in small municipalities
   This study investigates the actual situations and activities of public health nurses in small municipalities as they pursue community health actions to satisfy residents' needs.

Home Care Nursing

URL : http://www.jikei.ac.jp/univ/nurse/edu/e_homecare.html | E-mail :

Research activities in home care nursing

Japan has an aging society with a low birthrate. In this society an important issue has been to develop a comprehensive community care system that supports people to live with dignity in their own homes until the end of their lives. Therefore, our study aims to help people with health problems continue to live a better life at home or in a similar environment. Our support activities are aimed at a wide range of patients, from children to the elderly, and their families.



Overview of research activities in home care nursing

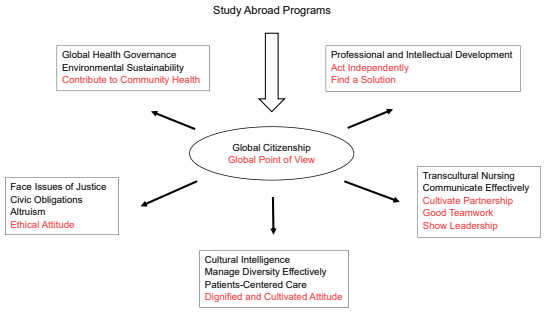
To ensure stable home care, caregiver support is essential. However, the number of family members who can fulfill their functions has decreased. This decrease is due to the aging of caregivers and the growing trend towards nuclear families. Furthermore, what the patients' families need and the type of support that would help stabilize their lives are unclear. Therefore, our research focuses on family caregivers of elderly people with dementia, children in medical care, and children with severe mental and physical disabilities, which have recently become more common. In-home nursing care is a complex interplay of people who need medical in-home care, their families, and environmental factors, including home care service providers. Therefore, in our study, we use case studies and a variety of qualitative and quantitative research methods.

Health Science

URL : http://www.jikei.ac.jp/univ/nurse/edu/e_kenkou.html E-mail : m.uchida@jikei.ac.jp

Developing study-abroad programs that contribute to the promotion of global citizenship

To develop study-abroad programs that help promote global citizenship, programs are assessed every year so that students better acquire professional knowledge and cultural intelligence. Empirical research is performed. We have 8 Diploma Policies (DP: red letters in the Figure), all of which students are expected to achieve while becoming global citizens. Students' professional and intellectual growth will bring about an attitude of acting independently (DP 1) and the ability to find a solution (DP 2). Students will be able to communicate effectively through transcultural nursing and learn how to cultivate partnerships (DP 3). They are also expected to study while maintaining teamwork and showing leadership when needed (DP 7). Cultural intelligence refers to the students' ability to effectively manage diversity and is important for providing patient-centered care and keeping a dignified and cultivated attitude (DP 6). Studying abroad will make students aware of their responsibility and obligation to act and encourage them to face issues of justice. Civic obligations, especially altruism, will foster an ethical attitude (DP 5). Students will realize the importance of both global health governance from a global point of view (DP 8) and environmental sustainability. Students will consequently wish to contribute to community health (DP 4).



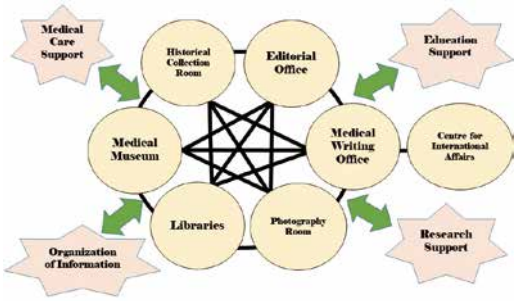
Global citizenship will enable students to achieve the 8 Diploma Policies of our faculty.

Academic Information Center

URL : http://www.jikei.ac.jp/academic/micer/ | E-mail : infctr@jikei.ac.jp

Support the activities of the university by providing comprehensive use of academic resources

The Academic Information Center consists of the Libraries (the Shimbashi Main Library and the Kokuryo Branch Library), the Editorial Office, the Medical Museum, the Photography Room, the Historical Collection Room, the Medical Writing Office, and the Centre for International Affairs (refer to p. 80).
The Libraries hold books and journals (total: 340,000) and maintain the title-list menu for bibliographic databases and more than 8,000 e-journals.
The Editorial Office is in charge of the journals published by the university.



