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[Inquiries concerning entrance examination and "Global Frontier in Life Science"]

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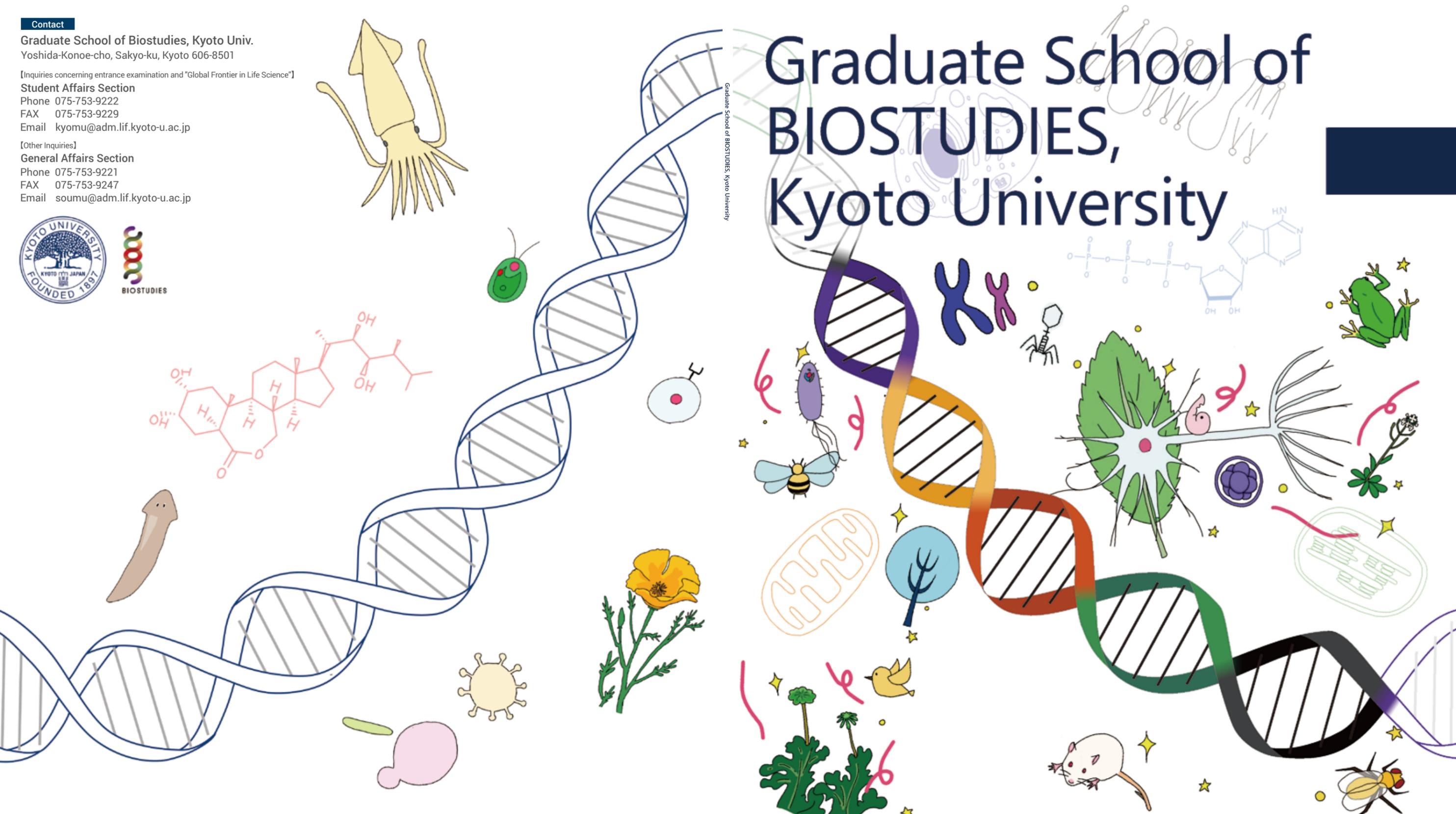
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Graduate School of BIOSTUDIES, Kyoto University



Let's Find Your Treasure!

The Graduate School of Biostudies was established in 1999 as Japan's first independent graduate school focused on life science research and education with the objective of developing individuals who can transcend the existing frameworks of science, agriculture, pharmacology, and medicine to discover and apply new knowledge related to biological phenomena. As of the end of the last academic year, a total of 1,533 students had earned their master's degree from our school, while 464 had earned their PhD; and these graduates are now contributing to life science research and the development of industry across life science related fields. This is an achievement that brings tremendous joy to all of the faculty members who have been involved in research and teaching at the Graduate School of Biostudies since its inception. In 2018, we set up two research centers, Radiation Biology Center and Research Center for Dynamic Living System, in our graduate school, aiming for a new education and research system toward 21st century biology and life science.

I believe that the greatest mission of this graduate school is to train exceptional PhDs. Since the majority of those who are reading this message are probably hoping to enroll in our school, I would like to offer my personal thoughts on earning a PhD (doctoral degree). When I was a student in the medical school, I had a strong desire to work overseas in the future. Since a Japanese medical license is not accepted overseas, I thought about going abroad as a researcher. To do so, I realized I would need to earn a PhD, so after completing my undergraduate degree, I immediately went on to graduate school and earned my PhD. When I explain what a PhD is, I tend to compare it to a driver's license. For example, if you have an F1 license, you are allowed to race F1 cars on circuits throughout the world. Similarly, if you have a PhD, you are allowed to carry out research at universities and research institutes around the world. I believe there is no other qualification that enables you to so freely do what you like. After I received my PhD, I was hired for a postdoctoral position at the Salk Institute for Biological Studies in the United States, where I was able to enjoy living abroad as I had hoped and to gain irreplaceable experiences. That was one of the most enjoyable times of my life.

So how can you earn your PhD? In order to do that, you must first find your personal treasure that gets you excited. It is like when you were a young child and you got all excited about discovering a pretty marble or seashell. But when it comes to this treasure, there are some conditions. It should have an element of being the "first in the world," and the method for finding this treasure should be through experimentation. The more experiments you carry out, the faster you will find such a treasure. In particular, when you produce an unanticipated result, you could be closing in on a large treasure, so it is important to verify your findings.

If you find your treasure, next you should teach others about it. That entails writing papers. Writing papers requires a bit of hard work, but you can ask senior students and professors in your lab to advise you, so there is absolutely no need to worry. After the paper has been presented, if you write your doctoral thesis based on that and successfully defend it, you will receive your PhD, making you qualified to work at universities and research institutes around the world. You will then use your experience to steadily find new treasures and write more papers. That is the work of a researcher. It is fun! Even if you do not become a researcher, I can assure you that the experience and confidence you will gain from discovering something that nobody else in the world knew about will serve you well no matter what type of work you do. For that reason, I hope that as you begin your graduate studies, you will devote all of your efforts to conducting lots of experiments and discovering your treasure. Then, once you have discovered your treasure, you can move on to your doctoral program with your mind at ease, further polish your skills, and obtain your PhD. Waiting on the other side of that goal line, you will find an exciting life that far exceeds your expectations. By all means, I hope that many of you will join our graduate school and will build the foundation for your future life. We, the members of the faculty, will dedicate ourselves to supporting your efforts and your growth.

Dean, MD, PhD. KAKIZUKA, Akira



MISSIONS of our GRADUATE SCHOOL

1 Provide education for pursuing the new biostudies at the world's top level

To meet the demands of the industry, college, research institutes and administrative organizations, individuals are educated in the life sciences and master the techniques for the society needs.

2 Train individuals to apply the new life sciences for the protection of the global environment and for human welfare

Integrate the knowledge and technology in the old fields of science, agriculture, medicine and pharmacology, and nurture individuals who can contribute to the human society in the 21st century.

3 Nurture individuals who can understand the various vital phenomena of the living organisms as a systemic function, and pursue these systemic functions

Nurture individuals who will be leaders in the human society to pursue their activities for the welfare and happiness of humans in the 21st century, where humans will be living in harmony with other living beings.



OPERATION POLICIES of our GRADUATE SCHOOL

1 Training of individuals with the most advanced knowledge of the life sciences for the next generation

The graduate student studies a higher level of life sciences beyond the structures of past life science-related fields at each undergraduate level to understand the integrated life sciences. The goal is to nurture a new type of individual with creative and innovative abilities to cope with the various unknown themes to be confronted by human beings in the next generation.

2 Training to establish self for society

In the Graduate School of Biostudies, individuals are trained to make a healthy and fair judgment based on the academic background of the staff and their prospects for the future; and, establish a new system to evaluate the effects of education from multiple aspects from the past.

3 Activation and flexibility of staff in the human relations

Research is pursued by each staff member independently to develop a new life science based on active exchange among the various laboratories in the graduate school.

4 Use of current post-doctoral system and evaluation of academic activities

Full use should be made of the current system, to provide the increasing necessary number of instructors per student, for the intensive training to become life scientists at an international level, for true development of a new research field.

Admissions Policy

Master's Program

As an advanced discipline that holds the key to the future of humankind, the life sciences today are undergoing a major evolutionary change. In response to this global trend, the Graduate School of Biostudies was founded in 1999 as Japan's first independent graduate school focused on the life sciences with the objective of building a world-class center for research and developing individuals who can lead the life sciences field into the next generation. Our school has engineered a true fusion of cutting-edge areas in several existing fields. By harnessing the common language of "cells, molecules, and genes" that together form the fundamental principles of life, we have developed an integrated understanding of diverse life forms and the environments they help shape, and have launched innovative efforts in research and education that will produce a new set of values for the future and dignity of life.

To meet the diverse expectations of society for advances in the life sciences, which are becoming increasingly sophisticated and complex, our school seeks students from a broad spectrum of backgrounds who share these ideals of our school, who possess basic academic skills and research aptitudes in the life sciences, and who demonstrate a strong sense of ethics and responsibility in their academic research. We especially welcome students who possess a pioneering spirit to help propel the comprehensive and advanced branches of the life sciences, free from preconceptions, while fully appreciating the dignity of life. Accordingly, the Graduate School of Biostudies endeavors to cultivate individuals with the following attributes:

1. Researchers ready to discover, or to shed fresh light on, fundamental principles of life, who will pioneer new areas of the life sciences;
2. Researchers and engineers committed to global environmental conservation and gains in human health, welfare, and well-being, who are ready to make social contributions through roles in public and private research institutions;
3. Educators and working professionals with a broad-based understanding of the varied phenomena of life in general, who are ready to make social contributions through roles in education, industry, the news media, and government;
4. Researchers, educators, engineers, and working professionals who possess strong communication skills that enable them to hold discussions with researchers and others from Japan and around the world in life science-related fields.

The entrance exam will comprise achievement tests that include a written exam to evaluate the applicant's ability to think logically in English, a skill that is required to read and analyze an article published in an international journal; a written exam to assess the applicant's general knowledge of molecular biology, cell biology, biochemistry, and other life science fields; a written exam to assess the applicant's fundamental knowledge as required to pursue his or her intended field of study; and an oral exam to assess the applicant's judgement, thinking ability, communication skills, initiative, and ethical perspective. Admissions decisions will be made based on the applicant's overall performance on these exams.

Doctoral Program

As an advanced discipline that holds the key to the future of humankind, the life sciences today are undergoing a major evolutionary change. In response to this global trend, the Graduate

School of Biostudies was founded in 1999 as Japan's first independent graduate school focused on life sciences with the objective of building a world-class center for research and developing individuals who can lead the life sciences field into the next generation. Our school has engineered a true fusion of cutting-edge areas in several existing fields. By harnessing the common language of "cells, molecules, and genes" that together form the fundamental principles of life, we have developed an integrated understanding of diverse life forms and the environments they help shape, and have launched innovative efforts in research and education that will produce a new set of values for the future and dignity of life.

To meet the diverse expectations of society for advances in the life sciences, which are becoming increasingly sophisticated and complex, our school seeks students from a broad spectrum of

backgrounds who share these ideals of our school, who possess broad academic knowledge and advanced expertise gained through their master's education, who possess strong research ability, and who demonstrate an even stronger sense of ethics and responsibility in their academic research. We especially welcome students who possess a pioneering spirit to help propel the

comprehensive and advanced branches of the life sciences, free from preconceptions, while fully appreciating the dignity of life. Accordingly, the Graduate School of Biostudies endeavors to cultivate individuals with the following attributes:

1. Researchers ready to discover, or shed fresh light on, fundamental principles of life, who will produce world-class research results in new areas of the life sciences;
2. Researchers and advanced engineers committed to global environmental conservation and gains in human health, welfare, and well-being, who are ready to assume a leading role in public and private research institutions;
3. Educational leaders and high-level working professionals with a broad-based understanding of the varied phenomena of life, who are ready to assume a leading role in education, industry, the news media, and government;
4. Researchers, educational leaders, advanced engineers, and high-level working professionals equipped with strong logical explanation and communication skills, who can convey their ideas broadly to others in Japan and around the world and assume a leading role in a variety of fields.

The entrance exam will comprise achievement tests that include a written exam to evaluate the applicant's ability to think logically in English, which is required for international communication; a presentation of the applicant's research findings during their master's program or elsewhere; and an oral exam to assess the applicant's judgement, thinking ability, communication skills, initiative, and ethical perspective. Admissions decisions will be made based on the applicant's overall performance on these exams.

Curriculum Policies of the Graduate School of Biostudies

Master's Program

The Master's Program offers courses that appropriately combine lectures, advanced studies, practical training, lab experiments, and seminars on specialized subjects in order to achieve the objectives set forth in the Diploma Policy. Courses conducted in English are also offered for international students. The curriculum is specifically designed in accordance with the following principles.

1. The curriculum is organized and delivered to cultivate broad scholarly knowledge spanning all domains of the life sciences, research capability in students' field of specialization, and specialized knowledge that will provide a foundation of competence for occupations that demand advanced expertise, based on the basic academic capabilities and specializations developed through education in the undergraduate program, as well as to enable the pursuit of cross-disciplinary study unencumbered by existing fields of specialization, which allows students to apply broad visions to put their own research into perspective and build systems of knowledge. Moreover, the curriculum includes practical training, lab experiments, workshops, and tutorials held in individual research labs that are designed to cultivate competence in research implementation, a capacity to explain research findings theoretically, communication skills, and firm ethical integrity and a sense of responsibility in academic research. Learning outcomes in each course are evaluated through written examinations, report examinations, and the outcomes of workshops, lab experiments, and practical training.
2. Emphasis is placed on students' proactive pursuit of a research theme that contributes academically or practically to the life sciences, mediated by research guidance and practical education, and leads to a master's thesis with theoretical value. This thesis is assessed by a panel of three examiners in accordance with the Diploma Policy.

The curriculum created on the basis of the above policies is presented in curriculum maps, and the details of each individual course are clearly stated in the syllabus.

Requirement for completing the Master's program

- The Life-Science Experiments and Exercises (20 credits : compulsory)
- Common Compulsory Subject (1 credit)
- Common Elective Subjects (at least 9 credits)

For graduation, the student must have enrolled for at least two years and have completed at least 30 credits. It is also required to pass the probation and an examination upon completion of the Master's thesis written under the supervision of faculty.

Doctoral Program

The Doctoral Program is comprised of lab-based research guidance and lectures designed to cultivate greater breadth of scholarly knowledge and advanced expertise in order to achieve the objectives set forth in the Diploma Policy. Courses conducted in English are also offered for international students. The curriculum is specifically designed in accordance with the following principles.

1. The curriculum is organized and delivered to further develop broad scholarly knowledge and advanced, specialized knowledge cultivated through education in the Master's Program, and to enable students to acquire the basic capabilities required of an independent researcher who can perform well in an international setting. Moreover, research guidance is provided through special seminars and special workshops in individual research labs to cultivate advanced competence in research planning and implementation, a capacity to explain research findings theoretically, communication skills, and firm ethical integrity and a strong sense of responsibility in academic research. Learning outcomes in each course are evaluated through written examinations, report examinations, and the outcomes of workshops, lab experiments, and practical training.
2. Special emphasis is placed on students' proactive pursuit of a research topic that contributes to an academic or practical area of the life sciences, mediated by research guidance and practical education, and leads to a doctoral dissertation that contributes to the generation of new knowledge. This dissertation is assessed by a panel of three examiners and one or more expert examiner in accordance with the Diploma Policy.

The curriculum created on the basis of the above policies is presented in curriculum maps, and the details of each individual course are clearly stated in the syllabus.

Requirements for completing the Doctoral program

- "The Life-Science Special Exercises" (8 credits : compulsory)
- Common Compulsory Subject (1 credit)
- Common Elective Subjects (at least 1 credit)

For graduation, the student must have enrolled for at least three years and have completed at least 10 credits. It is also required to pass the probation and the examination (thesis defense) upon completion of a Doctoral thesis written under the supervision of faculty.

Diploma Policy of the Graduate School of Biostudies

Master's Program

As an advanced discipline that holds the key to the future of humankind, the life sciences are currently undergoing a major evolutionary change. The Graduate School of Biostudies seeks to respond to this global change by building a world-class center for research and by training human resources to lead the life sciences field into the next generation. Our school has engineered a true fusion of cutting-edge areas in several existing fields and harnessed the common languages of cellular and molecular biology and genetics that together articulate the fundamental principles of life. Furthermore, it has developed an integrated understanding of diverse life forms and the environments they help shape, adding the perspective of mathematical science, and has launched innovative efforts in research and education that will define a new set of values for the future and dignity of life.

