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Institute for Frontier Life and Medical Sciences, Kyoto University

2019-2020

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A Message from the Director

Evolutional events have been also observed in human society. Two biomedical research institutes in Kyoto University, Institute for Virus Research and Institute for Frontier Medical Sciences, merged, and Institute for Frontier Life and Medical Sciences newly started in October 2016. Although evolutionary narratives are not teleological as described in Darwin' s famous book, "On the Origin of Species", we think this merge should promote innovative development.

Institute for Virus Research, being established in 1956, first identified human T-cell lymphotropic virus (HTLV) as the causative agent of adult T-cell leukemia (ATL), which was one of the representative achievements as a leading research institute in the field of viral infection as well as molecular biology in Japan. Institute for Frontier Medical Sciences, being established in 1998, has developed innovative foundation for regenerative medicine by successfully establishing embryonic stem cells (ES cells) and discovering induced pluripotent stem cells (iPS cells) as well as regulatory T cells.

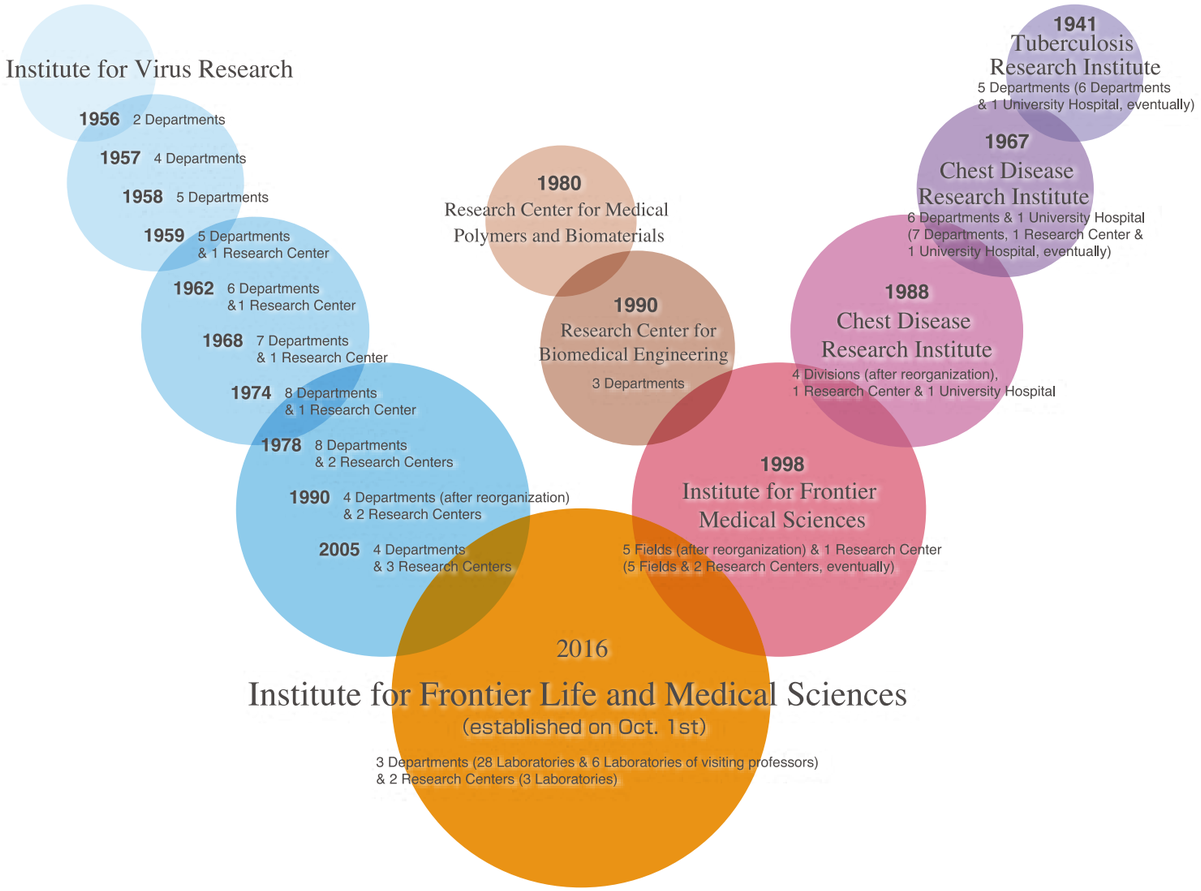
Our institute has been appointed as Joint Usage/Research Center for Transdisciplinary Collaboration on Tissue Engineering and Regenerative Medicine and as Joint Usage/Research Center for Fusion of Advanced Technologies and Innovative Approaches to Viral Infections and Life Science. In addition, we have many achievements to further develop the basic functions and to flourish as a biomedical research hub.

The process toward increasing globalization has brought varied issues and drastic growing of scientific knowledge to modern society. Thus, it becomes harder to follow results of all events. However, since this is a growing point of human society, we would like to positively enjoy such a situation. Our task is not only to promote scientific-development, but also to provide active support for motivated young people with higher education to be outstanding human resources. We are convinced to make efforts for contribution to human society. We appreciate your interest in supporting our activities.

May, 2019

Yoshio Koyanagi MD., Ph.D.
Director of Institute for Frontier Life and Medical Sciences

History



The original cover picture

The motif of the cover picture is from wall decorative paintings “Stoclefries”, one of the masterpieces of Gustav Klimt (1862-1918) in the late Austrian Empire.
Klimt’s work is described as giving the impression of the “chain of life and death” as well as the “permanency of life” because there is always scent of death in his gorgeously colored paintings. On this motif, we overlaid a “formula”, a common language of science, to express how a basic unit of life such as a nucleic acid molecule, a virus, a cell, an organ or a concrete life existence (consisted of the basic units of life) leads a dynamic life. This shows our direction to fulfill our mission to research into “variously structured cell society” of life in order to reveal the whole structure of strategy for life to exist.

Entwurf fur den Wandfries im Palais Stoclet in Brussel, Goldener Ritter - 1909

organization

Unveiling of Nameplate “Institute for Frontier Life and Medical Sciences Kyoto University” (October 3rd, 2016)

Establishment Ceremony of Institute for Frontier Life and Medical Sciences Kyoto University (December 21st, 2016)

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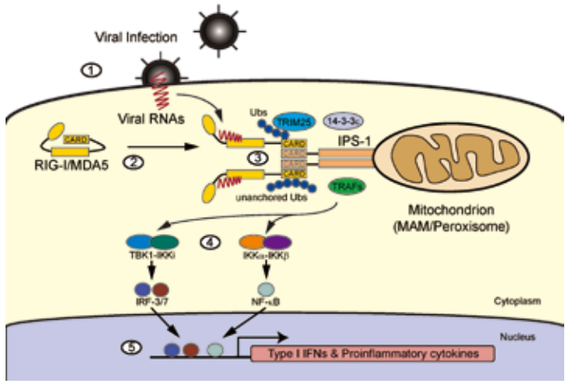
Lab. of Molecular Genetics

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. This laboratory belongs to Graduate School of Biostudies. Associate Professor Okabe studies on regulation of tissue-resident macrophage specialization and tissue homeostasis.



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/ex_ivr/Lab/bunshiiden/English/index.html*

Lab. of Virus Control

The major targets of our research are two human retroviruses, human T-cell leukemia virus type 1 (HTLV-1) and human immunodeficiency virus (HIV). We are studying the molecular mechanisms for pathogenesis of HTLV-1, and trying to develop the novel strategy for the treatment. Regarding HIV,our research purposes are understanding the dynamics of HIV infection and developing novel antiviral drugs.

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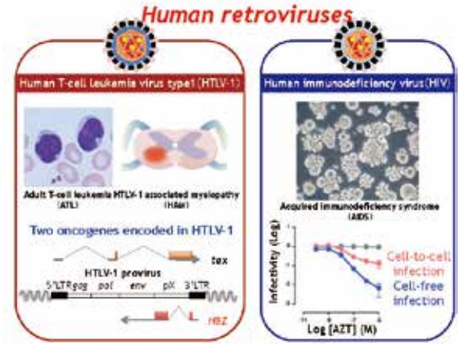

HTLV-1 is an etiological agent of a malignant disease, ATL, and several inflammatory diseases such as HAM. Two viral oncogenes, tax and HBZ, play important roles in the pathogenesis. HIV causes AIDS. HIV infects target cells through cell-to-cell and cell-free fashions, which have different sensitivity to anti-viral drugs.