Academic Information Center

The Medical Museum displays 1,800 gross specimens and 2,500 microscopic specimens, mainly for self-study by students.
The Photography Room supports the preparation of presentation materials by taking photographs, shooting videos, and modifying photographic and video image files.
The Historical Collection Room collects and keeps historical materials related to the university and to founder Dr. Kanehiro Takaki.
The Medical Writing Office helps students and researchers improve posters, presentations, and manuscripts submitted to journals. It also edits English journals published by the university.

Continuing Medical Education Center

URL : | E-mail :

Continuing Medical Education Center

The Continuing Medical Education Committee

Masahiro Abo, M.D., Yasuo Toriumi, M.D., Rimei Nishimura, M.D., Tatsuhiro Joki, M.D., Masanori Takeishi, M.D.

General Summary
The Continuing Medical Education (CME) Center was established in 1982 to commemorate the centennial of The Jikei University and to support the education of physicians outside the university hospital. Registered members consist of alumni throughout Japan, members of the local medical association, and physicians who have been approved by the CME Center. Members are allowed to use the facilities (video, library) of the CME Center and other facilities (medical library, medical museum) of the university. A telephone service is available at all times. Members can attend or participate in summer and monthly seminars sponsored by the CME Center.

2021 年度　慈恵医大月例セミナー
（日本医師会生涯教育講座）

開催時間　16:00～18:00
会場　慈恵大学病院 中央棟 8 階会議室

第 257 回

月日・時間	2021 年 4 月 10 日（土）16:00～17:00
テーマ	乳腺・甲状腺疾患の診断と治療
演者	乳腺・内分泌外科 田部井功 准教授
月日・時間	2021 年 4 月 10 日（土）17:00～18:00
テーマ	救急室で亡くなった症例を通して内分泌疾患を考える
演者	糖尿病・代謝・内分泌内科 山城健二 講師

第 258 回

月日・時間	2021 年 6 月 12 日（土）16:00～17:00
テーマ	睡眠薬との上手な付き合い方
演者	精神神経科 山寺亘 准教授
月日・時間	2021 年 6 月 12 日（土）17:00～18:00
テーマ	三叉神経痛
演者	脳神経外科 渡邉健太郎 助教

第 259 回

月日・時間	2021 年 11 月 13 日（土）16:00～17:00
テーマ	バイオフィルムの基礎研究と応用展開
演者	細菌学講座 杉本真也 准教授
月日・時間	2021 年 11 月 13 日（土）17:00～18:00
テーマ	消化器内視鏡領域におけるＡＩ技術の活用
演者	内視鏡部 樺俊介 助教

The Jikei University Monthly Seminar (Japan Medical Association Lifelong Education Course)

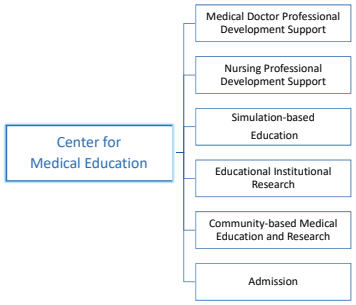
Activities
Registered members: 161 (as of April 1, 2021)
The CME Center News is mailed 3 times a year to the registered members.

Center for Medical Education

URL : http://www.jikei.ac.jp/academic/edu_center.html | E-mail : med.educ@jikei.ac.jp

The Center for Medical Education contributes to various activities in medical and nursing educations

