LiMe
Institute for Life and Medical Sciences
Kyoto University

**Institute for Life and Medical Sciences,
Kyoto University**

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https://www.infront.kyoto-u.ac.jp/en/

LiMe

Institute for Life and Medical Sciences
Kyoto University

2022-2023

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32 Lab. of Virus-Host Coevolution
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The Japanese name of this institute has been drastically changed from “Virus-Saisei-Ikagaku Kenkyu-sho (meaning Institute for Virus and Regenerative Medicine)” to “I-Seibutsugaku Kenkyu-sho (meaning Institute for Medical Biology)” since April, 2022. On the other hand, formal English name of this institute has been just slightly changed from “Institute for Frontier Life and Medical Sciences” to “Institute for Life and Medical Sciences”, just deleting “Frontier”. I will explain how the original Japanese name and new one was given, and the thoughts put in the new Japanese name.

Process of integration of two institutes and renaming

The Institute for Frontier Life and Medical Sciences was established in October 2016 by integrating the Institute for Virus Research (Virus-Kenkyu-sho) and the Institute for Frontier Medical Sciences (Saisei-Ikagaku Kenkyu-sho). At the time of the integration, the names of both laboratories could just be lined up one after the other, for the time being. Subsequently, discussions continued regarding the new name after the integration, and the name was changed at this occasion, five and a half years after the integration.

History up to integration

Prior to the integration, each institution had expressed a strong presence in the academia world. The Institute for Virus Research, established in 1956, had led not only virology but also the whole field of molecular biology, and the Institute for Frontier Medical Sciences, originally established in 1941 as Tuberculosis Research Institute, had led a wide range of fields including not only regenerative medicine but also immunology and bioengineering. For example, the Institute of Viruses has produced Dr. Yorio Hinuma, who discovered the causative virus of adult T-cell leukemia, and the Institute for Frontier Medical Sciences has produced Dr. Shinya Yamanaka, who invented iPS cells, and Dr. Shimon Sakaguchi, who discovered regulatory T cells.

Background that led to the integration and actions made after the integration

In recent years, life science has undergone major changes, and it becomes difficult to be competitive in academic field with the research activity conducted solely by individual laboratories. In order to develop as a research institute, it is necessary to create a strategy by looking ahead of the times, to accordingly re-build the organization, and to proceed with personnel affairs in line with the strategy. Such strategy requires a certain size of personnel, and the integration has made it easier to pursue such a strategy. Currently, the number of whole workers, that of faculty members, and that of professors, is about 300, 80, and 20, respectively.

In terms of re-organization of structure, for the time of integration in 2016, we have newly established the "Department of Biosystem Sciences", in addition to the department of the virus research and the regenerative medicine. This “Department of Biosystem Sciences” is the core department that is expected to develop new academic fields. In accordance with this, we have been putting a lot of effort into personnel affairs, such as recruiting young professors majoring in structural biology or theoretical biology, which we think has been very successful up to now.

Thoughts put in the word "I-Seibutsu-gaku (Medical Biology)"

I think the name of the new research institute more or less sounds old-fashioned with the word "Seibutsu-gaku (Biology)". Indeed, as it sounds, I think that this name proposes the idea of "emphasizing the viewpoint of biology".

Recently, there is a tendency for research activities to require a so-called "exit" like the former examples, but the essence of research is to get answer to the intellectual curiosity of human beings, and I think there exist fundamental fun there. There also may exist a point that research that seeks fun is more likely to lead to a big leap than the one that seeks actual profit.

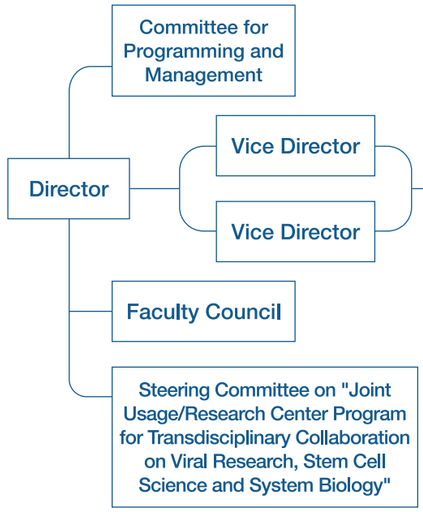
Launch of a new “Joint Usage/Research Center”

The former two institute had exerted the functions of research bases for virus research and regenerative medicine, respectively, and the integrated research institute has separately maintained the functions of the two bases. At the same time as this renaming, the two joint centers have been integrated, and a new base called "Joint Usage/Research for Transdisciplinary Collaboration on Viral Research, Stem Cell Science and System Biology" has been launched since April, 2022. As a core project of this center, we have established a system to financially support collaborations between the faculty members of this institute and outer researchers by up to 1 million yen per case, and in 2022, we adopted 30 projects as a result of the open call for participants.

Afterword

Although the function as joint center has been renewed as mentioned above in parallel with renaming of the center, the fundamental strategy that has been created after the integration will be basically inherited as it is, and thus we are not making major re-organization related to the renaming. However, taking the opportunity to change the name, all the staff members will strive hard together in unison so as to lead the era, with a sense of ownership as a member of “the research institute that has built the history of biology".

Hiroshi Kawamoto, MD., Ph.D.
Director and Professor
Institute for Life and Medical Sciences



Research Departments

Department of Virus Research

- Lab. of Molecular Genetics
- Lab. of Medical Virology
- Lab. of RNA Viruses
- Lab. of Ultrastructural Virology
- Lab. of Tumor Viruses
- Lab. of Cell Regulation
- Lab. of Immune Regulation
- Lab. of Bioresponse Analysis*
- Lab. of Viral Immunology*

Department of Regeneration Science and Engineering

- Lab. of Molecular and Cellular Biology
- Lab. of Biomaterials
- Lab. of Tissue Stem Cell Biology
- Lab. of Immunology
- Lab. of Tissue Regeneration
- Lab. of Developmental Epigenome
- Lab. of Integrative Biological Science
- Lab. of Immunopathogenesis
- Lab. of Experimental Immunology*
- Lab. of Material Biophysics*
- Lab. of Medical Engineering*

Department of Biosystems Science

- Lab. of Nano Bioprocess
- Lab. of Biomechanics
- Lab. of Developmental Systems
- Lab. of Systems Virology
- Lab. of Growth Regulation System
- Lab. of RNA System
- Lab. of Biological Membrane System
- Lab. of Tissue Homeostasis
- Lab. of Mathematical Biology
- Lab. of Stem Cell Genetics
- Lab. of Cell Fate Dynamics and Therapeutics
- Lab. of Deconstruction of Stem Cells
- Lab. of Regulatory Information*

*Visiting

Attached Research Facilities

Research Center for Infectious Diseases

- Lab. of Primate Model
- Lab. of Virus-Host Coevolution

Center for Animal Experiments

Center for Human ES Cell Research

- Division of Clinical Basis for ES Cell Research
- Division of Basic Technology Development for ES Cell Research

Department of Cell Biology

Department of Optical Biomedical Science

Research Administration Office

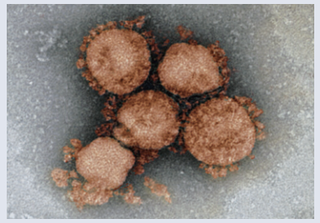
Division of Technical Support

Administration Office

The predecessor of the Institute, the Institute for Frontier Life and Medical Sciences (inFront), was formed by the merger of the Institute for Virus Research and the Institute for Frontier Life and Medical Science in 2016.
The Institute for Virus Research was known for its brilliant groundbreaking research in medical science, including the discovery of the human leukemia virus, and for pioneering work in molecular biology. The Institute for Frontier Medical Sciences, on the other hand, had built an innovative foundation in regenerative medicine by establishing human embryonic stem cells (ES cells) and discovering induced pluripotent stem cells (iPS cells) and regulatory T cells.
In April 2022, the Institute made a new start under the current name, The Institute for Life and Medical Sciences (LiMe), with the aim of exploring new academic fields in medical science and life science.

- **1941** Tuberculosis Research Institute
- **1956** Institute for Virus Research
- **1967** Chest Disease Research Institute
- **1980** Research Center for Medical Polymers and Biomaterials
- **1988** Chest Disease Research Institute (structural reorganization)
- **1990** Research Center for Biomedical Engineering
- **1998** Institute for Frontier Medical Sciences
- **2008** Joint Usage/Research Center Program for Transdisciplinary Collaboration on Tissue Engineering and Regenerative Medicine
- **2010** Joint Usage/Research Center Program for Fusion of Advanced Technologies and Innovative Approaches to Viral Infections and Life Science
- **2016** Institute for Frontier Life and Medical Sciences
- **2022** Institute for Life and Medical Sciences — Joint Usage/Research Center Program for Transdisciplinary Collaboration on Viral Research, Stem Cell Science and System Biology

Cell processing facility exclusive to human ES cells



Coronavirus image captured by an electron microscope

Unveiling ceremony for the establishment of the Institute for Frontier Life and Medical Sciences (inFront)

81 -year History

The origin of the Institute for Life and Medical Sciences (LiMe) dates back to 1941.

P5

Graduate Students **94**

The Institute accepts graduate students from six graduate schools.

P37

Faculty and Staff Members **192**

76 Faculty (**17** Professors)
46 Non-teaching researchers
70 Non-teaching staff

P37

Organization

3 Research Departments
3 Attached Research Facilities

The Iinstitute comprises three departments: the Department of Virus Research, the Department of Regenerative Science and Engineering, and the Department of Biosystems Science, and three attached research facilities: the Research Center for Infectious Diseases, the Center for Animal Experiments, and the Center for Human ES Cell Research.

P4

Laboratories

31 Laboratories
6 Visiting Laboratories

P4

Joint Research Projects adopted for Joint Usage/ Research Center Program **30**

P7

Expenditure in academic year 2021 **2.6** billion yen

P37

Overseas Partner Institutions **3** MOUs for academic cooperation and exchange

P37

Joint Usage/Research Center

The Institute for Life and Medical Sciences has been accredited by the Minister of Education, Culture, Sports, Science and Technology as a “Joint Usage/Research Center for Transdisciplinary Collaboration on Viral Research, Stem Cell Science and System Biology” since 2022, and provides the international research community with the resources and technologies of the Institute through collaborative research.

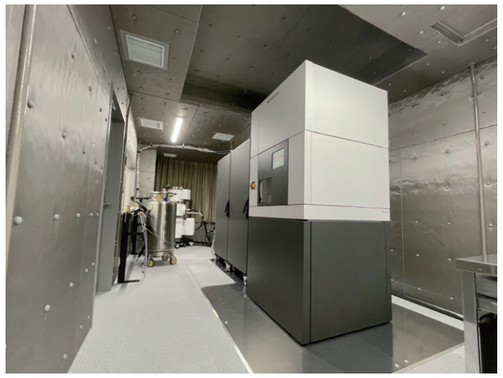
Since being formed by the merger of the Institute for Virus Research and the Institute for Frontier Life and Medical Science in 2016, the Institute for Life and Medical Sciences has promoted cutting-edge research in the life sciences in three divisions: the Department of Virus Research, the Department of Regenerative Science and Engineering, and the Department of Biosystems Science. There is collaboration across departments, as well as a system for conducting interdisciplinary research. The activities of the two joint centers, the “Joint Usage/Research Center for Fusion of Advanced Technologies and Innovative Approaches to Viral Infections and Life Science” and the “Joint Usage/Research Center for Transdisciplinary Collaboration on Tissue Engineering and Regenerative Medicine,” which continued at the Institute until FY2021, have been integrated into the new Center, which started activities in FY2022.