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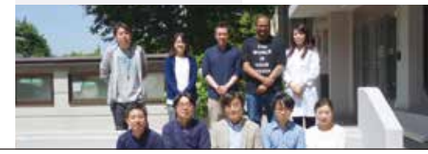

Lab URL *https://www.infront.kyoto-u.ac.jp/ex_ivr/Lab/VirusControl/index.html*

Topics

Laboratory of RNA viruses

One of my research project is "Paleovirology of RNA viruses by biological experiments and evolutionary analyses". In this project, I am studying the diversity of ancient viruses and the evolution of RNA viruses over tens of millions of years using "endogenous viral elements", sequences derived from viruses present in the genomes of eukaryotes.I am also conducting a virome project to understand the diversity of modern viruses. By integrating the knowledge obtained from these research projects, I am trying to comprehensively elucidate the diversity of viruses in the present and past and the deep evolutionary history of RNA viruses, and to prepare baseline data to take countermeasures against emerging viral infectious diseases.

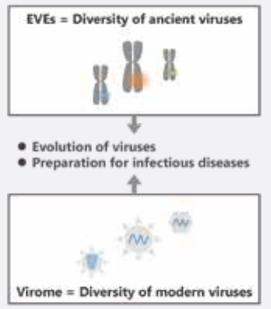

Figure 1 Schematic figure of my researchtopic.
EVEs: endogenous viral elements.

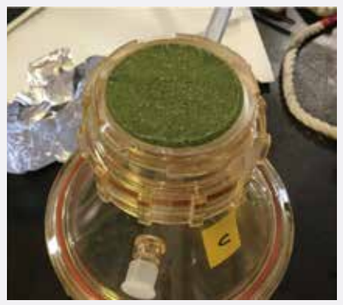

Figure 2 Phytoplankton samplefrom lake Biwa for virome analysis.

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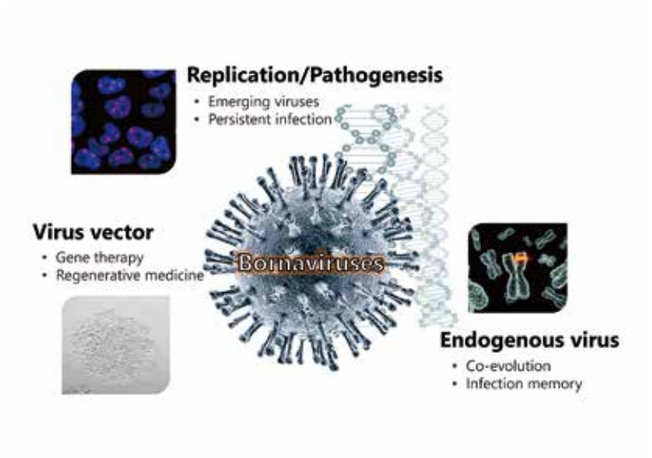
Lab. of RNA Viruses

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 researches 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 researches, we are investigating the replication and persistent mechanism of the bornaviruses in the cell nucleus. The understanding the biological and evolutional significances of the endogenous bornavirus-like elements (EBLs) found in the genomes of many mammalian 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 novel RNA virus vector using bornavirus, which can stably express foreign genes, including functional small RNAs, and be applied for gene therapy of stem cells, such as iPS cells.



In Laboratory of RNA viruses, we are working on several projects regarding replication/pathogenesis of bornaviruses, endogenous bornavirus and development of novel RNA virus vectors using bornavirus.

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

Lab. of Ultrastructural Virology

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.

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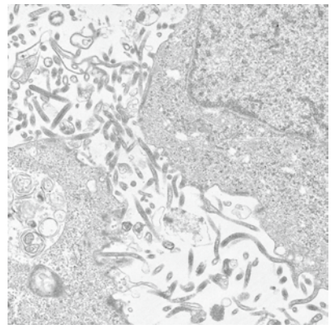


Figure 1 Transmission electron microscopic image of filamentous Ebola virus particles budding from infected cells.

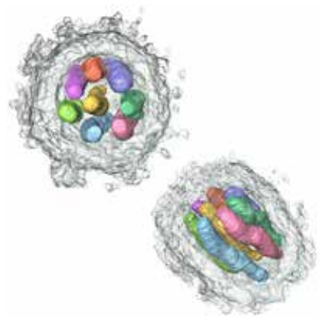
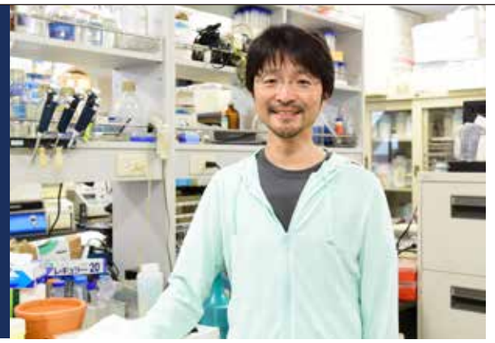


Figure 2 Three dimensional model of an influenza virus particle reconstructed by electron tomography. Eight RNPs arranged in a characteristic "1+7" pattern are present within the virion.

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



Lab. of Tumor Viruses

Papillomavirus infection and its tumorigenic potential: The infection of papillomavirus induces benign tumors, such as warts and condylomas, and occationally 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.

Lab URL ***https://www.infront.kyoto-u.ac.jp/ex_ivr/Lab/sakai2012/Home2.html***

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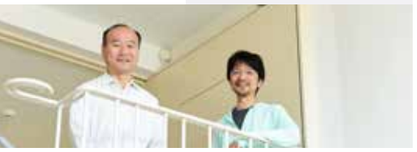

Horn-shaped warts induced by Shope papillomavirus infection

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

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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.

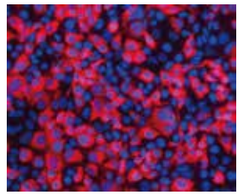

Figure 1 Cultured liver cancer cells infected with HCV. HCV infected cells are indicated by immunofluorescence using anti-HCV proteins antibody (red).

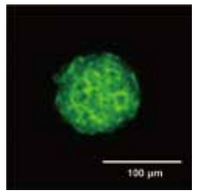

Figure 2 Immortalized human hepatocytes producing the HBV receptor molecule cultured in three-dimensional condition. The HBV receptor molecule is visualized with fused green fluorescent protein.

Lab. of Cell Regulation

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.

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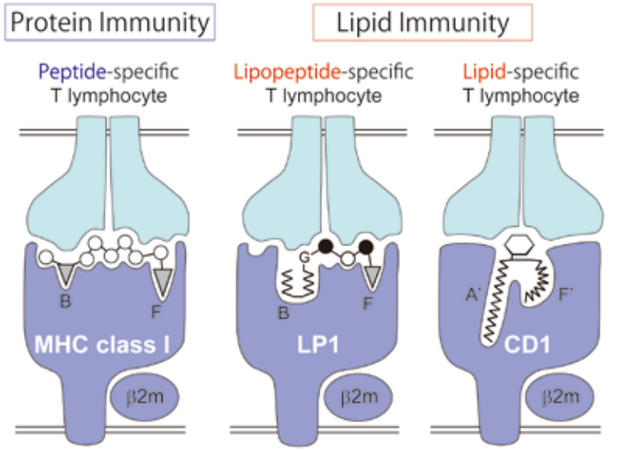
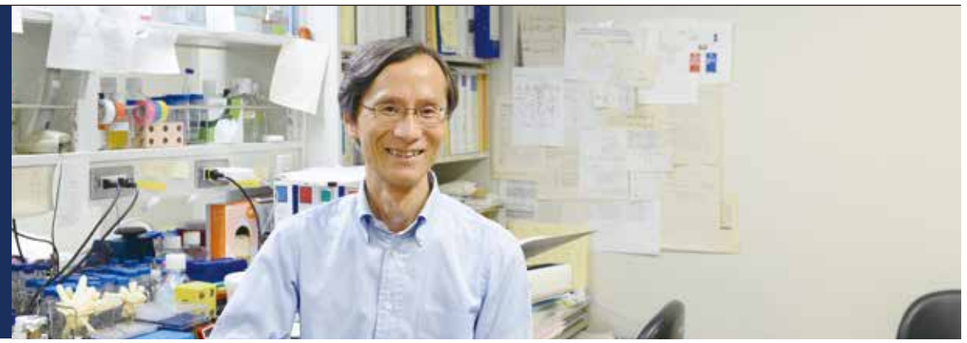


Whereas MHC molecules bind peptide antigens and present them to T lymphocytes, LP1 and CD1 molecules bind lipopeptide and lipid antigens, respectively, and present them to specific T lymphocytes. Our frontier research focusses on these new immune pathways that we call "lipid immunity".

