GUNMA UNIVERSITY Graduate School of Medicine

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# 群馬大学 大学院

医学系研究科生命医科学専攻【修士課程】 Course of Biomedical Sciences [Master's Program]

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Dean, Course of Biomedical Sciences **Takashi Minegishi** 

### A Message from the Dean

Course of Biomedical Sciences (Master's Program) was installed in 2007 at Graduate School of Medicine. Due to rapid development of life science, medicine, and information science, a possibility of utilizing the advance in bio-medical fields, in such as a bio-correlative industry, drug design, and advanced medicine, has increased. Therefore, Course of Biomedical Sciences was established in order to grow researcher, educator and high-level medical person, who can exercise leadership in life science, medicine and medical field.

In Course of Biomedical Sciences, the interdisciplinary field of medicine and life science is set as the main object of education and research. Namely, it aims at advancing a life process for analysis from a medical viewpoint, promoting the education and research of the interdisciplinary field in medicine and medical treatment, learning and developing new medicine and medical technology which aimed at improvement of health and the quality of life, raising advanced medical person, etc.

Although the graduates of this Course would be divided into the advanced profession people in each field, such as researcher, educator, medical person, and industrial person, or into those who go on to Course of Medical Sciences (Doctoral Program), playing an active part as a leader in each field will be expected, taking advantage of having learned at Course of Biomedical Sciences.

<Special Educational Course and Program>

1) Medical Physics Course

In Gunma University, heavy-ion cancer therapy was started from 2010 in Heavy-Ion Medical Center uniquely installed in Japan. Medical physicist, who takes charge of the cancer medical treatment using radiation, such as heavy-ion, is very insufficient in Japan. So, Medical Physics Course that aimed at cultivation of medical physicist was installed.

2) Asian Nuclear Medicine Graduate Program (ANMEG PROGRAM)

<Japanese Government (Monbukagakusho: MEXT) Scholarships Program>

This is a special program for foreign student from Asia. The mission of this program is to train specialists in Nuclear Medicine who will become leading clinicians and researchers, both in their home countries and at international level.

# Outline of Biomedical Sciences (Master's Program)

#### Aim of Master's Program for Biomedical Sciences

Recent advances in life sciences and information sciences have opened up abundant prospects for applying the achievements of basic research within bio-related industries and new medical services, including drug discovery and regenerative medicine. At the same time, there is a need to solve many challenges, such as medical ethics and information security that are associated with advanced medical technology, and community healthcare support in our aging society, which are opening up a wide range of potential roles for medical researchers and health professionals. Many doors are being opened to non-medical school graduates and trained researchers, educators, and/or highly skilled workers who can exercise leadership in the life sciences and medical fields. However, there is a looming shortage of researchers/educators able to respond to the needs of society and who can take an active role in Biomedical Sciences, this new interdisciplinary field between life sciences and medicine.

There is also a growing number of non-medicine, non-veterinary, and non-dentistry graduates who are hoping to pursue their interest in life science research or medical fields; however, before these graduates can enter a graduate school of medicine to take a PhD course, they either need to have obtained a Master's Degree or must have more than two years' research experience at a university or research institute. Gunma University Graduate School of Medicine has been shifting its focus of interest to new interdisciplinary fields. For example, in 2003, we re-organized our Medical Sciences Course (Doctoral Program) and our research and educational system into a basic plus clinical integrated style, and established a PhD program in health sciences, now being run by the Graduate School of Health Sciences. The implementation of a day/evening course system for both programs allowed us to offer the course to mature students not from only the medical and health science fields, but also from related fields. However, we were still unable to accept graduates from facilities other than medicine, veterinary, or dentistry directly to our medical sciences course.

In response to increasing demand, and to broaden our intake of graduates from other faculties, we have established a Biomedical Science Course (Master's program) within the Graduate School of Medicine. This program aims to educate non-medical school graduates in the fundamental knowledge and skills needed to engage in the type of independent research that increasingly underpins medical and life sciences, and to foster leadership in medical-related fields on the part of health professional experts.

#### **2** Research conducted in Biomedical Sciences

Biomedical Sciences is a general term for the life sciences field, which overlaps medicine, life sciences, and other medical interdisciplinary fields. The Biomedical Sciences Course is designed to draw together life sciences and traditional basic medicine/clinical medicine as educational and research subjects to promote the elucidation of biological processes from a medical perspective and to establish Biomedical Sciences as a discipline that is aimed at the creation of new medical care: not only diagnosis and treatment, but also the promotion of health and improvement of quality of life.

#### **3** Career options after earning Master's Degree

This Master's course will train students in the biomedical sciences. It is hoped they will acquire basic knowledge of medicine, and come to understand the relationship between medicine and life sciences. We hope graduates will become researchers who can propose and conduct original research in biomedical sciences and academic medicine.