Research conducted at the Center

The Center is involved in activities on three main themes (1) viral infection research, (2) stem cell and tissue regeneration research, and (3) biosystems research, and the technologies and methodologies developed by the Institute are deployed both domestically and internationally. The Center aims to conduct cutting-edge, interdisciplinary research. Specific initiatives include (1) viral infection experiments and analysis of the microstructure and molecular structure of viruses, (2) the use of human ES cells, stem cell research and the development of tissue regeneration technology through the Human ES Cell Research Center, and (3) activities to explore various life phenomena as systems in collaboration with faculty members from diverse backgrounds in the Biosystems Research Group. In 2022, the first year of the program, 30 projects were adopted and implemented.

Total number adopted in 2022	
(1) Viral infection research	7
(2) Stem cell and tissue regeneration research	9
(3) Biosystems research	14
Total	**30**

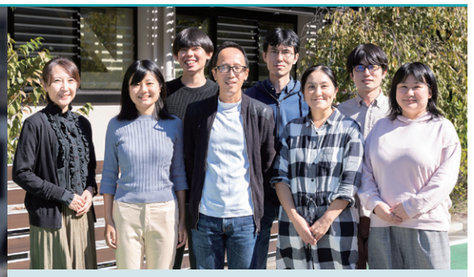
A list of these proposals is available in Japanese on the Institute’s website at:
https://www.infront.kyoto-u.ac.jp/kyoten/01-list



Cryo-TEM Glacios (ThermoFisher Scientific)

Lab. of Medical Virology

LiMe Bldg. No.2

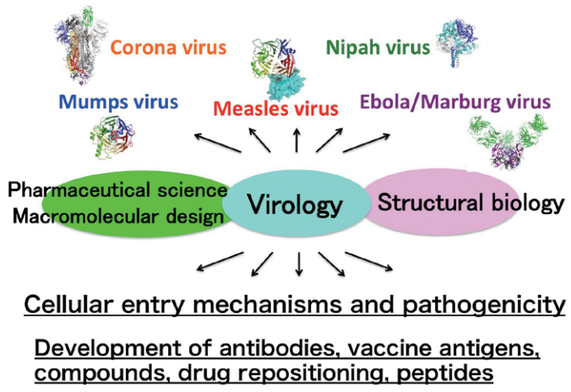


Prof. **Takao Hashiguchi**
Assist. Prof. **Tateki Suzuki**
Assist. Prof. **Kanako Kimura**
Assist. Prof. **Yuma Sato**

Infectious diseases still have remained a fatal threat to children, worldwide. To solve the problem, we have been studying on pediatric virology. In particular, we focus on the mechanisms of viral entry into cells and the inhibition of entry by compounds, peptides, glycans, and antibodies, using a combination of virological and structural biological approaches. Our major goals are the elucidation of viral pathogenesis and the development of preventive and therapeutic methods for viral diseases. Our laboratory was newly joined in this institute in September 2020, and started to research on paramyxoviruses and coronaviruses.

Measles virus (MeV) and mumps virus (MuV), members of the family Paramyxoviridae, are important human pathogens causing respiratory and neural infections. Globally, MeV has been causing outbreaks recently and over 200,000 deaths were reported in 2019. MeV usually causes acute measles, but in rare instances induces fatal and intractable neurological diseases. MuV causes epidemic parotitis, meningitis, encephalitis and deafness. Large outbreak of mumps occurs once every four to five years in Japan. Currently no licensed therapeutic agents are available for both viruses, and the mechanisms that cause CNS diseases remain unknown. Therefore, we are currently working on research to solve these problems.

Our laboratory has been also studying the development of new drugs for infectious diseases caused by SARS-CoV-2, Ebola and Marburg viruses, and Nipah virus, for which biosafety level 3 or 4 is required. One of our goals is to develop vaccines, therapeutics, and new methods of immunoanalysis using structural information.



Enveloped viruses possess glycoproteins that interact with receptors and other host factors to invade target cells via sequential membrane fusion and exert pathogenicity against humans. On the other hand, viral glycoproteins are also critical antigens in human immune responses and are one of the targets of antiviral drugs. Therefore, they are important not only in viral pathogenicity but also in the development of vaccines and new drugs. In our laboratory, we aim to elucidate the detailed mechanisms of infection and its inhibition by integrating virology with structural biology and drug discovery science.

Lab URL
https://medvirology.infront.kyoto-u.ac.jp/

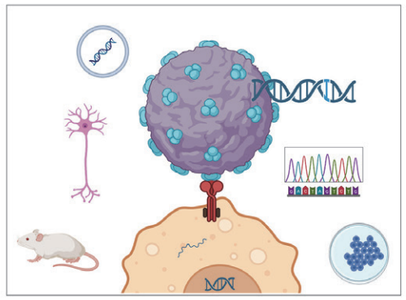
Lab. of RNA Viruses

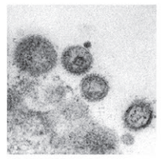
LiMe Bldg. No.3

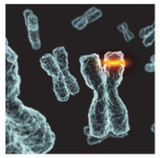
Prof. Keizo Tomonaga
Assoc. Prof. Akiko Makino
Assist. Prof. Makoto Kitabatake
Assist. Prof. Takehiro Kanda
Assist. Prof. Hiromichi Matsugo
Program-Specific Assist. Prof. Ryo Komorizono

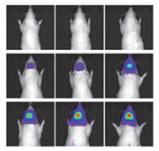
All viruses rely on the cellular machinery to complete their replication cycles. Therefore, the study of viruses can provide fundamental knowledge and understanding not only of viral pathogenesis and host responses but also of cellular function. The research carried out in this laboratory are focused on negative strand RNA viruses replicating in the cell nucleus, especially bornaviruses. All our projects aim to understand the fundamental mechanisms of the replication, pathogenesis and evolution of bornaviruses. In current research, we are investigating the replication and persistent mechanism of the bornaviruses in the nucleus. The understanding the biological and evolutional significances of the endogenous bornavirus-like elements (EBLs) found in the genomes of many vertebrate species is one of the main focuses of our laboratory. Furthermore, we are analyzing emerging bornaviruses, which include avian bornaviruses as well as a squirrel bornavirus that may be highly pathogenic to humans. We also aim to develop a next-generation RNA viral vector based on bornavirus for applying to gene and cellular therapy using stem cells.

朝長研究室 Tomonaga Laboratory









Replication/pathogenesis

- Persistent infection
- Neuropathogenesis
- Emerging viruses

Endogenous viruses

- Co-evolution
- Endogenization
- Paleovirology

Viral vectors

- Gene therapy
- Cellular therapy
- Regenerative medicine

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

Lab. of Ultrastructural Virology

LiMe Bldg. No.3

Prof. Takeshi Noda
Assoc. Prof. Yukihiko Sugita
Assist. Prof. Masahiro Nakano
Assist. Prof. Yukiko Muramoto

Our laboratory has been studying negative-strand RNA viruses such as influenza virus and Ebola virus, which are pathogenic for humans and animals. Especially, we have focused on: 1. The packaging mechanisms of influenza virus eight-segmented genome, 2. Mechanisms of influenza virus genome transcription and replication, 3. Mechanisms of Ebola virus helical nucleocapsid formation, 4. Generation of neutralizing monoclonal antibodies inhibiting influenza virus and Lassa virus replication, 5. Development of antiviral drugs by drug repositioning, and 6. The structure of influenza virus mRNAs. So our interests cover not only fundamental, but also practical research. In addition, our laboratory is skilled at imaging analyses by using microscopes. In addition to conventional virological, molecular biological, and cellular biological techniques, we employ microscopic analyses such as transmission electron microscopy, cryoelectron microscopy, and high-speed atomic force microscopy to understand virus replication mechanisms from an ultrastructural point of view. We would like to contribute to the progress of virus research as well as the control of infectious virus diseases through our research.

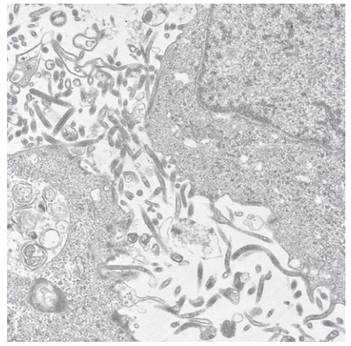


Figure 1 Transmission electron microscopic image of filamentous Ebola virus particles budding from infected cells.

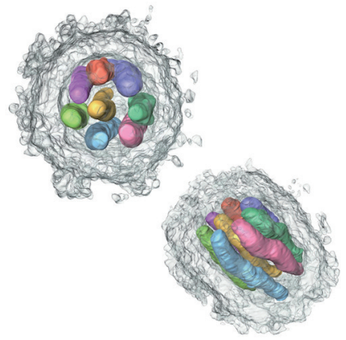
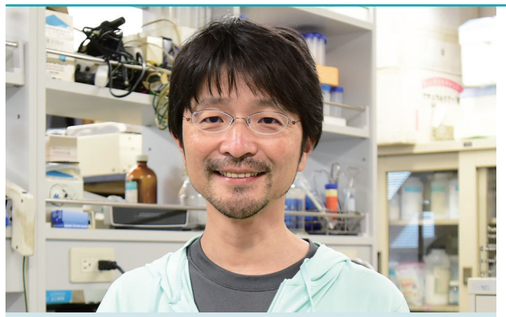


Figure 2 Three dimensional model of an influenza virus particle reconstructed by electron tomography. Eight RNPs arranged in a characteristic "1+7" pattern are present within the virion.

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

Lab. of Tumor Viruses



Assoc. Prof. **Hiroyuki Sakai**
LiMe Bldg. No.2

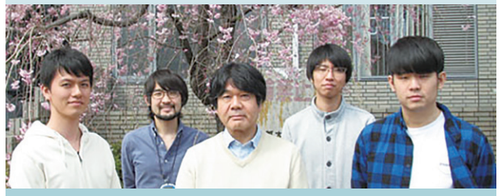
Lab URL
https://www2.infront.kyoto-u.ac.jp/sakai2012/Home2.html

Papillomavirus infection and its tumorigenic potential: The infection of papillomavirus induces benign tumors, such as warts and condylomas, and occasionally they are converted into cancers. We are investigating the molecular mechanisms of the virus replication and the virus-related tumor progression.

Analysis of Wnt intracellular signaling pathway: Wnt signaling regulates a variety of adult and developmental processes and mutations in several components of the Wnt pathway are oncogenic. I am analyzing this pathway in vitro and in vivo.

Horn-shaped warts induced by Shope papillomavirus infection

Assoc. Prof. **Makoto Hijikata**
South Research Bldg. No.1 LiMe Bldg. No.1



Lab URL
https://www2.infront.kyoto-u.ac.jp/HCV/

The main purpose our research group is to clarify the molecular mechanisms of carcinogenesis caused by the infection of human hepatitis viruses. Molecular and cellular biological analyses of the viral lifecycle and the cellular events related with viral infection have been investigated. We have found several candidates of the drugs against HCV and HBV through those studies.

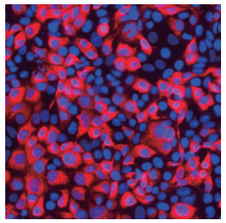


Figure 1 Cultured liver cancer cells infected with HCV. HCV infected cells are indicated by immunofluorescence using anti-HCV proteins antibody (red).