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



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Lab. of Immune Regulation

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.

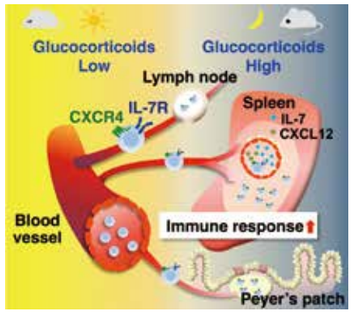

Figure 1 Immunoenhancing effects of glucocorticoids
Glucocorticoids drive diurnal oscillations in T cell distribution and responses by inducing IL-7R and CXCR4.

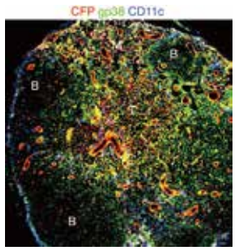

Figure 2 IL-15-expressing cells in lymph nodes
Immunohistochemistry of lymph nodes from IL-15-CFP knock-in mice. IL-15/CFP (red), fibroblastic reticular cells (green), dendritic cells (blue). IL-15 production is detected in stromal cells and blood vascular endothelial cells. B, B cell-rich follicles;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

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

Bioresponse Regulation Laboratory (Visiting)

Influenza has been recognized in history for hundreds of years. Yet, while medicine has advanced, influenza continues to cause epidemics and take lives every year. In addition, pandemic viruses appear about every ten years. In 2009, pandemic (H1N1) 2009 influenza arose and spread quickly around the world. Meanwhile, highly pathogenic H5N1 avian influenza viruses continue to circulate, and avian H7N9 and H9N2 viruses have infected humans. Therefore, we need to monitor these viruses. We study the mechanisms responsible for the high pathogenicity and transmissibility of influenza viruses, focusing on viral and host factors. To better understand pathogenesis and to improve the efficacy assessment of anti-viral drugs, we study influenza virus infection in a macaque model in the BSL-3 non-human primate facility at this institute. In addition, we are working on the development of new vaccines that are more effective than the current inactivated influenza vaccines., Lastly, we have developed a live imaging technique using two-photon microscopy.

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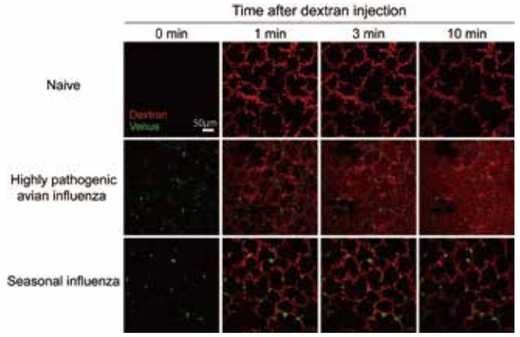

Figure 1 Pulmonary permeability in influenza virus-infected lungs of mice. Time-lapse imaging using 2-photon microscopy. Fluorescent dextran (red) was injected intravenous into the mice during image acquisition. In lungs infected with highly pathogenic avian influenza virus, we could observe that fluorescent dextran gradually leaked from blood vessels into the alveolar cavity. Green indicates virus-infected cells.

Figure 2 Analysis of influenza viruses in a macaque model at the BSL-3 non-human primate facility at this institute.

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Lab. of Bioresponse Regulation (Visiting)

Hepatitis viruses constitute a serious public health problem affecting more than 300 million people worldwide, which function as exogenous ligands inducing an inbalance of physiological condition to restricted hosts. We study these viruses to establish an experimental model evaluating infection and its cellular responses, to analyze spatio-temporal virus dynamics and its principle for survival during interaction with environment, and to develop a strategy for controlling these virus infections. Especially, our chemical genetics approach using chemical probes that manipulate virus infection enables to progress basic virology in concert with drug development.

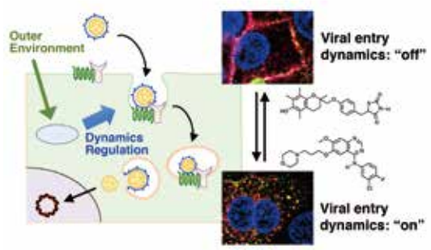

Figure 1 Chemical probes manipulating the dynamics of hepatitis B virus cell entry

Topics

Lab. of Systems Virology

Motto of my lab is "Virus Research from Cellular to Global Level".

Infectious diseases are responsible for substantial morbidity and mortality and continue to be of great concern. Viruses are among the most common causes of infectious diseases. To ensure better control of viral infections, I have been tackling the issue as a medical doctor, molecular biologist, informatician, epidemiologist, and public health officer. Building on the experience, I would like to integrate clinical medicine, theoretical modelling, evolutionary biology, genetics, and molecular biology to gain a more comprehensive understanding of viral diseases. These findings would make a contribution to place where outbreak/epidemic/pandemic exists.

Figure 1 Discussion with director general of Nigeria Centre for Disease Control for outbreak response

Program-Specific Assist. Prof.
Yuki Furuse (right)

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Lab. of Viral Immunology (Visiting)

Human T-lymphotropic virus type 1 (HTLV-1) is widespread in the tropics and subtropics. Ninety percent of people infected with this virus are unaware of the infection and remain healthy, but 5% develop a leukaemia or lymphoma, known as ATL, and up to a further 5% develop a chronic inflammatory disease of the nervous system known as HAM/TSP, which results in paralysis of the legs. HTLV-1 is the main cause of adult leukaemia in southern Japan.

We aim to answer the questions:

- why do some HTLV-1-infected people develop these serious diseases, while the majority remain healthy? and
- how does HTLV-1 persist lifelong in the individual, despite a strong immune response?

In the Imperial College laboratory we study the immunology and virology of HTLV-1 infection, using a wide range of molecular, cellular and mathematical techniques. We have longstanding and valuable collaborations with colleagues in the UK and overseas, especially in Japan.

Continuing our collaboration with colleagues in Japan, we have discovered (Satou et al 2016: Proc. Nat. Acad. Sci. USA; Melamed, Yaguchi et al 2018: eLife) that HTLV-1 alters the structure and transcription of host chromatin. This highly unexpected observation raises new hypotheses about the pathogenesis of the leukaemia associated with HTLV-1 infection, and about the evolution of transposable elements in the mammalian genome. In addition, we found (Kirk et al 2016: Nature Microbiology, doi: 10.1038/NMICROBIOL.2016.212) that HTLV-1 and other exogenous retroviruses integrate into a shared, non-palindromic DNA sequence motif, unlike what has been believed for the last 25 years.