Graduates of this Master's Program can expect to become:

- 1. Educators and/ or researchers in the area of biomedical sciences (eg. life sciences or medical science related fields)
- 2. Highly trained experts in the fields of medicine, welfare, pharmacology, biology-related industries
- 3. Those who continue their education in Medical Sciences (Doctoral program) course



### Outline of Biomedical Sciences (Master's Program)

#### 4 Curriculum

- 1) Subjects are categorized as Basic Subjects, Practical Subjects, and Research Subjects.
- 2) Basic Subjects are taken in the 1st year. In "required subjects", basic knowledge on life sciences and medical sciences, and basic techniques necessary in biomedical research will be acquired. In "required elective subjects," basic biomedical knowledge needed in multiple fields will be acquired (9 credits of required subjects, 4 credits of required elective subjects <10 or more credits for Medical Physics Course>).
- 3) Practical Subjects are electives selected according to research theme and/ or postgraduate career. Practical and applied knowledge needed for specialization and/ or research in chosen fields will be acquired (4 or more credits of Practical Subjects<10 or more credits for Medical Physics Course>).
- 4) In Research Subjects, students will conduct biomedical research in their chosen field and compose a master's thesis. They will acquire knowledge and techniques needed to propose and conduct research, and present research findings (13 credits of Research Subjects).

Requirements for degree award

- -Acquisition of required credits
- -Successful completion of Master's thesis review process and passing final examination

# **Graduation Requirements**

Curriculum										
		units Te		Teac	Teaching methods					
subdivision	Subject	An academic year	Required subjects	selectable Required subjects	Elective subjects	Lecture	Seminar	Technical Course		Remarks
	Introduction to Clinical Sciences	1	2			0			)	
	Philosophy	1	2			0				<b>-</b>
	Basic Scientific Language	1	2			0			}	Take all these required subjects
	Statistical Informatics	1	2				0			required subjects
	Bio-Scientific Training	1	1					$\circ$	Į	
Basic	Anatomy	1		2		0				Take more than 2 out of 5 subjects for 4
	Analytical Physiology	1		2		0				units or more.
	Biomolecular Chemistry	1		2		0			}	%[Analytical Physiology]
	Socio-Environmental Medicine	1		2		0				corresponds to
	Laboratory Animal Science	1		2			0		J	"Interative Physiology" or "Neurophysiology"
	subtotal (10 subjects)	-	9	10	0					
	Molecular and cellular biology	2			2	0			)	
	An Introduction to Pathology	2			2	0				
	Bacteriology & Infection Control	2			2	0				
	Neuroscience lecture	2			2	0				
	Reproduction, Regeneration and Development	2			2	0				
	Informational Management	2			2	0				Take 2 subjects for 4
Practical	International Public Health	2			2	0			ſ	units or more.
	Ion beam technology for bioengineering	2			2	0				
	Drug Discovery	2			2		0			
	Clinical Trial and Research	2			2		0			
	Exercises in Genomic Medicine	2			2		0			
	Rihabilitation Medicine & Sociology	2			2		0		)	
	subtotal (12 subjects)	-	0	0	24					
	Biomedical Scineces Methodology	1~2	2				0		٦	
rocorab	Biomedical Sciences Research	1~2	10				0		ł	required subjects
research	Research Discussion Seminar	2	1				0		J	
	subtotal (3 subjects)	-	13	0	0		-			
total (25 subjects)		_	22	10	24		-			
Degree Master (Biomedical Science)										
Required terms									rms	
Students should 1) obtain units described above, 2) write a dissertation with mentors' guidance, and 3) pass the thesis defense.							terms per year			two terms
							school weeks per terms			15 weeks
							time of one class			60-90 minutes

#### Asian Nuclear Medicine Graduate Program (ANMEG Program)

(Special Programmes with MEXT Scholarships Guaranteed for International Students)

This program started in autumn 2013.

The mission of this program is to train specialists in Nuclear Medicine destined to become leading clinicians and researchers, both in their home countries and at the international level.

Applicants eligible for the Master's Course are individuals licensed as radiologic technologists or who have completed a Bachelor's Course in natural sciences in their home countries. Technologists and researchers based in universities and university hospitals are preferred, but this is not an absolute requirement.

URL:http://www.med.gunma-u.ac.jp/en/anmeg/ANMEG\_Program.pdf

### Educational Policy

Course of Biomedical Sciences in Graduate School of Medicine, Gunma University (Master's Program)

#### Admission Policy

~The Biomedical Sciences course is looking for the following candidates.~

We accept the following candidates who have scholastic knowledge and ability for learning and research in our course.

- 1. Person who are willing to contribute to social development as an expert in the field of medical sciences, medical cares and medical welfare.
- 2. Person who are willing to contribute to human and social development as a researcher in medical sciences by proceeding to doctoral program after taking the Biomedical Sciences course.

#### **Curriculum Policy**

#### $\sim$ The Biomedical Sciences course is doing the following education and research. $\sim$

The Biomedical Sciences course which is interdisciplinary region between life sciences and medical sciences is doing the following education and research.

- Promoting the elucidation of biological processes from a medical perspective, and to do the systematic education in area of Biomedical Sciences who will deliver new forms of medical care : not only diagnoses and treatments, but also the promotion of good health and improved quality of life.
- After proceeding fundamental knowledge of life sciences/medical sciences/ medical treatments, basic techniques and morals that we need, applicable and practical knowledge that is appropriate to the research project or the student's career options after earning a Master's Degree.
- 3. The knowledge needed to propose, implement and apply a research project and techniques for presenting research result will be acquired. Also, research will be carried in a specialized field and the research outcome will be compiled as a thesis for growing the leader.

