Graduate School of BIOSTUDIES, Kyoto University

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2019

BIOSTUDIES

Contact

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BIOSTUDIES

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 1,447 students had earned their master' s degree from our school, while 433 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. From this fiscal year (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.

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.

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.

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.

Attached Research Centers

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.

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/Genetic Information/ 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.

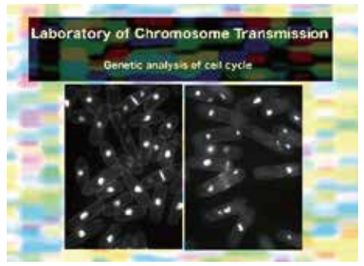
Laboratory of Chromosome Transmission

Assoc. Prof.
NAKASEKO, Yukinobu

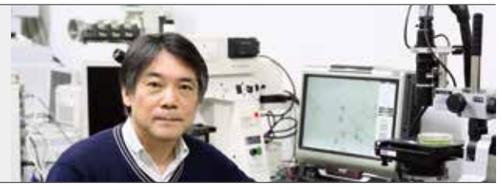
Main theme

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.



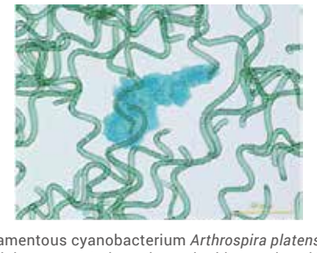
Laboratory of Gene Biodynamics



Assoc. Prof.
SHIRAISHI, 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

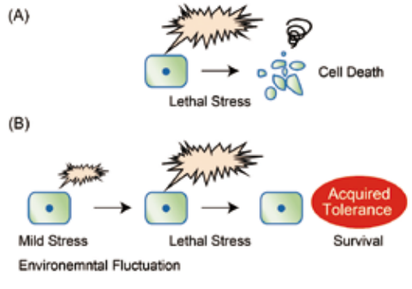
Professor
ISHIKAWA, Fuyuki

Assoc. Prof.
MIYOSHI, Tomoichiro

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.



Ingeneral, 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**

Laboratory of Cell Recognition and Pattern Formation

Professor
UEMURA, Tadashi

Lecturer
USUI, Tadao

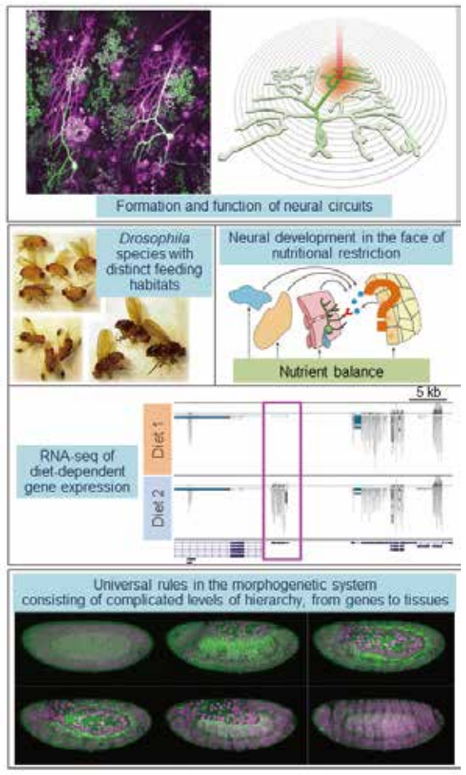
Assist. Prof.
HATTORI, Yukako

Program-Specific Assist. Prof.
KONDO, Takefumi

Program-Specific Assist. Prof.
TSUYAMA, Taiichi

Main theme

Diet is a critical environmental determinant that affects life-history traits. We are studying dietary responses that govern animal growth. We are also dissecting neuronal circuits that evoke selective behaviors in response to sensory stimuli.
Furthermore, we are finding the universal rule(s) in the morphogenetic system of multicellular organs consisting of complicated levels of hierarchy, from genes, cells to tissues.



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

Laboratory of Signal Transduction

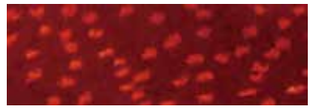
Lecturer
KUSAKABE, Morioh

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**

TOPICS

ES cell-derived presomitic mesoderm-like tissues for analysis of synchronized oscillations in the segmentation clock

The team of Professor Ryoichiro Kageyama, Marina Matsumiya, a graduate student, and others succeeded in inducing presomitic mesoderm (PSM)-like tissues from mouse ES cells. Somites, which give rise to vertebrae, ribs, and skeletal muscles, are periodically formed by segmentation of the anterior parts of the PSM. This periodicity is controlled by the segmentation clock gene *Hes7*, which exhibits synchronized oscillations in the PSM. Despite intensive studies, the exact mechanism of such synchronous oscillatory dynamics of *Hes7* expression still remains to be analyzed. Detailed analysis of the segmentation clock has been hampered, because it requires the use of live embryos, and establishment of an in vitro culture system would facilitate such analyses. This study established a simple and efficient method to generate mouse ES cell-derived PSM-like tissues, in which *Hes7* expression oscillates synchronously. Furthermore, in these tissues, segmentation occurs, forming somite-like structures. By using this system, the team examined the activities of 80 compounds and found that BET family proteins are involved in *Hes7* oscillations in the PSM. Thus, this method is applicable to gene and chemical library screening and will facilitate the analysis of the molecular nature of the segmentation clock.

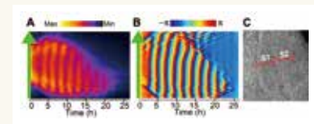
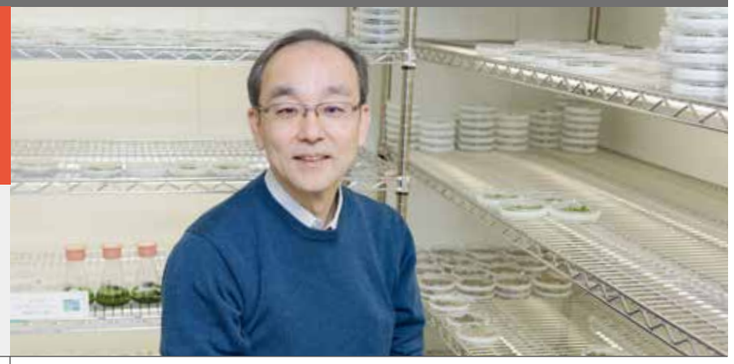


Figure: *Hes7* oscillations and segmentation of induced PSM-like tissues.

The findings were published in Development.
For further information, please refer to the URL below.
https://www.ncbi.nlm.nih.gov/pubmed/29437832
The interview article is available from the following URL.
http://thenode.biologists.com/people-behind-papers-marina-matsumiya-ryoichiro-kageyama/interview/