To meet the diverse expectations of society for advances in the life sciences, which are becoming increasingly sophisticated and complex, the Graduate School of Biostudies confers the degree of Master of Biostudies on students who maintain enrollment for the requisite period, complete curricular courses, earn the prescribed number or more of credits in accordance with the Curriculum Policy, and pass a review and examination of a master's thesis prepared after undergoing the required research guidance. A further prerequisite for degree conferment is the attainment of the following:

1. Broader-based scholarly knowledge; research capability in their field of specialization; and advanced, specialized knowledge required for occupations that demand advanced expertise
2. Firm ethical integrity and a sense of responsibility in academic research in the life sciences field
3. Appropriate capabilities in research implementation in order to set topics and themes based on scholarly knowledge, techniques, and skills in the life sciences field, and to achieve solutions and development thereof
4. Appropriate skills in theoretical explanation and communication required to promote one's research findings to researchers in one's own specialization and fields related thereto, and to deepen mutual understanding
5. A master's thesis, presented with theoretical rigor and clarity, with appropriate setting of research goals, planning, and execution of experimental work related thereto and discussion in regard to the findings thereof

Doctoral Program

As an advanced discipline that holds the key to the future of humankind, the life sciences are currently undergoing a major evolutionary change. The Graduate School of Biostudies seeks to respond to this global change by building a world-class center for research and training human resources to lead the life sciences field into the next generation. Our school has engineered a true fusion of cutting-edge areas in several existing fields and harnessed the common languages of cellular and molecular biology and genetics that together articulate the fundamental principles of life. Furthermore, it has developed an integrated understanding of diverse life forms and the environments they help shape, adding the perspective of mathematical science, and has launched innovative efforts in research and education that will define a new set of values for the future and dignity of life.

To meet the diverse expectations of society for advances in the life sciences, which are becoming increasingly sophisticated and complex, the Graduate School of Biostudies confers the degree of Doctor of Biostudies on students who maintain enrollment for the requisite period, complete curricular courses, earn the prescribed number or more of credits in accordance with the Curriculum Policy, and pass a review and examination of a doctoral dissertation prepared after undergoing the required research guidance. A further prerequisite for degree conferment is the attainment of the following:

1. Broad-based scholarly knowledge and advanced, specialized knowledge to engage as independent researchers or lead careers in advanced professional occupations
2. Firm ethical integrity and a strong sense of responsibility in academic research in the life sciences field
3. Advanced capabilities in research planning and execution in order to set unique topics and themes based on scholarly knowledge, techniques, and skills in the life sciences field, and to achieve solutions and development thereof through planning and implementation of joint research with other research institutions as necessary
4. Advanced skills in theoretical explanation and communication required to promote one's research findings to researchers in one's own specialization and fields related thereto, and to deepen mutual understanding
5. Doctoral dissertation that includes research findings demonstrating new discoveries or concepts that contribute academically or practically to the life sciences

Candidates considered to have made outstanding progress in their studies and research may be eligible for completion of the doctoral program in a reduced period of enrollment.

Composition of Departments

Research Laboratories in the Graduate School of Biostudies

Division of Integrated Life Science

In this division, education and research are focused on the elucidation of basic mechanisms regulating the chromosome transmission, chromosome replication, RNA architecture, cell cycle, cellular transport, cell polarity, signal transduction, growth and development, developmental plasticity, bioconversion, and environmental adaptation. Experimental approaches are taken with microorganisms, plants, and animals. We pursue education and research to elucidate the molecular aspects of Integrative Life Science.

Dept. of Gene Mechanisms Chromosome Transmission/Gene Biodynamics/Cell Cycle Regulation — 9

Major interest is the molecular mechanism of higher order phenomena (cell proliferation, morphogenesis, canceration, aging, etc.) and the cellular function (cell cycle, chromosome replication, segregation, maintenance and repair, etc.) in unicellular and multicellular organisms.

Dept. of Cell and Developmental Biology Cell Recognition and Pattern Formation/Signal Transduction — 11

We are studying signal transduction mechanisms that control organogenesis and animal growth in response to nutrition and growth factors. We are also dissecting operating principles of neuronal circuits that evoke behaviors to sensory stimuli.

Dept. of Plant Gene and Totipotency Plant Molecular Biology/Molecular and Cellular Biology of Totipotency — 13

The department pursues the basic research and application of molecular and cellular principles related to plant growth and development. We take approaches by cell biology, chemical biology, molecular and cellular biology, molecular genetics, and genomics.

Dept. of Applied Molecular Biology Biosignals and Response/Applied Molecular Microbiology/Molecular Biology of Bioresponse — 15

Signal response mechanisms have evolved in organisms through adaptations to fluctuations or changes in the natural environment. These mechanisms are being elucidated using various model organisms at different levels (individual, organ, tissue, cell, molecule and gene), and directing this knowledge toward applications with benefits to human welfare is a priority.

Dept. of Responses to Environmental Signals and Stresses Plant Developmental Biology/Plasma Membrane and Nuclear Signaling — 18

We aim at understanding fundamental systems underlying environmental responses by organisms through structural-functional study of information molecules involved in environmental responses and study of regulatory mechanisms of development in response to environmental signals.

Dept. of Molecular and Developmental Biology Developmental Neurobiology/Biochemical Cell Dynamics — 20

The development, function, and maintenance of tissues and organs are regulated by a coordinated interplay of cell-intrinsic programs and intercellular signals. We seek their mechanisms at cellular, organellar and molecular mechanisms using various model systems, including the brain and immune systems.

Dept. of Molecular and Cellular Biology Molecular and Cellular Immunology/Mammalian Molecular Biology/Developmental Dynamics/Ultrastructural Virology — 21

We study on mammalian development, differentiation, aging and viral immunity. We utilize molecular biology and developmental engineering as tools of analyses to elucidate mechanisms at molecular, cellular and animal levels.

Radiation Biology Center Radiation System Biology/Mutagenesis/Late Effects Studies/Genome Repair Dynamics/Chromosome Function and Inheritance/Stress Response — 43

Our center is trying to elucidate basic mechanisms behind biological responses to irradiation as well as chromosomal damages, and thereby pursue fundamental basis for evaluation of radiation exposure risks and for efficacious radiation therapy. To achieve the goals, our center is acting as a joint usage research center to promote collaborations among researchers in the community.

Research Center for Dynamic Living Systems Cutting-edge Bioimaging/Data-driven Modeling/Multiscale Biomechanics/Developmental Dynamics System/Physiological Network/Biological Function Manipulating — 45

We aim at understanding the life as dynamic living systems. We observe the dynamic behavior of molecules and cells with cutting-edge technologies of microscopy, optogenetics, and mouse genomics. Based on the accumulated multidimensional data, we will uncover the working principles of life by the approaches of mathematics and informatics.

Attached Research Centers

Division of Systemic Life Science

In this division, education and research are focused on the elucidation of the fundamentals of molecular and systemic biology, cell biology and immunology. Experimental approaches are taken with viruses, microorganisms, cultured cells and animals. We pursue education and research to elucidate the molecular aspects of Systemic Life Science.

Dept. of Molecular and System Biology Single-Molecule Cell Biology — 23

We will challenge direct viewing of biomolecular dynamics using single-molecule imaging and multi-target super-resolution microscopy IRIS. By elucidating the molecular basis of morphogenesis and the action of drugs, we will pursue principles in biology and seeds for drug development.

Dept. of Animal Development and Physiology Molecular and Cellular Biology/Immunobiology/Molecular Cell Biology and Development — 24

The objectives of our studies are to clarify the mechanisms that regulate hierarchical structures composing cells, tissues, organs, at the molecular, cellular, and individual levels, especially about cell growth, differentiation, cell death, cell-cell interactions, and histogenesis.

Dept. of Signal Transductions Molecular Neurobiology/Genetics — 26

Cancer, autoimmune diseases, and life-style related diseases can be caused by genetic abnormalities and aberrant response mechanisms. We aim to reveal dysfunctional biological mechanisms of cell proliferation, cancer, and immunological, genetic diseases.

Dept. of Functional Biology Functional Biology — 28

Using animal models of human diseases, such as neurodegenerations, cancers, and obesity-related diseases, and using metabolite imaging techniques, we aim to elucidate molecular bases of such diseases and develop new strategies to cure or prevent them.

Dept. of Biology Education and Heredity Science Communication and Bioethics/Science Communication/Bioeducation/Chromosome Function and Inheritance — 29

Development of effective teaching materials for biological sciences.

Dept. of Systems Biology Bioimaging and Cell Signaling/Theoretical Biology/Brain Development and Regeneration — 32

By the use of cutting-edge technologies of microscopy, optogenetics, and chemical biology, we will study the information that living organism perceive. Based on the accumulated information, mathematical models are built to understand systematically the mechanism of information processing of living organisms.

Dept. of Genome Biology Genome Maintenance/Genome Damage Signaling/Cancer Cell Biology/Chromatin Regulatory Network — 35

Genome and epigenome information are maintained by an intricate molecular system acting against exogenous and endogenous perturbations. We aim to study defects in these mechanisms that result in human disorders.

Dept. of Mammalian Regulatory Network Cell Regulation and Molecular Network/RNA Viruses/Cell Division and Differentiation/Cellular and Molecular Biomechanics — 39

Laboratories consisting of this Department study multi-dimensional networks of life signals that contribute to the integrity of higher organisms. Studies also include those utilizing viruses, animal models, and biomaterials, serving to establish basic principles in life science.

Dept. of Advanced Imaging Laboratory of Spatiotemporal Optical Control / Optical Cellular and Molecular Physiology — 41

We will understand the principle of biological functions by measuring and manipulating dynamics of genes and molecules multidimensionally with cutting-edge imaging, optical control technologies, and optical probes.

Industry-Academia Collaboration Course

Laboratory of Chromosome Transmission

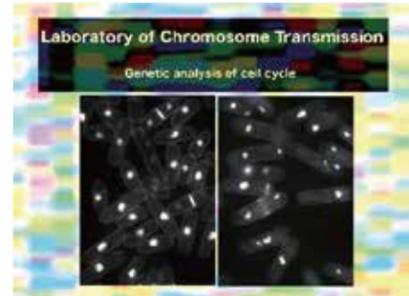
Assoc. Prof.
NAKASEKO, Yukinobu



Main theme

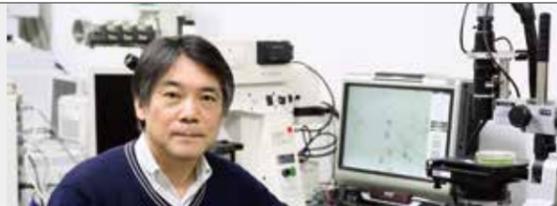
We are focusing on analyzing the genes involved in regulation of chromosome function. Especially, the genes essential for mitosis have been studied. Fission yeast *Schizosaccharomyces pombe* is used as a model system. This yeast has all basic features essential for eukaryotic cell division. Many genes have been identified which regulate the cell cycle of this yeast. Also, their functions as well as their primary structure have been shown to be conserved among all eukaryotic cells. We are trying to characterize these genes and their functions by genetical approach.

Elucidation of whole functional network of these genes is one of a goal in our research.



Laboratory of Gene Biodynamics

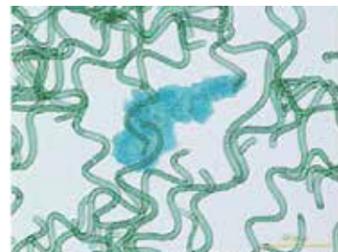
Assoc. Prof.
SHIRAIISHI, Hideaki



Main theme

We are interested in the mechanism of growth, development and evolution of photosynthetic microorganisms and currently focusing on the study of the edible cyanobacterium *Arthrospira (Spirulina) platensis*. *A. platensis* is a filamentous alkalophilic cyanobacterium that has been traditionally consumed as food by people living along the shores of alkaline lakes in several regions in the world. Because it can be cultured under alkaline conditions where growth of other microalgae is suppressed, it can be produced in mass cultures outdoors as an almost single algal strain. Because of its easiness of mass culture, it is commercially produced in many subtropical areas in the

world and consumed worldwide as food, food additives, and feed for animals and fishes. We are currently focusing on developing tools for molecular genetic studies of this cyanobacterium.



Filamentous cyanobacterium *Arthrospira platensis* and the aggregated expolysaccharides produced by them

Lab URL <http://kuchem.kyoto-u.ac.jp/seika/>

Laboratory of Cell Cycle Regulation

Professor
ISHIKAWA, Fuyuki

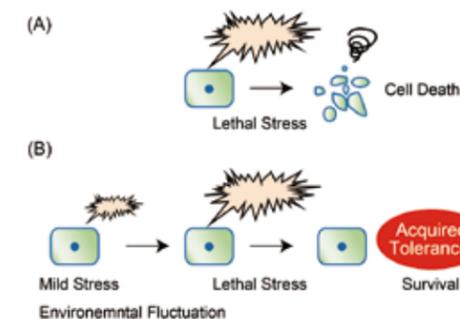


Main theme

Stable maintenance of genetic information is essential for cell viability. Genetic instability, a condition in which the genome is not properly maintained, causes numerous pathologies including cancer and aging. Telomeres, the ends of chromosomes, play a pivotal role in this process. We are interested in how telomeres protect genetic information from intrinsic and extrinsic insults. Aging can be defined as the accumulation of damaged cells caused by various stresses. Stress is generally considered to be non-adaptive. However, low-dose stress can act in an adaptive role by fostering cell resistance to prospective lethal stresses. This process is termed acquired tolerance (or hormesis) and its molecular mechanisms remain largely unknown. We are trying to understand how acquired tolerance is induced molecularly. Arguably, cancer cells

in vivo acquire stress resistance through experiencing ever-lasting environmental changes. As such, inhibiting the acquired tolerance in cancer cells may lead to fragility of cancers to various stresses, including iatrogenic ones.

- Molecular understanding of how telomeres protect DNA ends in fission yeast and mammals.
- Functional roles of acquired tolerance in various physiological and pathological conditions.
- Mechanism of retrotransposition and its impact on genomic instability in the mammalian genome.
- Development of therapeutic strategies for cancer by elucidating the mechanisms of cellular senescence.
- Mechanism of genomic instability induced by chromosome end-to-end fusions.



In general, cells exposed to lethal stress undergo cell death (A). However, cells preconditioned with mild stress can become resistant to subsequent lethal stresses (B). This process is called acquired tolerance or hormesis: an adaptive behavior that is crucial for survival in an ever-changing environment. In vivo, cancer cells can experience environmental changes such as hypoxia and iatrogenic stress. This is in contrast to normal cells that live in a stable niche given by the tissue. It is possible that cancer cells are pre-conditioned by the environmental changes to prepare for the prospective lethal stress. Therefore, inhibition of this acquired tolerance may make cancer cells sensitive to anti-cancer therapeutics.

<http://www.fish.lif.kyoto-u.ac.jp/> Lab URL

Assoc. Prof.
MIYOSHI, Tomoichiro



Assist. Prof.
NAKAOKA, Hidenori

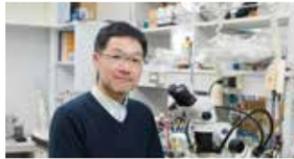


Laboratory of Cell Recognition and Pattern Formation

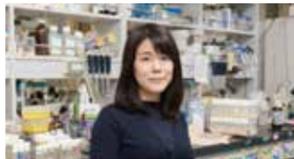
Professor UEMURA, Tadashi



Senior Lecturer USUI, Tadao



Assist. Prof. HATTORI, Yukako



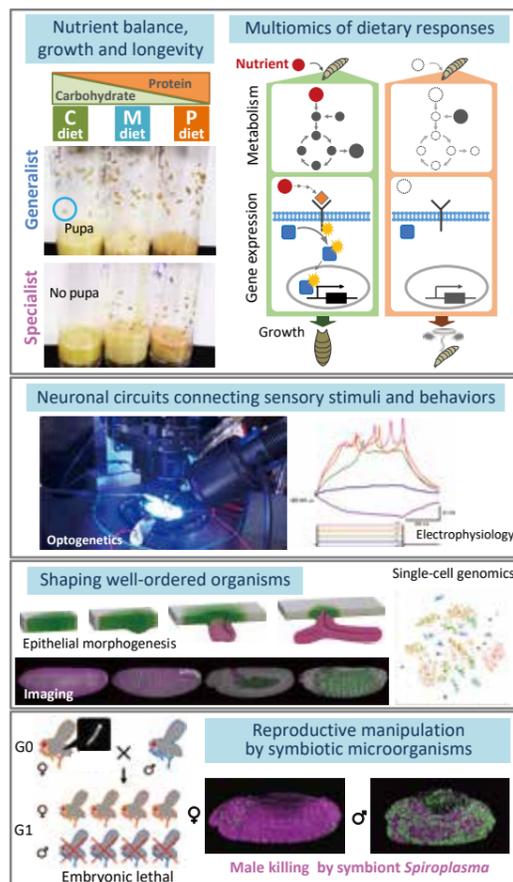
Program-Specific Assist. Prof. KONDO, Takefumi



Main theme

We are interested in:

- Contributions of nutrients and associated microbes to animal growth and aging
- Neuronal circuits that evoke selective behaviors in response to sensory stimuli
- Epithelial morphogenesis consisting of complex levels of hierarchy
- Reproductive manipulation ("male killing") caused by insect symbionts



Lab URL <http://www.cellpattern.lif.kyoto-u.ac.jp/>

Laboratory of Signal Transduction

Senior Lecturer KUSAKABE, Morioh

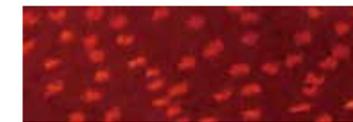
Assist. Prof. MIYATA, Yoshihiko

Main theme

We are interested in identifying and elucidating molecular mechanisms that regulate cell proliferation, cell differentiation, cell cycle, aging and developmental processes. The current topics include 1) regulatory mechanisms and functions of the MAP kinase cascade pathways, 2) identification of novel signal transduction mechanisms, 3) molecular mechanisms for life span regulation, 4) roles of protein kinases in cell cycle progression and regulation, 5) growth factor signaling mechanisms in developmental processes, 6) regulatory mechanisms for mammalian circadian clock.