#### **Diploma Policy**

#### $\sim$ The Biomedical Sciences course grow the following candidates. $\sim$

We grow the person who are based on the deep moral and knowledge and have a skill of self-research though our education.

We will be prized the diploma the following person who fulfill the graduated terms that we made.

- 1. People who proceeded the special knowledge and advanced skill that could be active by life sciences, medical sciences, medical treatments and medical welfare.
- 2. People who can participate the research taking the leadership in Biomedical Sciences course.

### Introduction of Research Area

#### **Basic Medicine**



The basic medicine consists of 14 fields.

Research and education of biomedical sciences will be conducted based on basic medicine.

#### **Clinical Medicine**



The clinical medicine consists of 16 fields (Including 2 Internal Medicine subdivision and 1 Surgical Medicine subdivision). Research and education of biomedical sciences will be conducted based on clinical medicine.

#### Cooprative and joint Department



The cooperative department and joint department consist of 9 fields of Institute for Molecular and Cellular Regulation, 2 clinical division of University Hospital, 2 fields of Heavy Ion Medical Center, and 1 field of Takasaki Advanced Radiation Research Institute, Japan Atomic Energy Agency.

#### Anatomy

Anatomy and Cell Biology Molecular and Cellular Neurobiology Biochemistry Integrative Physiology Neurophysiology and Neural Repair Neurobiology and Behavior Genetic and Behavioral Neuroscience Molecular Pharmacology and Oncology Bacteriology Parasitology Public Health Legal Medicine Medical Philosophy and Ethics Cardiovascular Medicine (Internal Medicine Subdivision) Endocrinology and Metabolism (Internal Medicine Subdivision) Gastroenterological Surgery (Surgical Medicine Subdivision) Radiation Oncology **Diagnostic Radiology and** Nuclear Medicine **Psychiatry and Neuroscience General Practice Medicine Rehabilitation Medicine Clinical Laboratory Medicine** Human Pathology **Diagnostic Pathology Pediatrics Obstetrics and Gynecology** Urology Otolaryngology-Head and NeckSurgery Clinical Pharmacology

(University Hospital) Clinical Trials and Regulatory Science Medical Informatics

(Institute for Molecular and Cellular Regulation)

Molecular Traffic

Medical Neuroscience

Secretion Biology

Molecular Membrane Biology Molecular Endocrinology and Metabolism

Developmental Biology and Metabolism

Metabolic Signaling

**Molecular Genetics** 

**Genome Sciences** 

(Heavy Ion Clinical Medicine) Medical Physics and Biology for Ion Therapy

Heavy Ion Clinical Medicine

(Takasaki Advanced Radiation Research Institute, National Institute for Quantum and Radiological Sciences and Technology)

Quantum Biology

Note : Inquiries about admission should be made directly to supervisors in desired Research Area of Study (from page 8 on) prior to the actual application process. Major Department can be changed at the end of the 1<sup>st</sup> semester of the 1<sup>st</sup> year.

#### Basic Medicine

#### Anatomy

Research themes of our laboratory are 1) molecular cell biology of functional proteins of the skeletal muscle and 2) expression and function of cell adhesion molecules during early development. For the former, we are now concentrating on studying cytoskeletal anchoring systems to the sarcolemma and vesicular sorting systems. For the latter, we are studying cadherin-superfamily proteins with in situ hybridization technique using zebrafish embryos that are characterized by transparency in early development. [Keywords] skeletal muscle, cytoskeleton, vesicular sorting system, embryogenesis, cell adhesion proteins

#### Anatomy and Cell Biology

We are interested in membrane channel proteins and transporter proteins, especially in water channel aquaporins. Our goal is to understand their physiological functions and relationships between these proteins and diseases. To understand the physiological functions of these proteins, we carefully investigate their tissue distributions and cellular localizations as well as their changes by using bio-imaging techniques such as immunofluorescence microscopy and immunoelectron microscopy, as well as techniques in molecular biology. [Keywords] membrane protein, water channel, transporter, immunofluorescence microscopy, immunoelectron microscopy,

molecular biology

#### Molecular and Cellular Neurobiology

We are studying the cells in the CNS from their birth to death. We aim to elucidate the molecular basis of the control of proliferation, differentiation, and survival of neural precursor cells, hoping that our results will contribute to the treatment of intractable CNS diseases in the near future. We are also studying theinteraction between neural cells and vascular cells in the CNS.

#### [Keywords] neural stem cells, neuronal precursor cells, glial precursor cells, glial cells, vascular cells, regenerative medicine

#### Biochemistry

Our research projects aim to clarify turnover of cell membrane hospholipids on various kinds of stimulation, production of bioactive lipids (lipid mediators), signal transduction through their GPCRs, and function of these bioactive lipids, using methods of biochemistry, molecular biology and cell biology. Lipid mediators may be involved in various pathological processes such as inflammation, allergic reaction, neurological disorders, and cancer proliferation. We are also working on analysis of signal transduction through DNA double strand break, and exhaustive analysis of protein and metabolite by mass spectrometry.