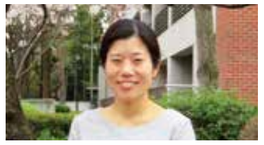
Laboratory of Plant Molecular Biology



Professor
KOHCHI, Takayuki

Assoc. Prof.
NISHIHAMA, Ryuichi

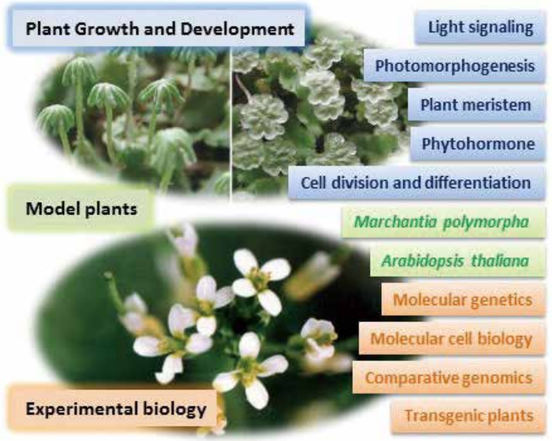
Assist. Prof.
YASUI, Yukiko



Program-Specific Assist. Prof.
YOSHITAKE, Yoshihiro

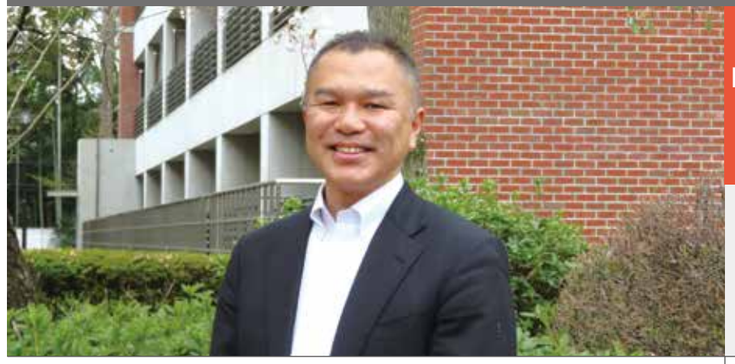
Main theme

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

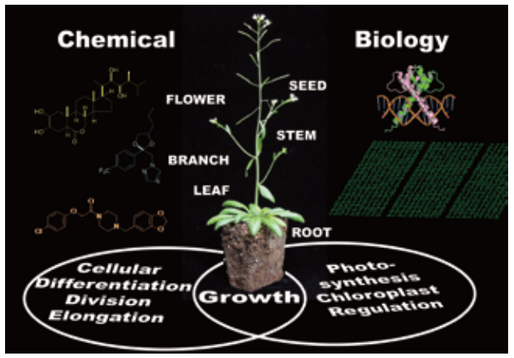
Assist. Prof.
IFUKU, Kentaro

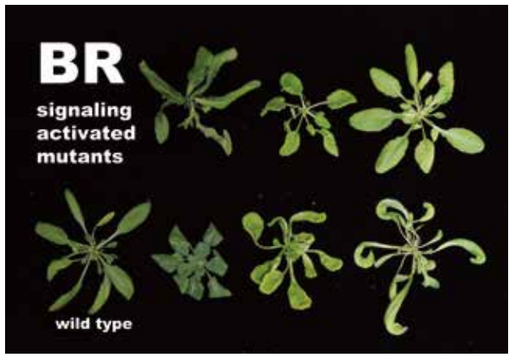
Main theme

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



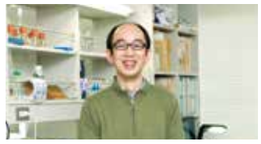


http://www.callus.lif.kyoto-u.ac.jp Lab URL

Laboratory of Biosignals and Response

Professor
NAGAO, Masaya

Assoc. Prof.
KAMBE, Taiho

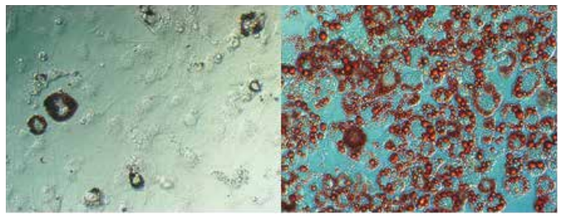


Assist. Prof.
NISHINO, Katsutoshi

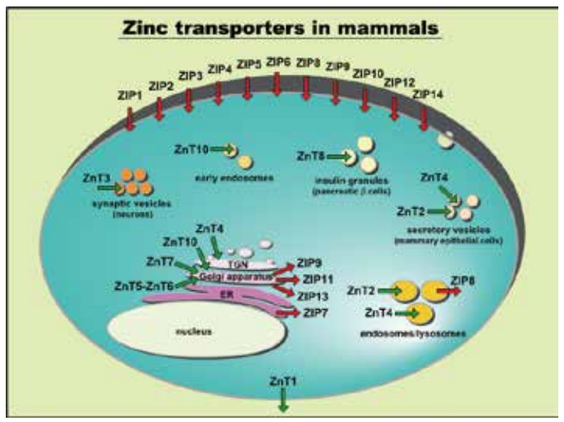
Main theme

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.

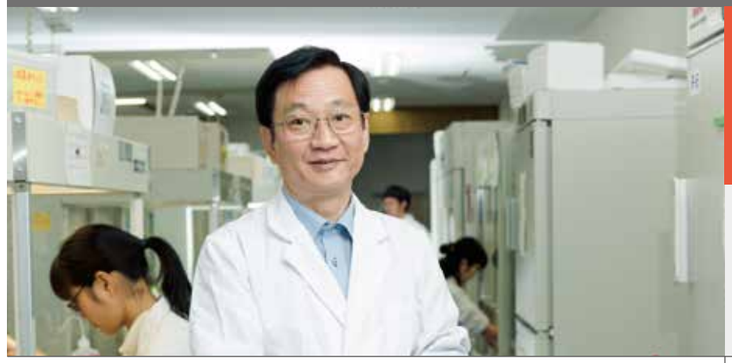


Stimulation of lipid accumulation by plant extracts



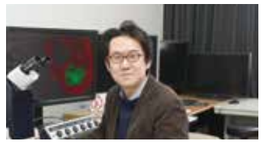
Lab URL http://www.seitaijoho.lif.kyoto-u.ac.jp/

Laboratory of Applied Molecular Microbiology



Professor
FUKUZAWA, Hideya

Lecturer
YAMANO, Takashi



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

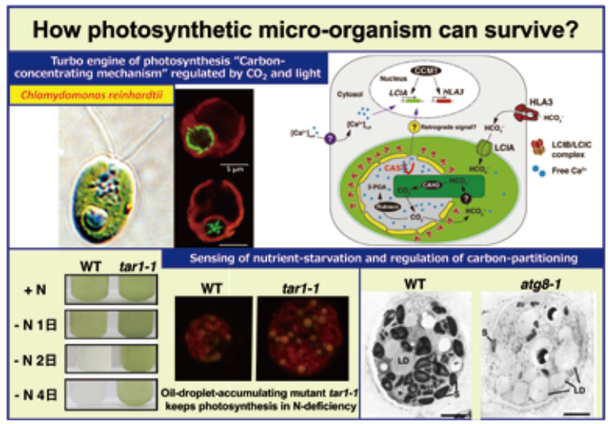
(1) Molecular characterization of the carbon-concentrating mechanism (CCM) supporting photosynthetic carbon fixation, biofuel production, and cell proliferation.

(2) Elucidation of regulatory systems controlling photosynthesis and carbon/nitrogen metabolisms by sensing environmental factors including changes of levels in CO_2 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

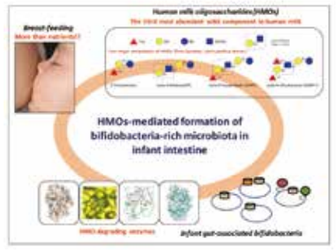
Assist. Prof.
KATOH, Toshihiko

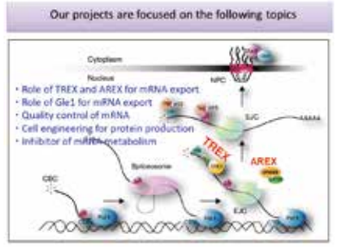
Main theme

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 matabolism to apply to medical care.





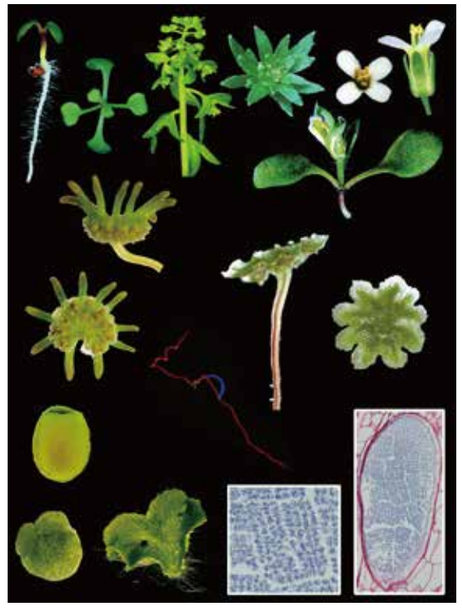
Lab URL http://www.bunshioutou.lif.kyoto-u.ac.jp/

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:

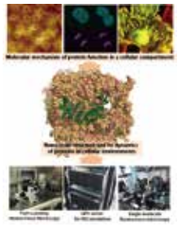
(1) Cytoskeletal dynamics in cell motility and metastasis: intracellular dynamics of actin cytoskeleton is elucidated by our live-cell nano-imaging technique.

(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

Observing how a living cell takes up signaling molecules into the cell

Cells communicate with their environments via the plasma membrane and various membrane proteins. Endocytosis plays a central role in such communication and proceeds with a series of multiprotein assembly, deformation of the plasma membrane, and production of a membrane vesicle that delivers extracellular signaling molecules into the cytoplasm. A research group of the Laboratory of Plasma Membrane and Nuclear Signaling in the Graduate School of Biostudies (S.H. Yoshimura, associate professor and A. Yoshida, former doctoral student) established a home-built correlative imaging system comprising high-speed atomic force microscopy (HS-AFM) and confocal fluorescence microscopy in collaboration with Olympus Co. Ltd. By utilizing this imaging system, the group successfully captured morphological changes of the plasma membrane and protein localization during clathrin-mediated endocytosis in a living cell.