Microinjection into *Xenopus laevis* embryos at the cleavage stage



Multiciliated cell differentiation in a salt-and-pepper pattern

<http://www.signal.lif.kyoto-u.ac.jp/> Lab URL

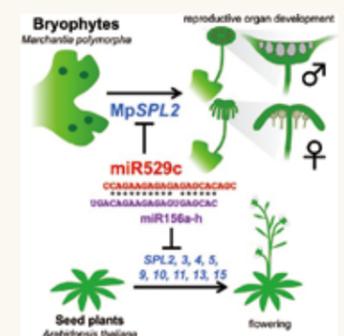
A molecular switch that regulates reproductive development is evolutionarily conserved in land plants - Short RNA molecules conserved from bryophytes to flowering plants regulate the transition from vegetative to reproductive growth phase -

This study was published in *Current Biology* on 7th October, 2019.

The research group of ex-graduate students, Ms. Chikako Inoue, Mr. Kan Kunimoto, Mr. Takashi Oogami, Assistant Research Staff, Dr. Yuki Tomita, Assistant Professor Keisuke Inoue, Associate Professor Shohei Yamaoka, Professor Takayuki Kohchi and Professor Takashi Araki, in collaboration with Professor Yuichiro Watanabe in the University of Tokyo, Associate Professor Takahiro Hamada in Okayama University of Science, and Associate Professor Masaki Shimamura in Hiroshima University, elucidated an evolutionarily conserved regulatory module that switches plant growth from vegetative to reproductive phase in land plants.

Comments from the research group: The mir156/529 microRNAs are evolutionarily conserved in land plants, and repress the expression of the SPL class of transcription factors to promote flowering in seed plants. Bryophytes also undergo

sexual reproduction by developing reproductive organs. We revealed that miR529 represses MpSPL2 expression to promote reproductive organ development in the liverwort *Marchantia polymorpha*. This study revealed a novel molecular switch for sexual reproduction in land plants, and provided novel insights and future prospects into the principle of land plant reproduction and its regulation technology.

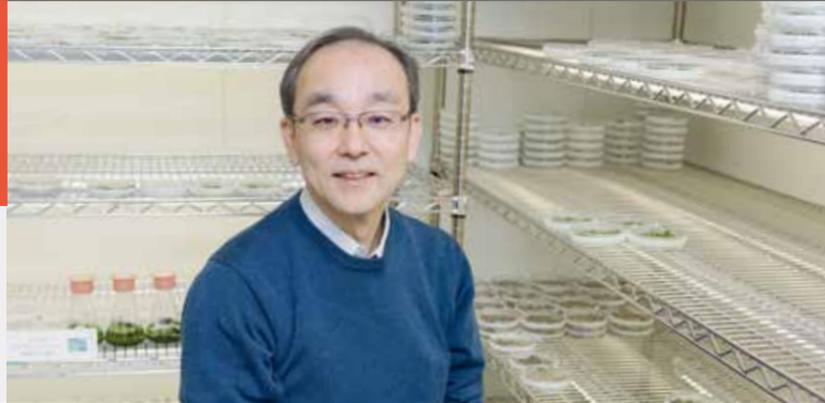


For further information, please visit the journal URL below (Open access): [https://www.cell.com/current-biology/fulltext/S0960-9822\(19\)31008-5](https://www.cell.com/current-biology/fulltext/S0960-9822(19)31008-5)

TOPICS

Laboratory of Plant Molecular Biology

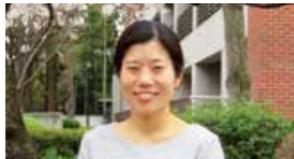
Professor KOHCHI, Takayuki



Assoc. Prof. NISHIHAMA, Ryuichi



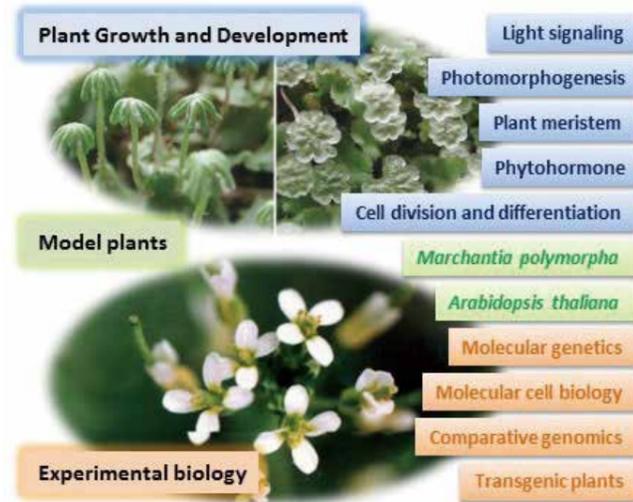
Assist. Prof. YASUI, Yukiko



Main theme

Research in this laboratory focuses on the adaptive regulation of growth and development to environmental conditions and its evolution by using model photosynthetic organisms. Especially with the liverwort *Marchantia polymorpha*, which is a basal land plant ideal for comparative evolutionary

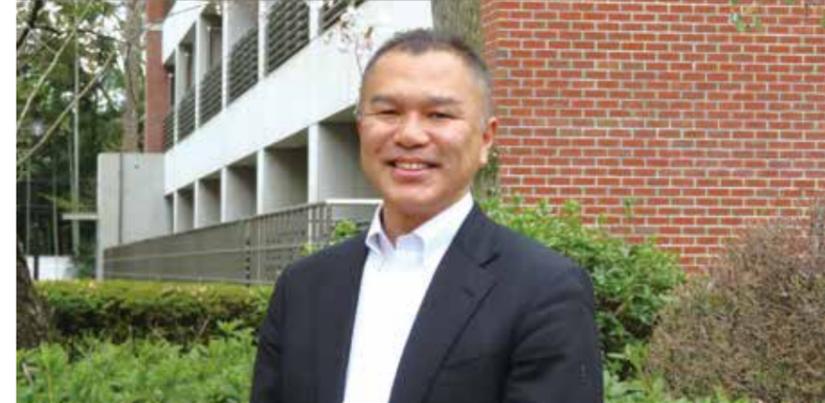
studies and amenable to molecular genetic manipulation, we aim to elucidate principles and ancestral molecular mechanisms of photomorphogenesis, growth phase transition, phytohormone signaling, meristem function, cell division, and cell differentiation in land plants.



Lab URL <http://www.plantmb.lif.kyoto-u.ac.jp/>

Laboratory of Molecular and Cellular Biology for Totipotency

Professor NAKANO, Takeshi

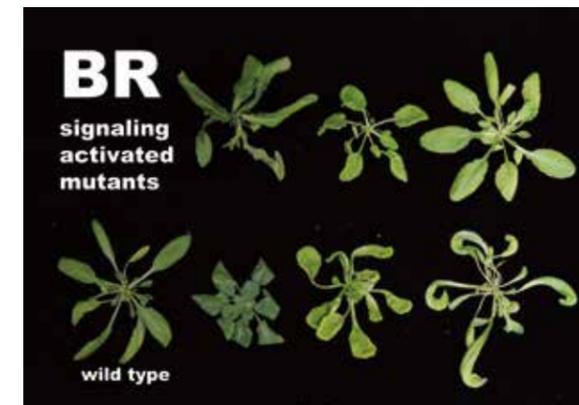
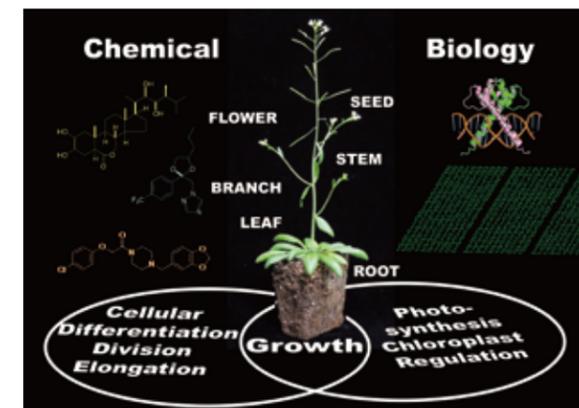


Main theme

Plant growth has been administrated by cooperative regulations between plant cell differentiation/division/elongation and photosynthesis. Based on these scientific aspects, our laboratory is trying to reveal the plant growth mechanisms by 'chemical biology' and 'molecular and cellular biology'.

Major research topics are:

- (1) Signaling of plant hormones
- (2) Chemical functions to regulate plant growth and differentiation
- (3) Plant biomass production regulated by chemicals and genes
- (4) Evolution and diversity of steroid hormones
- (5) Response and adaptation of photosynthesis to environmental factors



<http://plantchembio.sun.bindcloud.jp/index.html> Lab URL

Assoc. Prof. IFUKU, Kentaro



Laboratory of Biosignals and Response

Professor
NAGAO, Masaya



Assoc. Prof.
KAMBE, Taiho



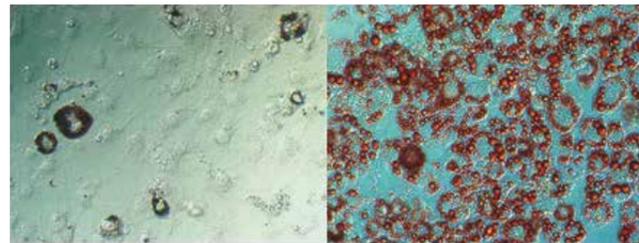
Assist. Prof.
NISHINO, Katsutoshi



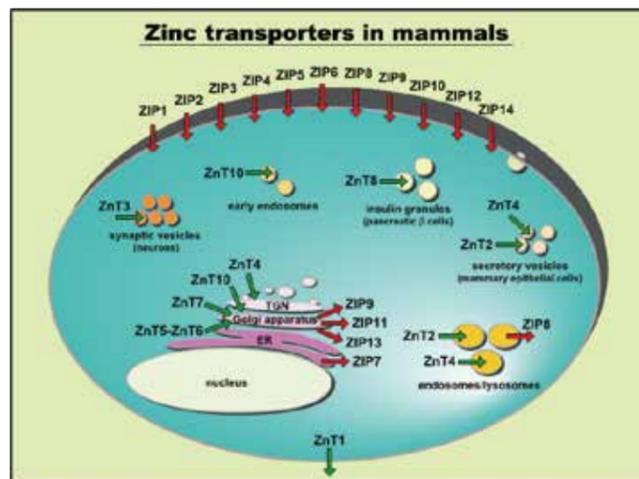
Main theme

Bio-prospecting, a research strategy searching for compounds that possess beneficial activity for health from natural sources, is one of the projects in this laboratory. Especially, compounds that are useful for treatment of lifestyle-related diseases and cancer are the main targets of our bio-prospecting.

We are also studying how organisms perceive environmental signals and transduce these signals into changes in gene expression, focusing mainly on the molecular and cellular basis of zinc metabolism (such as uptake, storage, delivery, and maintenance of metal concentration in cells) in mammal.



Stimulation of lipid accumulation by plant extracts

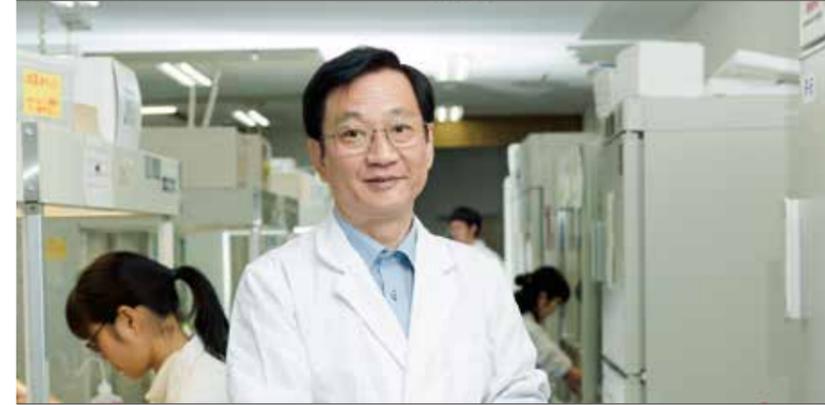


Lab URL <http://www.seitaijoho.lif.kyoto-u.ac.jp/>



Laboratory of Applied Molecular Microbiology

Professor
FUKUZAWA, Hideya



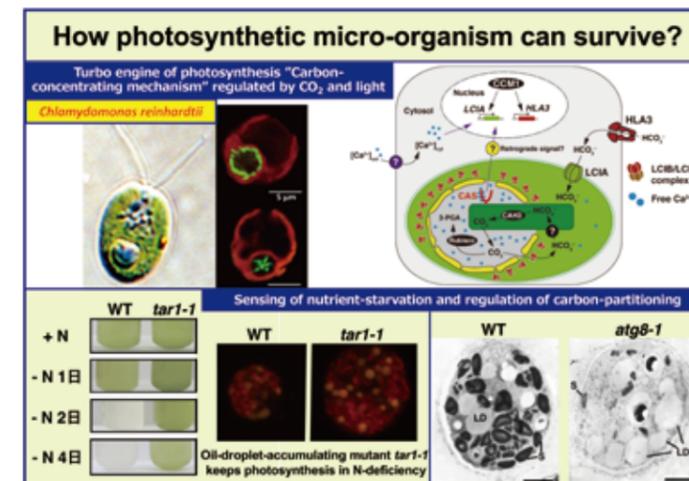
Main theme

We are focusing on the molecular basis of biological functions of microalgae contributing to production of food, biofuel and industrial materials through photosynthesis. Especially, we employ a green alga, *Chlamydomonas reinhardtii*, as a model eukaryotic photosynthetic microorganism using genomic, proteomic, genetic, molecular and biochemical techniques.

The current projects are

(1) Molecular characterization of the carbon-concentrating mechanism (CCM) supporting photosynthetic carbon fixation, biofuel production, and cell proliferation.

- (2) Elucidation of regulatory systems controlling photosynthesis and carbon/nitrogen metabolisms by sensing environmental factors including changes of levels in CO₂ concentration, light and nutrients.
- (3) Metabolic engineering for production of industrial important fatty acids, glycerolipids and carbohydrates.
- (4) Molecular control and signaling of sexual reproduction and oil production by nutrient starvation.
- (5) Identification of factors essential for intracellular signal transduction including calcium-dependent retrograde signal from chloroplast to nucleus and DYRK family of protein kinases supporting cell survival.



<http://www.molecule.lif.kyoto-u.ac.jp/> Lab URL



Laboratory of Molecular Biology of Bioresponse

Professor
KATAYAMA, Takane



Assoc. Prof.
MASUDA, Seiji



Assist. Prof.
KATO, Toshihiko



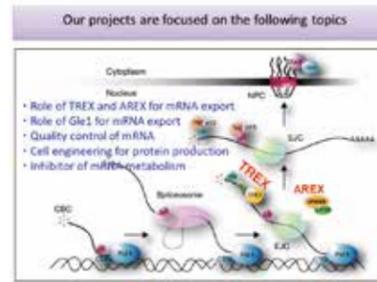
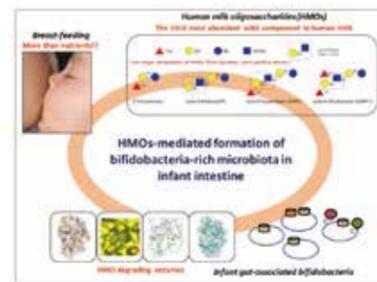
Main theme

The aim of our laboratory is to understand the fundamental life processes of microbes and human, and to develop food- and health-oriented application research. The research activities mainly include (1) elucidation of the molecular mechanism underlying symbiosis and co-evolution between gut microbes and host, and (2) elucidation of the mechanism of mRNA processing, export and quality control in the nucleus in human and its industrial applications.

(1) Recent studies have shown that the consortium of gut microbes exerts a considerable influence on host health. Most researchers approach this topic from "host" side using a mouse model, but we believe that approaches from "microbe" side are

equally needed to understand the symbiosis between them. To this end, we are genetically and enzymatically analyzing unique metabolic pathways in gut microbes, which should uncover the cross-kingdom communications between bacteria and host in intestine.

(2) The main projects are (i) the role of TREX and AREX, which couple transcription and export of mRNA, (ii) the molecular mechanism of RNA quality control in the nucleus, (iii) cell engineering for the protein production using mRNA export mechanism in mammalian cells to apply to industrial applications and (iv) identifying the active compounds which inhibit the mRNA metabolism to apply to medical care.



Lab URL <http://www.bunshioutou.lif.kyoto-u.ac.jp/>

Laboratory of Plant Developmental Biology

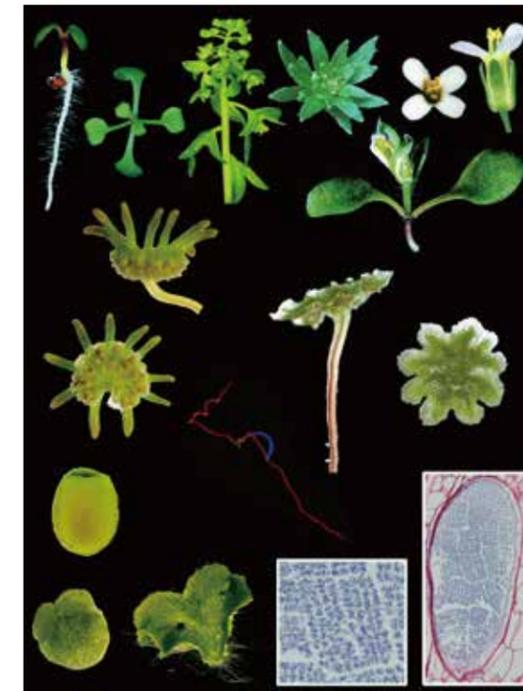
Professor
ARAKI, Takashi



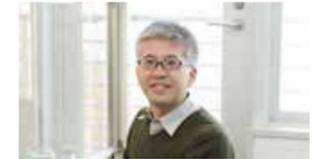
Main theme

We are interested in molecular mechanisms underlying plant's responses to environment. Plants have evolved plastic developmental programs with both genetic and epigenetic basis to adapt their sessile mode of life to changing environment. Using an angiosperm, *Arabidopsis thaliana* and a liverwort, *Marchantia polymorpha* as

model systems, we have been investigating (1) regulation of growth phase transition (especially reproductive transition) in response to environmental signals, (2) long-distance systemic signaling (e.g. florigen) in the control of development, (3) sexual reproduction processes (especially, germline specification and gametogenesis), and (4) origin and evolution of regulatory systems for plastic development.