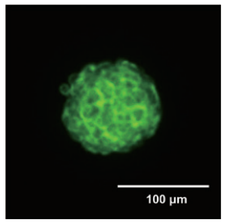
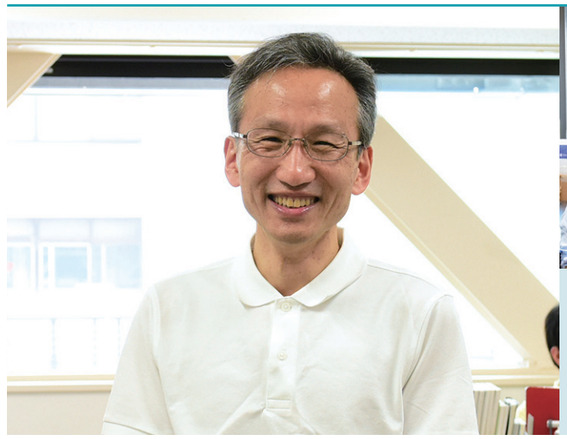


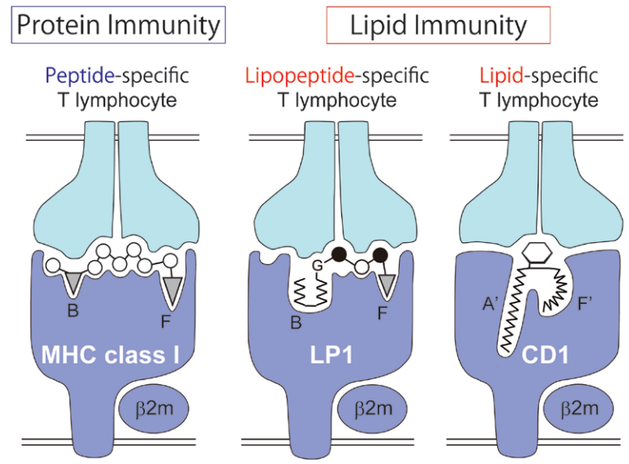
Figure 2 Immortalized human hepatocytes producing the HBV receptor molecule cultured in three-dimensional condition. The HBV receptor molecule is visualized with fused green fluorescent protein.

Lab. of Cell Regulation LiMe Bldg. No.2



Prof. **Masahiko Sugita**
Assist. Prof. **Daisuke Morita**
Assist. Prof. **Tatsuaki Mizutani**

The universe of antigens recognized by the immune system has recently been expanded to include not only protein antigens but also lipid and lipopeptide antigens. By orchestrating immunological, cell biological, biochemical and structural approaches and by developing valuable animal systems, our laboratory aims to establish the molecular and cellular basis underlying “lipid immunity” and disclose its relevance to cancer, microbial infections, and autoimmunity. These studies have important medical implications, including development of a new type of lipid-based vaccines. We have recently identified monkey molecules, LP1, capable of binding lipopeptide antigens and presenting them to lipopeptide-specific T lymphocytes. This study has guided us to the identification of human LP1, and previously unappreciated human immune pathways are now beginning to be unraveled in our laboratory.



Whereas MHC molecules bind peptide antigens and present them to T lymphocytes, LP1 and CD1 molecules bind lipopeptide and lipid antigens, respectively, and present them to specific T lymphocytes. Our frontier research focusses on these new immune pathways that we call "lipid immunity".

Lab URL
https://www2.infront.kyoto-u.ac.jp/SugitaLab/

Lab. of Immune Regulation LiMe Bldg. No.4

Prof. Koichi Ikuta
Assist. Prof. Takahiro Hara
Assist. Prof. Guangwei Cui

The immune system has acquired sophisticated control mechanisms as a result of evolution at the front line of the battles between hosts and pathogenic microorganisms. Cytokines are a group of proteins important for controlling the immune system. Interleukin-7 (IL-7), one of the cytokines, plays important roles in differentiation, maintenance and response of lymphocytes and innate lymphoid cells, and is essential for organogenesis of lymphoid organs. We are pursuing research on development and response of the immune system, focusing on IL-7. We are now carrying out the following projects: (1) function of IL-7 receptor in differentiation, maturation and response of immune cells; (2) regulation of IL-7 receptor expression during lymphocyte development and immune response; (3) circadian control of dynamics and function of lymphoid cells by steroid hormones and sex difference in the immune system; and (4) visualization and local function of cytokine-producing cells, in relation with tumor immunity.

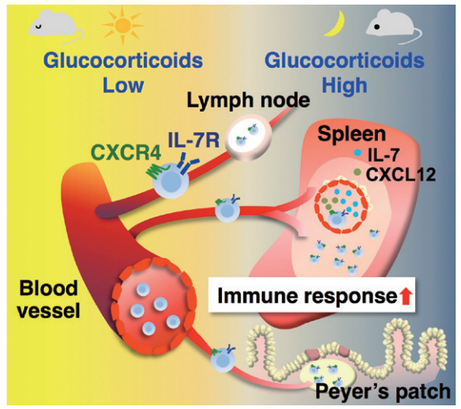


Figure 1 Immunoenhancing effects of glucocorticoids
Glucocorticoids drive diurnal oscillations in T cell distribution and responses by inducing IL-7R and CXCR4.

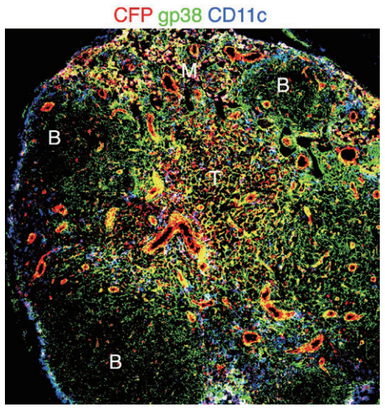


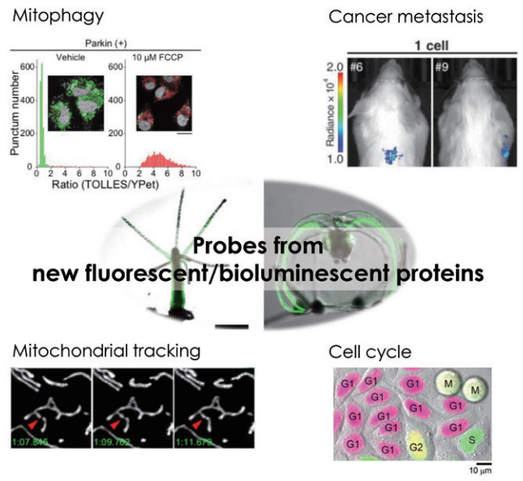
Figure 2 IL-15-expressing cells in lymph nodes
Immunohistochemistry of lymph nodes from IL-15-CFP knock-in mice. IL-15/CFP (red), fibroblastic reticular cells (green), dendritic cells (blue). IL-15 production is detected in stromal cells and blood vascular endothelial cells. B, B cell-rich follicles; T, T-cell zone; and M, medulla.

Lab URL
https://www2.infront.kyoto-u.ac.jp/Ikuta-Lab/

Lab. of Bioresponse Analysis (Visiting)

Visiting Prof. Atsushi Miyawaki

In a signal transduction diagram, arrows are generally used to link molecules to show enzymatic reactions and intermolecular interactions. To obtain an exhaustive understanding of a signal transduction system, however, the diagram must contain three axes in space and the time base, because all events are regulated ingeniously in space and time. The scale over time and space is ignored in biochemical approaches in which electrophoresis is applied to a specimen prepared by grinding millions of cells. We advocate employing the so-called real-time and single-cell imaging technique to fully appreciate cell-to-cell heterogeneity. We also steadfastly pursue the creation of a reliable gate that would enable researchers to better understand the "feelings" of individual cells. Over the past two decades, various genetically encoded probes have been generated principally using fluorescent or bioluminescent proteins and are used to investigate the function of specific signaling mechanisms in a variety of biological systems. We believe that these approaches will continue to improve due to the various features of fluorescent/bioluminescent proteins that serve as the interface between light and life.



Lab. of Bioresponse Analysis is developing fluorescent and bioluminescent probes to study various biological processes, such as mitophagy and cancer metastasis.

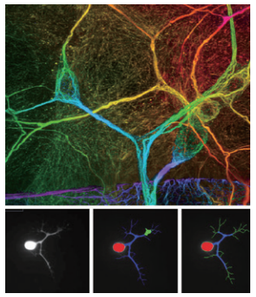
Lab URL
https://cfds.riken.jp/

Lab. of Bioresponse Analysis (Visiting)

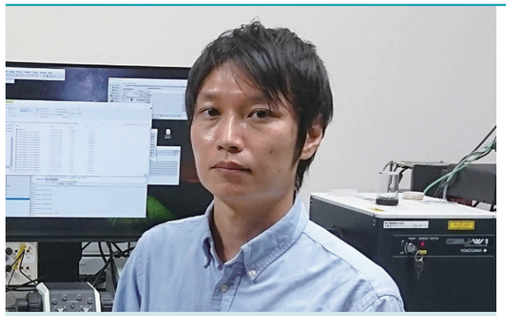
Visiting Assoc. Prof. **Adrian Walton Moore**

Lab URL
https://cbs.riken.jp/en/faculty/a.moore/

As neurons differentiate and assemble into circuits, they form among the most complex and diverse structures of any cell type. They construct complex dendrite arbors that connect them to their partners, and which must be patterned to support the precise connectivity and computational requirements of each neuron. The differentiation programs that create this pattern and connectivity are genetically programmed, and when they fail this leads to neurodevelopmental disorders. To reveal the molecular control processes of neuron differentiation, my lab is using multidisciplinary approaches in Drosophila, mouse and human experimental systems. Our work connects from transcriptional and genomic level controls, through cell biological cytoskeleton effector interaction networks, to in vivo mapping of neuron structural differentiation, and arbor pattern formation over time.

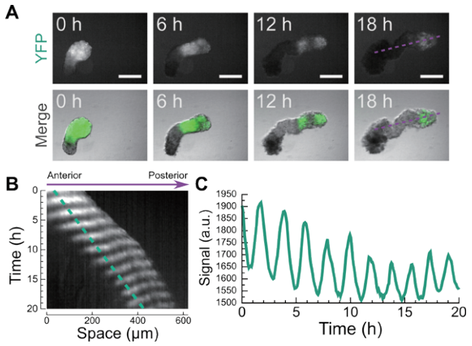


Drosophila sensory neurons.
Top: A super-resolution image of neuronal microtubules.
Bottom: AI-based feature extraction from in vivo imaging of dendrite arbor differentiation



Program-Specific Assoc. Prof. **Akihiro Isomura**
LiMe Bldg. No.2

Our major research interest is spatio-temporal pattern formation in biological systems. We are focusing on somitogenesis where spatially periodic structures of somites are formed in a temporally oscillatory manner. To gain mechanistic insight into the emergence of rhythms and patterns in multi-cellular systems , we are developing novel techniques for visualization and manipulation of gene expression and signaling dynamics.



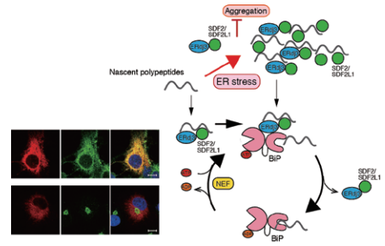
Time-lapse imaging of pre-somitic mesoderm tissues derived from mouse embryonic stem cells revealed that propagation of transcriptional waves from posterior to anterior regions with the periodicity of 2-h.

Lab. of Molecular and Cellular Biology South Research Bldg. No.1 LiMe Bldg. No.1

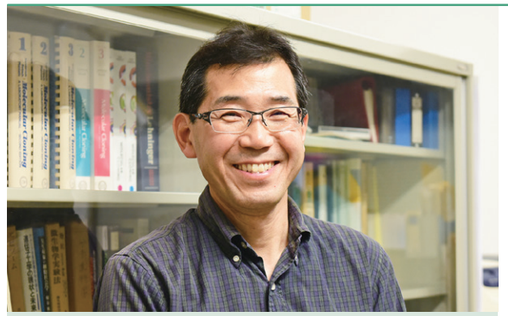
Assoc. Prof. **Nobuko Hosokawa**

Lab URL
http://www2.infront.kyoto-u.ac.jp/bf01/j/home.html

In Hosokawa G, we study on the quality control mechanism of proteins and on the molecules such as chaperones and lectins that are involved in this system. Protein misfolding occures when cells are exposed to various stresses, or when mutations occur in the genes that encode proteins. We are also analyzing the protein degradation mechanism named ERAD (endoplasmic reticulum-associated degradation), and the intracellular transport of proteins.