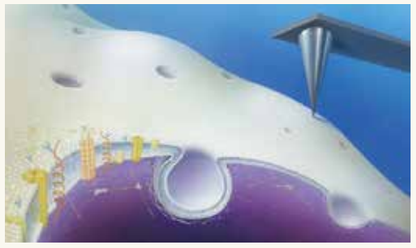


Figure: Cells take up various extracellular molecules into the cell via dynamic process called endocytosis, which proceeds with assembly of a number of proteins and dynamic morphological changes of the plasma membrane. (Copyright: S. Yoshimura, Kyoto University / Art: Tomo Narashima)

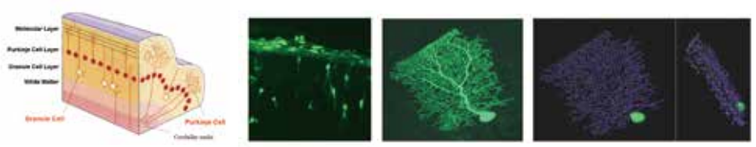
The findings were published in PLOS Biology, 16(5):e2004786 (2018).
For further information, please refer to the URL below.
https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2004786

Professor
KENGAKU, Mineko

Laboratory of Developmental Neurobiology

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 clarity 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

Professor
SUZUKI, Jun

Laboratory of Biochemical Cell Dynamics

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
FUJITA, Takashi

Main theme

Virus infections, such as influenza A epidemic, Ebola hemorrhagic fever, Middle East respiratory syndrom, 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.

Lab URL http://www.virus.kyoto-u.ac.jp/Lab/bunshiiden2012/English/index.html

Laboratory of Developmental Dynamics

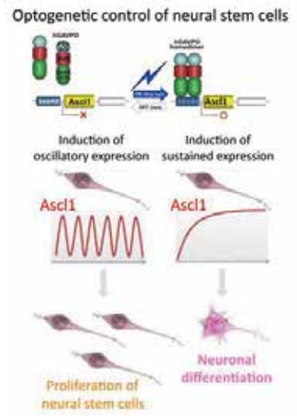
Professor
KAGEYAMA, Ryoichiro

Assoc. Prof.
OHTSUKA, Toshiyuki

Assist. Prof.
KOBAYASHI, Taeko

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.



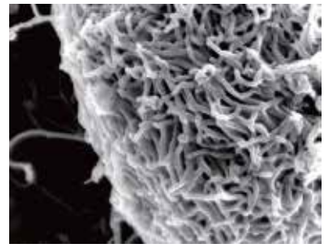
Lab URL http://www.infront.kyoto-u.ac.jp/research/lab28/

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.

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

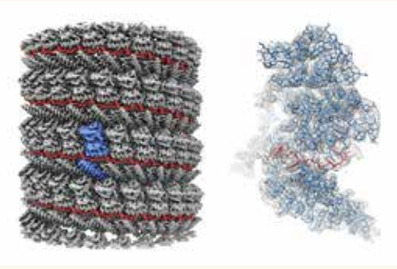
Assist. Prof.
NAKANO, Masahiro

Assist. Prof.
MURAMOTO, Yukiko

TOPICS

Structure of the Ebola virus nucleoprotein-RNA complex

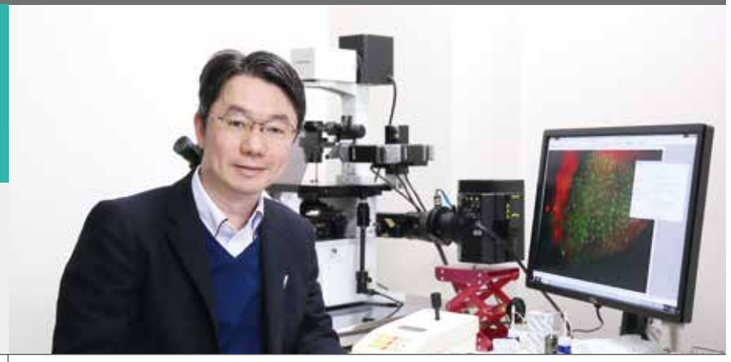
Ebola virus causes hemorrhagic fever with a high fatality rate in humans and non-human primates. However, there is no licensed antiviral drug and vaccine available against Ebola hemorrhagic fever. Prof. Takeshi Noda, Laboratory of Ultrastructural Virology, Graduate School of Biostudies, in collaboration with Prof. Matthias Wolf and Dr. Yukihiko Sugita at Okinawa Institute of Science and Technology Graduate University and with Prof. Yoshihiro Kawaoka at Institute of Medical Science, University of Tokyo, solved the structure of the Ebola virus nucleoprotein-RNA complex at 3.6 angstrom resolution by cryo-electron microscopy. Our findings provide a detailed molecular basis for understanding nucleocapsid assembly and virion morphogenesis, which may contribute to a development of the antiviral drug.



(Left) Structure of the helical Ebola virus NP-RNA complex solved by cryo-electron microscopy. The NP molecule is colored blue, and single-stranded RNA is in red. (Right) An atomic model of an NP molecule and an RNA comprising 6 nucleotides.

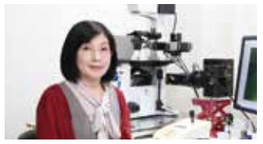
The findings were published in Nature 563: 137-140, 2018. For further information, please refer to the URL below.
http://www.infront.kyoto-u.ac.jp/achievements/post-3814/

Laboratory of Single-Molecule Cell Biology



Professor
WATANABE, Naoki

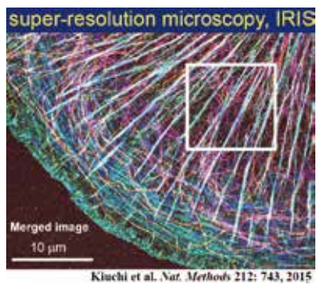
Lecturer
YAMASHIRO, Sawako



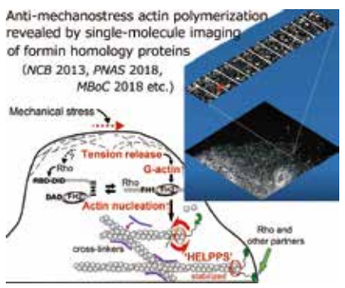
Assist. Prof.
MIYAMOTO, Akitoshi

Main theme

Our laboratory aims at bridging the gap between molecular activities and cell physiology in life systems. We are trying to visualize signal transduction and cell structure remodeling processes directly in living cells by fluorescence single-molecule microscopy. We have also recently invented new super-resolution microscopy called IRIS, which achieves ultra-high density labeling of multiple targets in a single specimen. By direct viewing using these advanced optical techniques, our laboratory elucidates the mechanism and the dynamics of pathophysiological cell signaling.



Kiuchi et al. *Nat. Methods* 212: 743, 2015



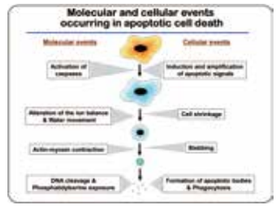
Lab URL http://www.pharm2.med.kyoto-u.ac.jp/

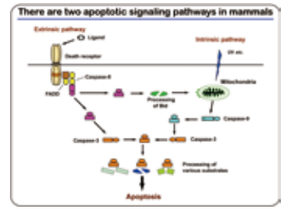
Assoc. Prof.
SAKAMAKI, Kazuhiro

Laboratory of Molecular and Cellular Biology

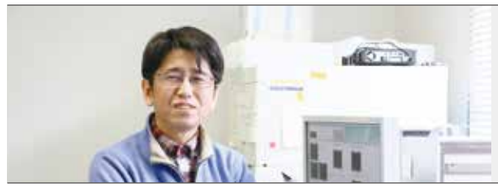
Main theme

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**

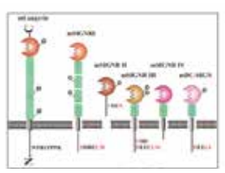


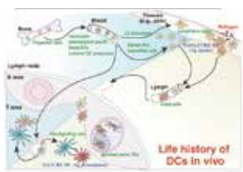
Assoc. Prof.
TAKAHARA, Kazuhiko

Laboratory of Immunobiology

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**

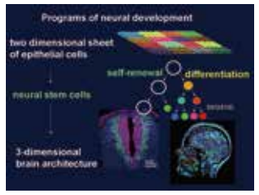
Laboratory of Molecular Cell Biology and Development

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 gyrification. 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

Assoc. Prof. 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.

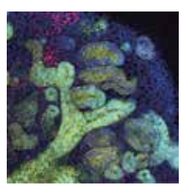
Prometaphase belt of chromosomes

Lab URL http://www.cdb.riken.jp/lcs/

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

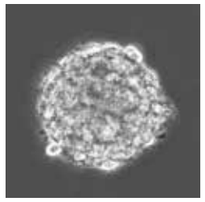
Assoc. Prof. KATOH, Hironori

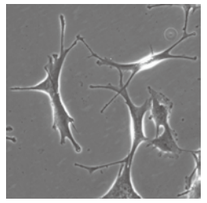
Laboratory of Molecular Neurobiology

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.