[Keywords] Lipid mediator, GPCR, Signal transduction, DNA double strand break, Proteome, Metabolome

#### Integrative Physiology

Small lipophilic hormones such as steroid and thyroid hormones play a crucial role in development and functional maintenance of various organs including the central nervous system. On the other hand, there are drugs and environmental chemicals whose constitutions are similar to those of these hormones. Such chemicals may disrupt endogenous hormone actions as either an agonist or antagonist. We study the effect of small lipophilic hormones on organ development and plasticity, and modulation by environmental chemicals and drugs on such process, using various techniques including behavioral analysis with gene modified animals, and cellular and molecular biological techniques.

[Keywords] hormone, development, plasticity, regeneration, environmental factors, endocrine disruption

#### Neurophysiology and Neural Repair

We are studying the mechanism underlying memory, learning and motor control as well as brain disorders and aging in terms of molecular, cellular, network and behavioral aspects. Our challenge includes development of novel therapies effective for the brain disorders. To pursue these aims, we are developing cutting-edge techniques such as novel viral vectors, genome editing technology and disease model non-human primates. Our laboratory has sufficient experimental setup to perform world top-level research.

[Keywords] Memory; Learning; Motor control; Regenerative medicine; Viral vector; Neurodegenerative disease; Marmoset; Non-human primate model; Aging; Stem cell therapy; Gene therapy; Patch clamp.

#### Neurobiology and Behavior

To understand the regulatory mechanisms of synapse morphology and function, we have studied the actin cytoskeleton in postsynaptic sites. For this research, primary cultured neurons, human iPS cells-derived neurons and knockout mice have been used with various experimental techniques including cell biology, biochemistry, molecular biology, neuronal cell culture, histochemistry, imaging and behavioral analysis. In addition, we have also studied about the effects of radiation on the synapses. These studies will shed light on the mechanisms of brain function and development of new diagnostic and therapeutic methods for neurological and psychiatric disorders. [Keywords] Synaptic morphology and function, Actin cytoskeleton, Imaging techniques, Human iPS cells-derived neurons,

#### Radiation damage

#### Noriyuki Koibuchi

Hirokazu Hirai

Tomoaki Shirao

Toshiyuki Matsuzaki

Yasuki Ishizaki

Takashi Izumi

Hiroshi Yorifuji

#### Genetic and Behavioral Neuroscience

We are studying the role of neurotransmitter GABA in brain functions such as emotion and the properties of GABAergic neurons through the generation and analyses of genetically engineered rodents such as conditional knockout mice and transgenic rats. We are also interested in the relationship between the deficits in GABAergic neurons and neuropsychiatric disorders. We have established model mice for schizophrenia or epilepsy and are characterizing them to elucidate the pathogenesis and/or pathophysiology of these disorders. [Keywords] neurotransmitter, GABA, knockout mice, transgenic rats, neuropsychiatric disorders, model mouse

#### Molecular Pharmacology and Oncology Masahiko Nishiyama

The development of molecular targeting drugs has accellerated advances in drug treatment for cancer. Students study the interaction of drugs in the levels of molecular, cellular, tissue, organ and an individual in order to better understand the mechanisms, and challenge translational research that facilitates the translation of findings from basic science to practical applications, which might lead to new drug discoveries, identification of novel biomarkers, and development of novel anticancer therapies: Students experience a variety of research processes of drug development from genome-wide screening of novel medical seeds to mega-clinical trial to evaluate the efficacy and toxicity of new drugs or therapies.

[Keywords] cancer, translational research, drug action mechanisms, genome-based drug discovery, oncology biomarker

#### Bacteriology

Nosocomial infections caused by multi-drug resistant (MDR) bacteria have increased and become a worldwide social problem. Our research is focused on the major causative MDR bacteria including methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), MDR Pseudomonas aeruginosa and MDR Acinetobactor baumanni . The drug resistances and pathogenecities of MDR bacteria are examined by molecular biological methodology. The molecular mechanisms of bacterial genetic exchange system which is a significant factor for the spread of drug resistance and virulence genes are also studied.

#### [Keywords] multi-drug resistant bacteria, VRE, MDRP, enterococcus, bacteriocin, conjugative plasmid, transposon

#### Parasitology

Malaria is one of the most life-threatening infections like AIDS and tuberculosis. Our research interest is host-parasite relationship in malaria. Specifically, immune responses to malaria parasites and pathogenesis of malaria parasites are analyzed in detail. We aim to develop vaccines and drugs to control malaria by revealing host-parasite relationship from both host and parasite points of view. [Keywords] Malaria, host-parasite relationship, immunity, vaccine

#### Public Health

Public Health is the art and science to delineate the environmental and social determinants of health, and to reduce the harmful factors and to promote the supportive factors for health through the organized community efforts. Our research topics include, the protective effect of trace elements on the development of cancer and metabolic syndrome, analytical studies of trace elements using HPLC-ICP-MS method, depression screening-test for the suicide prevention, and the epidemiology of the relationship between QOL and insurance system and community organization. We also examine health equity and public health ethics.