1. Prof. Nakamura was the course director of Medicine in General I to VI and director of several educational units. Prof. Onoue, assistant prof. Okazaki, and assistant prof. Suzuki were also in charge of several educational units. Regarding graduate school education, Drs. Nakamura, Onoue, Ishibashi, and Okazaki were in charge of medical education in the common graduate school curriculum.
2. Director Takahashi organized the Branch for Nursing Professional Development Support.
3. The Branch for Educational Institutional Research analyzed students' performance data for implementation of educational activities.
4. The Branch for Simulation-based Education engaged in the improvement of the educational environment for undergraduate students and hospital staff.
5. Nurse Hazama participated as a facilitator in simulation-based education of immediate cardiac life support, basic life support, and a rapid response system and carried out the training programs of intravenous injection at levels 3 and 4 and teamwork for sudden changes in the ward for nurses working in all affiliated hospitals.
6. Prof. Nakamura was involved in several activities in the Japan Accreditation Council for Medical Education. Regarding the Common Achievement Tests Organization, Profs. Nakamura and Ishibashi were members of computer-based testing committees and were sent to several schools as test monitors, and assistant prof. Okazaki was a member of objective standardized clinical examination committees and was sent as an examination monitor.



Organization chart of the Center for Medical Education

Clinical Research Support Center

URL : http://www.jikei.ac.jp/academic/rinshoukenkyuu_center.html | E-mail :

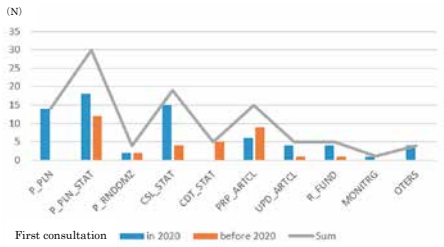
Support of clinical researches and education to improve literacy about clinical trials

The Clinical Research Support Center was founded in April 2014 to promote the proper conduct of clinical research. The center has the following functions: protocol planning, statistical analysis, data management, monitoring, support for clinical research conduct, and education. We started consulting for clinical research, including grant applications, in September 2014. From April 2019 through March 2020, we had 65 protocols of consultation. The number of matters consulted for are shown in Figure 1.

We have held "Methodology for Clinical Trial" as a course for graduate students which is open to all staff members of The Jikei University School of Medicine.

Ethical guidelines for medical and health research involving human subjects have been implemented since April 2015. The Clinical Trials Act has been enforced since April 2018, and a certified review board was established at our university in November 2018. To meet these requirements, we prepared common forms of protocol, an informed consent form, a standard operating procedure for monitoring, and other documents.

For research activities, we collaborate with many researchers to plan and conduct various types of clinical studies.



P_PLN; research planning, P_PLN_STAT; protocol planning and statistics, P_RNDOMZ; protocol for randomization/allocation/concealment of emergency key, CSL_STAT; consultation of statistical analyses, CDT_STAT; conducting statistical analysis, PRP_ARTCL; preparation of articles, UPD_ARTCL; Update of articles due to reviewers comments, R_FUND; application for competitive research fund, MONITRG; Monitoring

The number of protocols by consultation category from April 2019 through March 2020

Jikei Academic Nursing Practice Center

URL : http://www.jikei.ac.jp/univ/nurse/janp/ | E-mail : janp@jikei.ac.jp

Overview and initiatives of the Jikei Academic Nursing Practice Center

The Jikei Academic Nursing Practice (JANP) Center was established in 2018 as a place where faculty members and students of the Department of Nursing of The Jikei University School of Medicine collaborate with the local government, healthcare welfare facilities, and local residents to engage in health support and lifestyle activities for people in the community with a focus on nursing care. Academic nursing practice is the intentional integration of education, research, and clinical care from an academic standpoint with the aim of developing nursing science and improving the quality of health care. The center aims to contribute to the development of nursing science practice based on a research approach involving collaboration with people from various professions to improve health within the community.

Report on the activities

The JANP Center has 3 departments: "Everyone's Activities," "Everyone's Health Office," and "Everyone's Learning Place." In addition to the above activities, the center continues to contribute to the health of local residents by conducting community health nursing activities with nursing students and faculty members which were previously held in person.

Education at School of Medicine, The Jikei University School of Medicine

University mission

Based on its founding spirit of "Treat the patient, not the disease," our university aims to contribute to the health and welfare of humankind through the training of physicians and nurses, the promotion of medical and nursing research, and the practice of medical care.