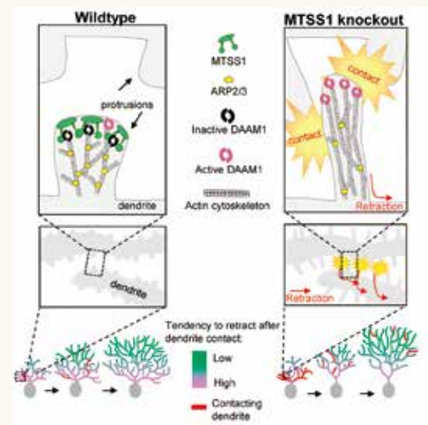


http://www.negishi.lif.kyoto-u.ac.jp/e/Top.html **Lab URL**

TOPICS

Building trees: the protein controlling neuron branching in the brain

Neurons in the brain form elaborate branches that connect with branches of other neurons, building complex neural networks. Kelly Kawabata and Mineko Kengaku of the Laboratory of Developmental Neurobiology found that the loss of a protein called 'Metastasis Suppressor-1' (MTSS1) causes growth restriction of neuron branches. MTSS1 binds to and inhibits a protein called DAAM1 that enhances polymerization of actin filaments in fine protrusions on the surface of neuron branches. The loss of MTSS1 leads to excess actin polymerization and abnormal elongation of the protrusions until they come in contact with neighboring ones, causing retraction of the neuron branches to avoid redundant neural network formation. Kengaku thinks this novel mechanism of the formation of neuron branches can help in the development of therapies for damaged brains.

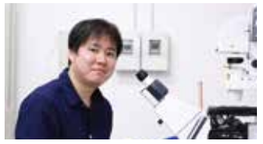


This study was published in the journal *Cell Reports*.
https://doi.org/10.1016/j.celrep.2018.06.013

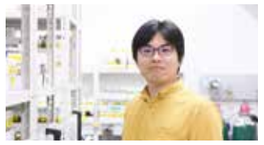
Laboratory of Genetics

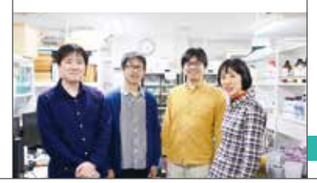
Professor
IGAKI, Tatsushi

Assist. Prof.
ENOMOTO, Masato



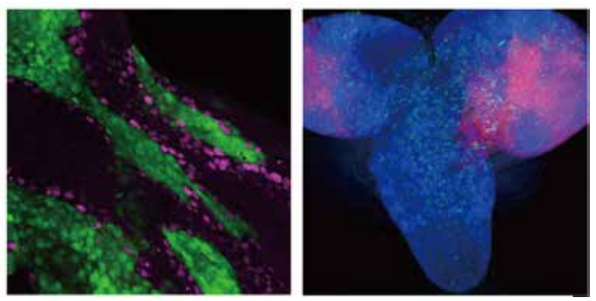
Program-Specific Assist. Prof.
TANIGUCHI, Kiichiro





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



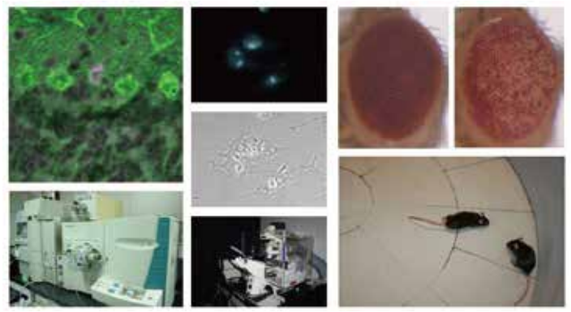
Left: Polarity-deficient cells (green; losers) are eliminated from epithelium by wild-type cells (magenta; winners) through cell competition.
Right:Malignant tumor cells (magenta) are invading and metastasizing from the eye disc to the brain (blue) in Drosophila larva.

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

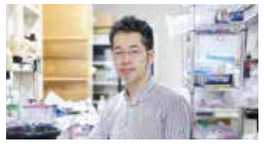
Laboratory of Functional Biology

Professor
KAKIZUKA, Akira

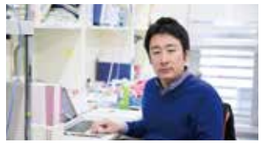
Main theme
Using animal models of human diseases, such as neurodegenerations, cancers, and obesity-related diseases, and using metabolite imaging techniques, we aim to elucidate molecular bases of such diseases and develop new strategies to cure or prevent them.
One of the main features of life science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



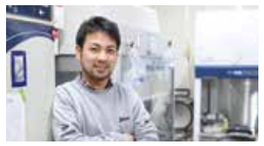
Assoc. Prof.
IMAMURA, Hiromi



Assist. Prof.
SASAOKA, Norio



Program-Specific Assist. Prof.
YOSHIDA, Tomoki



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

Laboratory of Science Communication

Professor
HEJNA, James Alan

Main theme

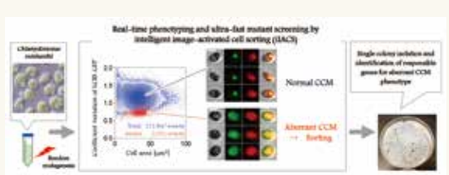
Our laboratory engages in the development and implementation of new approaches to the internationalization of science education and communication, based on principles of active learning. The particular challenges we are addressing often involve overcoming the differences in culture and pedagogical traditions 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

Development and use of the Intelligent Image-Activated Cell Sorter
Laboratory of Applied Molecular Microbiology
Takashi Yamano and Hideya Fukuzawa

A fundamental challenge of biology is to understand how cellular composition, structure, and morphology are linked to cellular physiology. Conventional technologies, such as FACS, are limited in uncovering these relations. Here, we present an "intelligent image-activated cell sorting (iIACS)" that realizes real-time and image-based cell sorting at an unprecedented rate. We applied it to screening of *Chlamydomonas* mutant cells based on CO_2-dependent protein relocation of low-CO_2 inducible protein (LCIB) in the chloroplast to understand the mechanism of photosynthetic carbon-concentrating mechanism (CCM). A coefficient of variation of the LCIB-GFP fluorescence signal was quantified in real time to distinguish the localization patterns in the chloroplast. The iIACS detected 221,947 events and sorted 2,021 mutant cells with aberrant LCIB localization. It is important to note that this identification and isolation processes normally takes several months using conventional techniques, but the iIACS could conduct it in only less than 40 min (6,500 times faster). We will use the iIACS to make phenotype-enriched library of algal cells based on the organelle and metabolite formation, localization, and accumulation for machine-based new scientific discovery in cell biology.



The findings were published in the Journal of "Cell, 175 (1): 266-276 (2018)" .
For further information, please visit the URL below
https://doi.org/10.1016/j.cell.2018.08.028

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

Elucidation of a novel regulatory mechanism of cell proliferation in vivo
-Visualizing activity of cell proliferation signals and its alteration in tumors-

This study has been published in Nature Communications on June 5th, 2018.
A research team from the Prof. Michiyuki Matsuda' s laboratory has succeeded in visualizing activity of ERK MAP kinase, a key protein regulating cell proliferation, in the intestinal epithelium of living mice, and showed that changes in the functions of this protein are involved in intestinal tumorigenesis.
In multicellular organisms, cell proliferation is strictly regulated to maintain tissue homeostasis, where growth factor signaling represents a critical mechanism to initiate and promote cell proliferation. Upon binding of growth factors to their specific receptors present at the cell surface, a key signaling protein ERK is activated to promote cell proliferation. Constitutive activation of the growth factor-ERK signaling pathway has been implicated in various cancers, and drugs targeting this pathway have been used clinically to treat several cancers. However, it had remained technically difficult to investigate when, where, and how ERK functions in living tissues or animals. In this study, by using the cutting-edge microscopy technologies, we have established a method to visualize ERK activity in the intestinal epithelium of living mice. The following analyses with this method revealed that dynamics of ERK activity is defined by two different growth factor receptors, EGFR and ErbB2. Notably, we also found that, during intestinal tumorigenesis, EGFR signaling is augmented and alters ERK activity dynamics, which renders cells highly sensitive to EGFR inhibitors that are currently used in the treatment of colorectal cancer. These results reveal how cell proliferation signals through the growth factor-ERK pathway are activated and transmitted in the mammalian intestinal epithelium, and show that changes in ERK activity dynamics underlie tumor cell-specific traits.

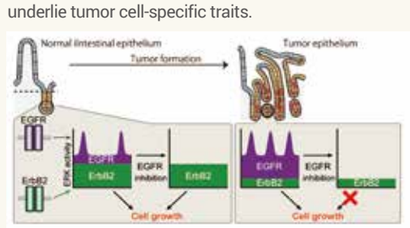


Figure: Dynamics of ERK activity during intestinal tumor development

For further information, please refer to the URL below.
http://www.kyoto-u.ac.jp/ja/research/research_results/2018/180605_2.html

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

TOPICS

Why is zinc deficiency associated with so many diverse symptoms?