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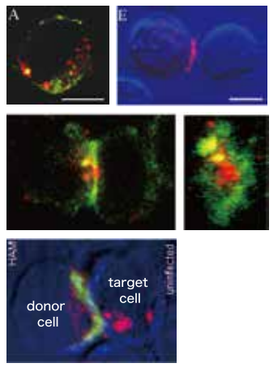
Discovery of the virological synapse (VS): triggered, directional transfer of HTLV-1 from cell to cell

Gag protein complexes (red) polarize to the cell-cell contact area

- which contains organized adhesion domains (green)

Gag is then transferred with the HTLV-1 genome to the target cell



Igakura et al 2003: Science **299**, 1713-6

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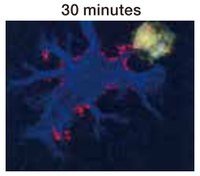

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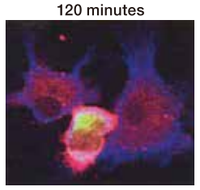

Dendritic cells (blue) can also be efficiently infected by contact with an HTLV-1-infected cell (green)

Lab. of Molecular and Cellular Biology

Our research focuses on the following three projects: Analysis of the quality control mechanism of proteins and the molecules such as chaperones and lectins that are involved in the mechanism (Hosokawa G); Analyses of transition stage from the formation of pre-initiation complex to elongation using RNA aptamer (Hirayoshi G); Analysis of illegitimate V(D)J recombination within T cell receptor β chain gene during normal T cell development in relation to tumorigenicity (Fujimoto G).

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 endcode proteins. We are also analyzing the protein degradation mechanism named ERAD (endoplasmic reticulum-associated degradation), and the intracellular transport of proteins.

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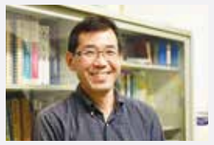

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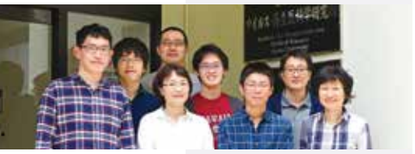
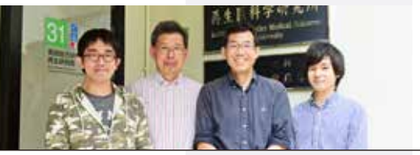
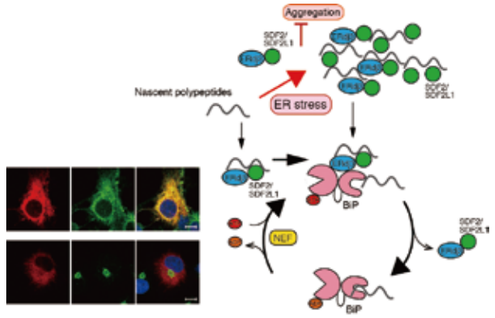
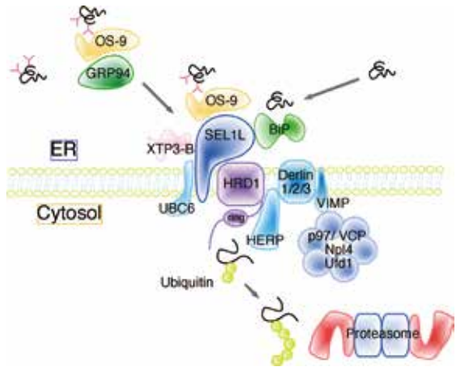






Chaperone protein complex in the endoplasmic reticulum (ER)
Newly snthesized proteins in the ER obtain their native conformations by the assistance of ER chaperon proteins. Some chaperone proteins make a complex to assist protein folding and to inhibit protein aggregation.

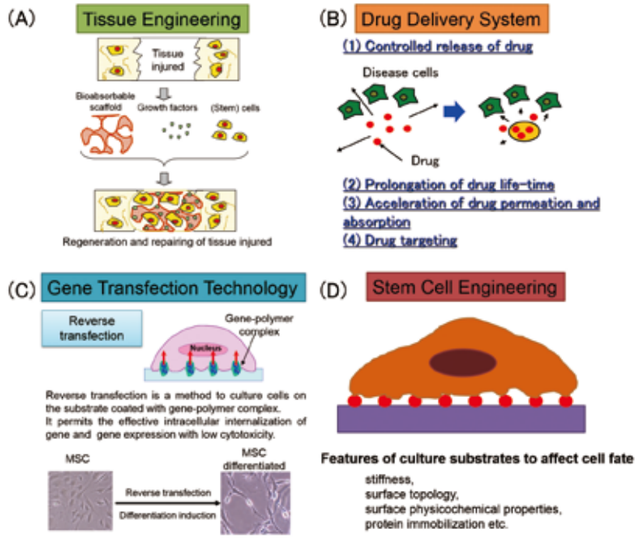


Ubiquitin-ligase complex in the endoplasmic reticulum (ER) membrane
Proteins that have misfold in the ER are degraded by the cytoplamic proteasome, a mechanism named ERAD. The ubiquitin-ligase complex in the ER membrane regulates ERAD. Chaperone proteins and lectins associate with this complex from the lumenal side.

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

Lab. of Biomaterials

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, 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.

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Lab. of Immunology

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 culture method by which CTLs expressing CD8 αβ heterodimer with high antigen specific cytotoxic activity can be generated (Figure 2). This new method provides a convincing rationale for application of this strategy in clinical settings.

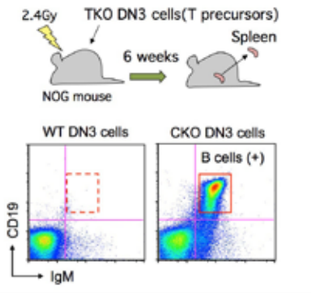


Figure1
Conversion of T cells to B cells by inactivation of polycomb-mediated epigenetic suppression
In T cell-specific Ring1A/B deficient mice, T cell development was severely blocked at an immature stage. We found that these developmentally arrested T cell precursors gave rise to functional B cells upon transfer to immunodeficient mice (Ikawa et al, Genes & Development, 2016).

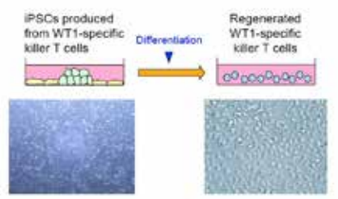


Figure2
Regeneration of antigen specific T cells using the iPSC technology
iPS cells were firstly produced from WT1-spcific CTLs, and then CTLs were regenerated from these iPSCs. Our novel culture system has made it possible to regenerated high quality CTLs with antigen specific cytotoxicity comparable to original CTLs (Maeda et al, Cancer Research, 2016). Applying this method to regenerate WT1 tumor antigen-specific CTLs, we showed that they prolonged survival of mice bearing WT1-expressing leukemic cells.

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

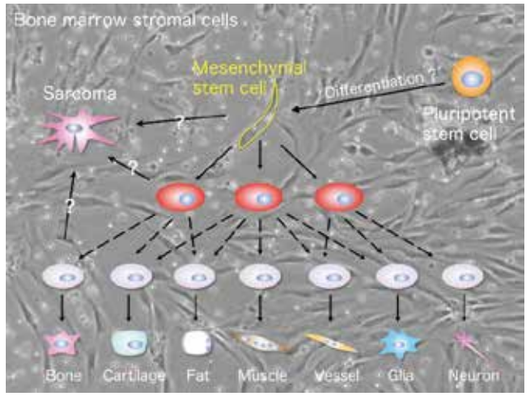
Department of Regeneration Science and Engineering

Lab. of Tissue Regeneration

The objectives of our department are to disclose the pathology of disorders in mesenchymal tissues at the molecular level and to develop new therapeutic modalities by understanding physiological growth and differentiation of mesenchymal cells. Following projects are currently undertaken.

1. Research on the regeneration of mesenchymal tissues.
We have analyzed on the growth and differentiation property of mesenchymal stem cells (MSC) that exist among bone marrow stromal cells and performed a clinical trial of cell therapy for the condition know as osteonecrosis.

2. Research on the transformation of mesenchymal cells
Sarcomas are malignant tumors derived from mesenchymal tissues. We have analyzed the genomic and epigenomic mechanisms of the development of sarcomas using MSC and pluripotent stem cells (PSC).



Our laboratory is investigating the mechanis of differentiation and proliferation of mesenchymal stem cells to achieve regeneration of mesenchymal tisseus, and also the mechanism of sarcoma development from mesenchymal tisseus.