[Keywords] trace element, selenium, cancer prevention, depression screening, and epidemiology, public health ethics

#### Legal Medicine

Legal medicine is essentially the application of scientific methods and techniques to matters involving the public: that covers a lot of ground. Every science from chemistry to medicine, from biology to statistics, from dentistry to anthropology, can be a forensic science if it has some applications to the law or public matter. Especially, our group has been focusing on personal identification, which is one of the important matters of legal medicine in Japan. We have performed researches on ABO blood group, which is one of the important genetic markers in human identification. Recently, we have succeeded in identifying the erythroid cell-specific enhancer and found the deletion or impairment of the enhancer element in variant blood type Bm, leading to the development of valuable methods for the genetic diagnosis of Bm based on PCR analysis.

[Keywords] Legal medicine, personal identification, ABO blood group, enhancer

#### Medical Philosophy and Ethics

Medical practices in the clinical setting as one of existential situations are fraught with troublesome problems in terms of actual human ways of life. Clinical ethics is tackling them by, not applying some general principles or abstract doctrines mechanically to every case, but paying close attention to the individual circumstances of each case. We have been involved in the groundwork for the methodology of clinical ethics from the perspective of hermeneutics and philosophy of literature. Ethical problems in preventive medicine, the method of teaching medical ethics, meta-ethical approaches to medical ethics, and critically examining the fundamental concepts such as health and disease, are also of our core concern.

[Keywords] clinical ethics, medical ethics, philosophy of medicine, medical ethics education

### Hajime Hisaeda

Haruyoshi Tomita

Yuchio Yanagawa

#### Hiroshi Koyama

Yoshihiko Kominato

Kenji Hattori

#### **Clinical Medicine**

Cardiovascular Medicine Masahiko Kurabayashi (Internal Medicine Subdivision)

According to the change of life style and an increase in aged population, the prevalence of hypertension, diabetes, and metabolic syndrome is rapidly increasing. These changes lead to the increase in cardiovascular disease such as myocardial infarction, stroke and heart failure. This department has been interested in the pathogenesis of atherosclerosis and heart failure. In addition, this department aims to identify the molecular target to prevent or treat the fatal arrhythmia. Furthermore, we are interested in the molecular mechanism of pulmonary fibrosis. Since the completion of human genome sequence determination, life science enters into post-genome era that make possible development of tailor-made medicine, and advances in high-throughput genotyping herald a rapid expansion of genomic information in human disease. Recently, this department has been interested in the identification of biomarkers that have incremental value for prevention of cardiovascular and pulmonary disease, and key molecules that are targetable by drugs. With identification of putative risk alleles for heart failure or pulmonary fibrosis, the next step will be exploration of the function of the genes and prospective clinical trials evaluating the benefits of genotype-directed treatment of cardiovascular and pulmonary disease.

[Keywords] vascular biology, atherosclerosis, heart failure, myocardial infarction, transcription factors

Endocrinology and Metabolism Cancer, and apoplexy and myocardial infarction due to arteriosclerosis, which account for two thirds of deaths in Japan, are caused by

abnormalities of endocrine and metabolic systems, various gene mutations, and/or viral infection. We have investigated the pathogenesis of these disorders using animal models such as knockout mice, and examined gene abnormalities of samples obtained from the surgery to establish new methods of the diagnosis and therapy.

[Keywords] lifestyle-related diseases, endocrine-metabolic disorders, diabetes mellitus, respiratory allergy disorders, hepatometabolic-digestive disorders

#### Gastroenterological Surgery

In Division of Gastroenterological Surgery, researches for whole digestive tract are included. A wide variety of research, which including mechanism of carcinogenesis, growth and invasion of tumor, metastasis of tumor, suppressive research of malignancy and gastrointestinal motility research with conscious dogs, it will read to new therapeutic treatment have been energetically performed. Moreover, several clinical researches including development of excellent diagnostic method and therapeutic method have been performed continuously for the future.

[Keywords] gastrointestinal surgery, carcinogenesis, gastrointestinal motility, excellent diagnostic method, development of therapeutic method

#### **Radiation Oncology**

The Department of Radiation Oncology practices radiation therapy for various cancers comprehensively. It undertakes basic research on radiation induced apoptosis, modulation of radiation sensitivity by cell cycle regulatory proteins, hypoxia, cell- proliferation proteins, oncogenes, and cancer vasculature. In addition, clinical researches on heavy ion radiotherapy, combination of molecular targeted therapy with radiation, image based brachytherapy, and high precision radiotherapy (IMRT,SBRT, etc) are extensively conducted and promoted. [Keywords] radiation therapy, heavy ion therapy, radiation biology, radiation oncology, radiation pathology

#### Diagnostic Radiology and Nuclear Medicine Yoshito Tsushima

After the discovery of X-ray CT, there have been incredible advances in diagnostic imaging and it is now indispensible to modern medical care. In addition to CT, MRI, Ultrasound, PET, and SPECT, and the image-guided, minimally invasive techniques of interventional radiology and radioisotope therapy contribute to patient quality of life, and are also hoped to advance medical care. This field researches and new techniques in combining morphological and functional imaging and developing "patient-friendly" treatment methods such as interventional radiology and radioisotope therapy.