Zinc is a trace nutrient indispensable for life. It plays crucial roles in numerous biological processes, and thus, its deficiency causes myriad pathophysiological symptoms in human patients and animal models. However, why distinct phenotypes are generated by zinc deficiency remains unclear. In a study in Communications Biology, the laboratory of Taiho Kambe examines whether zinc deficiency affects extracellular adenine nucleotide metabolism. Zinc deficiency impairs adenine nucleotide metabolism in both cell and rat models leading to delays in extracellular ATP clearance and adenosine generation. Since the finely tuned balance between extracellular adenine nucleotides and adenosine is critical for purinergic signaling, these findings provide a novel insight into why zinc deficiency in humans results in diverse symptoms.

The findings were published in the Journal of “Communications Biology” .

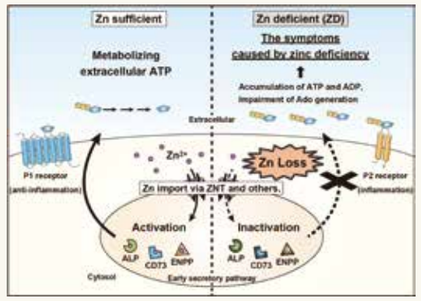


Figure: Zinc deficiency impairs extracellular adenine nucleotide metabolism leading to delays in extracellular ATP clearance and adenosine generation.

For further information, please refer to the URL below.
https://www.nature.com/articles/s42003-018-0118-3

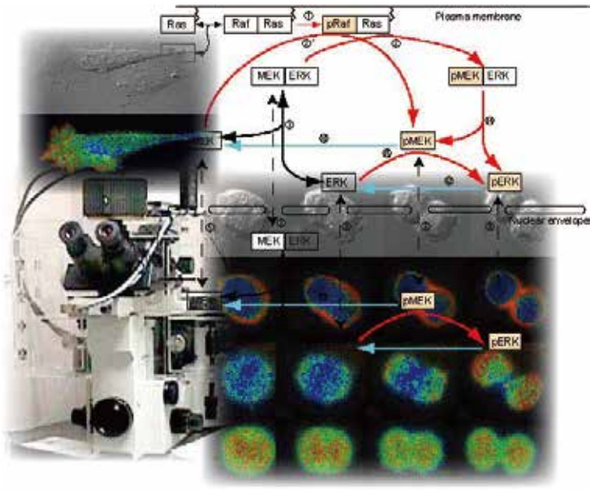
Laboratory of Bioimaging and Cell Signaling

Professor
MATSUDA, Michiyuki

Assoc. Prof.
TERAI, Kenta

Main theme

We are visualizing the growth signal transduction cascades in living cells by using biosensors based on the principle of Foerster resonance energy transfer (FRET). These FRET videos are used to characterize the property of each signaling molecule. We are also developing transgenic mice expressing FRET biosensors to observe the signaling status in living mice with two-photon excitation microscopes. We also study development and plasticity of nervous system by using in vivo imaging of mouse brain.



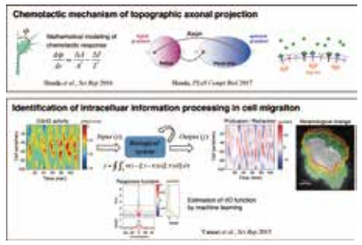
http://www.fret.lif.kyoto-u.ac.jp/mi.htm **Lab URL**

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.



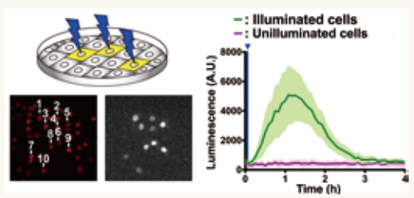
Lab URL https://sites.google.com/view/theoretical-biology/

TOPICS

Hybrid tool combines light with chemicals to fine-tune gene expression

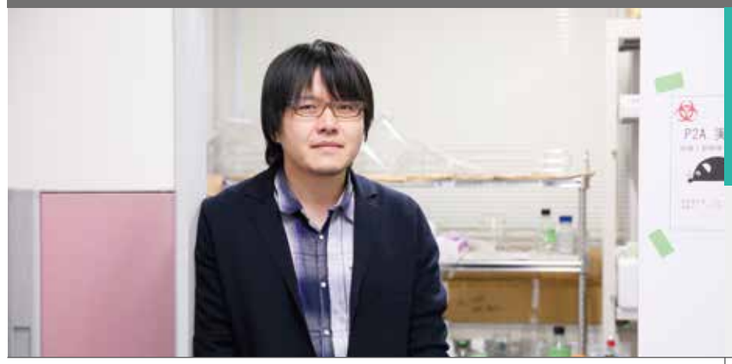
The laboratory of Itaru Imayoshi and Mayumi Yamada characterized a novel light-control system of cellular gene expressions.
For mammalian cells, the Tet system is one common, chemically-regulated system that can activate specific genes. It utilizes a small molecule called Doxycyclin -- or Dox -- to move the Tet transcription activator on or off of the DNA, thereby controlling gene expression.
The researchers designed the Tet transcription factor and photo-activatable (PA) protein switch to bind together in the presence of blue light, resulting in two versions of PA-Tet: PA-Tet-ON and PA-Tet-OFF. In this case of the PA-Tet-ON system, the Tet element activates with Dox, but when the light is turned off, the protein complex splits apart and ceases all activity. This new tool was shown to increase or decrease activity depending on the concentration of Dox as well as due to light intensity, and even short bursts of light could pulse gene expression levels.

"We can now accurately control gene expression inside a living mouse's body, such as in the brain and under the skin," states Yamada.
Lead researcher Itaru Imayoshi concludes, "Our lab's main focus is neural development and regeneration of the brain. Neural stem cells show dynamic changes in gene expression in a precise and timed manner. This PA-Tet system will help not only our field of research but the wider study of genetics and cell biology."



The blue-light induced gene expression in the targeted cells.

For further information, please refer to the URL below.
https://www.cell.com/cell-reports/fulltext/S2211-1247(18)31456-6

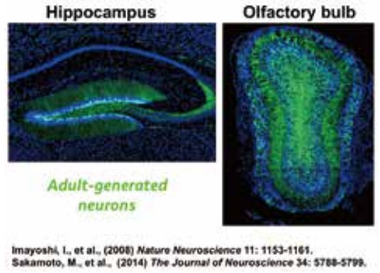


Laboratory of Brain Development and Regeneration

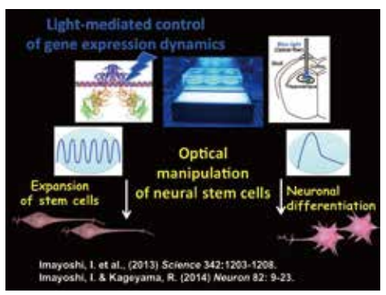
Professor
IMAYOSHI, Itaru

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.



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

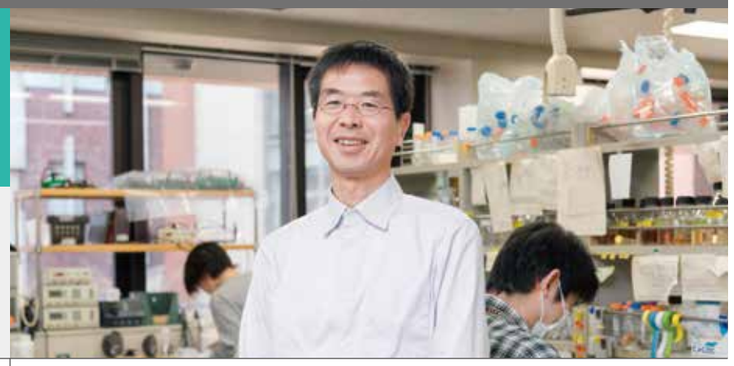


Imayoshi, I. et al., (2013) *Science* 342:1203-1208.
Imayoshi, I. & Kageyama, R. (2014) *Neuron* 82: 9-23.