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Lab. of Organ and Tissue Reconstruction

The target organs currently being considered for this development project are the heart, heart valves, esophagus, stomach, intestine, gallbladder, trachea, lung, liver, kidney, peripheral nerves, spinal cord, cornea, tendons, ligaments, cartilage, bone, fatty tissue, periodontal tissue, and permanent teeth. We plan to employ the two majour methods as described below.

in situ Tissue Engineering and Field theory

Cells (or living tissues) of patients are complexed (mixed) with purified ECM or bioabsorbable material. Using this complex, reconstruction of the failing tissues or organs will be attempted. Mesenchymal stem cell (MSC) obtained from the bone marrow is now applied to this method.

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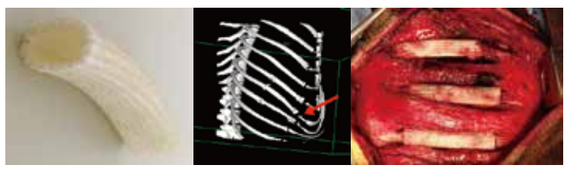

PLA-fiber woven rib coaptation socket system. (Dr. T. Komatsu)

Our major mission is to develop regenerative medicine for endocrine (primarily diabetes) and metabolic (liver etc.) diseases. We are studying devices for 3D cell culture, tissue (primarily islets) preservation, cell fusion for cancer therapy and so on. In the studies of regenerative medicine, our macro-encapsulation device that protects cell/tissue against immune attack and allows full retrieval without cell leakage awaits wide application for various diseases.

Lab URL ***https://www2.infront.kyoto-u.ac.jp/ca03/en/g_info.html***

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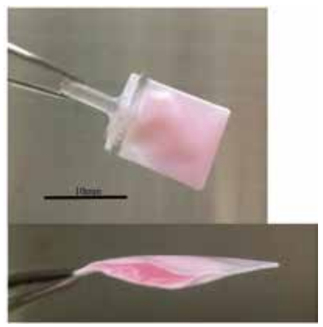
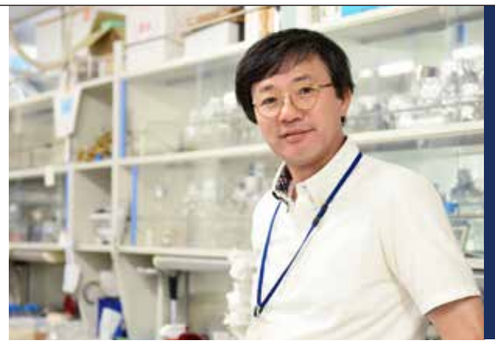


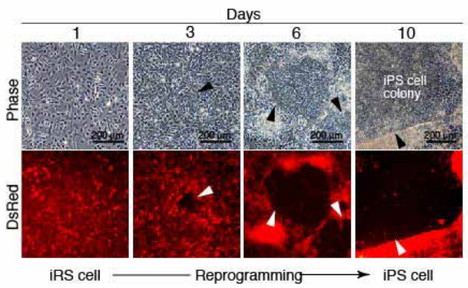
Highly histocompatible and porous EVOH bag that keeps cells inside securely (top) and immune-isolating chitosan hydrogel in it (bottom).

Lab. of Developmental Epigenome

Regenerative medicine and aging are closely linked subjects. Stem cell functions in repair and replacement of old tissues with young tissues. Induced pluripotent stem (iPS) cell generated through transformation of somatic cell by forced expression of reprogramming factors is expected to contribute to regenerative medicine. Anti-aging factors, which function in maintaining to keep body young, could be related to stem cell. Reprogramming and anti-aging sharing rejuvenation as a goal are regulated by the molecular mechanism of epigenome.



Lab URL ***https://www2.infront.kyoto-u.ac.jp/es03/index.html***



Reprogramming of iRS (intermediately reprogrammed stem) cell to iPS cell

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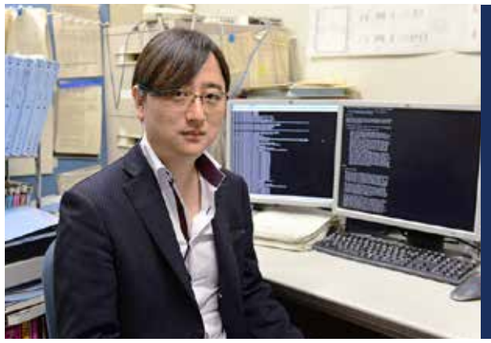
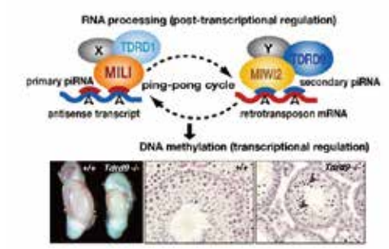
During development of multicellular organisms, genetic stability is differentially regulated depending on developmental stages, cellular lineages and physiological conditions etc. We are currently investigating (1) how pluripotent stem cells and germline cells maintain their genome and epigenome integrity, 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.



Lab URL ***https://www2.infront.kyoto-u.ac.jp/rc01/index-j.htm***



Tdrd1 and Tdrd9 protect the germline genome and epigenome from retrotransposon activity through the piRNA pathway

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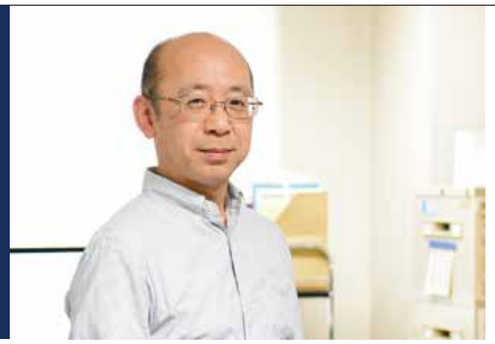

Lab. of Embryonic Stem Cell Research

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.

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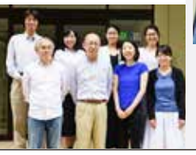

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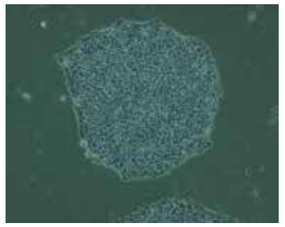


Figure 1 Human Embryonic Stem Cell

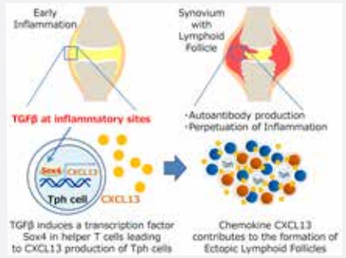
Figure 2 Clinical-grade hESC Processing Facility

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

Topics

Lab. of Tissue Regeneration

Human CXCL13-producing PD-1^{hi}CXCR5^{-}CD4^{+} T cells, which were identified in our study to figure out what happens in the inflamed joints of patient with rheumatoid arthritis, have been recognized as a new human CD4^{+} T cell subset, peripheral helper T (Tph) cells. In FY 2018, we identified Sox4 as a new transcription factor relating to the pathogenic function of Tph cells. We further investigate human immune responses at inflammatory sites to achieve more understandings of human immunology.



Assoc. Prof.
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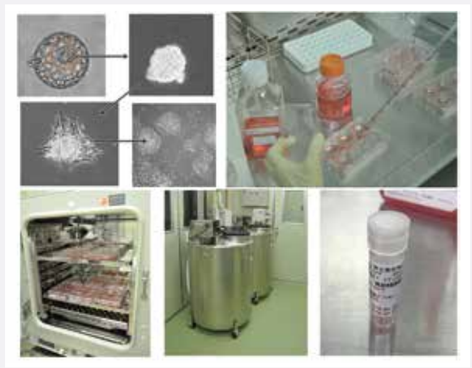
Laboratory of Embryonic Stem Cell Research

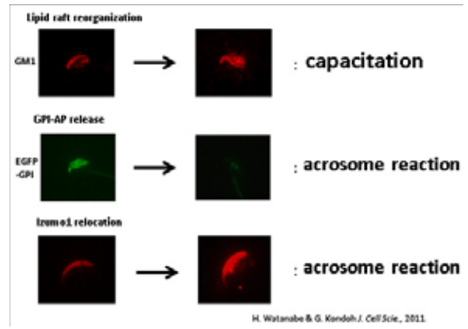
For clinical application of hES cells, we started derivation of clinical-grade hESC lines after governmental approval of the project. We reported the derivation of the first clinical-grade hESC line, KthES11, in May 2018, and in total 3 cell lines at present. Frozen stock of these cell lines have been distributed to research institutes aiming clinical application of hESCs.