[Keywords] Diagnostic Radiology, Nuclear Medicine, CT, MRI, US, SPECT, PET, Interventional Radiology

#### Psychiatry and Neuroscience

Development in neurosciences and brain sciences is just revealing brain dysfunctions for etiology and pathophysiology of psychiatric disorders using neuroimaging and genetic studies. Department of Psychiatry and Neuroscience endeavors to clarify etiology and pathophysiology of "mental dysfunction" employing structural neuroimaging such as MRI, functional neuroimaging such as PET and NIRS, neurophysiology such as MEG, neuroendocrine stress responses such as DST, and animal model of psychiatric disorders. [Keywords] psychiatric disorder, neuroimaging, stress, mental illness, brain function

#### General Practice Medicine

In our department, we are going to study about many problems in gerontology, especially methods of nutrition for old people. We are interested in the effects of the lack of trace elements on immune systems or protection to infectious disease. [Keywords] general medicine, gerontology, primary care, nutrition

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Takashi Nakano

Masato Fukuda

Junichi Tamura

Hiroyuki Kuwano

Masanobu Yamada

(Internal Medicine Subdivision)

(Surgical Medicine Subdivision)

#### **Rehabilitation Medicine**

Rehabilitation medicine is a transverse field of diagnostic as well as therapeutic medicine for infant-to-elder patients with a great variety of diseases. The course of rehabilitation medicine consists of basic knowledge of rehabilitation medicine, which are kineology, central and peripheral nerve system, respiratory, cardiac systems and psychiatry. The students discuss the methods for evaluation of disabilities and the equipment for the measurements. The indications of scales, rating scores and other evaluation methods for functional and mental disorders will be studied. Biological and cytological methods are also applied to the analysis, and the cellular reaction by physical stimulation will be observed. Statistical analysis will be indicated for the measurements and evaluations. Investigation of the results and publishing some conclusions in the journal is the purpose of the courses. [Keywords] disability medicine, diagnostic medicine, therapeutic medicine

#### Clinical Laboratory Medicine

Modern medicine and preventive medicine aim at the evidence based medicine (EBM). Clinical laboratory medicine plays a key role in EBM. Therefore the research field of clinical laboratory medicine extends to every field. We are investigating sports medicine and pathophysiology of diabetes, thyroid diseases, atherosclerosis and infectious diseases using gene analysis and new methods. [Keywords] gene analysis, diabetes mellitus, thyroid disease, atherosclerosis, infectious diseases, sports medicine, clinical laboratory medicine, lifestyle-related disease

#### Human Pathology

Pathology has dual aspects, one is basic science that aims to investigate causes of diseases, and the other is pathological diagnosis and classification of diseases. We shed light on neuropathology for years, and investigate pathogenesis, pathological diagnosis, and novel therapy of various diseases of the nervous system. Especially, our research group consistently plays a central role of brain tumor pathology of Japan for decades. We chiefly handle human samples, and also possess original transgenic animals prone to brain tumors. [Keywords] neuropathology, brain tumor, molecular and cytogenetics of tumor, glial cells, translational research

#### Diagnostic Pathology

Cancer is a "genetic disease" and oncogene and tumor suppressor genes have a great influence to carcinogenesis. Most cancers develop by multi-step accumulation of genetic mutation with environmental and morphological changes. The main purpose of the course is to clarify the genetic change from morphological change or gene-related protein expression during cancer development and feedback to the diagnostic tumor pathology.

[Keywords] cancer morphology, multi-step carcinogenesis, oncogene, tumor suppressor gene, protein expression

#### Pediatrics

Chromatin is the most gigantic intra-cellular structure, which consists of genomic DNA with a length of more than 2 meters and associated proteins. Understanding of how this gigantic structure is organized and stored in the nucleus with a radius of ~10 micro meters while being ready to exert a wide variety of its coordinated functions is a central question. Our aim is to reveal regulatory mechanisms of gene expression in differentiating neural cells and post-mitotic neurons to understand brain development and its functions. We specifically focus on sub-nuclear spatial organization and post-translational modifications of chromatin, and their relevance in gene regulation in the nervous system.

[Keywords] Chromatin, nuclear organization, epigenetics, transcription, neural cells

#### Obstetrics and Gynecology

The understanding of hormonal effects and interactions on the hypothalamo-pituitary-ovarian axis is important for comprehending reproductive physiology and pathophysiology. The hormones work on the axis in a well-coordinated way and maintain physiological homeostasis. The aim of our research is to understand the functions of hormones at the molecular level, leading to the discovery of biologically active substances such as hormones and growth factors and their functional mechanisms. Our research involves the interrelationship between structures and functions of hormone receptors to elucidate the functions and mechanisms of actions of gonadotropin receptors.