Lab URL https://brainnetworks.jimdofree.com

Program-Specific Assist. Prof.
SUZUKI, Yusuke

Laboratory of Genome Maintenance

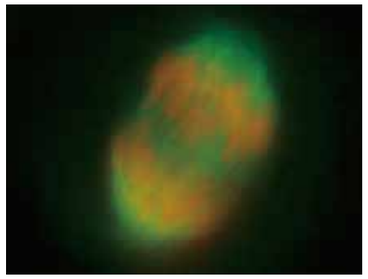


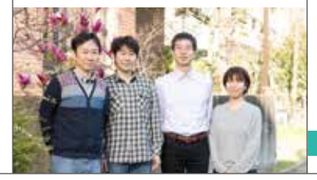
Professor
MATSUMOTO, Tomohiro

Lecturer
FURUYA, Kanji

Main theme

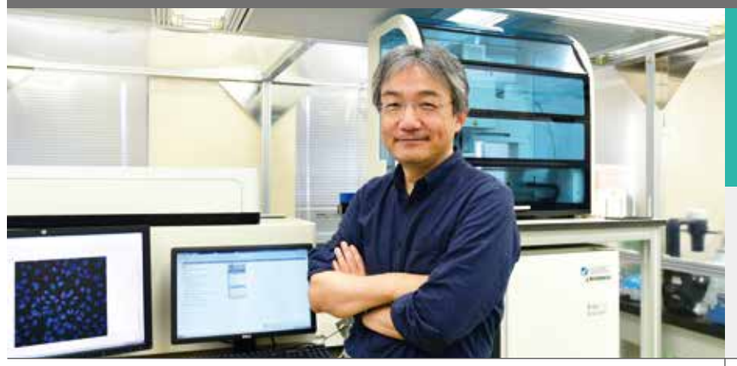
The spindle checkpoint, our major research subject, is a surveillance mechanism to regulate cellular apparatus for compliance with this rule. It is a unique negative feedback that converts/amplifies a physical signal sensed by kinetochores (attachment of the spindle and/or tension) and regulates the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

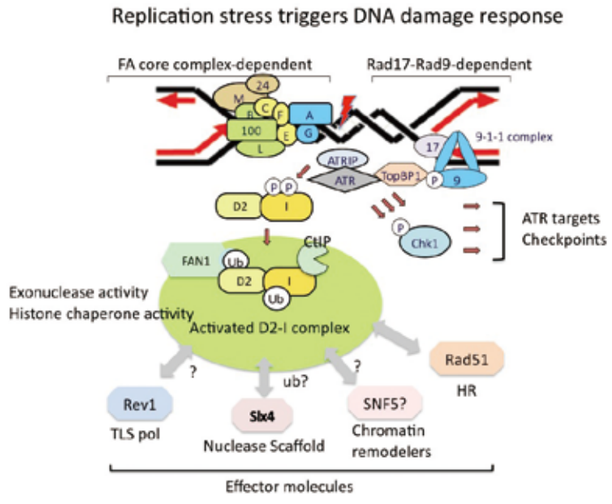


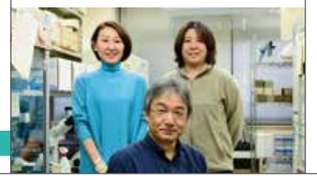
Professor
TAKATA, Minoru

Program-Specific Assist. Prof.
KATSUKI, Yoko

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.



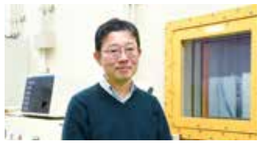


http://house.rbc.kyoto-u.ac.jp/late-effect Lab URL

Laboratory of Cancer Cell Biology

Professor
HARADA, Hiroshi

Assoc. Prof.
KOBAYASHI, Junya



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 at elucidating molecular mechanisms responsible for cellular adaptive responses to the tumor-specific microenvironments and malignant progression of cancer cells (Figure 2).

- Cellular adaptive responses to diverse and complex tissue microenvironments
- Molecular mechanisms underlying malignant progression and radioresistance of cancer cells
- Regulatory mechanisms of carbohydrate metabolic pathway

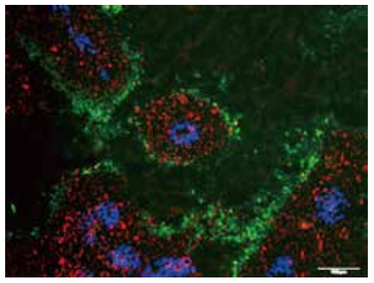


Figure 1: Hypoxic tumor cells (green) distant from blood vessels (blue) are resistant to radiation-induced DNA damage (red).

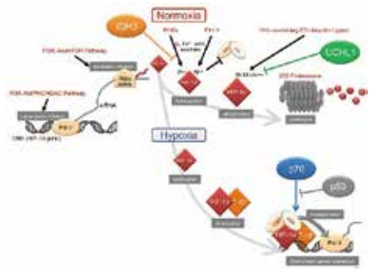
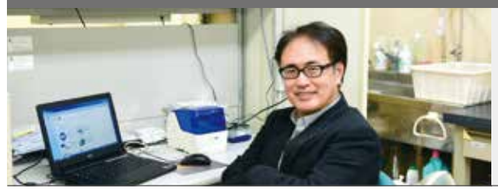


Figure 2: HIF-1-mediated gene networks responsible for both adaptive responses to hypoxia and malignant progression of cancer cells.

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



Laboratory of Chromatin Regulatory Network

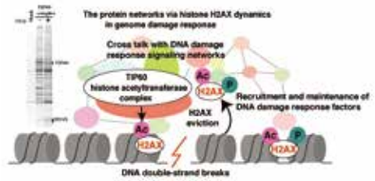
Assoc. Prof.
IKURA, Tsuyoshi

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



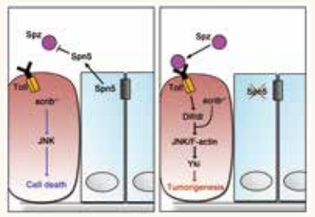
Lab URL http://house.rbc.kyoto-u.ac.jp/mutagenesis2/index1

TOPICS

Identifying the mechanism of tumor suppression by cell competition in flies.

This study has been published in *Current Biology* on May 24th, 2018.

Using fruit fly *Drosophila* as a model organism, the research group of Professor Tatsushi Igaki (Lab of Genetics, Graduate School of Biostudies) and Dr. Mitsuko Katsukawa (a former graduate student in the Graduate School of Biostudies) identified the mechanism of tumor suppression by 'cell competition' , a cell-cell interaction whereby cells with higher fitness eliminate neighboring cells with lower fitness by inducing cell death.
Most cancers originate from epithelia, which has clear apico-basal cell polarity. It has been shown in *Drosophila* imaginal epithelia that newly emerged oncogenic polarity-deficient cells are eliminated via cell-cell interaction with surrounding normal cells, a phenomenon called tumor-suppressive cell competition. However, the regulatory mechanisms behind this cell elimination are not fully understood. The research group searched for factors that regulate tumor-suppressive cell competition in *Drosophila* and found that a secreted protease inhibitor Serpin5 (Spn5) is required for surrounding normal cells to eliminate neighboring oncogenic cells. Downregulation of Spn5 in wild-type cells results in elevation of Toll signaling in neighboring oncogenic cells, which causes tumorous overgrowth. Mechanistically, Toll signaling activation in polarity-deficient cells leads to activation of the Hippo pathway effector Yorkie that blocks cell death and promotes cell proliferation. These observations suggest that manipulation of innate immune signaling could be a novel strategy of cancer therapy via activation of tumor-suppressive cell competition.



(left) Spn5 secreted from normal cells (blue) suppresses the Toll ligand SpZ, thereby inhibiting Toll signaling in oncogenic polarity-deficient *scrib*$^{-/-}$ cells (red) and promoting their elimination.
(right) Downregulation of Spn5 in normal cells causes activation of Spz, which leads to elevation of Toll-Dif/dl signaling in oncogenic *scrib*$^{-/-}$ cells, thereby resulting in Yki-dependent tumorous overgrowth.

Details can be read here:
https://www.cell.com/current-biology/fulltext/S0960-9822(18)30450-0

Laboratory of Cell Regulation and Molecular Network

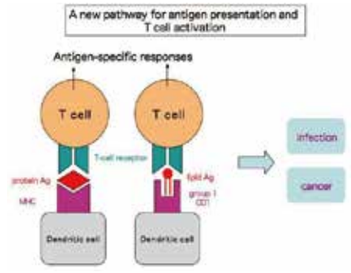
Professor
SUGITA, Masahiko

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

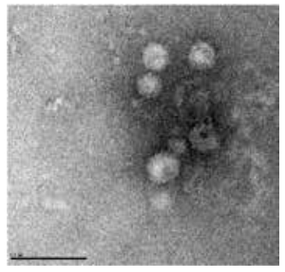
Professor
TOMONAGA, Keizo

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/

Professor
TOYOSHIMA, Fumiko

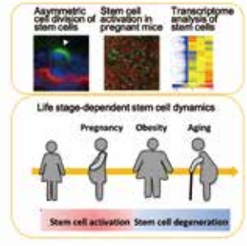
Laboratory of Cell Division and Differentiation

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.

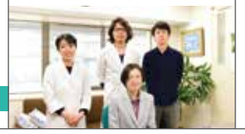
Research subjects

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



Asst. Prof.
ODA, Yukako

Assist. Prof.
ISHIBASHI, Riki



Lab URL http://www.virus.kyoto-u.ac.jp/Lab/toyoshima.html

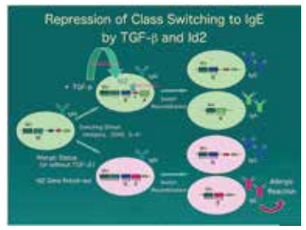
Laboratory of Genetic Information

Professor
SHIMIZU, Akira

Main theme

Major goal of research in this laboratory is to understand molecular and cellular mechanisms underlying highly systemic functions of living things, such as immune and neural systems. For this purpose, structure and regulation of genetic information responsible for such systemic functions are being analyzed using model animals, for example, transgenic or gene disrupted mice. Our research is focused on the following subjects:

1. Analysis of molecular mechanisms and regulation of chromatin modification, gene expression, gene rearrangements and RNA processing during lymphocyte differentiation.
2. Making and characterization of model mice of immunodeficiency or autoimmune by introduction of, or targeted disruption of interleukin, immunoglobulin or other genes.
3. Analysis of molecular and cellular mechanism for lymphocyte mobility and formation of immunomicroenvironment during development and immune reaction.