Educational philosophy

The educational philosophy of the school of medicine is to cultivate a deep understanding of medicine by learning the basic knowledge, techniques, and philosophy of medicine and to nurture a rich humanity and the ability to make ethical and scientific judgments.
Our goal is to lay the foundation for practicing holistic medicine and medical care based on the founding spirit of "Treat the patient, not the disease."

The tradition of our university that lives in the present age

Kanehiro Takaki, who studied medicine in England, founded Sei-I-Kwai with the intention of spreading throughout Japan the British style of medical practice in 1881 (Meiji 14). British medicine emphasized humanitarianism, rather than German medicine, which, at that time, emphasized science. The training school of medical education became the starting point of our university. Our university inherited the passion of instructors who wanted to train physicians who see a patient as a "person" without being limited to the illness, based on our founding spirit of "Treat the patient, not the disease." The Jikei University have cultivated physicians and nurses who greatly contribute to human health and welfare through medical research and medical practice. Today, holistic medical care is advocated by many medical and medical education institutions but has been inherited as a tradition at our university since its foundation.

Passion, vitality, and wisdom for educational programs

The educational environment is designed to foster a rich sense of humanity, understanding in a wide range of fields, and the solid knowledge and skills of medicine and medical care. Over the years, the university's environment and curriculum have been improved in many ways. The first-year students are exposed to medicine and medical care on the green, leafy Kokuryo campus, where they learn the essence of various academic fields and aim to build a foundation for life in society. For clinical training in the later years, the affiliated teaching hospitals of the university, which have abundant medical records, also provide an excellent

educational environment. The university continues to devote its passion, vitality, and wisdom to the practice and improvement of educational programs. The driving force is the enthusiasm of the founder, who inherited the founding spirit

To the future

At the Nishi-Shimbashi Campus, the affiliated hospital has been expanded around an outpatient center so that its funsctions are enhanced and better medical care is provided. A suitable environment is provided for clinical training, medical practice, postgraduate training, and medical research. Information and communication technology, which is also included in the functions of our new outpatient building, will surely change society, including medical care and medicine, as a whole. If artificial intelligence provides support for diagnosing illnesses, healthcare professionals will be able to focus more on treating patients. With the passion, vitality, and wisdom of our university, which inherited the spirit of its founder, The Jikei University provides educational programs for future medicine and medical care to students who want to contribute to the health and welfare of humankind.

Diplomacy policy

Medical students are required to have mastered the curriculum of our university and have the following abilities by the time you graduate.

1. Medical ability to independently carry out research activities and prepare and publish treatises
2. Human competence as a medical researcher
3. Diverse leadership for medical research, education, and social contribution, and a wealth of academic knowledge that serves as a foundation for such leadership

Education at The Jikei University School of Nursing

University mission

Based on the founding spirit of "Treat the patient, not the disease," our university aims to contribute to the health and welfare of humankind through the training of physicians and nurses, the promotion of medical and nursing research, and the practice of medical care.

Educational philosophy

The educational philosophy of the School of Nursing is defined as to "Fostering creative and highly qualified nurse who can contribute to the development of nursing science by forming a rich humanity based on human dignity and by developing the basic ability of nursing to respond to professional and social demands." In other words, the philosophy is to nurture excellent nursing practitioners who have not only the knowledge and skills necessary for their profession but also a sensitivity that is close to the hearts of the sick and reasoning that can deal with the ethical and moral aspects of medical care.

Founder's words "Doctors and nurses serve as two wheels"

Nursing education at the The Jikei University can be traced to the start of nursing in Japan. While studying in the United Kingdom, the founder Kanehiro Takaki saw a nurse, in the Nightingale Ward of St. Thomas Hospital, cooperated with a doctor to provide patient-centered nursing. He stated that "Doctors and nurses serve as two wheels."
Takaki's idea is reflected by the establishment in 1992 of the Department of Nursing in the Faculty of Medicine instead of the Faculty of Nursing. In addition to the joint start-up training of the medical and nursing departments, we have incorporated many co-educational subjects, such as liberal arts subjects and clinical ethics exercises.