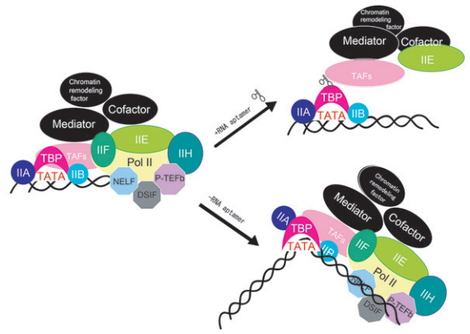
Chaperone protein complex in the endoplasmic reticulum (ER)
Newly snthesized proteins in the ER obtain their native conformations by the assistance of ER chaperone proteins. Some chaperone proteins make complexes to assist protein folding and to inhibit protein aggregation.



Sr Lect. **Kazunori Hirayoshi**

Lab URL
https://www.infront.kyoto-u.ac.jp/laboratory/lab11/

In Hirayoshi G, we analyze transition stage from the formation of pre-initiation complex to elongation using RNA aptamer.



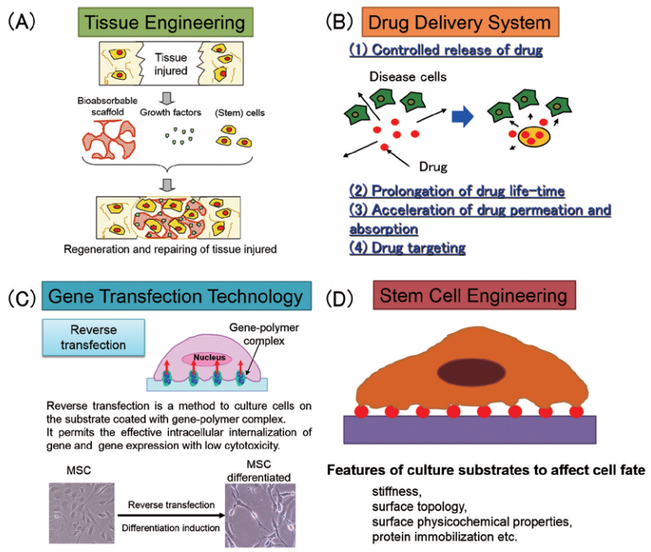
Basal transcription factors on the gene. RNA aptamer,which we selected, prevents the binding of factors and inhibits the formation of transcription complex and inhibits the transcription.

Lab. of Biomaterials

South Research Bldg. No.1 LiMe Bldg. No.1

Prof. Yasuhiko Tabata
Assist. Prof. Mitsuru Ando

The main objective of our department is to proceed the research and development of methods, procedures, and technologies applicable to basic research of biology and medicine, and medicines (therapy, diagnosis, and prophylaxis) from the viewpoint of material sciences. The biomedical materials (biomaterials) to use in the body and to contact biological substances are being designed and created from biodegradable and non-biodegradable materials. Our goal is not only to carry out researches of tissue regenerative therapy (tissue engineering, cell transplantation, cell research, and drug discovery), drug delivery system (DDS), biomedical engineering, gene engineering technology, and stem cell technology, but also put the research results to clinical and practical uses.



Technologies developed in this laboratory.

(A)Tissue engineering is the research and development of biomaterial technologies to realize the regenerative therapy by making use of cell-based natural healing potential. Biomaterials can enhance the cell-based potential to achieve the regeneration and repairing of tissues.

(B)Drug delivery system is technologies and methodologies to maximize the action of drugs (substances with a certain biological activity and function) by the combination with biomaterials. Drugs include therapeutic, diagnostic, and preventing drugs or cosmetics.

(C)Reverse transfection enables genes to safely internalize into weak cells of mesenchymal stem cells (MSC) and achieve the prolonged gene expression.

(D)Behavior of stem cells is modified by the stiffness, surface topology, and physicochemical properties of materials (hydrophilicity and charge etc.) and the extent of protein immobilized to materials. The objective of stem cells engineering is to create materials which mimic the cell environment in the body for cell research and drug discovery.

Lab URL
http://www2.infront.kyoto-u.ac.jp/te02/index-j.php3

Lab. of Immunology

South Research Bldg. No.1 LiMe Bldg. No.1

Prof.
Hiroshi Kawamoto
Assoc. Prof.
Masaki Miyazaki
Assist. Prof.
Seiji Nagano
Program-Specific Assist. Prof.
Yuka Kobayashi
Program-Specific Assist. Prof.
Junji Uehori
Program-Specific Assist. Prof.
Hiromi Sumita
Program-Specific Assist. Prof.
Riyo Konishi
Program-Specific Assist. Prof.
Yosuke Nagahata
Inter-Organ Communication Research Team
Program-Specific.Assoc. Prof.
Shinpei Kawaoka

The major aim of our laboratory is to elucidate the molecular mechanisms that regulate cell fate decisions in the process of lineage restriction from multipotent hematopoietic stem cells to unipotent progenitors. Among various events occurring during hematopoiesis, we are mainly focusing on the process towards the production of T cells. We have recently clarified the mechanisms for the maintenance of T cell lineage (Figure 1).

As another project, we have been developing an approach aiming to apply our culture method in clinical settings. Whereas cytotoxic T lymphocytes (CTLs) represent the most promising therapeutic avenue in cancer immunotherapy, adaptive transfer of antigen-specific CTLs has faced difficulty in efficient expansion of CTLs from patients in ex vivo culture. To solve this issue, we have proposed a strategy to use iPSC technology for cloning and expansion of tumor antigen specific CTLs; iPSCs produced from T cells (T-iPSCs) should inherit rearranged TCR genes, and thus all regenerated T cells from T-iPSCs should express the same TCR. Based on this idea, we have succeeded in regenerating MART1-specific CTLs from a melanoma patient (Vizcardo et al, Cell Stem Cell, 2013). Recently we have developed a method by which CTLs are regenerated from iPS cells transduced with exogenous TLR gene(TCR-iPSCs) (Figure 2). This new method provides a convincing rationale for application of this strategy in clinical settings.

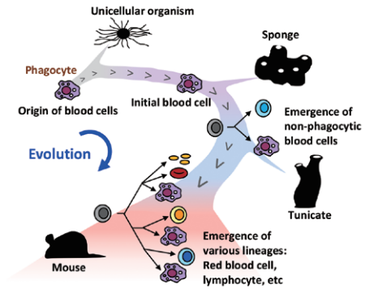


Figure 1 Evolutionary history of blood cells
In order to trace the evolutionary history of blood cells, gene expression profiles of blood cells in mouse, tunicate, and sponge were compared. Those of phagocytes/macrophages in the 3 animal species were similar to each other, and to a eukaryotic unicellular organisms. CEBPa and its homologs were found to determine this similarity. Collectively, we revealed that the initial blood cells emerged by inheriting a phagocytic program from ancestral unicellular organisms, and various lineage blood cells have stepwisely evolved from the prototypic phagocytes (Nagahata et al, Blood in press).

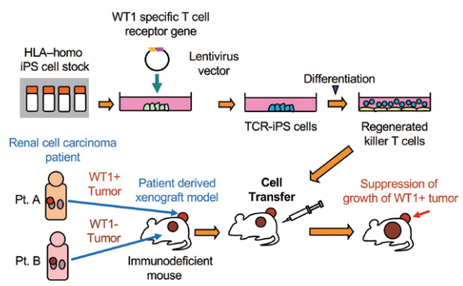


Figure2 Regenerated killer T cells showed efficacy in a PDX solid tumor model
iPS cells obtained from CiRA were transduced with WT1 antigen-specific T cell receptor that had been clinically tested, and killer T cells were regenerated from the iPS cells. The regenerated killer T cells were transferred to the PDX (patient derived xenograft) model mouse of renal cell carcinoma in which both of WT1 positive and negative tumor tissues had been transplanted, resulting in the suppression of the growth of solely the WT1 positive tumor.

Lab URL
http://kawamoto.frontier.kyoto-u.ac.jp

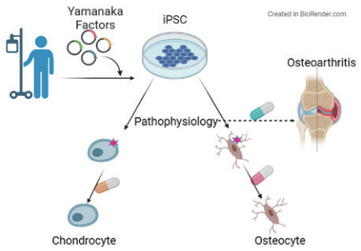
Lab. of Tissue Regeneration

South Research Bldg. No.1 LiMe Bldg. No.1

Assist. Prof.
Yonghui Jin

iPS cells established from individuals possess genetic information and can be differentiated into target cells to elucidate pathological mechanisms in vitro. We establish iPS cells from patients with intractable bone and cartilage diseases such as fibrodysplasia ossificans progressiva, and the pathophysiology and drug discovery research are conducted using the osteogenic or chondrogenic differentiation induction methods originally developed by our laboratory. The findings obtained from these researches are also expected to contribute to bone and cartilage regenerative medicine.

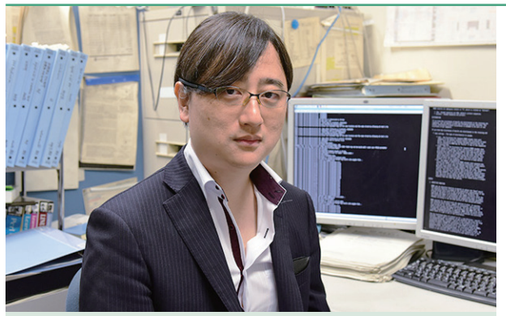
Lab URL
https://www.infront.kyoto-u.ac.jp/laboratory/lab15/



Using patient-derived iPS cells, the molecular mechanism of intractable diseases will be elucidated by experimental reproduction in vitro. The research results can also be applied to regenerative medicine for osteoarthritis and other diseases.

Lab. of Developmental Epigenome

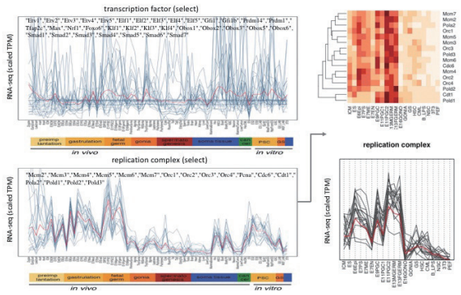
South Research Bldg. No.1 LiMe Bldg. No.1



Assoc. Prof. Shinichiro Chuma

Lab URL
http://www2.infront.kyoto-u.ac.jp/rc01/

During development of multicellular organisms, genetic stability is differentially regulated depending on developmental stages, cellular lineages and physiological conditions etc. We are currently investigating (1) how pluripotent stem cells and germline cells maintain their genome and epigenome integrity, and (2) how the genome and epigenome stability is coordinated with developmental programs of the germline-stem cell cycle. We also aim to identify genes and pathways with which the genetic stability of stem cell resources can be improved.



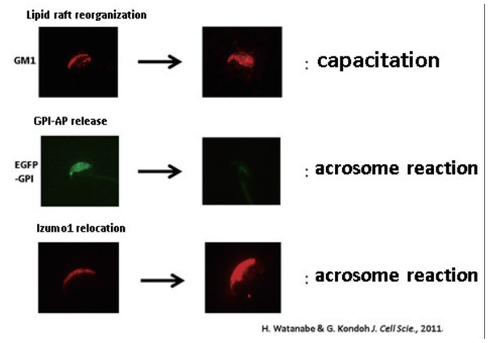
Synchronized co-expression of DNA replication genes during developent

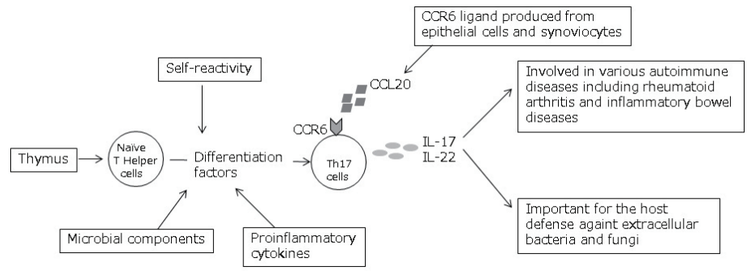
Lab. of Integrative Biological Science

South Research Bldg. No.1 LiMe Bldg. No.1 / No.5

Prof. Gen Kondoh
Assoc. Prof. Keiji Hirota
Assist. Prof. Hitomi Watanabe (concurrent)

Mammalian sperm undergo multiple maturation steps after leaving testis to be competent for fertilization. Serial important changes occur in the female reproductive tract on sperm, although the molecular mechanisms underlying these processes remain unclear. In our early study, we found that angiotensin-converting enzyme (ACE) releases GPI-anchored proteins (GPI-AP) from the cell membrane and plays a critical role in mammalian fertilization. We also found that sperm undergoing GPI-AP release associated with reorganization of lipid raft and acrosome reaction acquire fertilization potential. In terms of identifying factors triggering these processes in vivo, we found Lipocaline2 as a sperm maturation factor of female. Recently, we started new research projects elucidating character and function of new helper T cell, Th17 cell, to clarify the mechanism of inflammation.