Laboratory of Cellular and Molecular Biomechanics

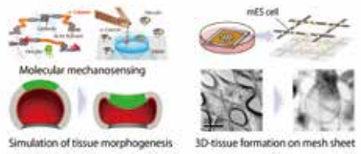
Professor
ADACHI, Taiji

Assist. Prof.
KAMEO, Yoshitaka

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.

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



Morphogenesis of biological tissues is regulated by mechanical forces generated through multicellular interactions. This study aims to clarify the mechanism of tissue morphogenesis using experiments and simulations.

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

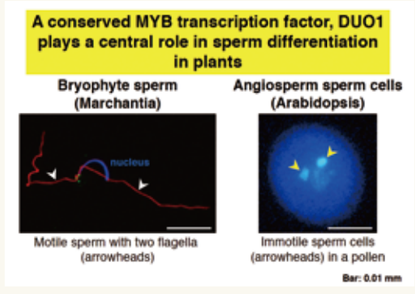
TOPICS

The evolution of sperm started with a single molecular change

How new cell types evolve remains a major question in biology. Across multi-cellular organisms, reproduction generally occurs via small, motile sperm that fertilize large immotile eggs. However, the widely varied morphology of sperm makes one wonder whether this cell type evolved from a single common ancestor or perm identity was defined by distinct events in separate group of organisms.

In work published in *Nature Communications* on Dec. 11, 2018, an international collaborative project between the Takashi Araki lab at Kyoto University and the Frederic Berger lab at the Gregor Mendel Institute of Molecular Plant Biology, an Institute of the Austrian Academy of Sciences, found that a single molecular event which occurred 700 million years ago was responsible for the evolution of sperm in all land plants.

"Our research will stimulate applied researches to develop various male-sterile crop and other useful plants, because DUO1 gene function is widely conserved among all land plants" said Takashi Araki and Asuka Higo, a former graduate student and a post-doctoral fellow of Araki lab (currently, a research stuff in Kihara Institute for Biological Research at Yokohama City University).



For further information, please refer to the URL below.
https://www.oeaw.ac.at/gmi/detail/news/article/the-evolution-of-sperm-started-with-a-single-molecular-change/

TOPICS

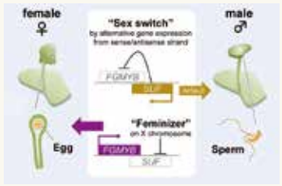
Sex differentiation genes evolutionarily conserved in land plants and sex switching mechanism in bryophyte were identified

- The liverwort *Marchantia polymorpha* switches female and male by alternate gene expression from sense and antisense strands of the sex differentiation gene locus -

This study was first published in the on-line version of *The EMBO Journal* on 4th January, 2019.

The research group of Professor Takayuki Kohchi and ex-graduate student Keitaro Okahashi collaborated with Professor Keiji Nakajima and ex-postdoc Tetsuya Hisanaga in Nara Institute of Science and Technology, and the research groups in Hiroshima University, Kindai University, and Monash University (Australia) to identify the evolutionarily conserved *FGMYB* genes, the regulatory genes for female differentiation in land plants. In the male plant of the liverwort *Marchantia polymorpha*, an extant bryophyte diverged in the earliest stage of land plant evolution, a long non-coding RNA expressed from the antisense strand of the Mp*FGMYB* gene suppresses the Mp*FGMYB* gene expression to promote male differentiation. Thus *Marchantia* switches female and male by an alternate gene expression between sense and antisense strands of DNA.

Comments from the research group:
This study identified evolutionarily conserved regulatory genes for sex differentiation in land plants, and revealed a sex switching mechanism by alternate gene expression from the sense and antisense strands of the sex differentiation gene locus in *Marchantia*. These findings have an impact on the research field of plant sexual reproduction and evolution, and also provide insights and future prospects into the development of plant breedings and innovations.

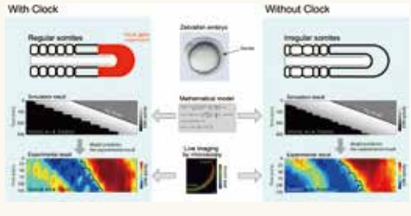


For further information, please visit the journal URL below (Open access):
http://emboj.embopress.org/content/38/6/e100240

How are somites accurately developed by cooperation of noisy unreliable cells

- Noise cancellation mechanism by internal clock -

The embryonic development is a remarkably reproducible phenomenon. However, individual cellular behaviors are not as accurate as machine, but are so stochastic that they behave differently even under the same conditions. How such noisy unreliable cells in a developing embryo cooperate to precisely form a body has been a fundamental question in the field of developmental biology. To address this issue, Associate Professor Naoki Honda (Theoretical Biology lab) and the collaborative research group at Nara Institute of Science and Technology Graduate School focused on somite formation in vertebrates. Somites are body segments repeatedly produced along the body axis during development. It has been known that regular-sized somites are formed to match the rhythm of the internal clock, and that the somites are irregularly formed in clock-deficient embryos. However, how the somites are reproducibly formed by the action of the clock was unclear. In this research, by combining the mathematical model and the experiment, it was clarified that the rhythm of the clock has the effect of canceling the noise, and as a result, the clock acts like the orchestra's conductor to cooperate noisy and unreliable cells for accurate somite formation.



The findings were published in PLoS Computational Biology.
For further information, please visit the URL below.
https://doi.org/10.1371/journal.pcbi.1006579

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. Now the center is integrated with Graduate School of Biostudies and will 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 (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.

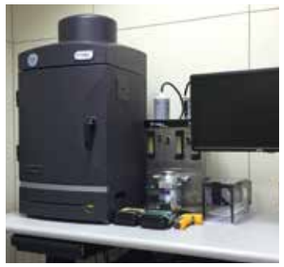
[Staff] HARADA, Hiroshi (Prof.)
KOBAYASHI, Junya (Assoc. Prof.)

Dept. of Stress Response

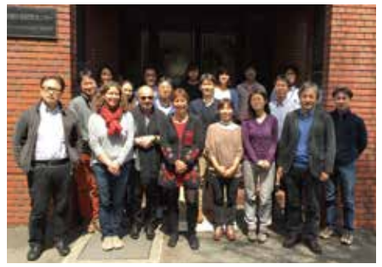
We will elucidate what kind of molecular reactions cells would display upon low dose irradiation in terms of stress response. Our main research targets are regulatory mechanisms of chromatin dynamics, translational regulation on ribosomes, acquired resistance mechanisms to low dose irradiation.

[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

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.)

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.)

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.)

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.)

Developmental Dynamics System (Kageyama Lab)

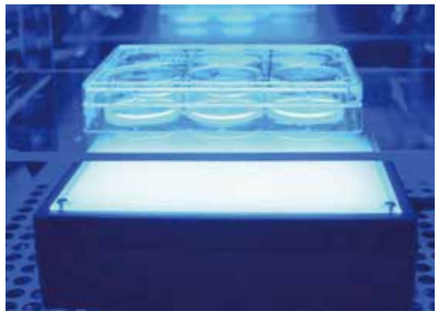
We will elucidate the significance of oscillatory gene expression by live imaging with luminescent and fluorescent reporters and by optogenetic perturbation in cultured cells and tissues.

[Staff] KAGEYAMA, Ryoichiro (Prof.)

Biological Function Manipulating Team (Imayoshi Lab)

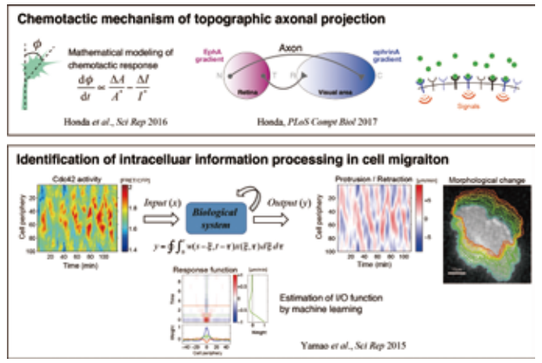
We will develop genetic and virus vector methods for expressing fluorescent proteins and functional molecules in specific cell types of the model organisms, especially mice. We will also develop novel optical methods to manipulate cellular and biological functions. By integrating these cutting-edge technologies,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

Data

As of April, 2019

Number of Students

*Students who pass Interim Exam will recieve master's degree.