Assoc. Prof.
YAMAOKA, Shohei



Assist. Prof.
INOUE, Keisuke



<http://www.plantdevbio.lif.kyoto-u.ac.jp/> Lab URL

Laboratory of Plasma Membrane and Nuclear Signaling

Assoc. Prof. YOSHIMURA, Shigehiro



Assist. Prof. KUMETA, Masahiro



Main theme

Our laboratory studies dynamic properties of cellular proteins and membrane in cellular environments by using a variety of techniques in biochemistry, cellular biology and biophysical approaches. We are also interested in how those dynamics of cellular architectures are related to diseases.

Specific research topics include:

- (1) Cytoskeletal dynamics in cell motility and metastasis: intracellular dynamics of actin cytoskeleton is elucidated by our live-cell nano-imaging technique.
- (2) Molecular mechanism of signal transduction: how plasma membrane and membrane-bound proteins coordinates endocytic process.

(3) Virus vs host cell at cell surface: imaging viral particle at the host plasma membrane to elucidate the mechanism of viral infection and proliferation.

(4) Proteins in molecular crowding: dynamic assembly and disassembly of proteins and nucleic acids in cellular environments.

(5) How do cells feel force?: elucidating molecular mechanism of mechano-sensing and -responses by combining various biophysical approaches



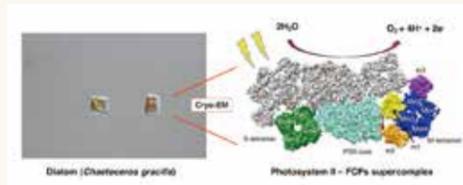
Lab URL <http://www.chrom.lif.kyoto-u.ac.jp/>

TOPICS

“Structural basis for energy harvesting and dissipation in a diatom PSII–FCPs supercomplex”

Diatoms are one of the important groups of oxyphototrophs and possess fucoxanthin chlorophyll *a/c*-binding proteins (FCPs) as light harvesters for photosynthesis. The organization and association pattern of FCP with the photosystem II (PSII) core are unknown. The research group of Kentaro Ifuku, in collaboration with Okayama University, Osaka University, etc., solved the structure of PSII–FCPs supercomplexes isolated from a diatom, *Chaetoceros gracilis*, by single-particle cryoelectron microscopy (Cryo-EM). The PSII–FCPs forms a homodimer. In each monomer, two FCP homotetramers and three FCP monomers are associated with one PSII core. The structure reveals a highly complicated protein–pigment network that is different from the

green-type light-harvesting apparatus. Comparing these two systems allows the identification of energy transfer and quenching pathways. These findings provide structural insights into not only excitation-energy transfer mechanisms in the diatom PSII–FCPs, but also changes of light harvesters between the red- and green-lineage oxyphototrophs during evolution.



The above findings were published in the Journal of “Nature Plants” . For further information, please refer to the URL below. <https://www.nature.com/articles/s41477-019-0477-x>

Laboratory of Developmental Neurobiology

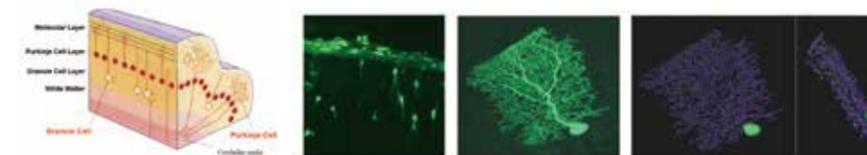
Professor KENGAKU, Mineko



Main theme

Neurons in the mammalian brain are orderly arranged in cortices and nuclei for integration into specific neural circuits. During development, neurons directionally migrate from the birthplace to their destination within the cortex, and then arborize well-patterned dendrites and axons to contact with their specific synaptic counterparts. The major goal of our research is to clarify the

mechanisms of cortical lamination and functional wiring of neurons in the brain. We seek to identify the molecular signals regulating neuronal migration and dendrite patterning. We also aim to develop imaging techniques for real-time observation of molecular and cellular dynamics of neuronal migration and dendrite patterning to discover novel phenomena and rules in neuronal motility in the developing brain.



<http://www.kengaku.icems.kyoto-u.ac.jp> Lab URL



Laboratory of Biochemical Cell Dynamics

Professor SUZUKI, Jun



Main theme

In principle, we identify specific genes involved in the biological phenomenon with our interests. The main approaches are as follows: Expression cloning using cDNA library, functional screening using sgRNA library in a CRISPR/Cas9 system, biochemical approach in combination with mass spectrometry. By establishing the robust experimental systems, we try to understand the biological phenomenon with interests. Currently, we are interested in the biological phenomenon called phospholipid scrambling that regulates blood coagulation, engulfment of dead cells, cell fusion, cancer progression, regulation of brain/bone/muscle functions and so on. In spite of its importance in various biological systems, much is unknown about how phospholipid scrambling is regulated. We are going to

uncover the mechanisms of lipid scrambling.

Research Topic

- Identification of novel scramblases on plasma membranes
- Identification of novel scramblases on intracellular membranes
- Identification of regulators or subunits in scramblases
- Involvement of scramblases on synaptic engulfment
- Understanding how diseases occur by scramblase deficiency
- Screening the chemical substances regulating the scramblases
- Exploring the new phenomenon discovered in the above projects

<http://www.callus.lif.kyoto-u.ac.jp> Lab URL

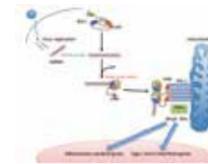
Laboratory of Molecular and Cellular Immunology

Professor
NODA, Takeshi
(Concurrent post)

Main theme

Virus infections, such as influenza A epidemic, Ebola hemorrhagic fever, Middle East respiratory syndrome, Zika virus infection are important diseases and outbreaks of newly emerging viruses are serious problems for modern society. Higher animals, including humans, are genetically equipped with mechanisms, collectively known as innate immunity, to counteract viral infections. During the course of replication, many viruses generate double-stranded (ds)RNA, which is virtually absent in normal cells and likely serves as a "foreign molecule" in cells. An RNA helicase, RIG-I, functions as a sensor for viral dsRNA. RIG-I is composed of three domains: a Caspase recruitment domain (CARD), a

DExD/H helicase domain, and a C-terminal domain (CTD)(Figure). CTD senses viral dsRNA produced in the cytoplasm, leading to a conformational change. This conformational change releases CARD, which signals to downstream, resulting in the activation of genes including those for type I interferon and other cytokines. The purpose of our project is to clarify the molecular mechanism underlying the antiviral innate immunity regulated by RIG-I, and to develop new diagnostic and therapeutic means for viral infections.

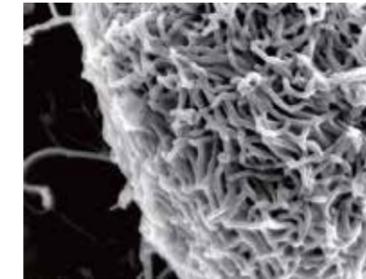


Laboratory of Ultrastructural Virology

Professor
NODA, Takeshi

Main theme

Virus infections are accompanied by numerous ultrastructural changes in viral and cellular components. Our laboratory has been investigating the replication mechanism of influenza and Ebola viruses from the ultrastructural point of view, by using different microscopic methods such as electron microscopy and high-speed atomic force microscopy. Visualization and characterization of the virus life cycle at the nano-mesoscopic level give us unique knowledge and novel paradigms, which will advance our understanding of molecular basis of the replication mechanism.



Scanning electron micrograph of Ebola viruses budding from cell surface.

Assist. Prof.
NAKANO, Masahiro



Assist. Prof.
MURAMOTO, Yukiko



<https://www.facebook.com/NodaLab/> Lab URL

Laboratory of Developmental Dynamics

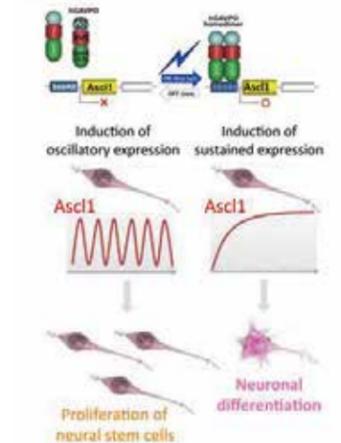
Professor
KAGEYAMA, Ryoichiro



Main theme

We analyze the molecular mechanism of embryonic development by using the most advanced methods such as imaging, optogenetics and transgenic mouse technologies. We evaluate mathematical modeling by using transgenic mice and seek to understand the principles of developmental dynamics. We found that oscillatory gene expression is important for many developmental processes such as brain morphogenesis and somite formation.

Optogenetic control of neural stem cells



Assoc. Prof.
OHTSUKA, Toshiyuki



Assist. Prof.
KOBAYASHI, Taeko

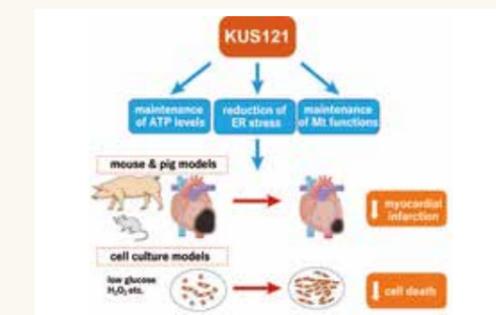


Lab URL <http://www.infront.kyoto-u.ac.jp/research/lab28/>

Cardioprotective Effects of VCP Modulator KUS121 in Murine and Porcine Models of Myocardial Infarction

Professor Kakizuka's research group in our Graduate School has developed KUS121 (Kyoto University Substance 121) as a compound that specifically inhibits the ATPase activity of VCP (valosin-containing protein), the major intracellular ATPase, and has shown that KUS 121 is effective in suppressing neuronal cell death and dramatically improving pathological conditions in model animals such as glaucoma, retinitis pigmentosa, and Parkinson's disease. KUS 121 was found to be effective in treating myocardial infarction. In the past, there was a method of restoring blood flow through a catheter to treat myocardial infarction, but the effect of preventing myocardial necrosis was limited. At the site of myocardial infarction, the decrease in blood flow prevents oxygen from being supplied, resulting in a decrease in ATP and the death of heart muscle cells. In a joint study with the Department of Cardiovascular Medicine, Graduate

School of Medicine, Kyoto University, KUS121 was administered to a mouse model of myocardial infarction. It was also found that ATP levels in the heart rapidly recovered and ER stress (endoplasmic reticulum stress) was reduced. In addition, intracoronary KUS121 reduced the infarct area in a dose-dependent manner in a more human-like porcine model of myocardial infarction (Figure).

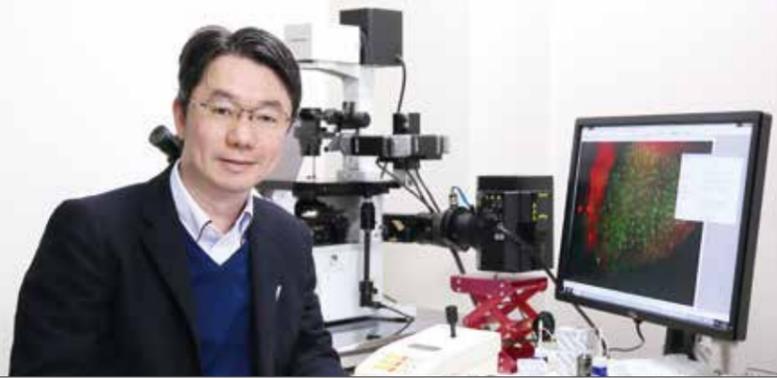


The results were published in the U.S. international journal "JACC: Basic to Translational Science" on 2019 29 10. <https://doi.org/10.1016/j.jacbts.2019.06.001>

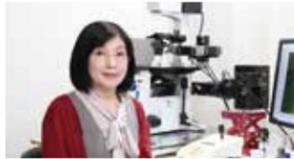
TOPICS

Laboratory of Single-Molecule Cell Biology

Professor
WATANABE, Naoki



Senior Lecturer
YAMASHIRO, Sawako



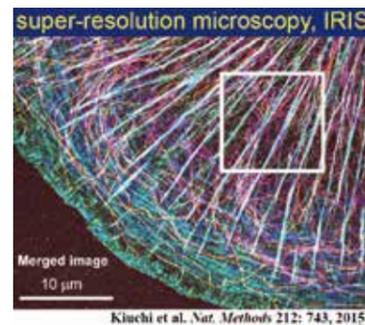
Assist. Prof.
MIYAMOTO, Akitoshi



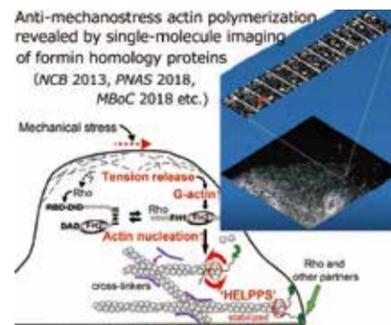
Main theme

Our laboratory aims at bridging the gap between molecular activities and cell physiology by visualizing signal transduction and cell structure remodeling processes with live-cell fluorescence single-molecule (eSIMS) microscopy. We have also invented new super-resolution microscopy called IRIS,

which achieves ultra-high density (= high-fidelity) labeling of multiple targets in a single specimen. By real-time and high-resolution monitoring of cell structure and adhesion molecules using these advanced optical techniques, our laboratory unveils mechanisms and dynamics of pathophysiological cell signaling and body structure remodeling.



Kiuchi et al. *Nat. Methods* 12: 743, 2015



Anti-mechanostress actin polymerization revealed by single-molecule imaging of formin homology proteins (NCB 2013, PNAS 2018, MBoC 2018 etc.)

Lab URL <http://www.pharm2.med.kyoto-u.ac.jp/>



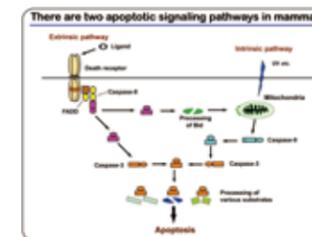
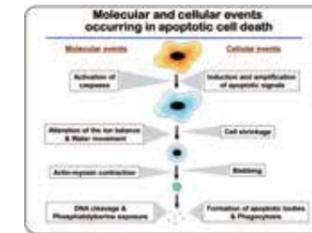
Laboratory of Molecular and Cellular Biology

Assoc. Prof.
SAKAMAKI, Kazuhiro



Main theme

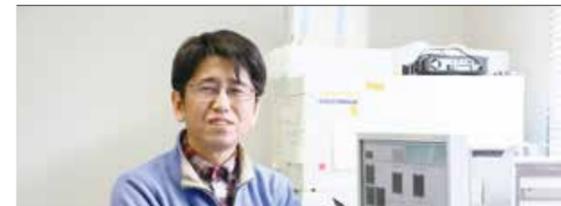
Apoptosis, or programmed cell death, plays an important role in many biological processes, including embryogenesis, maintenance of tissue homeostasis, and elimination of improper cells such as unfunctional or harmful cells in both animals and plants. Our main research project is to understand the molecular and cellular mechanisms of apoptotic cell death in vitro and in vivo, using cultured cells, medaka and mouse as model systems. We also investigate to develop new methods and techniques for imaging and simulating of such a vital phenomenon. In conjunction with these studies, we have been challenging to pursue the biological significance of cell death.



<http://www.MCB.lif.kyoto-u.ac.jp/> Lab URL

Laboratory of Immunobiology

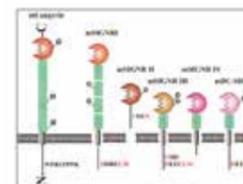
Assoc. Prof.
TAKAHARA, Kazuhiko



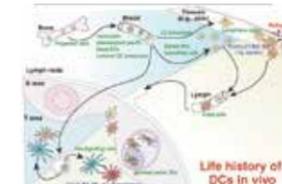
Main theme

Our interest is the induction and control of immunity. We focus on dendritic cells (DC), which are a primary antigen-presenting cell in the immune system. We are especially interested in functions of lectin molecules expressed on DC and its relative, macrophage, that recognize polysaccharides on pathogenic agents. The study includes analyses of interaction between polysaccharides and

lectins, and subsequent cellular and systemic responses in co-operation with TLR signaling. In this study, we found that certain lectin-polysaccharide interaction induced immune suppressive environment, ameliorating excessive and lethal inflammation. By these studies, we would like to develop new methods to control immune system.



Mouse lectins expressed on DCs/macrophages



<http://zoo.zool.kyoto-u.ac.jp/imm/> Lab URL



Laboratory of Molecular Cell Biology and Development

GBS's Collaboration Course in the RIKEN KOBE BDR

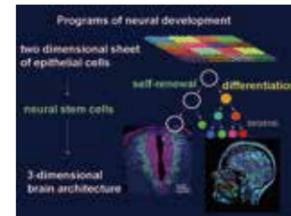
Professor MATSUZAKI, Fumio



Main theme

All the vertebrate brains develop from a single layer of epithelial cells that function as neural stem cells, which go through common processes: the initial proliferative phase, and the subsequent neurogenic phase, at which neural stem cells undergo asymmetric cell divisions to generate self-renewing and differentiating daughter cells. Especially, the mammalian brain has rapidly evolved to explosively increase the neuron number and brain size, leading to gyrication. We explore both the principles underlying common

processes for brain formation as well as specific mechanisms that allowed the mammals to develop into such complex brains, ultimately enabling human to gain intelligence. We use *Drosophila*, mouse and ferret that form the folded brain as models.