[Keywords] LH receptor, FSH receptor, mutation, intracellular signal transduction, epigenetics

#### Urology

Our department has focused on understanding of the pathophysiology of prostate cancer. Basic studies cover genetic analysis, the role of lipids and intratumoral hormonal environments. Clinical studies cover the role of the tumor marker PSA and screening of prostate cancer. [Keywords] Urological tumor, prostate cancer, androgen dependency, screening

#### Hirokazu Arakawa

Takashi Minegishi (Due to retire in March 2017.)

Hideaki Yokoo

Tetsunari Oyama

Kazuhiro Suzuki

### Masami Murakami

Naoki Wada

Kazuaki Chikamatsu

Koujirou Yamamoto

#### Otolaryngology Head and Neck Surgery

Antitumor immunity plays an important role in protection against the development of malignancy. However, with a developing tumor, tumor cells acquire various mechanisms to corrupt the host antitumor responses, escape from immunosurveillance system, and grow in the host. The followings are current studies being conducted. 1) Immunological analysis of T cells in patients with head and neck cancer 2) Analysis of interaction between tumor cells and stromal cells in head and neck cancer.

[Keywords] head and neck cancer, immunosuppression, cancer vaccine, tumor microenvironment

#### Clinical Pharmacology

Recently, many new drugs with novel mechanisms have produced to improve the clinical efficacy of drug therapy, however, the development of new drugs also have produced a lot of new problems to be solved. In the pharmacotherapy, the choice of appropriate therapy or drugs for each individual patient is imperative. To establish safe and effective pharmacotherapy, we focus the variation factors for clinical efficacy of drug therapy for several diseases with gene analysis and pharmacokinetic approaches. [Keywords] Clinical pharmacology, pharmacokinetics, genetic polymorphisms, individualization of drug therapy

### **Cooperative and Joint Department**

#### (University Hospital)

**Clinical Trials and Regulatory Science** Tetsuya Nakamura

Clinical trials and research are advanced very rapidly and changed dramatically in recent years. We conduct and support a variety of clinical trials in our hospital and in our community to establish highly qualified clinical evidence. We continuously improve our knowledge and skills about trial design, data management, statistical methods, regulatory science or ethical issues in daily practice. We are trying to open a door for new world of clinical research science.

[Keywords] clinical research, study design, statistics

#### Medical Informatics

Yuichiro Saito (Associate Professor)

Today's rapid growth of hospital information systems produces huge amount of data and excellent infrastructure to let clinicians to access them. This seminar aims to learn methodology contributing human health care using medical information system. It has been exploring and presenting required data via hospital information system using ubiquitous computing technologies. [Keywords] medical information, health care, hospital information system

#### (Institute for Molecular and Cellular Regulation)

Molecular Traffic

Membrane trafficking plays essential roles not only in secretion and nutrient uptake but also in various physiological processes such as the endocrine system, the metabolic system, the nervous system, and animal development. In our laboratory, we study the molecular mechanisms and physiological functions of membrane trafficking in multicellular organisms by using the nematode Caenorhabditis elegans and mice as model systems.

Ken Sato

Akiko Hayashi-Takagi

[Keywords] membrane trafficking, secretion, metabolism, development, C. elegans, knockout mouse

#### Medical Neuroscience

The deterioration of the synapses has attracted attention as the pathophysiology of neuropsychiatric disorders. Thus, we examine the relationship between the structural and functional property of synapse and behavioral manifestations by utilizing in vivo 2-photon imaging. Furthermore, we also utilize novel optogenetic tools, which can manipulate the plasticity of the synapse in order to alter neurocircuits by extension changing the behaviors. By these two strategies, we pursue the cellular mechanism of neuropsychiatric disorders to identify a novel therapeutic target for disorders.

[Keywords] europsychiatric disorders, synapse, 2-photon imaging, signal transduction, drug discovery

#### Secretion Biology

Seiji Torii (Associate Professor)

With the decrease of neuroendocrine function, a variety of diseases increase, which include metabolic syndrome and neuronal disorders. To understand fundamental mechanisms on such human diseases, we investigate the biosynthesis and secretion of peptide hormones, and the regulation of cell survival and death, with use of molecular and cellular technical approaches. In a collaborative study with some engineering researchers, we are also developing fluorescent or luminescent probes for analyzing cancer, diabetes, and ischemia. [Keywords] peptide hormones, insulin, fluorescent probes, molecular imaging, tumor cells ,cell death

#### Molecular Membrane Biology

Eukaryotic cells are composed of several membrane-bound organelles. The shape and composition of cells are dynamically regulated during cell differentiation and are also influenced by various changes in the extracellular environment. We are interested in the regulation of organelle dynamics during animal development and use C. elegans as a model system. In particular, we explore the mechanisms and physiological roles of autophagy and endocytosis in fertilized eggs by using genetic and cell biological approaches. [Keywords] C. elegans, embryonic development, organelle, autophagy, endocytosis

#### Molecular Endocrinology and Metabolism

To understand the physiopathology of multicellular organisms, it is important to know how differentiated cells communicate with each other to regulate their function as a whole body. We especially focus on the basic biology of pancreatic beta cells, adipocytes, and immune cells, because of their involvement in the pathogenesis of endocrine and metabolic diseases such as diabetes and obesity. We approach these themes at multiple levels from molecules to whole body, and by using varying techniques of molecular biology, biochemistry, cell biology, and genetics.