(🧍=10) total 263

1st year	2nd year	3rd year	4th year	5th year
71	92	24	22	54

Number of International Students

(🧍=10) total 62

Government-sponsored	Personally funded
20	42

Non-degree Students

(🧍=2) total 7

Japanese Students	International Students
2	5

International Students Numbers

total 62

Asia

Brunei	1
China	23
Hong Kong	1
India	1
Korea	9
Malaysia	3
Philippines	2
Sri Lanka	1
Taiwan	3
Thailand	1

Africa

Ghana	1
Nigeria	1
Sudan	1

Europe

Croatia	1
UK	1

Middle East

Kuwait	1
Palestine	2
Turkey	2

North America

Canada	1
Mexico	2
USA	4

Number of Staff

*( )The numbers in parentheses indicate number of visiting academic staff.
*〈 〉The numbers in brackets indicate affiliate academic staff, in addition to the regular staff.

(🧍=5) total 62

Academic Staff

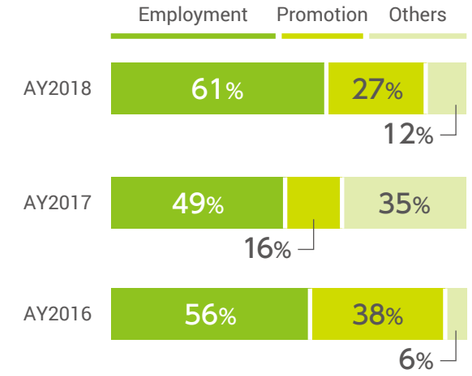
Professor	Associate Professor	Lecturer	Assistant Professor
18(3) 〈10〉	17(3) 〈2〉	5	11 〈9〉

Administration Office

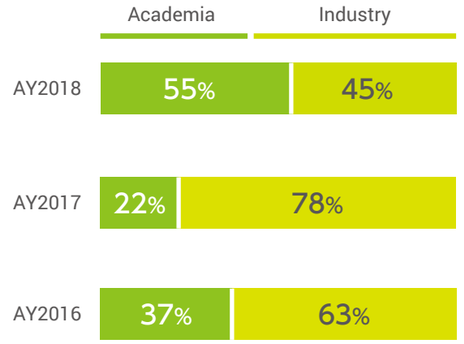
Administrative Staff	Technical Staff
10	1

Activity of Students following graduation

Master's degree holder



Employment of Doctoral degree holder



Number of Doctoral degree holder

(🧍=5)

AY2019	AY2017	AY2016
19	22	26

Places of Employment

Business

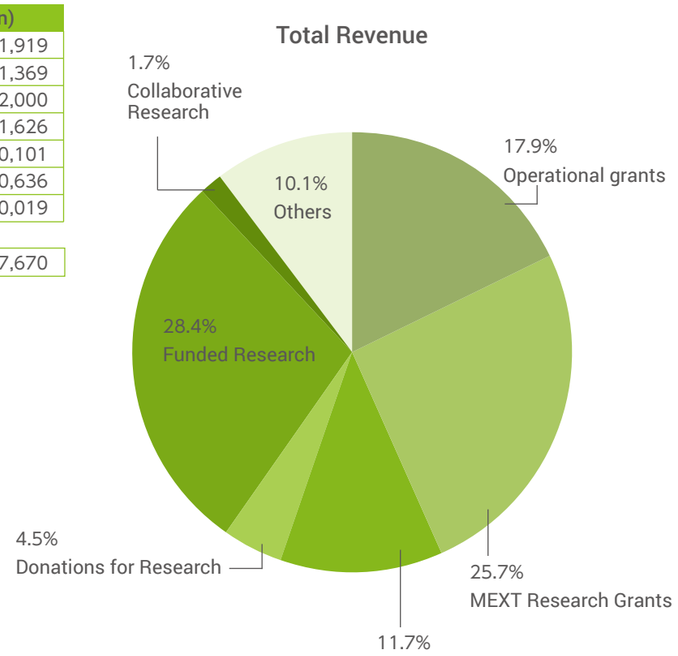
DENKA SEIKEN Co., Ltd. / KAWASUMI LABORATORIES. INC. / KOSÉ Corporation / Shionogi & Co., Ltd. / Astellas Pharma Inc. / Waqoo, Inc / choseido Pharmaceutical Co., Ltd. / TAKII & CO., LTD / Panasonic Corporation / Sumitomo Mitsui Card Co., Ltd. / KYORIN CO., LTD / SEIWA KASEI Co, Ltd. / Kyowa Hakko Kirin 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.

Others

Hokkaido University / University of Tokyo / Kyoto University / Shiga University of Medical Science / 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 2018

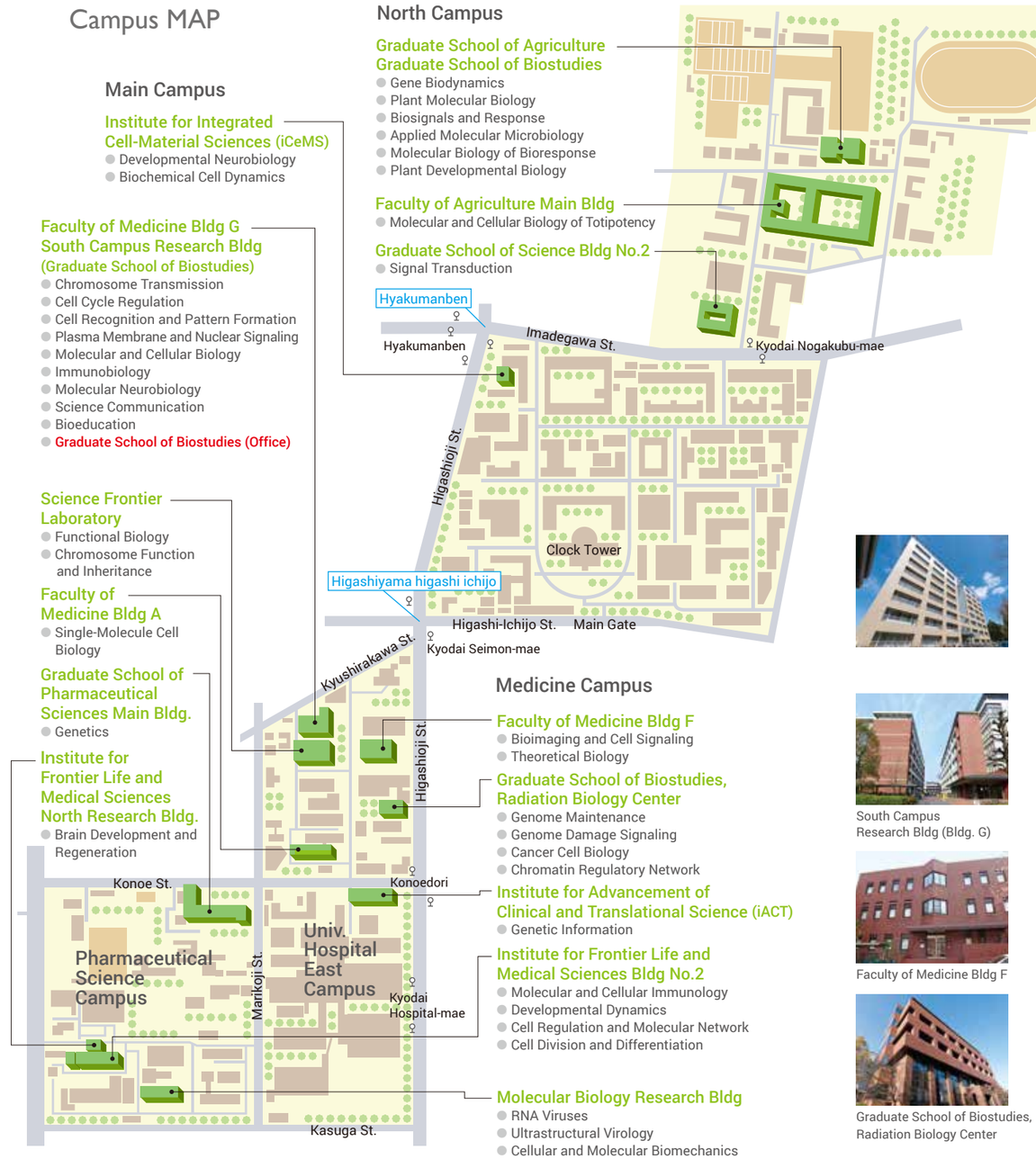
Category	Total (yen)
Operational grants	214,181,919
MEXT Research Grants	307,921,369
Other Research Grants	140,452,000
Donations for Research	54,531,626
Funded Research	340,210,101
Collaborative Research	20,480,636
Others	121,770,019
Total	1,199,547,670



Professors Emeriti As of April 1, 2019

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

Campus MAP



South Campus Research Bldg (Bldg. G)

Faculty of Medicine Bldg F

Graduate School of Biostudies, Radiation Biology Center

Access