Aiming to be a nurse who has reliable practice ability and can practice high-quality team medical care

To develop nurses in this department who can practice high-quality team medical care, nursing students should have a place to learn and think with medical students and to deepen a mutual understanding with them. In addition, the students are required to have a solid ability to practice nursing, that is, specialized knowledge based on scientific thinking, skills based on ethical values, and individual needs to grasp the physical, psychological, and social needs of people with health problems. We provide detailed education according to the individuality and abilities of each student so that they can be equipped with the ability to find

new skills.

Having a strong understanding of the founding spirit and educational philosophy of this university, the students are also required to have an attitude of actively learning the basic knowledge and skills necessary to become an excellent nursing practitioner and to have a strong will to survive four years of student life.

Diplomacy policy

Students are required to participate in the curriculum of this department based on the founding spirit and educational philosophy of our university and acquire the following abilities by the time of graduation.

1. Problem-solving ability
   Ability to analyze issues and find the best solution based on scientific evidence in nursing practice
2. Attitude to pursue nursing ethics
   Attitude to pursue the best interests of a patient and ability to respect each other and collaborate toward the agreed goals in accordance with Kanehiro Takaki's philosophy of "Treat the patient, not the disease"
3. Ability to collaborate with multiple professions and community medical care
   Ability to collaborate with multiple occupations by using the expertise of nursing in accordance with the Takaki's philosophy of "Doctors and nurses are like two wheels of a car" in the health care welfare system
4. Leadership
   Ability to utilize the power of the members of a health care team to improve the system and lead the organization by themselves
5. International perspective
   Ability to understand the characteristics of Japanese nursing and think about nursing from an international perspective

International Exchange Activities

The university founder Dr. Kanehiro Takaki studied at St. Thomas' Hospital Medical School in London from 1875 to 1881. His experiences in London inspired him to introduce humanistic ideas of English medicine in Japan.
Shortly after returning to Japan, Dr. Takaki and his colleagues founded Sei-I-Kwai Medical School and a charity hospital, which are the origins of The Jikei University School of Medicine and The Jikei University Hospital, respectively. Dr. Takaki also established the first nursing school in Japan.

To inherit Takaki's spirit, The Jikei University offers international exchange programs to provide students, doctors, and researchers with opportunities to study abroad and to broaden their international perspective.

Overseas Study Programs

Exchange program with King's College London GKT School of Medical Education and other partnership universities

Every year, medical students (5th or 6th-year) are selected to take 1-to-2-month clinical electives at King's College London GKT School of Medical Education (former St. Thomas' Hospital Medical School in London) or partnership universities (see below). Travel and living expenses are subsidized by the university or The Jikei Alumni Association.
Nursing students (4th-year) are also selected to take 1-to-2-month clinical practice at the Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care of the King's College London.
Instead, every year, more than 30 medical students from overseas partner universities also receive clinical training at The Jikei University School of Medicine.

Extramural studies for researchers

Every year, a full-time associate professor, lecturer, or assistant who has performed excellent research is recommended to study at other institutions (mainly overseas institutions) for up to 2 years. Travel and living expenses are subsidized by the university.

Centre for International Affairs

The Centre for International Affairs was established in 2015 to promote international exchange and collaborative activities of our university. The roles of the Centre are as follows :

・Sending students to overseas universities for their clinical electives
・Accepting overseas students for their clinical electives at our university
・Holding seminars related to academic and educational exchanges
・Encouraging to share overseas experiences among students, doctors, and researchers
・Promoting cooperation with other universities to enrich exchange programs

Partnership Universities

In 1978, a partnership agreement was signed between St. Thomas' Hospital Medical School in London (now King's College London GKT School of Medical Education) and The Jikei University School of Medicine. Since then, the number of partnership universities has increased (Table 1) and exchange programs are being developed.