[Keywords] genetically modified mouse, regulated exocytosis, endocrine and metabolic disease, live cell imaging, cell sorting

#### Developmental Biology and Metabolism Yoshio Fujitani

The dysfunction of pancreatic cells or brown adipocytes can cause diabetes and metabolic syndrome. We aim to elucidate the mechanism involved in the maintenance of homeostasis in these higher-order function cells, which is the key to glucose metabolism, from a variety of viewpoints, including developmental biology, molecular biology, and physiology. Recent studies have indicated that zinc not only plays a crucial role in the maintenance of protein structure, but is also involved in intracellular and extracellular signal transduction. Our second aim is to clarify the role of zinc signaling in diabetes and obesity. Furthermore, using our findings from basic medical research, we aim to establish a groundbreaking treatment for diabetes and obesity.

[Keywords] Pancreatic  $\beta$  cell, development, brown adipocyte, zinc biology, glucose metabolism, autophagy

#### Metabolic Signaling

In this laboratory, we are trying to elucidate the molecular mechanism by which metabolic syndrome occurs, using genetically manipulated animal models, such as knockout mice or transgenic mice. We hope that our research will contribute to the development of new strategies to treat or prevent diabetes and obesity.

[Keywords] diabetes, obesity, metabolic syndrome, transcription factor, knockout mouse, insulin, glucagon

#### Molecular Genetics

A wide variety of intrinsic and environmental stresses induce cellular senescence, apoptosis and genomic instability. These "stress responses" underlie the pathogenesis of aging-related diseases and tumor development. Specifically, we aim to clarify (i) the molecular mechanisms of oncogene-induced DNA replication stress in genomic instability and (ii) the regulatory role of HSF1, a master transcription factor of the heat shock response, in cellular senescence.

[Keywords] DNA replication stress, genomic instability, carcinogenesis, heat shock transcription factor 1, cellular senescence

#### **Genome Sciences**

Epigenetics is the study of heritable codes other than genetic codes written in A, G, C, and T. Monozygotic twins have the same genetic information; however, they have different epigenetic information and phenotype. DNA methylation and histone modifications (acetylation and methylation) serve as epigenetic code. Epigenetic status, namely, epigenome, is thought to be influenced by the environment, such as food, infection, and chemicals. This reprogramming of the epigenome by the environment could cause diseases such as cancer, and diabetes. We are going to clarify the role of epigenetic anomalies in diseases such as cancer, diabetes and obesity. [Keywords] epigenetics, epigenome, DNA methylation, microarray, genome-wide analysis

#### (Heavy Ion Clinical Medicine)

#### Medical Physics and Biology for Ion Therapy Masami Torikoshi Akihisa Takahashi

In this course, we aim to nurture researchers in the field of medical physics who are indispensable for ensuring the reliability of radiation therapy through sophisticated research and credible study of heavy ion and x-ray radiotherapies. To improve radiation therapy, we carry out in vitro and in vivo experiments regarding a variety of radiation-induced biological phenomena. Another important purpose of this course is to increase the expertise of those radiobiology specialists involved in radiation therapy.

[Keywords] Radiation therapy, particle therapy, medical physics, accelerator, radiation biology

#### Takayuki Yamashita

Tadahiro Kitamura



Izuho Hatada



Miyuki Sato (Associate Professor)

#### Heavy Ion Clinical Medicine

Tatsuya Ohno

Heavy ion radiotherapy for malignant tumors has several biophysical advantages compared with photon therapy. Heavy ion clinical medicine includes radiobiology, medical physics and engineering, tumor pathology, clinical oncology, and radiation diagnosis. This course is implemented to understand that the radiation oncology including heavy ion radiotherapy is comprehensive medical science which integrates and systematizes these wide varieties of scientific subfields to attain successful cancer treatment.

[Keywords] heavy ion radiotherapy, multimodality cancer therapy, biological response, high LET, hypofractionation, Image-guided adaptive radiotherapy

#### (Takasaki Advanced Radiation Research Institute, National Institute for Quantum and Radiological Sciences and Technology)

#### Quantum Biology

Yasuyuki Ishii Yasuhiko Kobayashi Tomihiro Kamiya

We are researching biological functions at the molecular, cellular and tissue levels using the physical and biological effects of ion beams at the ion beam irradiation facility of Takasaki Advanced Radiation Research Institute. Our final goal is the development of new methods of analyzing biological function not possible with previously established methods. The major subjects are as follows: • Making advances in micro-PIXE (Particle Induced X-ray Emission) analysis,

• Developing a technology to target and hit a cell or a tissue with a single-heavy-ion of several hundred MeV within  $1 \mu m$  spatial accuracy under microscope observation, Elucidating effects induced to normal or cancer human cells irradiated with heavy ions, and to those not irradiated (bystander effect).

[Keywords] ion beam, microbeam, micro-PIXE, single-ion hit, irradiation of targeted cell, radiomicrosurgery, bystander effect

### Location

(Showa Campus)

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