Lab URL <https://www.bdr.riken.jp/en/research/labs/matsuzaki-f/index.html>

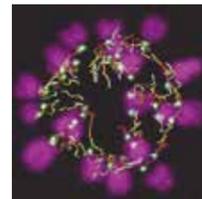
Professor KITAJIMA, Tomoya



Main theme

Meiosis in oocytes is prone to chromosome segregation errors and thus frequently produces aneuploid eggs. The aneuploidy of eggs is a leading cause of pregnancy loss and congenital diseases such as Down syndrome. We aim to understand the causes of chromosome segregation errors in oocytes. We will reveal molecular mechanisms of how unique features of oocytes and age-related effects predispose to chromosome segregation errors. The mechanisms in oocytes will be compared with those in eggs and zygotes, by which we will

understand differentiation of intracellular mechanisms through development. By understanding how aging affects chromosome segregation in oocytes, we will provide insights into how events at cell, tissue and organ levels are interconnected at different life stages.



Prometaphase belt of chromosomes

Lab URL http://chromosegr.riken.jp/index_en.html

Assoc. Prof. TAKASATO, Minoru



Main theme

In our previous study, we developed a protocol generating self-organizing kidney organoids from human iPS cells. While these kidney organoids comprise all anticipated renal tissues, they are still far from the real human kidney in terms of their size, tissue complexity, maturity and functionality. We study to achieve the ultimate goal of generating a functional and transplantable three-dimensional kidney. We appreciate knowledge from basic developmental biology that is essential for

such regenerative studies; therefore, we are also highly interested in studies of human embryology. Particularly, we are focusing on uncovering the developmental mechanisms of the human mesoderm and kidney.



A kidney organoid generated from human pluripotent stem cells

Lab URL <https://www.bdr.riken.jp/jp/research/labs/takasato-m/index.html>

Laboratory of Molecular Neurobiology

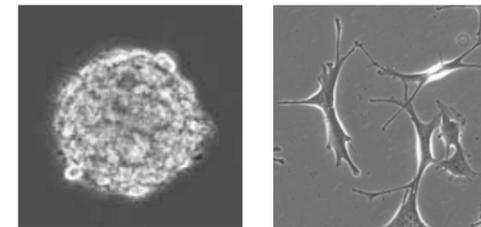
Assoc. Prof. KATOH, Hironori

Main theme

Our laboratory is seeking to understand the mechanisms underlying cancer development and progression. In particular, we study the relationship between cellular metabolism and signal transduction in cancer cells. Our current research focuses on the following

subjects:

1. Signal transduction in cancer cells under metabolic stress.
2. The expression and activity of amino acid transporters in cancer cells.
3. Regulation of amino acid metabolism in cancer cells.

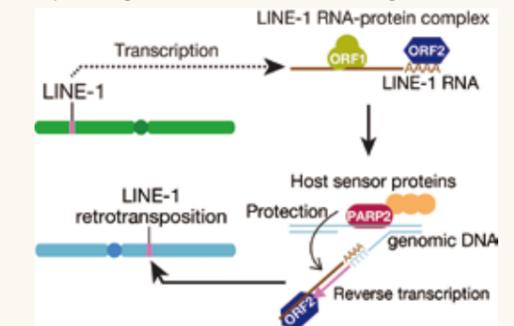


<http://www.negishi.lif.kyoto-u.ac.jp/e/Top.html> Lab URL

Identification of the host cellular mechanisms of human LINE-1 mobilization

Long interspersed element-1 (LINE-1) retrotransposons comprise approximately 17% of the human genome, and they are still actively moving in our genome. L1 encodes two proteins, ORF1p and ORF2p, required for retrotransposition. However, cellular factors involved in LINE-1 retrotransposition remained to be elucidated. In this research, Miyoshi et al (Laboratory of Cell Cycle Regulation) identified cellular proteins that regulate LINE-1 retrotransposition. They discovered that DNA replication factors, chromatin-binding proteins, and several DNA repair proteins interacted with ORF2p. Intriguingly, one of them, PARP2, a single-strand break repair protein, was found to recognize DNA breaks induced by ORF2p specifically. Furthermore, PARP2

recruits other host proteins that protect an intermediate of LINE-1 retrotransposition. These results suggest that the host DNA repair proteins facilitate LINE-1 mobilization, which will give an impact on genetic variation in the human genome.



The findings were published in the Journal of "Molecular Cell". For further information, please refer to the URL below. http://www.kyoto-u.ac.jp/ja/research/research_results/2019/190829_1.html

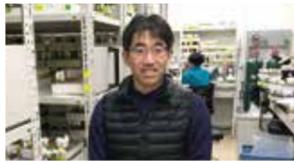
TOPICS

Laboratory of Genetics

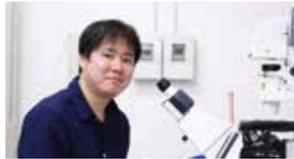
Professor
IGAKI, Tatsushi



Assoc. Prof.
KANDA, Hiroshi



Assist. Prof.
ENOMOTO, Masato

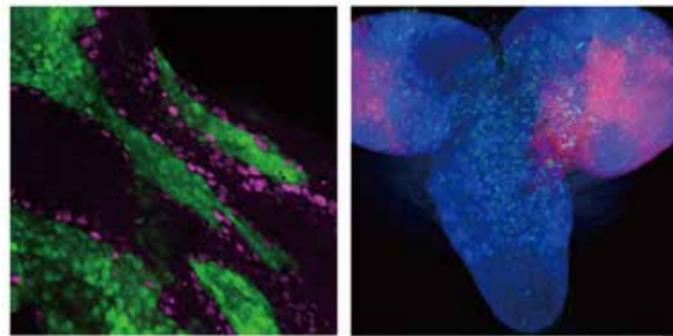


Main theme

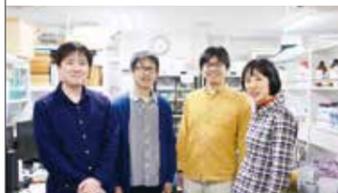
Our research focuses on the molecular basis of cell-cell communication that governs tissue growth, homeostasis, and cancer. We take advantage of the powerful genetics of *Drosophila*.

Research subjects

1. Mechanism of cell competition
2. Genetic basis of tissue growth regulation
3. Molecular basis of tumor progression and metastasis
4. Mechanism of aging



Left: Polarity-deficient cells (green; losers) are eliminated from epithelium by wild-type cells (magenta; winners) through cell competition.
Right: Malignant tumor cells (magenta) are invading and metastasizing from the eye disc to the brain (blue) in *Drosophila* larva.



Lab URL <http://www.lif.kyoto-u.ac.jp/labs/genetics/>

Laboratory of Functional Biology

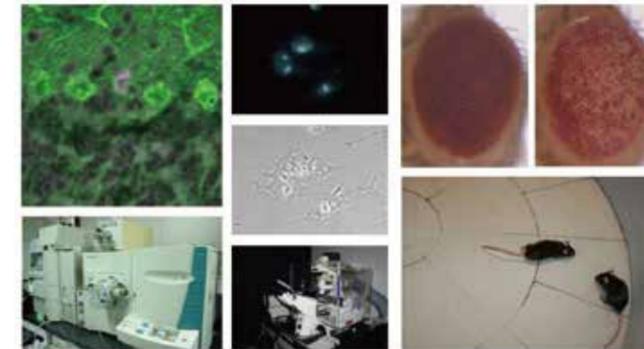
Professor
KAKIZUKA, Akira



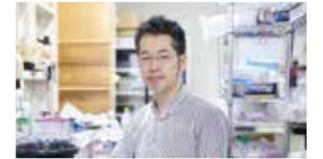
Main theme

Using animal models of human diseases, such as neurodegenerations, cancers, and obesity-related diseases, and using metabolite imaging techniques, we aim to elucidate molecular bases of such diseases and develop new strategies to cure or prevent them. One of the main features of life science research in the coming years will be that the results obtained from fundamental research should ideally be directly connected to the good of society. From this standpoint, in addition to handling

topics with high scientific significance, we aim to contribute to the development of treatments for neurodegenerative diseases, cancers, and obesity-related diseases from our research results. We hold the same view on scientific education, and through training individuals to communicate their ideas logically yet effectively, as well as by nurturing their creativity, in addition to strengthening their practical research skills, we aim to cultivate opinion leaders standing at the core of life science research in the 21st century.



Assoc. Prof.
IMAMURA, Hiromi



Assist. Prof.
KOIKE, Masaaki



<http://www.funcbiol.lif.kyoto-u.ac.jp/> Lab URL

Laboratory of Science Communication

Specially Assigned Professor HEJNA, James Alan



Main theme

Our laboratory engages in the development and implementation of new approaches to the internationalization of science education and communication, based on principles of active learning. The particular challenges we are addressing often involve overcoming the differences in culture and pedagogical traditions between Japanese and Western societies. Our efforts are chiefly in the educational arena, aimed at training the next generation of scientists to communicate their knowledge and expertise not only to the international scientific community but locally to the citizens who ultimately

support basic research. Our activities entail the following:

1. Increasing the exposure of Japanese students to foreign peers. We are forging new partnerships with foreign universities to foster joint courses, using live Internet connections, with active student participation in English.
2. Establishing partnerships with foreign universities to encourage short-term reciprocal exchanges of graduate students for collaborative research.
3. Expanding the opportunities for students to present their research in English to a broad audience.

TOPICS

An evolutionary trait of the human milk oligosaccharide transporter dictates bifidobacteria-infant symbiosis

The microbiota of breast-fed infant guts is generally dominated by bifidobacteria. In vitro studies have suggested that human milk oligosaccharides (HMOs) in breastmilk promote the formation of bifidobacteria-rich microbiota in the guts; however, the underlying molecular mechanism remains elusive. In the paper published in Science Advances, Prof. Katayama at the Laboratory of Molecular Biology and Bioresponse characterized two functionally distinct but overlapping fucosyltransferase transporters (FL transporter-1 and -2) from *Bifidobacterium infantis*. Fecal DNA and HMO consumption analyses revealed that FL transporter-2 is primarily associated with bifidobacteria-rich microbiota formation in the guts. Structural analyses of the solute-binding protein of FL transporter-2 complexed with 2'-fucosyllactose and 3-fucosyllactose highlight a unique adaptation

strategy of *Bifidobacterium* to HMOs, in which the gain-of-function mutations enabled the transporter to capture major fucosylated HMOs. Our results provide a molecular insight into HMO-mediated symbiosis between bifidobacteria and humans.

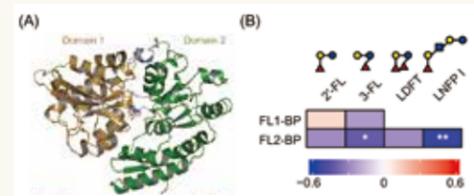


Figure: Structure of the solute-binding protein of FL transporter-2 (A) and the correlation between the abundance of FL transporter-2 gene and the abundance of fucosylated oligosaccharides in the feces of breast-fed infants (B).

For further information, please refer to <http://advances.sciencemag.org/content/5/8/eaaw7696>

Laboratory of Bioeducation

Professor CHISAKA, Osamu



Main theme

Our laboratory has been trying to improve study materials on biology.

1. Introduction of modern topics into study materials on biology
2. Introduction of active learning methods into biology lectures in English
3. Exploitation of new biology lab course protocols and materials

TOPICS

Identification of the mechanism of how normal cells eliminate abnormal neighbors in the epithelium

This study was published in *Developmental Cell* on September 19, 2019

The research group of Professor Tatsushi Igaki and graduate student Rina Nagata found the mechanism by which unfit or abnormal cells are eliminated by neighboring normal cells, a phenomenon called 'cell competition'. Cell competition is a quality control process that selectively eliminates unfit cells from the growing tissue. To dissect the mechanism of cell competition, they performed a genetic screen for genes required for elimination of unfit cells (cells with reduced protein synthesis ability) from *Drosophila* eye imaginal epithelium. As a result, they found that blocking autophagy in unfit cells abolished elimination of unfit cells. Consistently, autophagy was specifically elevated in unfit cells nearby normal cells. JNK

signaling was also activated in unfit cells, and simultaneous activation of JNK and autophagy cooperatively induces cell death. These findings may provide a novel strategy against cancer and aging.

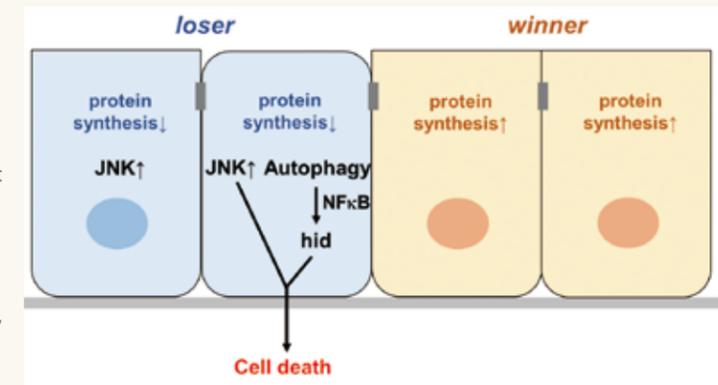


Figure legend: Unfit cells (blue: loser), which have reduced protein synthesis ability, elevate autophagy when surrounded by normal cells (yellow: winner). Elevated autophagy upregulates a proapoptotic gene *hid* via NFκB. Unfit cells also activate JNK, which cooperates with *hid* to effectively induce cell death.

For further information, please refer to the URL below. [https://www.cell.com/developmental-cell/fulltext/S1534-5807\(19\)30701-4](https://www.cell.com/developmental-cell/fulltext/S1534-5807(19)30701-4)

Laboratory of Chromosome Function and Inheritance

Assoc. Prof. CARLTON, Peter



Main theme

To create haploid gamete cells (sperm or egg cells) from diploid precursors in meiosis, homologous chromosomes must pair, recombine, and then separate from each other, reducing the genome by half. Recombination between homologous chromosomes is initiated in meiotic prophase by programmed DNA double-strand breaks; these breaks are then repaired through homologous recombination, giving rise to genetic crossovers that link homologous chromosomes until they divide. Using the model organism *Caenorhabditis elegans*, we are working to determine the molecular mechanisms of recombination initiation and repair in the context of chromosome dynamics,

combining molecular genetics, biochemistry and cytology with high-resolution microscopy and quantitative image analysis. Since errors during meiosis are common in humans and can lead to infertility and developmental defects, understanding these mechanisms is important for achieving improvements in human reproductive health.

Our current research focuses on the following areas:

- Understanding mechanisms of chromosome dynamics and regulation during meiosis
- Phosphoregulation of the synaptonemal complex
- Analysis of chromosome structures using super-resolution microscopy



Lab URL <http://www.carltonlab.org>



Laboratory of Bioimaging and Cell Signaling

Professor MATSUDA, Michiyuki



Main theme

Our research has been focused on the visualization of activities of various kinases and G proteins in living cells using biosensors based on the principle of the Förster resonance energy transfer (FRET). Our most recent study created FRET-based optogenetic tools which enables molecular activity control at single-cell resolution. These sensors and optogenetic tools will lead us to 'talk' with live cells under microscope to facilitate deeper understandings of the biological systems. Multiphoton microscopy of various tissues and organs of mice expressing our biosensor will reveal relationship between signal transduction and cellular behavior in physiological and pathological conditions.

Research objects

- Development of fluorescent and luminescent biosensors to visualize signal transduction in living cells.
- Development of optogenetics tools to control signal transduction.
- Inter-cellular/intra-cellular signaling in living cells and living mice.
- Analysis of inter-cellular communication mediated by mechanical force.
- Multiphoton live imaging of molecular activities in the neural retina.

Assoc. Prof. TERAU, Kenta



Assist. Prof. SATO, Shinya



Program-Specific Assist. Prof. HINO, Naoya



TOPICS

Interspecies comparative analyses reveal distinct carbohydrate-responsive systems among *Drosophila* species.

During evolution, organisms have acquired variable feeding habits. Some species are nutritional generalists that adapt to various food resources, while others are specialists, feeding on specific resources. However, much remains to be discovered regarding how generalists adapt to diversified diets. Yukako Hattori, Kaori Watanabe, and Tadashi Uemura (Laboratory of Cell Recognition and Pattern Formation) uncovered robust carbohydrate-responsive regulatory systems, which allow larvae of a generalist *D. melanogaster* to adapt to various nutrient balances. In contrast, a specialist *D. sechellia* is defective in the systems, culminating in reduced adaptation to carbohydrate-rich diets. We share a great deal of our metabolic

machinery with *D. melanogaster*, and the team ultimately aims to pursue comparative studies that explore how the interplay between our diet and our genetic background might contribute to metabolic disorders. The findings were published in "Cell Reports".

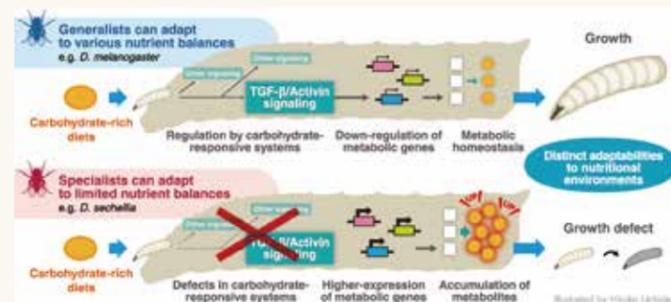
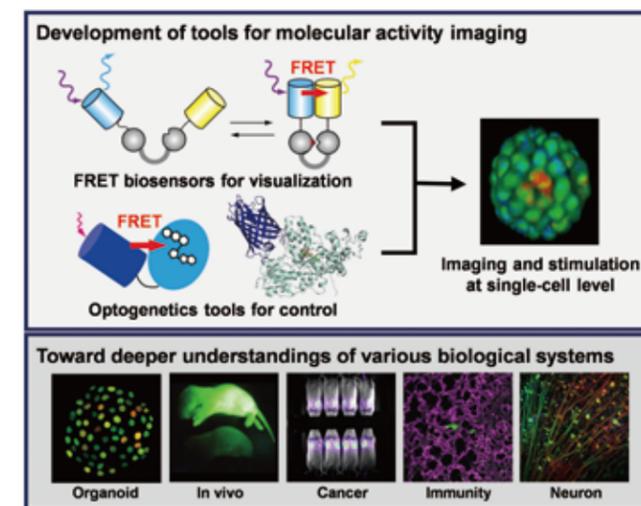
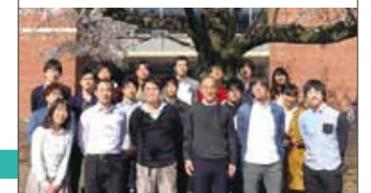


Figure: The specialist *D. sechellia* is defective in the carbohydrate-responsive systems of the generalist *D. melanogaster*, culminating in reduced adaptation to carbohydrate-rich diets.