Lab URL
http://an02-kaihen-anim.frontier.kyoto-u.ac.jp/

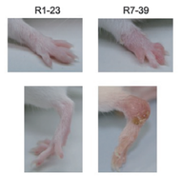
Lab. of Immunopathogenesis

South Research Bldg. No.1 LiMe Bldg. No.1

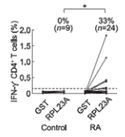
Prof. **Yoshinaga Ito**

We study an interplay between immune system and self-organs/tissues, with particular focus on its physiological roles and the mechanisms of disease development when the interaction becomes aberrant. We place autoimmunity and cancer immunology from an integrated perspective: both of them are ‘destruction of self-derived components by immune system’.

We strive to discover key molecular pathways shared by both autoimmune diseases and cancer immunotherapy in order to develop innovative treatment arms for these devastating diseases.

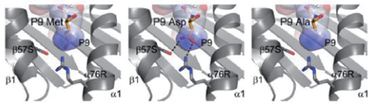


自己免疫疾患新規モデルマウス
A novel autoimmune disease model

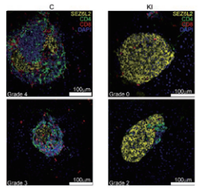


ヒト関節リウマチの標的自己抗原の同定
Identification of an autoantigen in rheumatoid arthritis

Ito Y et. al. *Science*. 2014



生化学的特性に基づく遺伝子改変モデルマウス設計
An animal model with a single amino acid substitution



自己免疫炎症の抑制
Control of autoimmune inflammation

Ito Y et. al. *J Exp Med*. 2018

By employing our own new technology, we will elucidate the whole repertoire of autoantigens critical for disease development in autoimmune diseases in order to establish antigen-specific therapeutics.

Lab URL
https://www.infront.kyoto-u.ac.jp/laboratory/lab21/

Lab. of Experimental Immunology (Visiting)

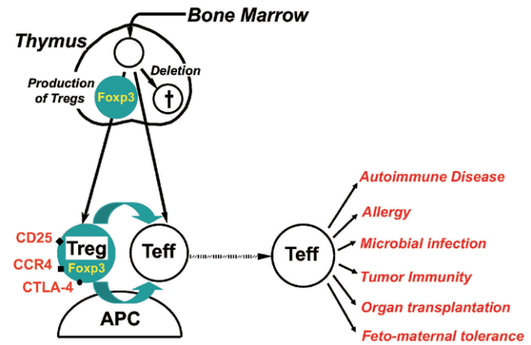
South Research Bldg. No.1 LiMe Bldg. No.1

Visiting Prof. **Shimon Sakaguchi**
Program-Specific Assist. Prof. **Ryoji Kawakami**

Our laboratory studies the mechanisms of immunological tolerance. We discovered naturally occurring regulatory T (Treg) cells as a T-cell subpopulation that is specialized for immune suppression and engaged in the maintenance of immunological self-tolerance and homeostasis. We have been studying the molecular and cellular basis of Treg cells development and maintenance, in mice and humans by using immunological, genetic and bioinformatics approaches. Since Treg cells are involved in various physiological as well as pathological immune responses, we are developing various ways to manipulate Treg cells for clinical application, which is a novel immuno-therapy for autoimmune diseases, allergy, infection, organ transplantation and cancer.

We are also studying the pathogenetic mechanism of rheumatoid arthritis by analyzing our newly developed model (SKG mouse). SKG mice have a mutation in the ZAP70 gene, which plays a critical role in T cell recepter signaling. Because of this mutaion, SKG mice show altered thymic selection and allow a leakage of self-reactive T-cell from the thymus. We are investigating how such impaired signal transduction causes autoimmune diseases.

Control of immune responses by Foxp3⁺CD25⁺CD4⁺ Tregs



CD25+CD4+ regulatory T (Treg) cells are produced by the normal thymus as a functionally mature T-cell subpopulation. They specifically express the transcription factor FoxP3. Reduction of Treg cells or attenuation of their suppressive activity may enhance tumor immunity and microbial immunity. In contrast, increase of the number of Treg cells or augmentation of their suppressive activity can treat autoimmunity and induce transplantation tolerance.

Lab URL
http://exp.immunol.ifrec.osaka-u.ac.jp/

Lab. of Biomechanics

South Research Bldg. No.1 LiMe Bldg. No.1

Prof. Taiji Adachi
Assist. Prof. Yoshitaka Kameo
Assist. Prof. Koichiro Maki

The Laboratory of Biomechanics aims to clarify the self-organized regulatory mechanisms of diverse biological phenomena through interdisciplinary approaches encompassing mechanics, life science, and medical science. Our research topics cover developmental processes (cell differentiation, morphogenesis, and growth) as well as tissue/organ remodeling and regeneration which underlie functional adaptation to the environment. A major focus of our research is to understand how well-organized dynamics of living systems emerges from complex molecular and cellular interactions. To this end, we are integrating biomechanics and mechanobiology approaches to highlight the roles of “adaptation to mechanical environment” and “hierarchy of structure and function” in the living organisms using mathematical modeling, simulation and experiments.

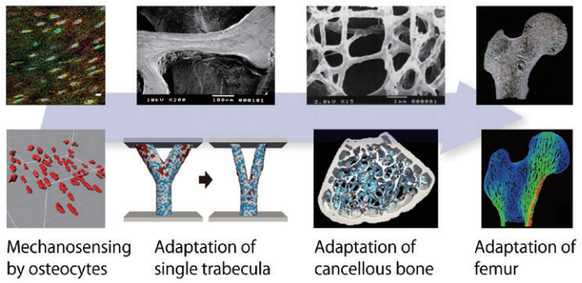


Figure 1 Bone can remodel its outer shape and inner structure to adapt to the surrounding mechanical environment. This study aims to clarify the mechanism of bone functional adaptation achieved through cooperative cellular activities.

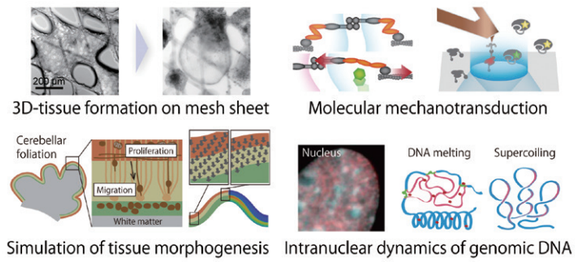
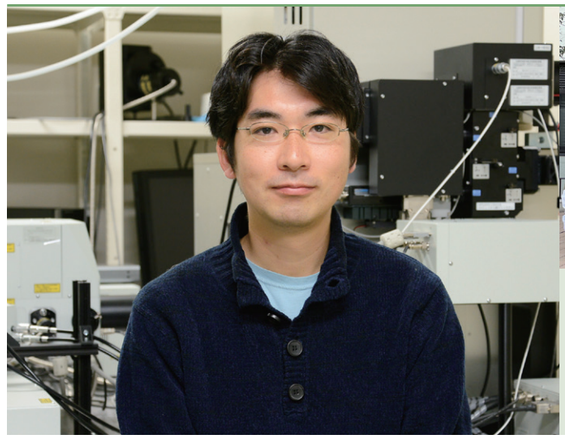


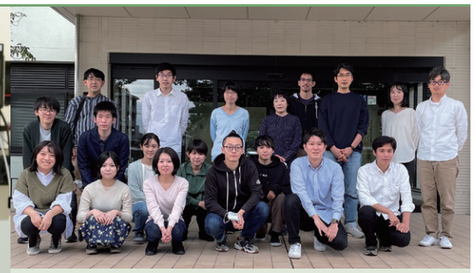
Figure 2 Morphogenesis of biological tissues is orchestrated by mechanical forces at the multiscale. By combining experiments and simulations, this study aims to clarify the mechanisms of tissue morphogenesis.

Lab URL
https://www2.infront.kyoto-u.ac.jp/bf05/index-e.html

Lab. of Developmental Systems

South Research Bldg. No.1 LiMe Bldg. No.1 / No.5

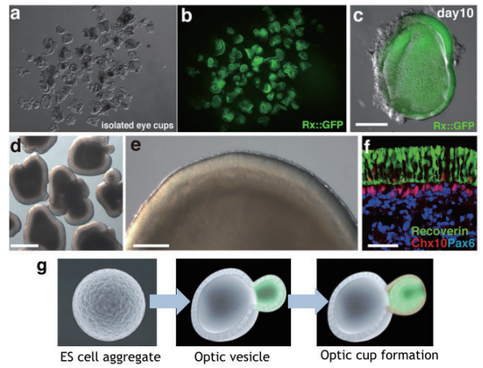




Prof. Mototsugu Eiraku
Assoc. Prof. Masatoshi Ohgushi
Assist. Prof. Yusuke Seto

Organogenesis is a highly dynamic process in which multicellular behaviors are regulated by mechanisms in multiple scales from molecules and cells to tissues. In vitro generation of functional organ with complex structure is a major challenge of cell biology. Toward this goal, it is a reasonable strategy to recapitulate the ontogeny that is the most efficient and robust process for organogenesis acquired through evolution. Our laboratory aims to clarify molecular and cellular mechanisms underlying organogenesis, and to develop new technologies for in vitro recapitulation, that is, three-dimensional functional organ generation from stem cells. We have previously established efficient three-dimensional cultures for generation of mouse and human ES/iPS cell-derived brain and retinal tissue as well as other ectoderm-derived tissues. Based on our past achievements in 3D tissue formations from pluripotent stem cells, we have been attempting to extend our limit of understanding for self-organization phenomena in neural development and advance the culture technology for generation of more complex tissues from ES/iPS cells in a more robust manner. To do that, we mainly focus on following points.

1) Elucidation of self-organization phenomena in neural development and morphogenesis
2) Development of novel technologies for in vitro formation of functional organ
3) Molecular analysis of species-specific regulation for developmental timing and tissue size determination.



in vitro formation of optic cup and layered retina from ES cells
a-c, Isolated optic cup structure generated from mouse ES cells. d-f, ES cell-deirved optic cup differentiate into layered retinal structure. g, Scheme of in vitro optic cup formation in ES cell culture.