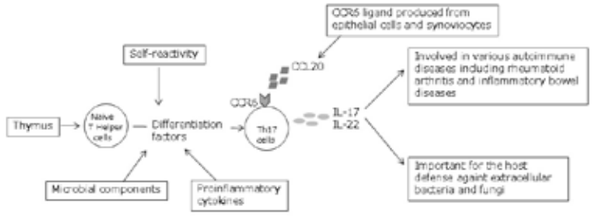


Assoc. Prof.
Hirofumi Suemori

Lab. of Integrative Biological Science

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.





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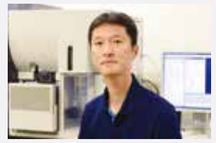

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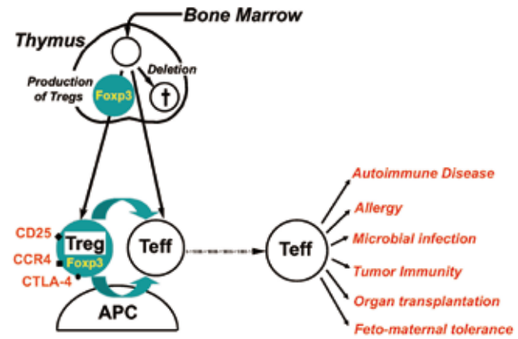
Our laboratory studies the mechanism of immunological tolerance. We discovered naturally occurring regulatory T (Treg) cells as a T-cell subpopulation that is specialized for immune suppression and engaged in the maintenance of immunological self-tolerance and homeostasis. We have been studying the molecular and cellular basis of Treg cells development and maintenance, in mice and humans by using immunological, epigenetic 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 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

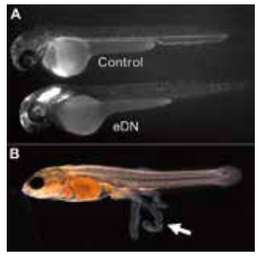


$CD25^+CD4^+$ regulatory T (Treg) cells are produced by the normal thymus as a functionally mature T-cell subpopulation. They specifically express the transcription factor FoxP3. Reduction of Treg cells or attenuation of their suppressive activity may enhance tumor immunity and microbial immunity. In 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 Tissue Stem Cell Biology

We are interested in biological mechanisms in two perspectives. One is a common system in the vertebrates. We are analyzing cardiovascular development using zebrafish. The other is unique trait in particular group of the teleost fish. We are investigating a viviparous system of goodeid species, which has no mammalian-like placenta and umbilical cords.



A. Cephalic hemorrhage in the endothelial cell-specific integrinβ1 inhibition zebrafish (eDN).
B. Intraovarian embryo of *Xenotoca eiseni* with trophotaenial placenta (arrow).

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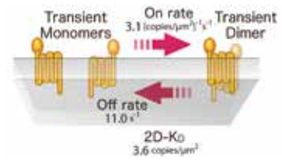
Lab. of Nano Bioprocess

A long-term goal of my laboratory is to uncover the mechanism of signal transduction process of receptors and molecules in the plasma membrane, leading to elucidate the conserved general feature of signal processing. We perform this research by applying the advanced optical microscopy techniques. Therefore, the new imaging techniques and analysis methods for image decoding have been developed, which allow us to directly observe elementary processes organized by single molecules in the plasma membrane. We' re particularly interested in G-protein coupled receptors or GPCR, and its signal transduction. By applying our imaging methods, we can now directly detect the association and dissociation of receptor molecules as well as other signaling molecules at the single molecule level.



Dynamic equilibrium between monomers and dimer of G-protein coupled receptor in the live plasma membrane

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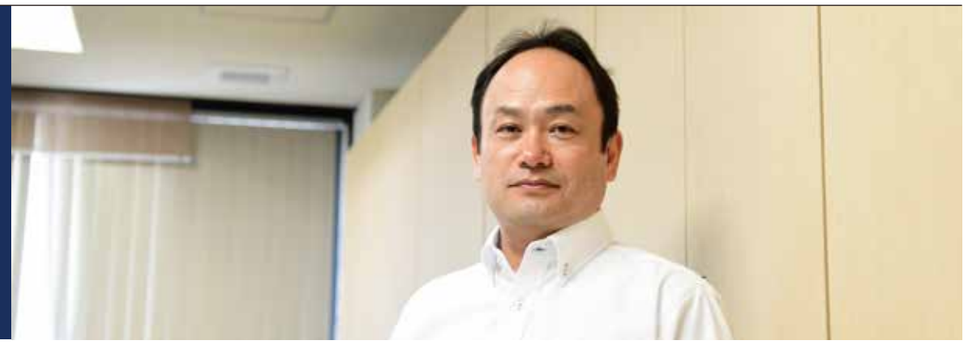
Topics

Lab. of Integrative Biological Science

It has been reported that immune cells play a key role in a wide range of diseases including cancer, lifestyle-related diseases, and cranial nerve diseases, and there is also a growing public interest in cancer immunotherapy with immune checkpoint molecule inhibitors including anti-PD-1 antibodies. Therefore, there is a high social demand for elucidating the pathogenesis of immune cell-associated diseases. My research team is working on how inflammatory T helper cells induce the development of autoimmune disease and how chronic tissue inflammation is mediated by a complex network of immune cells.

Assoc. Prof.
Keiji Hirota (left)



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Lab. of Biomechanics

The Laboratory of Biomechanics aims at clarifying the self-organized regulatory mechanisms of a diverse biological phenomena through interdisciplinary approaches encompassing mechanics, life science, and medical sciences. The major goal of our research is to understand how well-organized dynamics emerge from complex molecular and cellular interactions in living systems. Specifically, we are focused on highlighting the roles of “adaptation to the mechanical environment” and “hierarchy of structure and function” in living systems based on integrated biomechanics and mechanobiology studies using experiments and mathematical modeling and simulation. Our research topics cover developmental processes (cell differentiation, morphogenesis, and growth) and functional adaptation to the environment by remodeling and regeneration of tissues and organs.

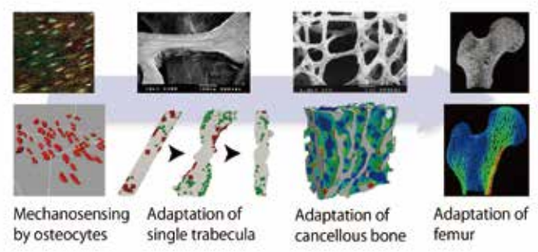

Figure 1 Bone can remodel its outer shape and inner structure to adapt to the surrounding mechanical environment. This study aims to clarify the mechanism of bone functional adaptation achieved by cooperative cellular activities.

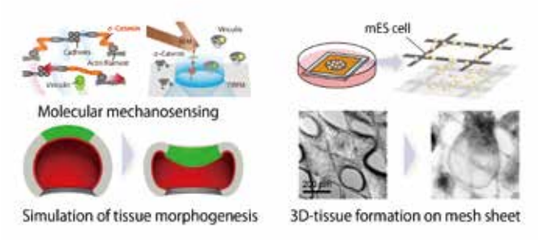

Figure 2 Morphogenesis of biological tissues is regulated by mechanical forces generated through multicellular interactions. This study aims to clarify the mechanism of tissue morphogenesis using experiments and simulations.