For details, please refer to the following https://www.kyoto-u.ac.jp/en/research/research_results/2019/190904_1.html



<http://www.fret.lif.kyoto-u.ac.jp/mi.htm> Lab URL



Laboratory of Theoretical Biology

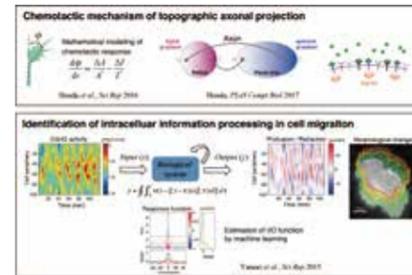
Assoc. Prof. HONDA, Naoki



Main theme

Our laboratory aims to elucidate theoretical logic of dynamic living systems. By developing and simulating mathematical models, we are trying to understand mechanisms underlying phenomena in a bottom-up manner. We are also utilizing machine learning to extract hidden rules of dynamic, complicated phenomena from experimental quantitative data in a top-down manner. By means of these theoretical approaches, we are studying neuronal wiring in the brain, emotional neural dynamics, noise-resistant embryonic development, mechano-chemical mechanism of collective

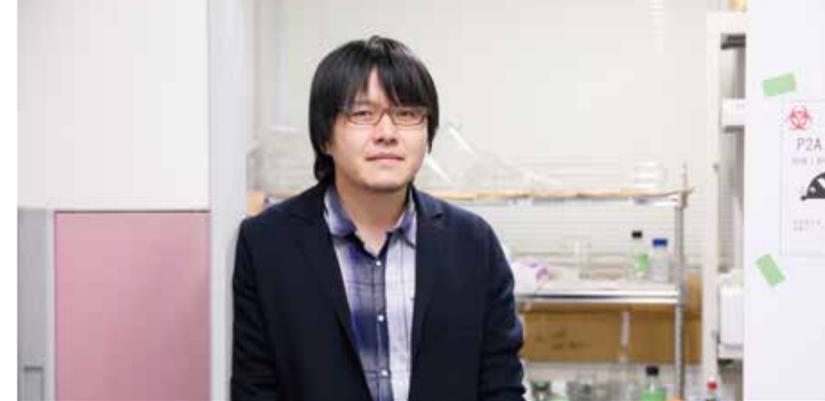
cell migration, cytoskeleton-based cellular morphogenesis, identification of intracellular information processing and animal behavioral strategy.



Lab URL <https://sites.google.com/view/theoretical-biology/>

Laboratory of Brain Development and Regeneration

Professor IMAYOSHI, Itaru



Main theme

Our laboratory aims at understanding the mechanisms of development and regeneration processes in the mammalian brain, and their functional outcomes on neural circuits, higher brain functions, and animal behaviors. We are focusing on the regulatory mechanism of cell growth, differentiation, and quiescence of neural stem cells. We are also focusing on the functional

contribution of newly-generated neurons to neural circuits and animal behaviors. Our laboratory is also developing novel optogenetic tools that can manipulate gene expression of cells by light.

Assist. Prof. SUZUKI, Yusuke

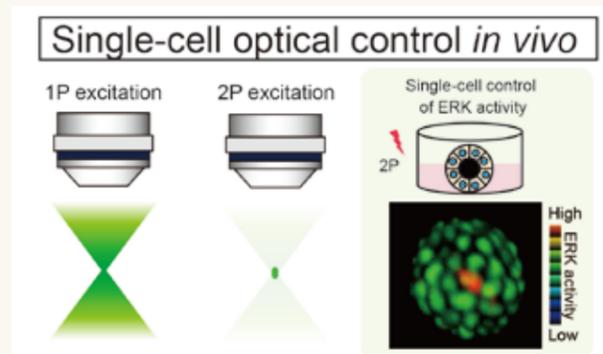


TOPICS

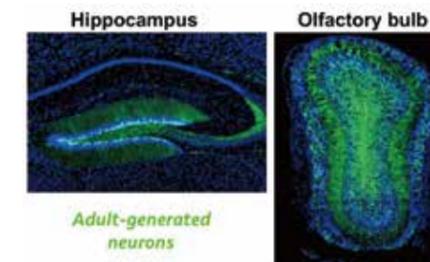
Single-cell control of ERK activity by optogenetic tool *in vivo*

Optical dimerizers have been developed to untangle signaling pathways, but they are of limited use *in vivo*, partly due to their inefficient activation under two-photon (2P) excitation. To overcome this problem, Kinjo et al. developed Förster resonance energy transfer (FRET)-assisted photoactivation, or FRAPA. In three-dimensionally cultured cells expressing 2paRAF, extracellular signal-regulated kinase (ERK) was efficiently activated by 2P excitation at single-cell resolution. Photoactivation of ERK was also accomplished in the epidermal cells of 2paRAF-expressing mice. We further developed an mTFP1-fused LOV domain that exhibits efficient

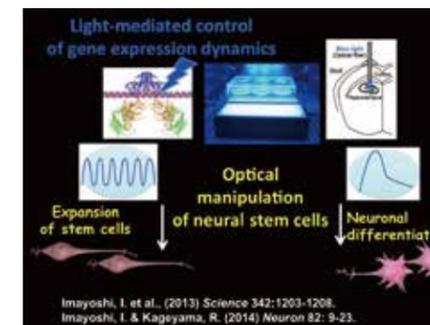
response to 2P excitation. Collectively, FRAPA will pave the way to single-cell optical control of signaling pathways *in vivo*.



The findings were published in the Journal of Nature Methods. For further information, please refer to the URL below. <https://www.nature.com/articles/s41592-019-0541-5>



Imayoshi, I. et al., (2008) *Nature Neuroscience* 11: 1153-1161. Sakamoto, M., et al., (2014) *The Journal of Neuroscience* 34: 5788-5799.



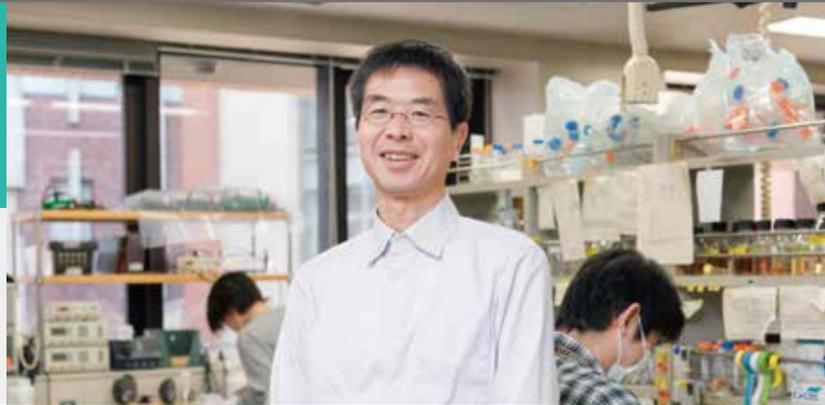
Imayoshi, I. et al., (2013) *Science* 342:1203-1208. Imayoshi, I. & Kageyama, R. (2014) *Neuron* 82: 9-23.

<https://brainnetworks.jimdo.free.com> Lab URL

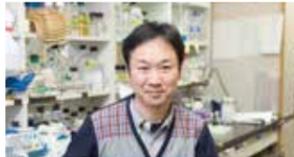


Laboratory of Genome Maintenance

Professor
MATSUMOTO, Tomohiro



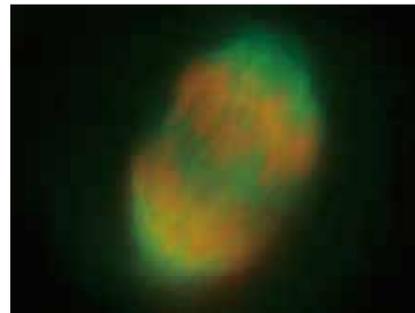
Senior Lecturer
FURUYA, Kanji



Main theme

The spindle checkpoint, our major research subject, is a surveillance mechanism to regulate cellular apparatus for compliance with this rule. It is a unique negative feedback that converts/amplifies a physical signal sensed by kinetochores (attachment of the spindle and/or tension) and regulates the timing of the sister chromatid separation. Mad2, a signal

carrier of this feedback, plays a vital role in the spindle checkpoint. It is specifically localized at unattached kinetochores that are the origin of the checkpoint signal. Mad2 targets CDC20 and inhibits its activity to promote sister chromatid separation. We study Mad2, a central player of the spindle checkpoint, to reveal mechanisms, which regulate the activity of Mad2.

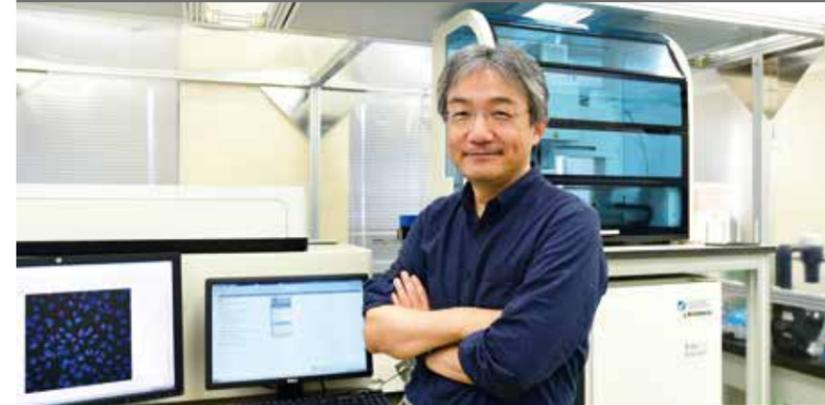


Lab URL http://www.rbc.kyoto-u.ac.jp/radiation_system/



Laboratory of Genome Damage Signaling

Professor
TAKATA, Minoru



Main theme

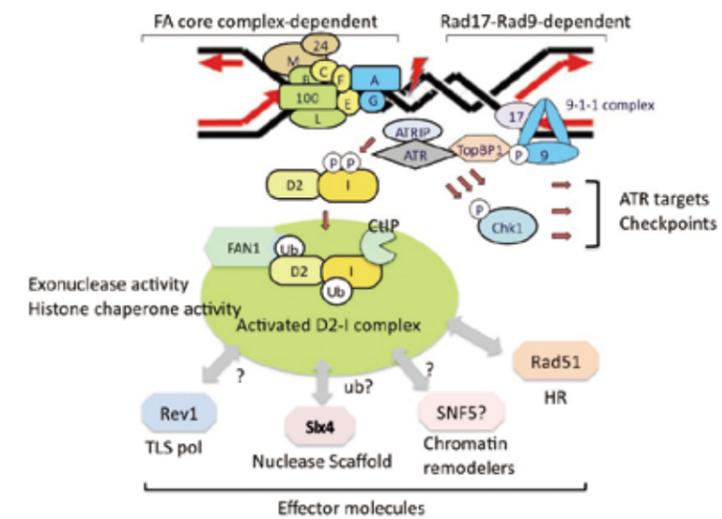
DNA damage response (DDR) is the fundamental mechanism that stabilizes our genome. Genome stability underlies all biological processes. We try to identify molecules involved in genome

stability/ replication stress/DDR by methods such as screening mutations in human patients, and further analyze their function using genome engineering in various cell lines, iPS cells, and model organisms.

Program-Specific Assist. Prof.
KATSUKI, Yoko



Replication stress triggers DNA damage response



Lab URL <http://house.rbc.kyoto-u.ac.jp/late-effect>



Laboratory of Cancer Cell Biology

Professor HARADA, Hiroshi



Main theme

Cells maintain their function and morphology by exploiting a suitable adaptive response system to diverse and complex tissue microenvironments. Several lines of evidence have suggested that hypoxic, acidic and nutrients-depleted microenvironments exist in solid tumors and induce malignant phenotypes and chemo/radioresistance of cancer cells (Figure 1). We aim to elucidate molecular mechanisms responsible for cellular

adaptive responses to the tumor-specific microenvironments and malignant progression of cancer cells (Figure 2).

- Cellular adaptive responses to tumor microenvironments, e.g. hypoxia
- Molecular mechanisms underlying malignant progression and chemo/radioresistance of cancer cells
- Regulatory mechanisms of carbohydrate metabolic pathway

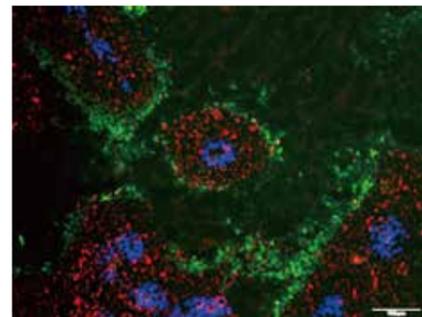


Figure 1: Hypoxic tumor cells (green) distant from blood vessels (blue) are resistant to radiation-induced DNA damage (red).

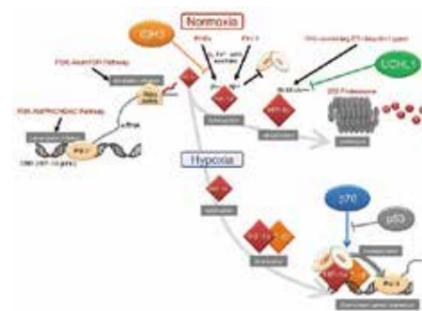


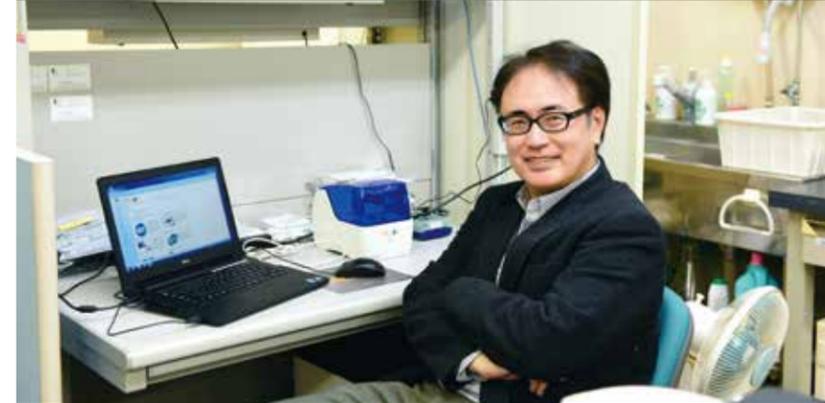
Figure 2: HIF-1-mediated gene networks responsible for both adaptive responses to hypoxia and malignant progression of cancer cells.



Lab URL http://www.rbc.kyoto-u.ac.jp/cancer_biology/

Laboratory of Chromatin Regulatory Network

Assoc. Prof. IKURA, Tsuyoshi

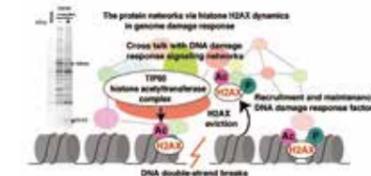


Main theme

The purpose of our research is to clarify the role of chromatin dynamics, which is required for the DNA metabolisms such as transcription, DNA replication, and DNA repair. In particular, we focus on the molecular mechanisms by which histone modifier complexes regulate the histone eviction as chromatin remodeling machinery upon DNA damage induced by ionizing radiation. Our goal is to understand how histone eviction activates DNA damage signaling pathways and functions as an anti-cancer signaling.

Main research topics

- Memory of genomic damage
- Cellular robustness in genomic stress response
- Solution of energy metabolism mechanism in specific cancer cell



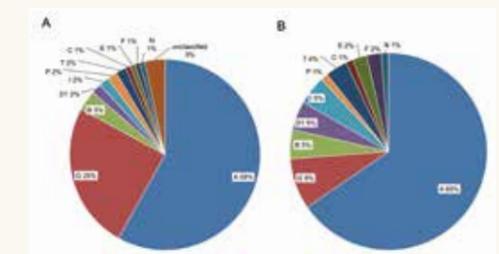
<http://house.rbc.kyoto-u.ac.jp/mutagenesis2/index1> Lab URL

"A landscape analysis of mutated genes responsible for the rare hematologic disease Fanconi anemia in Japan"

This research result was published in Haematologica, a hematology journal, in February 2019.

"Fanconi anemia" is a serious hereditary disease that causes aplastic anemia, leukemia, and cancer in children. The disease is very rare, but important for understanding hematopoiesis and cancer, and is also famous for having common genes (BRCA1 and BRCA2) with hereditary breast and ovarian cancer syndrome (HBOC). These and other causative genes (total 22) can function in repairing DNA damage when working normally. Conversely, if the causative gene loses its function due to mutation, it will not be able to repair DNA damage that occurs naturally in the body and will lead to developing anemia and leukemia. Dr. Minako Mori, a graduate student of the Graduate School of Medicine (currently a research fellow at the Graduate School of Biostudies), and Professor Minoru Takata have collaborated with many clinicians, including Dr. Miharuru Yabe of the Tokai University Hospital, to analyze samples of 117 cases regarding what kind of causative gene is mutated in Japanese, how does the mutation look

like, whether it affects symptoms, etc. Fanconi anemia research of this scale is unprecedented in Japan and provides the basic information that will support the future of research and treatment of Fanconi anemia in Japan.