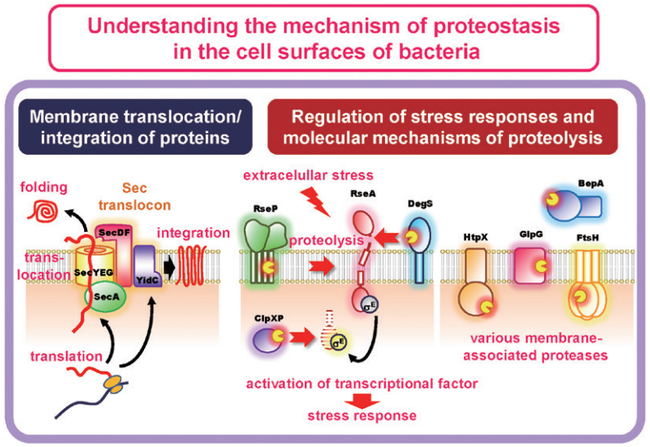
Lab URL
http://www2.infront.kyoto-u.ac.jp/bs01/

Lab. of Biological Membrane System

LiMe Bldg. No.2

Prof. Yoshinori Akiyama
Assoc. Prof. Hiroyuki Mori
Assist. Prof. Yohei Hizukuri

The research projects carried out in this group are concerned with dynamic aspects of cell surface proteins in bacteria including Escherichia coli and Vibrio alginolyticus. Specifically, processes of protein folding, protein translocation across and integration into the membrane, membrane protein proteolysis and extracytoplasmic stress responses are studied by combined molecular genetic, biochemical biophysical and structural approaches. We are mainly focusing on the following two topics. (1) Function and regulation of protein translocation machinery: Protein export across the bacterial cytoplasmic membrane is promoted by cooperation of the evolutionary conserved SecYEG translocon associated with auxiliary factors (such as SecDF) and the SecA ATPase motor. We are investigating the structure and molecular function of these and related cellular factors and regulation of their expression. (2) Membrane protein degradation and extracytoplasmic stress response: Membrane proteins play central roles in the functions of biological membranes. We are investigating the mechanism and physiological roles of membrane protein degradation by envelope proteases. We are also interested in the cellular system to sense and cope with abnormality of cell surface proteins.

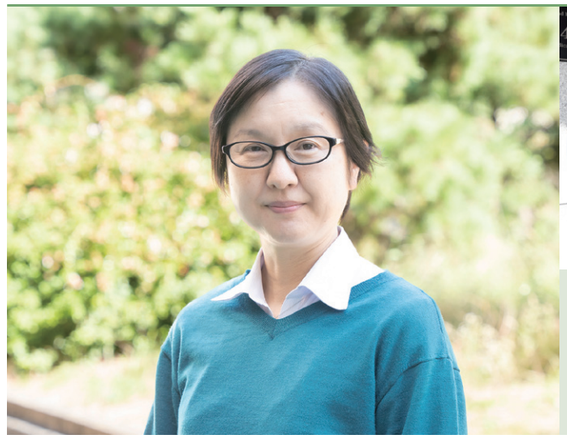


The research prejects carried out in the laboratory of Biological membrane system.

Lab URL
https://infront-biomembrane.jp

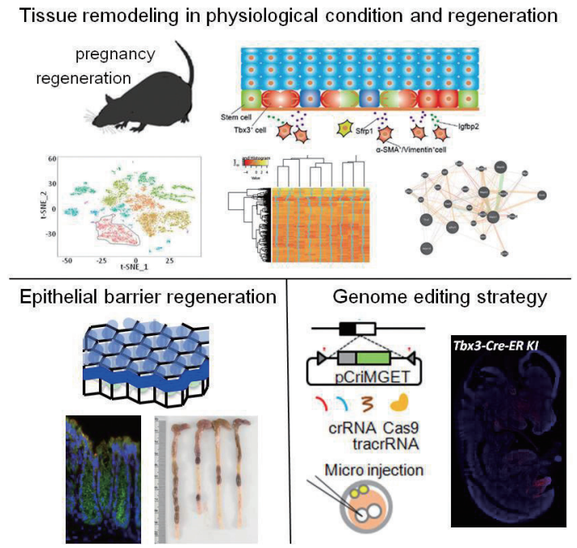
Lab. of Tissue Homeostasis

LiMe Bldg. No.2



Prof. Fumiko Toyoshima
Assoc. Prof. Alexis Vandenbon
Assist. Prof. Riki Ishibashi
Assist. Prof. Ryo Ichijo
Assist. Prof. Yoshihiko Kobayashi

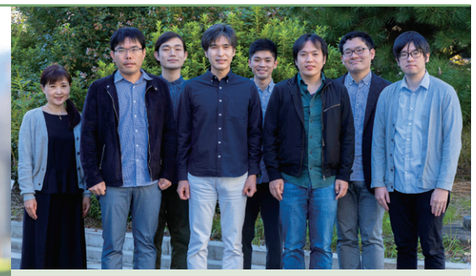
Each organ in the adult body responses to tissue damage or physiological changes of the body through regulating the multicelullar network by which organ size and functions are determined. Our laboratory studies the mechanisms of tissue remodeling especially focusing on a regenerating organ from acute and chronic damage, as well as maternal remodeling organ during pregnancy. How the tissue mechanics and secretory molecules affect the transcriptional network in the multicellular systems is one topic in the projects. These endogenous tissue remodeling mechanisms would be applied for regenerative medicine. We also interested in how the maternal tissue remodeling contributes to fetal growth or developmental origin of health and disease (DOHaD).



Lab URL
https://www2.infront.kyoto-u.ac.jp/Toyoshima-HP/

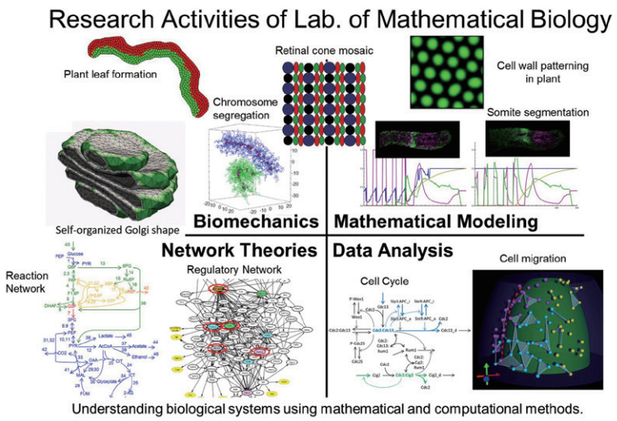
Lab. of Mathematical Biology

LiMe Bldg. No.3



Prof. Atsushi Mochizuki
Program-Specific.Assoc. Prof. Takashi Okada
Program-Specific.Assoc. Prof. Yuji Sakai

The progress of modern biology revealed that biological phenomena are governed by complex network systems including many molecules, cells or organs. For the aim of understanding the functions of complex systems, we adopt mathematical and computational methods. By theoretical approaches we decipher huge amounts of experimental information, and to give integrative understanding for the biological systems. Our final goal is to open a new bioscience which will progress by the repeats of the theoretical predictions and the experimental verifications. We are promoting multiple projects of collaborations with experimental biologists. One of our recent projects is studying dynamics of complex network systems in biology. We developed some theoretical frameworks to extract the important aspects of dynamics from network structure alone, without assuming other quantitative details. By combining our theory with experimental measuring and controling, we will determine mechanism of dynamical behaviours and understand the principles for the biological functions.

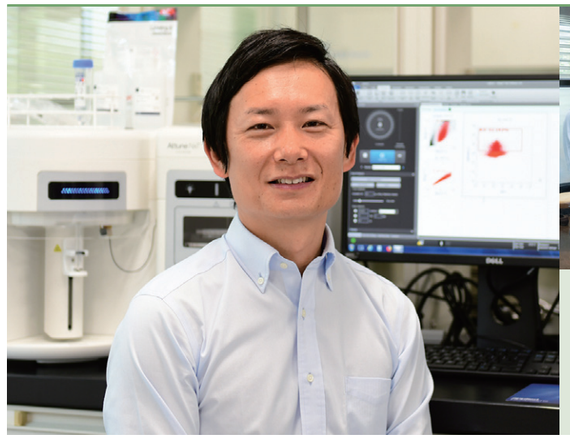


Research topics in lab. of Mathematical Biology

Lab URL
https://mathbio.infront.kyoto-u.ac.jp/

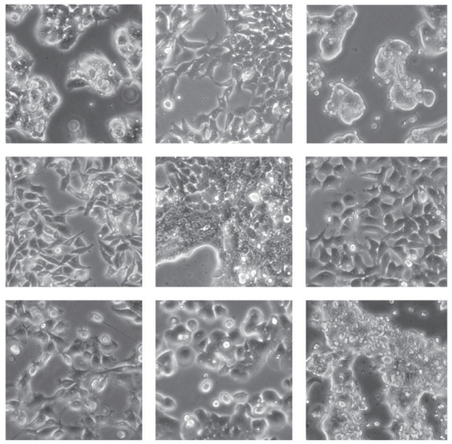
Lab. of Stem Cell Genetics

South Research Bldg. No.1 LiMe Bldg. No.1



Prof. Kosuke Yusa
Assist. Prof. Yusuke Tarumoto
Assist. Prof. Gohei Nishibuchi
Assist. Prof. Kazunari Aoki
Program-Specific Assist. Prof. Fumihiko Kawamura

Forward genetic approach can comprehensively reveal genes involved in a phenotype of interest. This approach was frequently applied in lower model organisms such as yeast, Caenorhabditis elegans and fruit fly to identify genes involved in fundamental biological processes. In contrast, forward genetic approach had been hampered in mammalian cultured cells as there was no efficient way to inactivate all copies of every gene. Our research has been focusing on developing novel genetic tools that enable us to apply powerful forward genetics in mammalian cells. We have recently developed a functional genetic screening method using the CRISPR-Cas9 system, which is highly efficient to genetically dissect a wide range of mammalian biology. Our current work focuses on molecular function studies of genes identified through CRISPR-based genetic screening in the following two research area: 1. Molecular mechanisms of pluripotency maintenance and differentiation of human pluripotent stem cells and 2. Genetic vulnerabilities in cancer cells and drug development. For the latter, we have recently completed an analysis of the CRISPR screening dataset of > 300 cancer cell lines and identified a number of promising drug targets. We will conduct detailed molecular studies of these candidates to further narrow down the list to the most promising drug targets.



Colorectal cancer cell lines showing various cell morphologies. This cancer type can be classified into a few sub-groups based on gene mutations and gene expression profiles. Drug targets that show specificity in certain groups are most valuable as these targets are associated with biomarkers that can be used for patient stratification, and prioritised in follow-up analysis and subsequent drug development process.

Lab URL
https://www.infront.kyoto-u.ac.jp/laboratory/lab40/

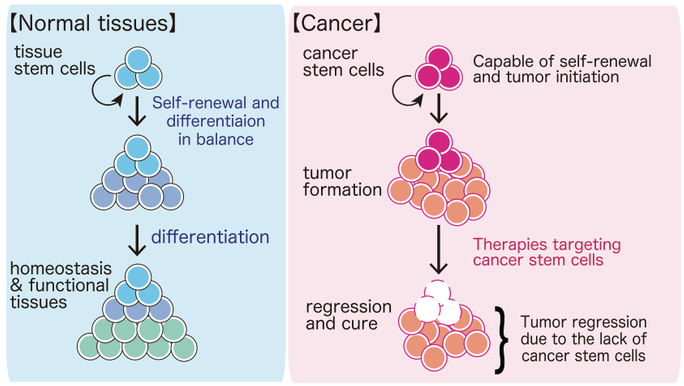
Lab. of Cell Fate Dynamics and Therapeutics

LiMe Bldg. No.3

Prof. **Takahiro Ito**
Assoc. Prof. **Ayuna Hattori**
Assist. Prof. **Kenkyo Matsuura**
Assist. Prof. **Sayumi Okigawa**

My laboratory studies the molecular basis of cell fate regulation in normal and malignant stem cells. We are currently investigating several pathways of hematopoiesis and skeletal muscle systems in mice and human. Stem cells have a remarkable ability to propagate themselves, self-renewal. It allows tissue regeneration and repair damaged tissue after injury. But this ability is a double-edged sword; the same mechanism of self-renewal can be a target of malignant transformation and lead to cancer development. In the past decades, we have learned a great deal about the mechanisms of cancer-causing transformation, and yet finding effective ways to eradicate cancer cells has remained an elusive goal in many types of cancers. This is partly because tumors are often complex and heterogeneous mixtures of neoplastic cells with different self-renewal and differentiation capacities. Unlike many differentiated cells within a tumor, some cancer cells have the ability to self-renew. These self-renewing cancer cells, or cancer stem cells, are therapy-resistant and can drive tumor relapse and metastasis following treatment cessation. Recent studies, including our own work, suggest that the normal and malignant stem cells operate on cell fate regulatory signals that are common or specific to each population. Our research program seeks to improve our understanding of stem cell and cancer biology, and to apply this knowledge to the development of novel and effective approaches to treat human disease and cancer.