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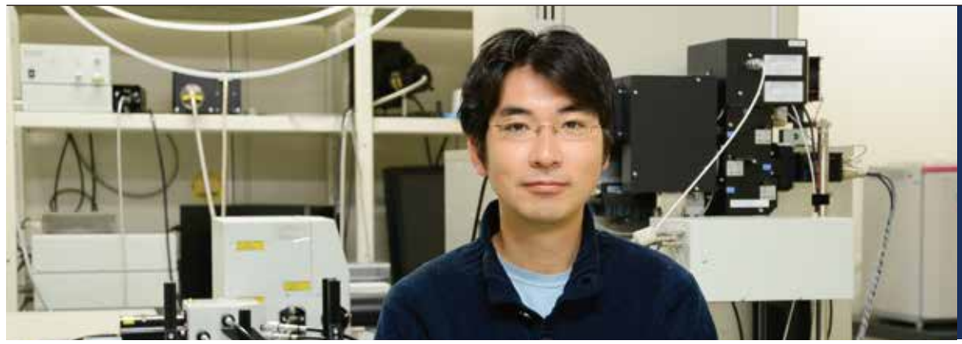
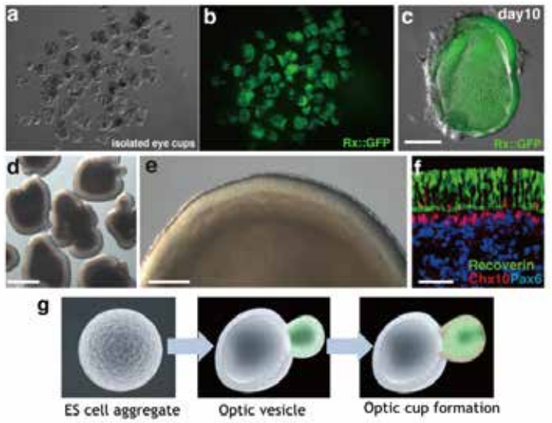


Lab. of Developmental Systems

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.

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Lab. of Systems Virology

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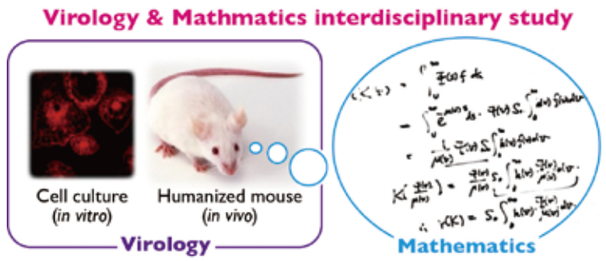
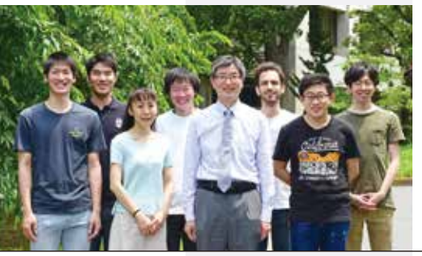
Virus infects cell and replicates. Viral genome transmits from infected cell to adjacent naive cells. This is a most significant characteristic of virus. The mechanism of this infection event is a primary theme of our laboratory. It has been found that various cellular factors positively and negatively associate with viral replication. However, we do not yet have the answer for how, which, and when cellular factors commit viral replication. The aim of our laboratory is to learn the mechanism how virus replicates in the cells. We address the mechanism of virus replication from the aspects of immunology and virology. The main subject of our research is HIV, which causes AIDS in human. The mechanism by which HIV infection results in AIDS remains unclear. We have been investigating how the immunodeficiency is triggered by HIV infection using in vitro (cell culture system) and in vivo (animal model) through the application of mathematics and bioinformatics. We developed a humanized mouse system in which the human immune system is reconstituted.



Virology and Mathmatics interdisciplinary study
Interdisciplinary research involves the combining of Virology from cell culture model and HIV-1-infection humanized mouse model generated by human hematopoietic stem cell-transplantation into NOG mice and Mathematical model application.



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Lab. of Growth Regulation System

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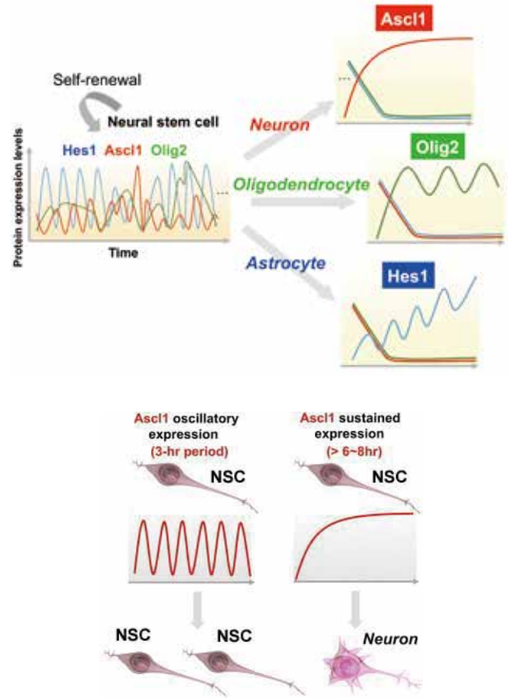
Neural stem cells have multipotency to produce three cell types, neurons, oligodendrocytes, and astrocytes. Fate determination factors responsible for production of each cell type have been identified, but it was found that these factors also have an opposing function – enhancement of maintenance and proliferation of neural stem cells. By using a time-lapse imaging method, we found that the expression of three cell fate determination factors oscillates in neural stem cells, whereas one of them becomes dominant and exhibits sustained expression during cell fate determination (upper Fig.) Our optogenetic approach showed that oscillatory expression of the neuronal fate determination factor activates the proliferation of neural stem cells, whereas its sustained expression induces neuronal differentiation (lower Fig.) This optogenetic technology allows us to control neural stem cell proliferation and neuronal differentiation at will by simply changing the light illumination patterns. We now plan to apply this technology to neural regeneration.



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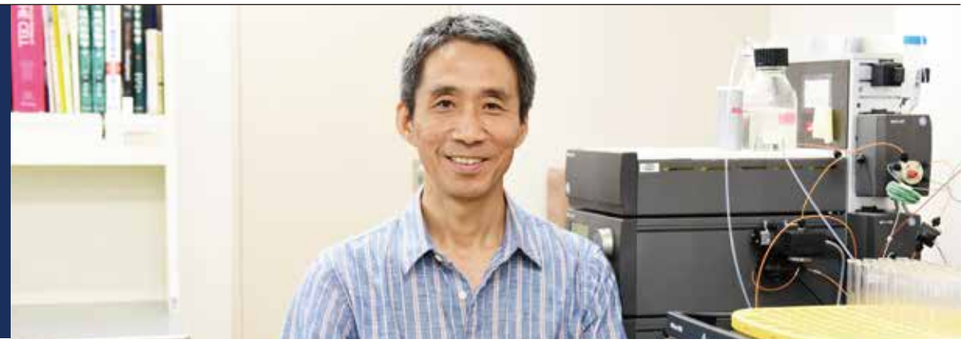

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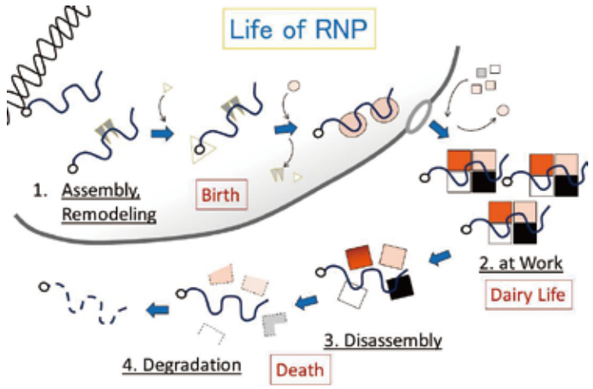
Lab. of RNA System

RNA in the cell is not naked but bound by various proteins. Specific RNA binding proteins gather onto the newly-made RNA and thus specific RNP (ribonucleoprotein) is born. RNA component usually undergoes maturation from its primary form through RNA processing. RNP frequently changes its protein composition. RNP is often transported to the place where it functions. If RNP becomes non-functional for various reasons, e.g. gene mutations, direct lesions, misassembly etc., it is disassembled and RNA component is degraded. Prof. Mutsuhito OHNO' s laboratory is studying various aspects (birth, dairy life and death) of such "Life of RNP". Major research subjects are (1) RNA processing and transport, (2) Regulation of RNA expression by HIV-1, (3) Quality control of the Ribosome, and (4) Sorting mechanisms between mRNAs and non-coding RNAs. This laboratory belongs to the Graduate School of Science, Kyoto University.