Frequency distribution of total (A) versus unique (B) Fanconi anemia (FA) gene mutations in the 117 Japanese FA patients. The frequency of the total FA gene mutation was based on subtyping of 117 FA cases, while the frequency of unique FA gene mutations was derived from 84 genetic variants detected in the 117 FA patients.

<http://www.haematologica.org/content/104/10/1962.full.pdf+html>

TOPICS

Laboratory of Cell Regulation and Molecular Network

Professor
SUGITA, Masahiko



Assist. Prof.
MORITA, Daisuke



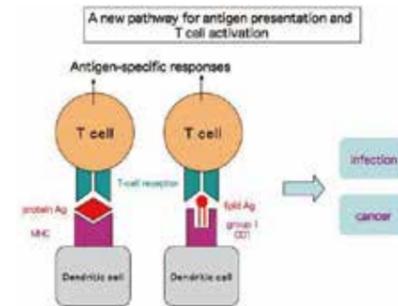
Assist. Prof.
MIZUTANI, Tatsuaki



Main theme

Full attention of this laboratory has been directed to previously unappreciated aspects of the acquired immunity that we call "lipid immunity". Unlike conventional MHC molecules that present protein-derived peptide antigens, molecules of the human group 1 CD1 family (CD1a, CD1b, CD1c) mediate presentation of "lipid" antigens to specific T lymphocytes. In addition, we have recently identified a novel lineage of antigen-presenting molecules, termed LP1, capable of mediating presentation of "lipopeptide" antigens. By taking cell biological, immunological and lipid chemical approaches, this laboratory wishes to establish a molecular and cellular basis for

lipid immunity and determine how CD1 and LP1 have been evolved to function critically in host defense. An important extension of this research is a challenge for developing a new type of lipid-based vaccines against cancer and microbial infection.



Lab URL http://www.infront.kyoto-u.ac.jp/ex_ivr/Lab/SugitaLab.html

Laboratory of RNA Viruses

Professor
TOMONAGA, Keizo



Assoc. Prof.
HIJIKATA, Makoto



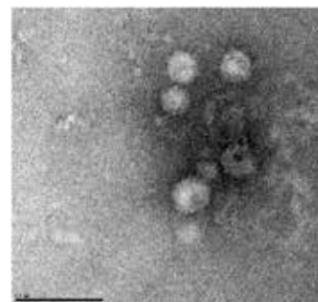
Assist. Prof.
MAKINO, Akiko



Main theme

The researches carried out in our laboratory are focused on several RNA viruses, including bornavirus, and hepatitis C virus. All our projects aim to understand the fundamental mechanisms of the replication and pathogenesis of these viruses. We are investigating the replication and persistent mechanism of the bornavirus in the cell nucleus. The understanding the biological significance of the endogenous element of bornaviruses in mammalian genomes is one of the main focuses of bornavirus researches. We also aim to develop a novel RNA virus vector using bornavirus, which can express stably functional small RNAs.

The understanding of the molecular mechanism of tumorigenesis caused by hepatitis viruses is also the main purpose of our laboratory.



Lab URL <https://t.rnavirus.virus.kyoto-u.ac.jp/>

Laboratory of Cell Division and Differentiation

Professor
TOYOSHIMA, Fumiko

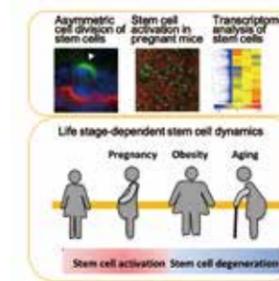


Main theme

How adult tissue stem cells adapt to physiological changes is a fundamental question in stem cell biology. Balance between self-renewal and differentiation of stem cells via symmetric/asymmetric cell division is essential for steady state homeostasis. Biased stem cell self-renewal or differentiation leads to changes in tissue organization and in organ size. Our group focuses on the mechanisms of symmetric/asymmetric stem cell division, stem cell differentiation, and cell lineage-commitment in tissues metabolism and regeneration. We further research on the stem cell regulation in response to the physiological changes of the body, including pregnancy, obesity and aging.

Research subjects

1. Symmetric and asymmetric stem cell division in tissue homeostasis
2. Maternal tissue stem cell dynamics during pregnancy
3. Obesity- and age-related stem cell degeneration



<https://www2.infront.kyoto-u.ac.jp/Toyoshima-HP/index-En.html> Lab URL

Assist. Prof.
ODA, Yukako



Assist. Prof.
ISHIBASHI, Riki



Laboratory of Cellular and Molecular Biomechanics

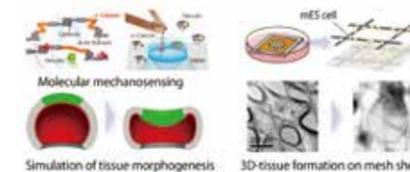
Professor
ADACHI, Taiji



Main theme

Our research group aims to clarify the mechanisms by which cells sense mechanical stimuli and regulate their activities in tissue adaptation, regeneration and stem cell differentiation in morphogenesis. To better understand the mechano-regulation of these dynamical processes through the complex hierarchical structure-function relationships, bridging spatial and temporal scales from microscopic molecular/cellular activities to macroscopic tissue behaviors is very important. Based on multiscale biomechanics, our group is involved in the integrated biomechanics and mechanobiology researches of modeling and simulation combined with experiments, focusing on mechano-biochemical couplings in the system dynamics.

2. Understanding mechanisms of tissue differentiation and regeneration emerged from multicellular dynamics.
3. Identifying mechanisms of tissue functional adaptation by remodeling to mechanical environment
4. Elucidation of mechano-biochemical coupling mechanisms in mechanosensory cells.
5. Nano- and microengineering of artificial systems combined with biomolecular and cellular systems.



1. Biomechanics and mechanobiology studies on stem cell differentiation, morphogenesis, and remodeling in tissue development and regeneration.

<http://www.infront.kyoto-u.ac.jp/research/lab25/> Lab URL

Senior Lecturer
OKEYO, Kennedy



Assist. Prof.
KAMEO, Yoshitaka



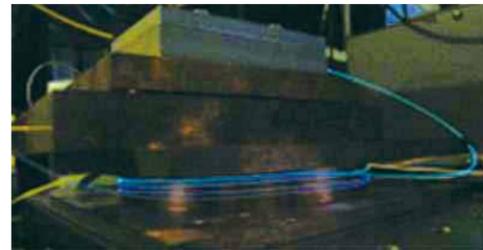
Laboratory of Spatiotemporal Optical Control / Laboratory of Optical Neural and Molecular Physiology

Main theme

This department was launched in January 2020 as an academic-industrial cooperation with Hamamatsu Photonics. In this department, scientists at Graduate School of biostudies and research groups at Hamamatsu Photonics will maximize their respective expertise to develop next-generation technologies for microscope. By integrating the knowledge and experience of academia and companies, we aim

to achieve innovative optical technology development through industry-academia collaboration and apply it to the elucidation of life phenomena. In this department, two laboratories ("Laboratory of Spatiotemporal Optical Control" and "Laboratory of Optical Neural and Molecular Physiology") were founded and they will develop cutting-edge imaging, optical control technologies, and probes. By measuring and manipulating

dynamics of genes and molecules multidimensionally, they will understand the principle of biological functions.



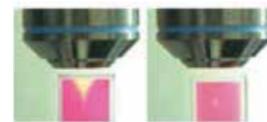
Laboratory of Spatiotemporal Optical Control
Program-Specific Professor
ISOBE, Keisuke



Main theme

Two-photon fluorescence microscopy has become a powerful tool for deep imaging of biological tissues. However, many biological phenomena in which intercellular interaction and communication networks play a crucial role are invisible because of insufficient imaging performance of commercial two-photon fluorescence microscopes. We aim to make the invisible visible by creating novel optical techniques. Our current research focuses on the following subjects;

1. Development of femtosecond lasers for ultra-deep imaging and their applications
2. Development of wide-field deep imaging techniques using spatiotemporal control of laser pulses and their applications
3. Development of 4-dimensional optical control techniques using multiphoton patterned illumination their applications



Laboratory of Optical Neural and Molecular Physiology
Program-Specific Assoc. Prof.
SAKAMOTO, Masayuki



Main theme

Probing functional neural circuits at high spatial-temporal resolution is crucial to understand how neuronal populations work together to achieve higher brain functions such as learning and memory. We aim to understand these circuit mechanisms with cutting-edge multiphoton imaging and optical control technology. Our current research focuses on the following subjects;

1. Dendritic voltage integration of synaptic potentials.
2. Circuit mechanisms underlying odor-induced behaviors.
3. Development of fluorescent probes for monitoring neural activity.



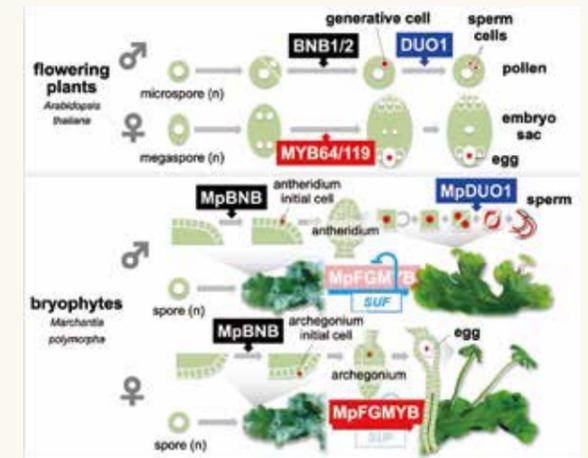
In vivo two-photon imaging from head-fixed mouse during learning

Marchantia polymorpha is a powerful model for elucidating molecular mechanism and evolution of gametogenesis in land plants

This review was published in *Nature Plants* on 8th July, 2019.

The research group of Associate Professor Shohei Yamaoka, ex-graduate student Dr. Asuka Higo, Professor Takashi Araki, and Professor Takayuki Kohchi, in collaboration with Assistant Professor Tomokazu Kawashima in University of Kentucky, Professor Keiji Nakajima in Nara Institute of Science and Technology, and Dr. Tetsuya Hisanaga and Senior Group Leader Frédéric Berger in Gregor Mendel Institute, published a review of the recent researches on land plant gametogenesis and the evolution. Comments from the research group: We have recently identified evolutionarily conserved core regulators of land plant gametogenesis: BONOBO, a fate determinant of plant germ cells including generative cell in pollen; DUO1, an essential regulator for formation of motile flagellate sperm in charophytes and bryophytes, and sperm cells passively transported through pollen tube in flowering plants; FGMYB, a key regulator for the regulation of embryo sac development in flowering plants and female

sex differentiation in bryophytes. These findings are based on the studies in the liverwort *Marchantia polymorpha*, a new model plant established in Kyoto University.



Hisanaga, T.*, Yamaoka, S.*, Kawashima, T.*, Higo, A., Nakajima, K., Araki, T., Kohchi, T., and Berger, F. Building new insights in plant gametogenesis from an evolutionary perspective. *Nature Plants* vol. 5, issue 7, pp. 663-669, 2019. (*co-first authors)

For further information on the genes shown in the review, see:
BONOBO: http://www.kyoto-u.ac.jp/ja/research/research_results/2017/180126_1.html
DUO1: http://www.kyoto-u.ac.jp/ja/research/research_results/2018/181211_1.html
FGMYB: http://www.kyoto-u.ac.jp/ja/research/research_results/2018/190104_1.html

Regulation of active and quiescent neural stem cells in the adult mouse brain

Neural stem cells generate new neurons; however, many of them are quiescent and only occasionally exhibit proliferation and neuronal differentiation in the adult brain. In a study in *Genes and Development*, the laboratory of Ryoichiro Kageyama revealed that high expression of the transcription factor Hes1 suppresses the expression of the proneural gene Ascl1, thereby maintaining a quiescent state.

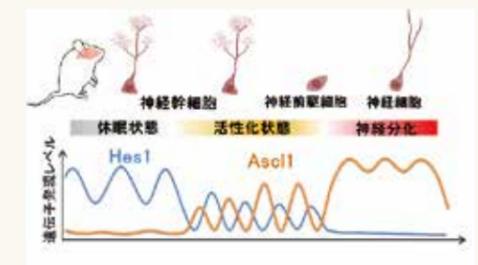


Figure: Expression dynamics of Hes1 and Ascl1 in neural stem cells.

The findings were published in the *Journal of "Genes and Development."*
For further information, please refer to the URL below.
https://www.kyoto-u.ac.jp/en/research/research_results/2018/190313_1.html

Radiation Biology Center (RBC)

Radiation Biology Center, Kyoto University



Message from Director of the Center

Hiroshi Harada

The Radiation Biology Center (RBC) was founded in 1976 to promote basic research on biological effects of radiation. As a Joint Usage Research Center, the RBC has been fulfilling its responsibilities as a hub for scientists in radiation biology and its related research fields. The center was integrated with Graduate School of Biostudies in 2018 to commence novel and deeper research activities from this privileged position as a part of "Biostudies" looking into the vast areas of life sciences.

Overview

The research in the RBC is in large part strongly linked with users of Joint Usage Research Center, but at the same time, each member of RBC pursues science with their own research direction.

Departments

Dept. of Radiation System Biology

We are pursuing mechanistic understanding of genetic and epigenetic inheritance by analyzing regulation of centromere structure, various cell cycle check points, and stress responses.

[Staff] MATSUMOTO, Tomohiro (Prof.)
FURUYA, Kanji (Senior Lecturer)

Dept. of Late Effects Studies, Lab of DNA Damage Signaling

We are studying (1) cellular and molecular mechanisms in response to endogenous DNA damage and replication stress, and (2) disorders caused by the defects in these mechanisms such as Fanconi anemia and hereditary breast and ovarian cancer. We employ technologies *in vitro* recapitulation of pathologies with iPS cell lines derived from patients, genome editing, and analysis of human materials.

[Staff] TAKATA, Minoru (Prof.)
KATSUKI, Yoko (Program-Specific Assist. Prof.)

Dept. of Chromosome Function and Inheritance

Using the model organism *Caenorhabditis elegans*, we are working to determine the molecular mechanisms of recombination initiation and repair in the context of chromosome dynamics. Understanding these mechanisms is important for achieving improvements in human reproductive health problems such as infertility and developmental defects.

[Staff] CARLTON, Peter (Assoc. Prof.)

Dept. of Mutagenesis, Lab of Chromatin Regulatory Network

How does the cell maintain its integrity in response to various stress such as radiation or UV? What kind of strategy is employed? To solve these questions and to elucidate mechanisms of cancer or lifestyle-related disorders, we focus on chromatin that is the characteristic of eukaryote's genome using proteomics analysis of chromatin regulator protein complexes, bioimaging, and mathematical and statistic approaches.

[Staff] IKURA, Tsuyoshi (Assoc. Prof.)

Dept. of Genome Repair Dynamics, Lab of Cancer Cell Biology

We are conducting studies on endogenous and exogenous factors that affect cellular radiation sensitivity/resistance such as genetics deficiencies and tissue microenvironments and on the effect of low dose and low dose rate radiation on our body. Our focus is ranging from molecules to individual mice.

[Staff] HARADA, Hiroshi (Prof.)

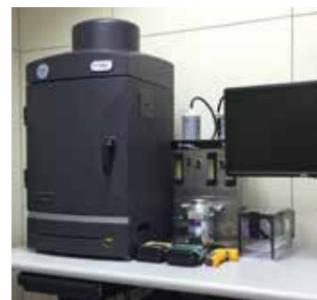
Dept. of Stress Response

We will elucidate what kind of molecular reactions cells would display upon low dose irradiation in terms of stress response. Our main research targets are regulatory mechanisms of chromatin dynamics, translational regulation on ribosomes, acquired resistance mechanisms to low dose irradiation.

[Staff] ISHIKAWA, Fuyuki (Prof.)
MIYOSHI, Tomoichiro (Assoc. Prof.)



Low Dose and Low Dose-rate Irradiation System



Optical In Vivo Imaging System



The 2nd RBC-CEA Joint Workshop



The 33rd International Symposium of Radiation Biology Center, Kyoto University

Research Center for Dynamic Living Systems

Research Center for Dynamic Living Systems



Message from Director of the Center Matsuda Michiyuki

Recent advent of biology largely depends on the reductionist's approach that has been deciphering the function of molecules of interest. New functions of molecules are still being discovered, leading to the discovery of new biological phenomena. Meanwhile, it will be also quite important to integrate the huge knowledge accumulated so far and to deduce common principles of biological phenomena. Theoretical biology, mathematical biology, or systems biology are the school of such research area, but their advancement depends on technological break-through of imaging and omics that fuels these theoretical research field with the ground-truth data and tools for validation. With this background, a MEXT-supported project named 'a research and education platform for innovative research on dynamic living systems' were launched by Graduate Schools of Medicine, Biostudies, and Informatics, and by Virus Research Institute and Institute for Frontier Medical Sciences. Here, to further promote this interdisciplinary approach, Research Center for Dynamic Living Systems has launched in 2018. Setting the cutting-edge microscopy as the core of technology, we attempt to understand the biological systems by the collaboration of theoretical researchers and experimental biologists.

Overview

- Course meeting of developmental biology, cell biology and systems biology. Monthly seminars are given by foreign or domestic top runners and by young researchers. Annual retreat will provide the graduate students with the opportunity to talk and discuss on their data.
- MACS education program: In collaboration with department of mathematics, graduate school of science, a series of lectures will be provided under the title of "Fusion of imaging technology and mathematics".
- Introduction to mathematics, statics, and computational biology. For the graduate students who belongs to the wet laboratories, the basics of mathematics and statistics and the use of mathematical software will be lectured.
- Kyoto University Live Imaging Center. Cutting-edge microscopes including multiphoton microscopes are available for researchers both in and out of Kyoto University. Technicians maintain the microscopes in good condition and help researchers for the operation.

Laboratories

Cutting-edge Bioimaging Team (Matsuda Lab)

By using fluorescence biosensors, we will visualize molecular activity and cellular function in the tissue culture cells and the living mice, and thereby decipher the principle of intercellular communication.

[Staff] MATSUDA, Michiyuki (Prof.)
TERAI, Kenta (Assoc. Prof.)