Stem cells in tissues and cancer

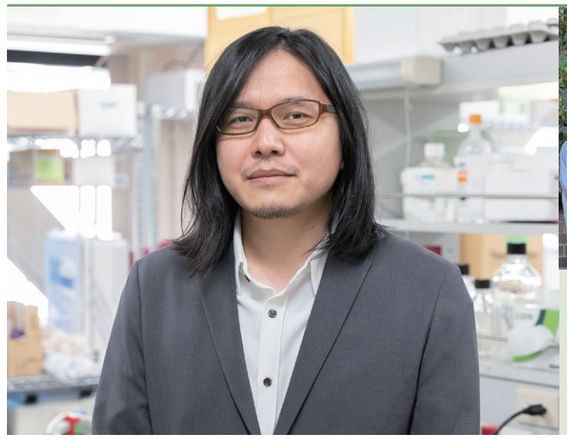


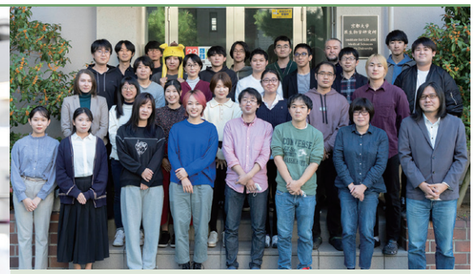
Stem cells in tissues and cancer. Stem cells maintain both normal and malignant tissues, and we seek to uncover the molecular basis of cell fate regulation essential for the stem cell functions.

Lab URL
https://cellfate.infront.kyoto-u.ac.jp/

Lab. of Deconstruction of Stem Cells

LiMe Bldg. No.2 / LiMe North Research Bldg

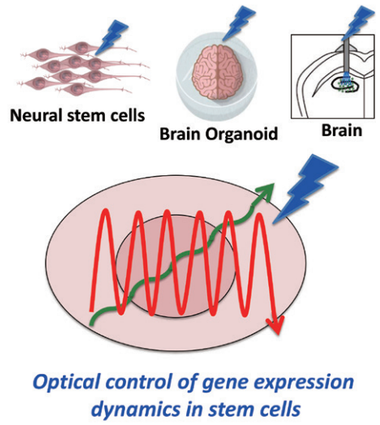




Prof. **Itaru Imayoshi** (concurrent)

The recent discovery of neural stem cells in the adult central nervous system has raised the possibility of repairing the damaged tissue by recruitment of their latent, endogenous regenerative potentials. Development of innovative methods that can noninvasively manipulate neural stem cells in the brain has been expected for regenerative medicine of the nervous system. We have recently demonstrated the first success of such an approach in artificial manipulation of proliferation and neuronal differentiation of neural stem cells by light. We are currently extending this regenerative approach to various types of neural disease models in mice and primates, such as traumatic injury, neurodegeneration or psychiatric disorder. In our laboratory, by applying the novel light-inducible gene expression system, we will try developing novel methods to selectively and efficiently induce various neural cell types from neural stem cells.

More specifically, we will focus on the dynamic expression changes of transcription factors in neural stem cells and manipulate them by the optogenetic approach. We will improve the specificity and efficiency of differentiation of neural stem cells and direct reprograming processes. We will apply these light-mediated control methods to neural stem cells in the brain and iPS cells-derived brain organoids, as well as to cultured neural stem cells.

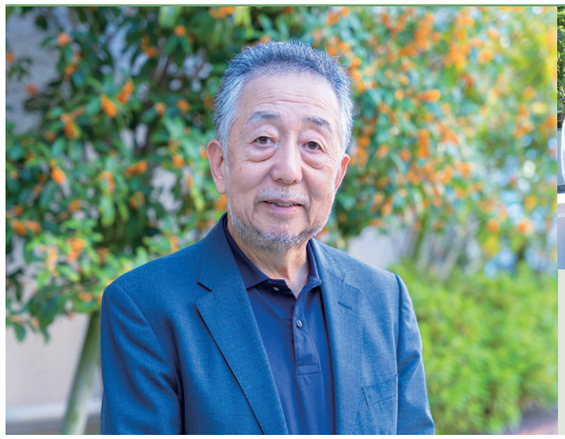


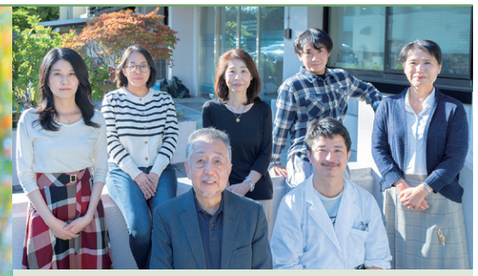
Optical control of gene expression dynamics in stem cells

Development of novel optical methods to regulate differentiation of neural stem cells in neural stem cell cultures, brain organoids, and living brains.

Lab URL
https://brainnetworks.jimdofree.com/

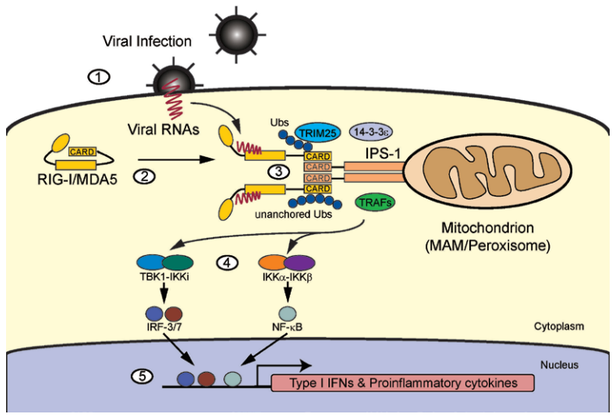
Lab. of Regulatory Information (Visiting) LiMe Bldg. No.2





Visiting Prof. **Takashi Fujita**
Program-Specific Assist. Prof. **Fumihiko Takeuchi**

Virus infections, such as influenza A epidemic and Chronic Hepatitis C virus infection are still 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. RIG-I, MDA5 and LGP2, collectively termed as RIG-I-Like Receptors (RLRs) function as sensor for viral dsRNA to initiate production of interferon (IFN) and proinflammatory cytokines (Figure), which block viral replication and promote acquired immunity against viruses. Recently we discovered that persistent activation of MDA5 leads to lupus-like autoimmune disorder in mice. The purpose of our project is to clarify the molecular mechanism underlying the antiviral innate immunity and autoimmunity regulated by RLR, and to develop new diagnostic and therapeutic tools for these diseases.



Sensing viral dsRNA and activation of RLR
When cells were infected with virus (1), viral dsRNA is sensed by RIG-I or MDA5 (2). CARD of RIG-I and MDA5 interacts with another CARD-containing protein expressed on mitochondria, termed Interferon Promoter Stimulator-1 (IPS-1) (3). AS a result of these molecular interactions, transcription factors, IRF-3, IRF-7 and NF-κB are activated (4). These transcription factors cooperatively activate several antiviral genes, including those of type I and type III interferon are activated (5).

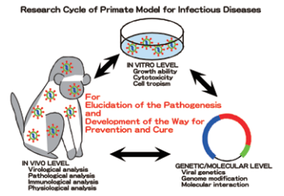
Lab URL
https://www.infront.kyoto-u.ac.jp/laboratory/lab50/

Lab. of Primate Model LiMe Bldg. No.2

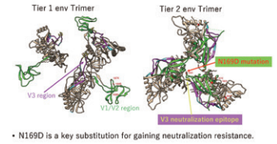
Assoc. Prof. **Tomoyuki Miura**

Lab URL
https://www2.infront.kyoto-u.ac.jp/primatemodelHP/

Since the nonhuman primate is the closest experimental animal to human, it is expected to establish the most useful model for human infectious disease in many aspects. Some pathogenic viruses (HIV-1, for example) can only infect primates. We have a large scale facility for infection experiments using nonhuman primates at P3 level. We establish infection and disease development models using macaque monkeys, and carry out the basic research for clarifying the in vivo pathogenesis and developing prevention and cure of infectious diseases.



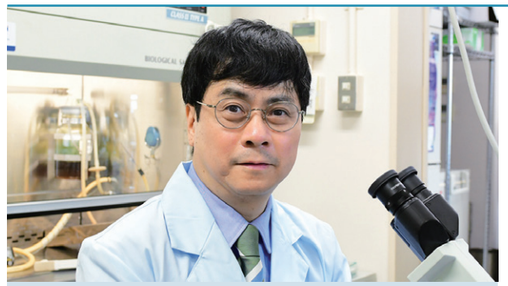
We will elucidate the pathogenicity and develop preventive and therapeutic methods of infectious diseases by comprehensive analysis at the level of molecules, cultured cells, and infected individuals.



The virus mutated in monkeys acquired neutralization resistance by structural shield of the target site.

• N169D is a key substitution for gaining neutralization resistance.

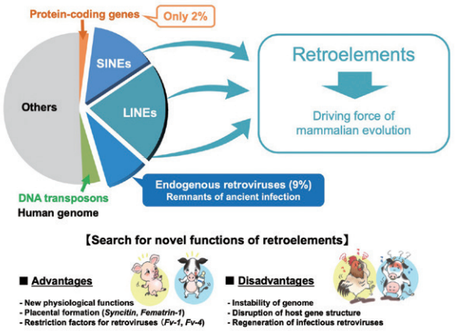
Lab. of Virus-Host Coevolution LiMe Bldg. No.2



Assoc. Prof. **Takayuki Miyazawa**

Lab URL
https://paleovirology.jimdofree.com/

Endogenous retroviruses (ERVs) occupy about 10% of mammalian genomes. New exogenous retroviruses arise from ERVs by recombination and induce diseases in the new hosts. On the other hand, cetrain ERVs are known to be involved in placental morphogenesis and reprogramming of somatic cells. In this laboratory, we aim to reveal the mechanisms of the emergence of new viral diseases and the process of coevolution between mammals and viruses.



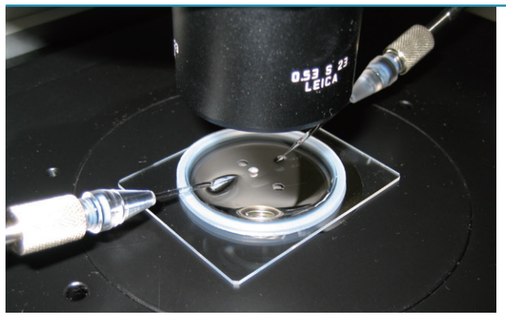
Animal Experiment Facility for Viral Infection

Molecular Biology Research Bldg.

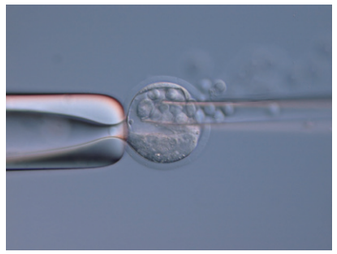
We have a laboratory facility for investigation of biological reactions with virus infection. The purpose of this facility is to analyze pathogenicity of human pathogenic viruses and develop useful vaccines. BSL2 and BSL3 rooms are in operation at each pathogen level. Small animals such as mice and medium animals such as monkeys can be used as experimental animals. After permission from the committee of faculty and technical staff (veterinarians), viral infection experiments are conducted under strict control.