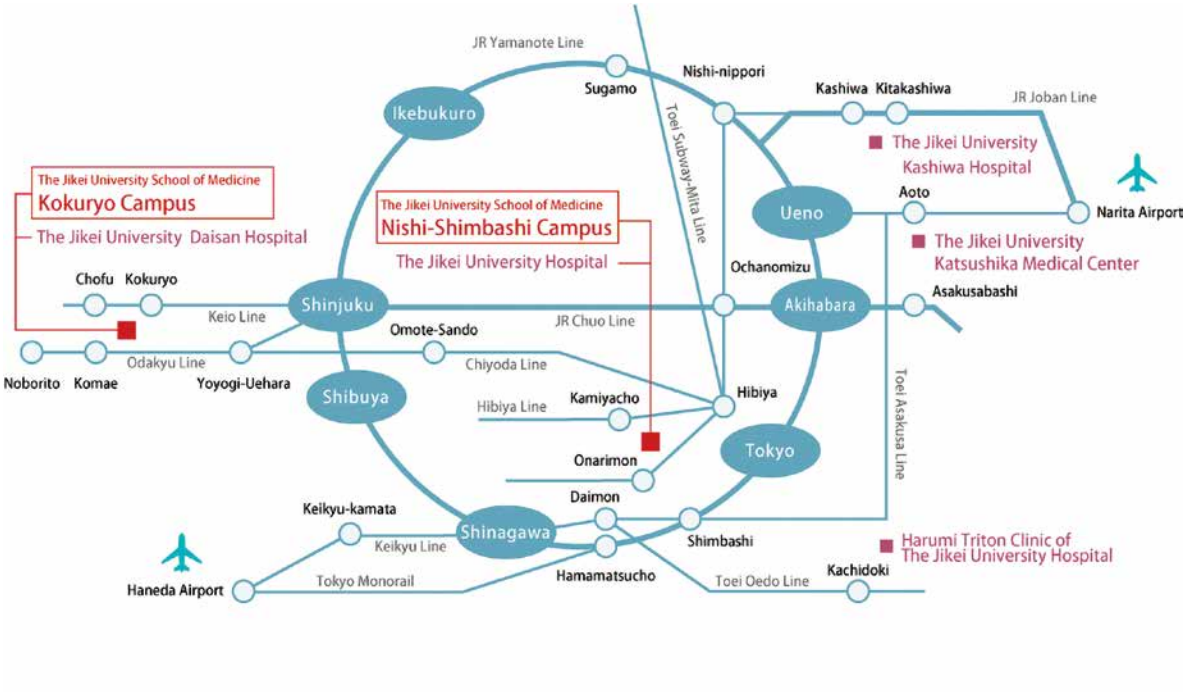
Table 1. Partnership Universities (as of May 2022)

(order of agreement dates)

King's College London GKT School of Medical Education
University of Leeds, the Faculty of Medicine
Faculty of Medicine Ludwig–Maximilians–Universitat Munchen (LMU)
National Taiwan University College of Medicine
University of California, Los Angeles (UCLA) David Geffen School of Medicine
Stanford University School of Medicine
National University of Singapore Yong Loo Lin School of Medicine
Chulalongkorn University Faculty of Medicine
University of Hawaii John A. Burns School of Medicine
Seoul National University College of Medicine
The University of Hong Kong LKS Faculty of Medicine
The University of Queensland
Mayo Clinic College of Medicine and Science
Medical University of Vienna

The Jikei University

www.jikei.ac.jp



The Jikei University School of Medicine

Nishi-Shimbashi Campus (School of Medicine)
3-25-8 Nishi-Shimbashi, Minato-ku Tokyo 105-8461, Japan
Tel : 81-(0)3-3433-1111

Kokuryo Campus (School of Medicine/Nursing)
8-3-1 Kokuryocho, Chofu-shi Tokyo 182-8570, Japan

University Hospitals

The Jikei University Hospital
3-19-18 Nishi-Shimbashi, Minato-ku Tokyo 105-8471, Japan

The Jikei University Katsushika Medical Center
6-41-2 Aoto, Katsushika-ku Tokyo 125-8506, Japan

The Jikei University Daisan Hospital
4-11-1, Izumihoncho, Komae-shi Tokyo 201-8601, Japan

Harumi Triton Clinic of the Jikei University Hospital
1-8-8 Harumi, Chuou-ku Tokyo 104-0053, Japan

The Jikei University Kashiwa Hospital
163-1 Kashiwashita, Kashiwa-shi Chiba 277-8567, Japan

Research Activities

The Jikei University School of Medicine/School of Nursing

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