Data-driven Modeling Team (Honda Lab)

By statistical analysis and machine learning of quantitative experimental data, we will extract hidden patterns and/or rules underlying dynamic and complicated biological phenomena, thereby providing basis for developing mathematical model.

[Staff] HONDA, Naoki (Assoc. Prof.)

Multiscale Biomechanics Team (Adachi Lab)

Roles of force in hierarchical living systems from molecular/cellular levels to tissue/organ levels will be clarified by multiscale biomechanics approach through integration of in-vitro and in-silico experiments.

[Staff] ADACHI, Taiji (Prof.)
KAMEO, Yoshitaka (Assist. Prof.)

Developmental Dynamics System (Kageyama Lab)

We will elucidate the significance of oscillatory gene expression by live imaging with luminescent and fluorescent reporters and by optogenetic perturbation in cultured cells and tissues.

[Staff] KAGEYAMA, Ryoichiro (Prof.)

Physiological Network Team (Uemura Lab)

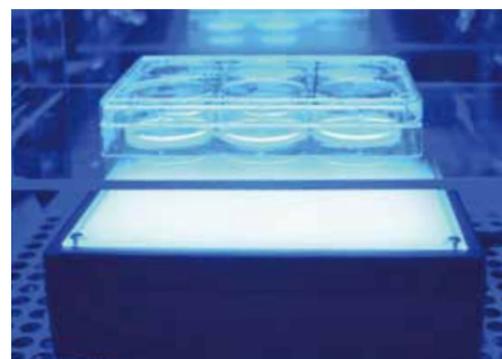
By taking multi-omics and genetic/optogenetic approaches, we will unravel operating principles of physiological mechanisms that control animal life-history traits and neuronal circuits that evoke selective behaviors, in response to nutrient balances or sensory stimuli.

[Staff] UEMURA, Tadashi (Prof.)

Biological Function Manipulating Team (Imayoshi Lab)

We will develop genetic and virus vector methods for expressing fluorescent proteins and functional molecules in specific cell types of the model organisms, especially mice. We will also develop novel optical methods to manipulate cellular and biological functions. By integrating these cutting-edge technologies, we will unveil the regulatory mechanisms underlying brain development, plasticity, and regeneration.

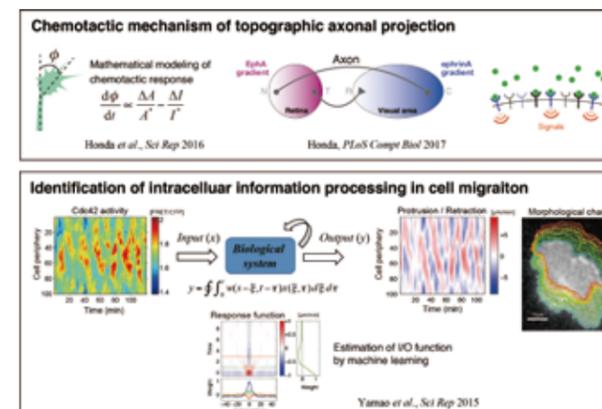
[Staff] IMAYOSHI, Itaru (Prof.)



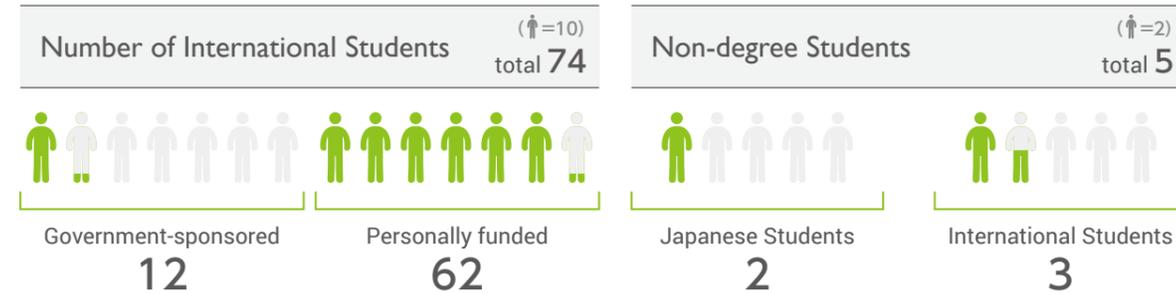
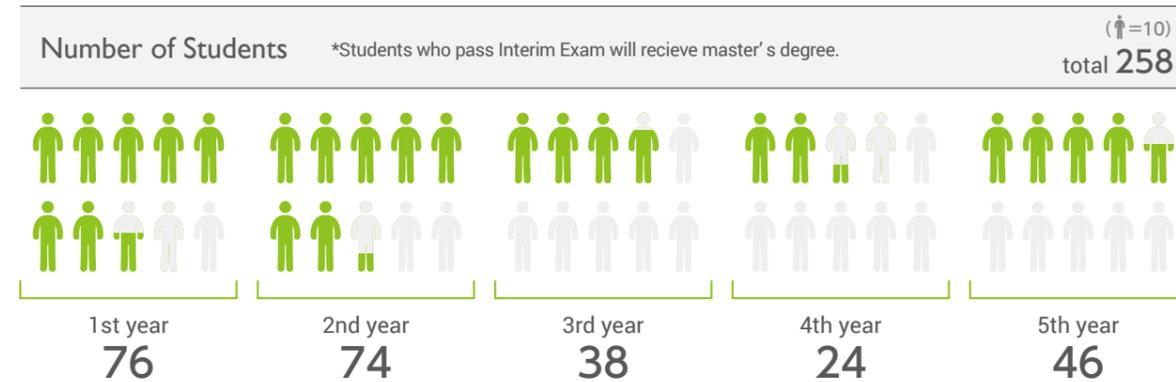
Blue light illumination to cultured cells expressing the light-induced gene expression system.



A transgenic mouse expression FRET biosensor (right).

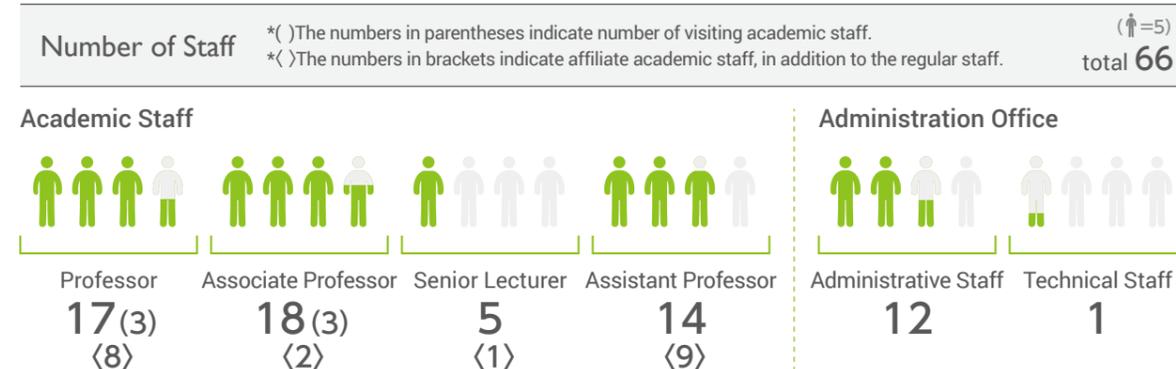


Scheme of projects: Chemotactic mechanism of topographic axonal projection and Identification of intracellular information processing in cell migration.

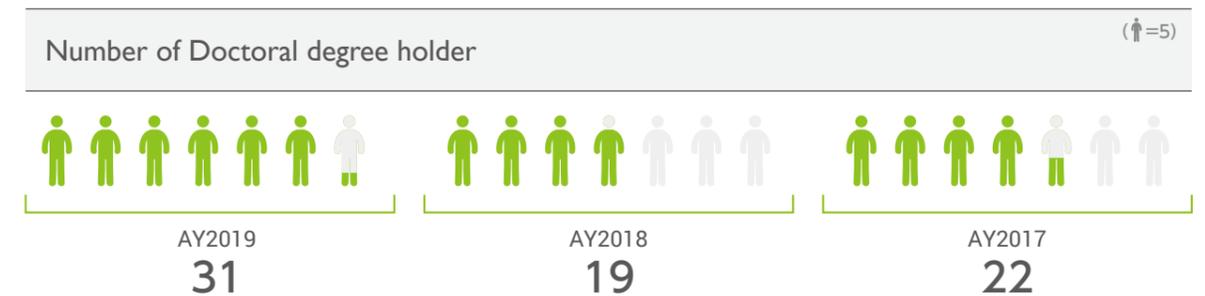
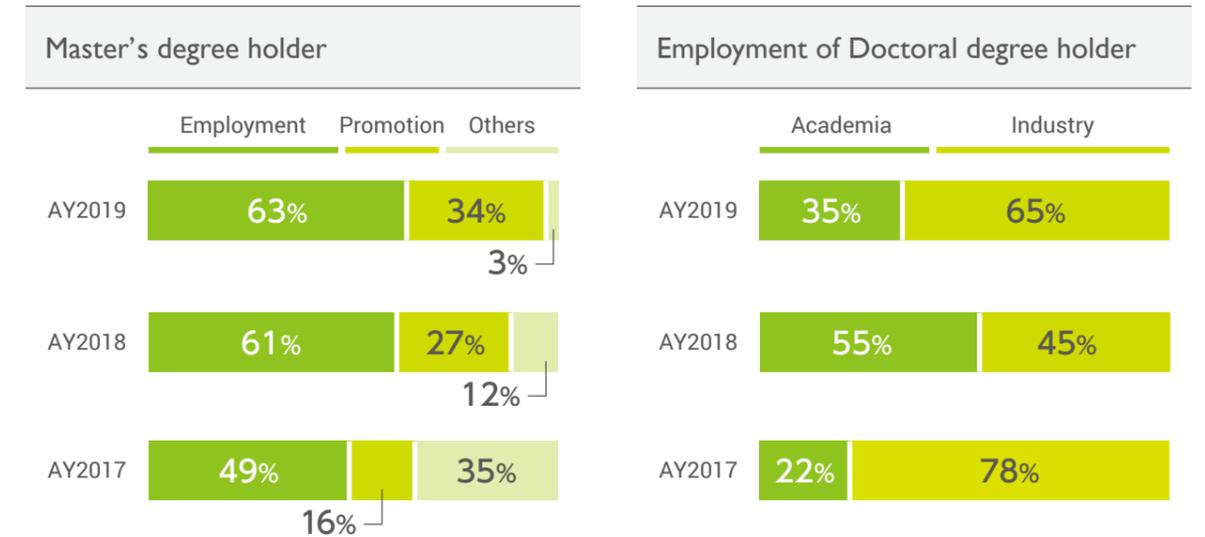


International Students Numbers (↑=10)
total 74

Region	Country	Number
Asia	China	33
	Hong Kong	2
	India	2
	Korea	11
	Malaysia	4
	Philippines	2
	Sri Lanka	1
	Taiwan	3
	Thailand	1
	Viet Nam	1
Africa	Ghana	1
	Nigeria	1
	Sudan	1
Europe	Croatia	1
	Germany	1
Middle East	Palestine	2
	Turkey	1
	North America	Canada
Mexico		2
USA		2



Activity of Students following graduation



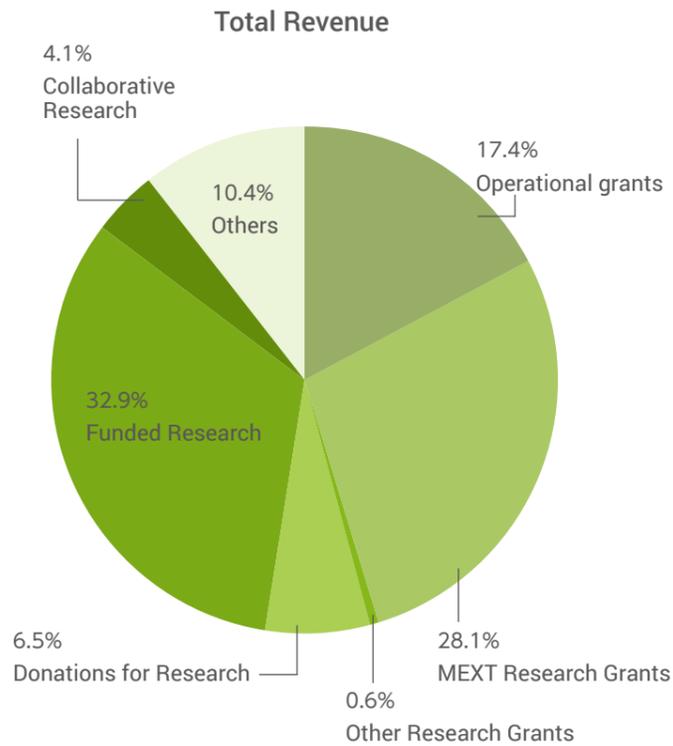
Places of Employment

Business
DENKA SEIKEN Co., Ltd. / KAWASUMI LABORATORIES, INC. / KOSÉ Corporation / Shionogi & Co., Ltd. / Astellas Pharma Inc. / Waqoo, Inc / choseido Pharmaceutical Co., Ltd. / TAKII & CO., LTD / Panasonic Corporation / Sumitomo Mitsui Card Co., Ltd. / KYORIN CO., LTD / SEIWA KASEI Co., Ltd. / Kyowa Hakko Kirin Co., Ltd. / JAPAN POST Co., Ltd. / Gakken Holdings Company, Limited / CMIC HOLDINGS Co., Ltd. / Mandom Corporation / DENTSU INC. / Toho Co., Ltd. / OSAKA GAS CO., LTD / Lion Corporation. / Maruho Co., Ltd. / Sysmex Corporation / NICHIREI CORPORATION / NISSIN FOODS HOLDINGS CO., LTD / Mediscience Planning Inc. / Linical.Co., Ltd / NBC Meshtec Inc. / NEXCO EAST Corporate / AIREX INC. / Works Applications Co., Ltd. / Sumitomo Dainippon Pharma Co., Ltd. / CHUGAI PHARMACEUTICAL CO., LTD / FUJIREBIO Inc. / fixpoint, Inc. / Daiichi Sankyo Healthcare Company, Limited / Taiyo Kagaku Co., Ltd. / Shiseido Company, Limited / KYOKUTO PHARMACEUTICAL INDUSTRIAL CO., LTD / SDS Biotech K.K. / AOHATA Corporation / JCR Pharmaceuticals Co., Ltd. / MORINAGA MILK INDUSTRY CO., LTD. / EUGLENA CO, LTD / ASAHI BREWERIES, LTD / ARKRAY, Inc. / SANYO FOODS.Co., Ltd. / Kobayashi Pharmaceutical Co., Ltd. / GLICO NUTRITION CO., LTD. / CHUGOKU ELECTRIC POWER CO., INC. / Sunstar Inc. / NIDEC CORPORATION / Takara Bio Inc. / Toyota Motor Corporation. / Idemitsu Kosan Co., Ltd. / Oriental Yeast Co., Ltd. / ROHTO Pharmaceutical Co., Ltd. / MANDA FERMENTATION CO., LTD. / Otsuka Pharmaceutical Co., Ltd. / P&G. / TOYO SHINYAKU Co., Ltd. / Santen Pharmaceutical Co., Ltd. / TSUMURA & CO. / AJINOMOTO CO., INC. / House Foods Corp. / Mizkan Holdings Co., Ltd. / Nissan Motor Corporation / The Nisshin OilliO Group, Ltd. / Sapporo Breweries Limited

Others
Hokkaido University / University of Tokyo / Kyoto University / Shiga University of Medical Science / Wakayama Medical University / Kumamoto University / Okinawa Institute of Science and Technology Graduate University / RIKEN / JICA / City of Kobe / Ministry of Education, Culture, Sports, Science and Technology / Ministry of Agriculture, Forestry and Fisheries

Total Revenue in Fiscal 2019

Category	Total (yen)
Operational grants	214,716,953
MEXT Research Grants	347,187,214
Other Research Grants	7,430,000
Donations for Research	80,315,443
Funded Research	405,747,892
Collaborative Research	50,176,800
Others	128,048,038
Total	1,233,622,340



Professors Emeriti As of April 1, 2020

Name	Laboratory	Enrollment period	
		from	to
SASAKI, Ryuzo	Biosignals and Response	April 1, 1999	March 31, 2001
TAKEICHI, Masatoshi	Cell Recognition and Pattern Formation	April 1, 1999	March 31, 2002
OHYAMA, Kanji	Plant Molecular Biology	April 1, 1999	March 31, 2003
KUMAGAI, Hidehiko	Applied Molecular Microbiology	April 1, 1999	March 31, 2004
YANAGIDA, Mitsuhiro	Chromosome Transmission	April 1, 1999	March 31, 2005
IZUI, Katsura	Plant Physiology	April 1, 1999	March 31, 2005
NAKANISHI, Shigetada	Neuroscience	April 1, 1999	March 31, 2005
YAMAMOTO, Kenji	Applied Molecular Microbiology	April 1, 1999	March 31, 2010
KOZUTSUMI, Yasunori	Membrane Biochemistry and Biophysics	April 1, 1999	March 31, 2012
TAKEYASU, Kunio	Plasma Membrane and Nuclear Signaling	April 1, 1999	April 30, 2014
INOUE, Tan	Gene Biodynamics	April 1, 1999	March 31, 2015
INABA, Kayo	Immunobiology	April 1, 1999	March 31, 2016
YONEHARA, Shin	Molecular and Cellular Biology	August 1, 2001	March 31, 2018
SATO, Fumihiko	Molecular and Cellular Biology of Totipotency	April 1, 1999	March 31, 2018
NISHIDA, Eisuke	Signal Transduction	April 1, 1999	March 31, 2018
NEGISHI, Manabu	Molecular Neurobiology	April 1, 1999	March 31, 2019
HEJNA, James Alan	Science Communication	November 1, 2010	March 31, 2020

Campus MAP



Access