Reproductive Engineering Team

LiMe Bldg. No.3



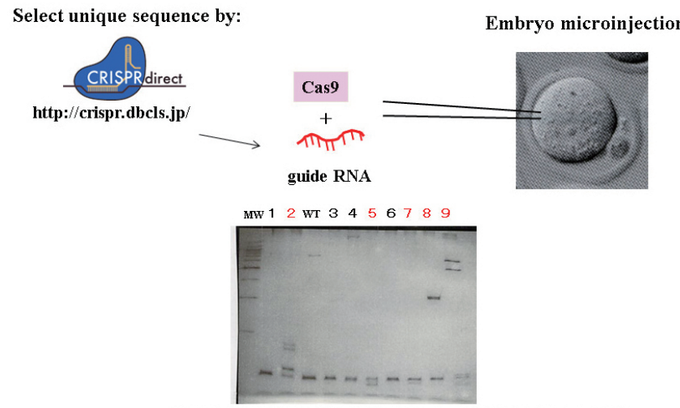
Reproductive engineering team is a support unit for generating transgenic mouse (Tg) and knockout mouse (KO). We also perform cryopreservation of mouse-fertilized eggs.



LiMe Bldg. No.3 / No.4

Prof. **Gen Kondoh** (concurrent)
Assoc. Prof. **Keiji Hirota** (concurrent)
Assist. Prof. **Hitomi Watanabe**

Experimental animals, such as mouse, rat and others, are housed in our Center under strict regulation of animal experimental committee and institutional guidelines for animal welfare. Moreover, we have been considered for long time: how to make gene-manipulated mice more rapidly and conveniently. Recently, genome engineering methods have been established using TALEN or CRISPR-Cas9 systems. We have searched for many methods and finally developed our own protocol making such mice more easily and reproducibly.



Detecting genome-edited mice by urea-denaturing gel electrophoresis

Our strategy for developing genome-edited mice using CRISPR-Cas9 system.

Lab URL
https://anif4.infront.kyoto-u.ac.jp/ [Internal Access Only]

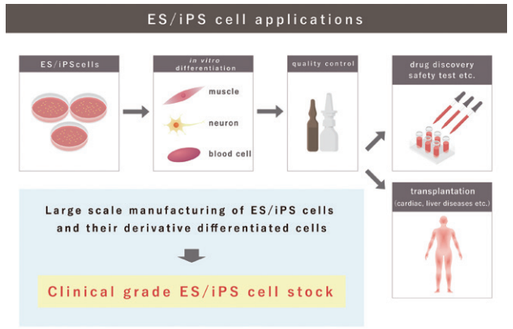
Our mission

The center for human ES cell research was newly established in April 2020, with a mission of promoting the establishment and distribution of human ES (ES) cell lines and the advancement of applied studies on them. ES cells are a type of pluripotent stem cells, known as widely as induced-pluripotent stem (iPS) cells, and human ES cells precede human iPS cells in the history of their first establishment. There are two institutes in Japan approved for the generation of hES cell lines, one being the national center for child health and development and the other being our institute, and currently we are manufacturing human ES cell lines for clinical use in our MHLW approved cell processing facility.

Regarding the importance of human ES cells in academic researches and their potential benefits in clinical applications, a robust and stable supply of high-quality human ES cells is essential for the advancement of regenerative medicine as well as basic researches. To realize the clinical application of human ES cells, we strengthen our current facility of ES cell production and, through further cooperation with other research organizations and hospitals inside and outside of Japan, we accelerate the progression of stem cell research and regenerative medi-cine.

History

Institute for life and medical sciences first succeeded in establishing human ES cell lines in 2002, and since 2017, directed by the the former laboratory of embryonic stem cell research, has been serving as the supplier of clinical-grade human ES cell lines in Japan (as of April, 2020). In order to enhance our capability and performance in research and development of human ES cells for clinical use, the facility under-went a reorganization in 2020, and the center for human ES cell research was newly founded.



Lab URL
http://chesr.infront.kyoto-u.ac.jp/

Organization overview

The center for human ES cell research comprises two divisions, namely, the division of clinical basis for ES cell research and the division of basic technology development for ES cell research. The division of clinical basis for ES cell research consists of two groups: the laboratory of embryonic stem cell research (associate professor Kawase), which is responsible for the establishment and distribution of human ES cell lines, and the laboratory of embryonic stem cell application (associate professor Chuma), which takes charge of quality control of and comparative genome/epigenome analyses of human ES cell lines. The division of basic technology development for ES cell research consists of three groups, which aim for research and development, with mid-to long-term vision, intended for clinical applications of human ES cells: the laboratory of organoids technology (professor Eiraku, Center Director and associate professor Ohgushi), the laboratory of regenerative immune cell therapy (professor Kawamoto and program-specific assistant professor Konishi) and the laboratory of ES cell differentiation (professor Yusa). Together, our center works toward the establishment of an international and stable research facility for human ES cell distribution, as well as the development of basic technologies required for its clinical application, such as quality control and cell/organoid culturing methods.

Center for Human ES Cell Research

Division of Clinical Basis for ES Cell Research

Lab. of Embryonic Stem Cell Research	Associate professor Kawase (full time)	• Establishment and distribution of hES cell lines • Library construction of hES cell lines
Lab. of Embryonic Stem Cell Application	Associate professor Chuma (concurrent)	• Quality control of hES cell lines • Comparative analyses of genome/epigenome regualion

Division of Basic Technology Development for ES Cell Research

Lab. of Organoids Technology	Professor Eiraku (Center Director/concurrent) Associate professor Ohgushi (concurrent)	• Generation of organoids from hES cells • Regenerative medicine & drug discovery by organoids
Lab. of Regenerative Immune Cell Therapy	Professor Kawamoto (concurrent) Program-Specific Assist. Prof. Konishi (concurrent)	• Regeneration of T cells from hES cells • Cancer immunotherapy by regenerative T cells
Lab. of ES Cell Differentiation	Professor Yusa (concurrent)	• Analyses of hES cell differentiation and lineage commitment • Development of hES cell differentiation methods

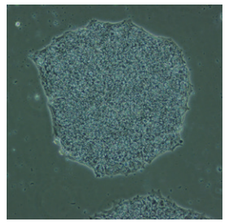
Division of Clinical Basis for ES Cell Research

Lab. of Embryonic Stem Cell Research LiMe Bldg. No.5

Assoc. Prof. Eihachiro Kawase

Lab URL
https://www2.infront.kyoto-u.ac.jp/es01/top.htm

Human ES cell lines are considered to have great potential in medical research and application such as cell transplantation therapy and drug discovery. We established human ES cell lines at a high efficiency and analyzed their characters in detail. We derived 5 ES cell lines, named KhES-1, KhES-2, KhES-3, KhES-4 and KhES-5, and distributed to over 50 research projects in Japan. We are also performing researches on molecular mechanisms of self-renewal and differentiation of human ES cells, and developing techniques for genetic manipulation of hES cells.
We have constructed a Cell Processing Facility (CPF) to develop core technologies to produce and supply clinical grade human embryonic stem (hES) cell lines.



Human Embryonic Stem Cell

Clinical-grade hESC Processing Facility

Faculty and Staff (As of October 1st, 2022)

Professor	17* (3)	Program-Specific Assoc.Prof.	6
Assoc.Prof.	14 (1)	Program-Specific Senior Lecturer	0
Senior Lecturer	2	Program-Specific Assist. Prof.	8
Assist.Prof.	29	SUBTOTAL	14
SUBTOTAL	62 (4)	**TOTAL**	**76 (4)**

(*) Including cocurrent faculty
Numbers in parenthesis indicate visiting faculty

Program-Specific Researcher	17	Re-employed staff	1
Technical Staff	8	Researcher (Part-Time)	29
Administrative Staff	3	Other	58
TOTAL	**116**		

Graduate Students (As of October 1st, 2022)

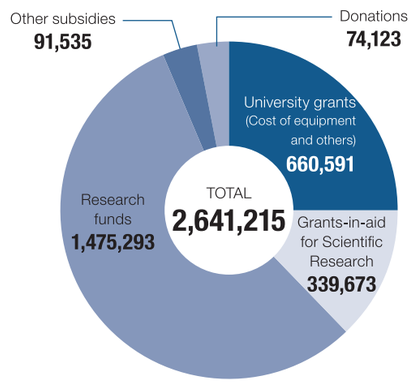
Graduate School of Medicine	16	Graduate School of Human and Environmental Studies	4
Graduate School of Science	7	Graduate School of Biostudies	25
Graduate School of Engineering	28	Graduate School of Pharmaceutical Sciences	14
TOTAL	**94**		

Research Fellows and Research Students (As of October 1st, 2022)

Special Research Student	2	JSPS* Research Fellow	0
Research Student	4	Contracted Researcher	7
Research Fellow	0	Private Sector Researcher	18
TOTAL	**31**		

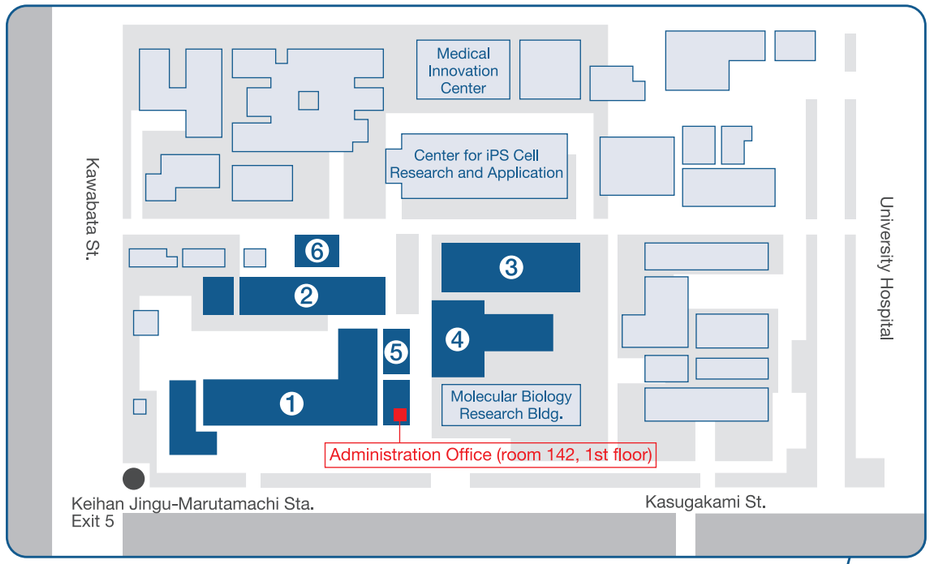
*The Japan Society for the Promotion of Science

Financial data in academic year 2021 [Unit: KJPY]



International exchange (As of October 1st, 2022)

Departmental-Level Academic Exchange Memoranda	**[China]** China Medical University China Rehabilitation Research Center **[Germany]** Bonn Institutes of Immunosciences and Infection, Medical Faculty, University of Bonn



① South Research Bldg. No.1 / Institute for Life and Medical Sciences (LiMe) Bldg. No.1
② Institute for Life and Medical Sciences (LiMe) Bldg. No.2
③ Institute for Life and Medical Sciences (LiMe) Bldg. No.3
④ Institute for Life and Medical Sciences (LiMe) Bldg. No.4
⑤ Institute for Life and Medical Sciences (LiMe) Bldg. No.5
⑥ Institute for Life and Medical Sciences (LiMe) North Research Bldg.

Access to LiMe

- From Kansai International Airport (KIX) by Train
  Take JR Kansai-Airport Express "HARUKA" to Kyoto Station.
  It takes about 80 minutes.
- From Kyoto Station by Taxi
  It takes 20 minutes and costs 2,000 yen, approximately.
- From Kyoto Station by City Bus
  Take a No. 206 bus bound for "Higashiyama St. and Kitaoji Bus Terminal", and get off at "Kumano Jinja-mae". Walk two blocks to the west. It takes 5 minutes.
- From Kyoto Station by Subway
  Take Subway Karasuma Line and get off at "Marutamachi". Walk east for about 20 minutes.