In the current world of life, the main genetic material is DNA, but the major functional molecules are both protein and RNA. Therefore, the current world of life can be called "RNP world". RNP, just like human, goes through a cycle of birth, life and death. Very important biological themes can be found in each step.

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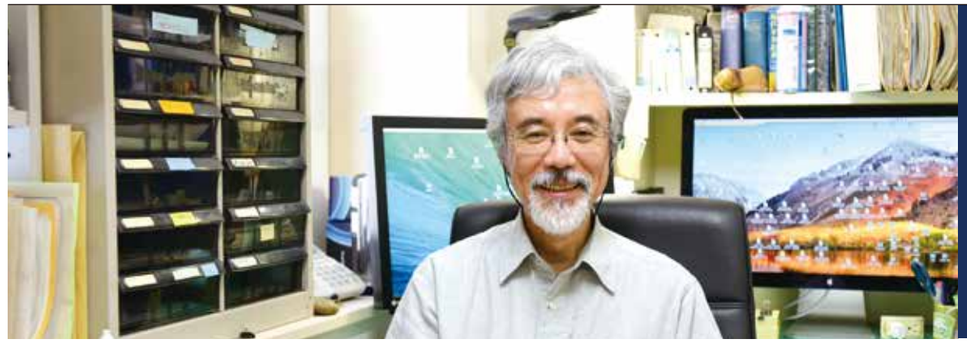
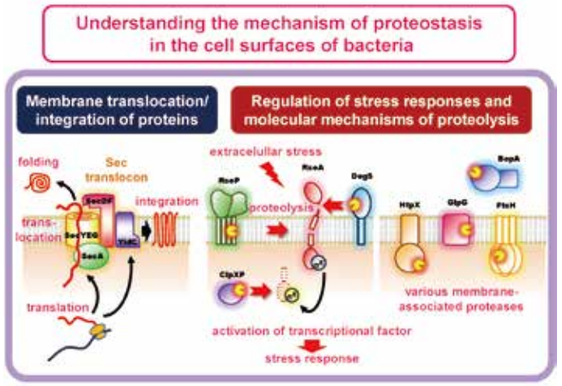


Lab. of Biological Membrane System

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 of protein translocation machinery: Protein export across the bacterial cytoplasmic membrane is promoted by cooperation of the evolutionary conserved SecYEG translocon associated with auxiliary facotrs (such as SecDF) and the SecA ATPase motor. We are investigating the structure and molecular function of these and related cellular factors. (2) Membrane protein degradation and extracytoplasmic stress response: Membrane proteins play central roles in the functions of biological membranes. We are investigating the functional mechanism and cellular roles of membrane 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.

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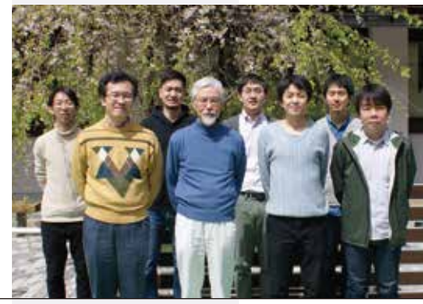

Lab URL ***https://infront-biomembrane.jp***

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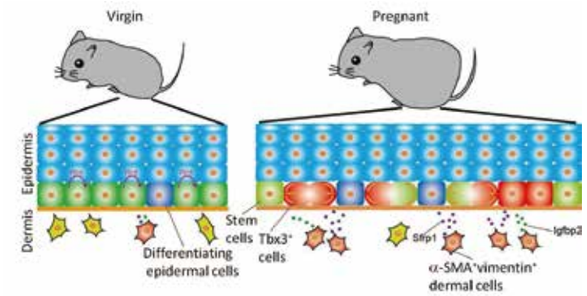
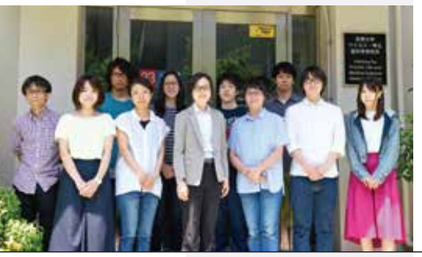
Lab. of Tissue Homeostasis

Stem cells in adult tissues exist in a quiescent state. When they are needed in tissue homeostasis or repair, they exit a quiescent state and undergo symmetric/asymmetric cell division to give rise to differentiation-committed progenitor cells. Our group seeks to explore the molecular mechanisms underlying oriented stem cell division, stem cell activation, and cell fate determination. We also want to know how stem cells adopt to physiological changes in the body. Current Projects; 1) Epidermal stem cell proliferation and differentiation in skin homeostasis. 2) Cell fate determination of lymphoid cells via symmetric/asymmetric cell division. 3) Tissue stem cell activation during pregnancy.



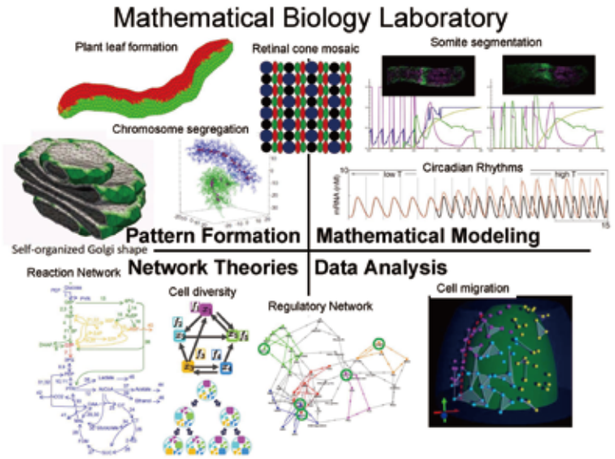
Epidermal stem cell dynamics during abdominal skin expansion in pregnant mice



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

Lab. of Mathematical Biology

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

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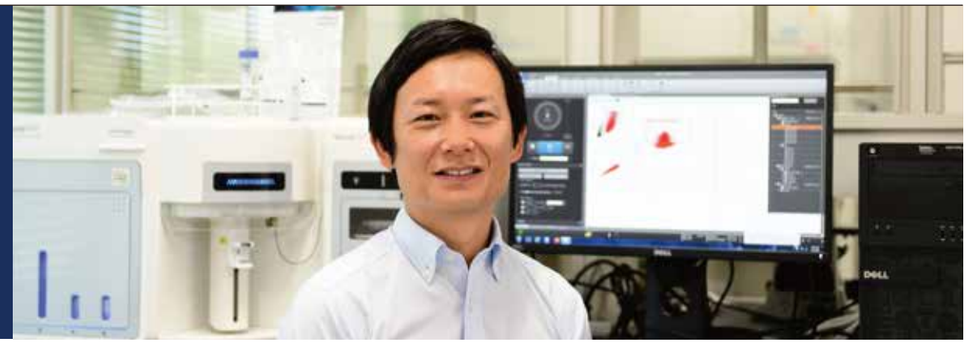

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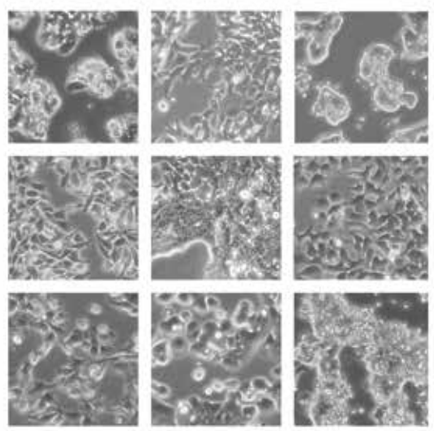
Lab. of Stem Cell Genetics

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. of Cell Fate Dynamics and Therapeutics

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.

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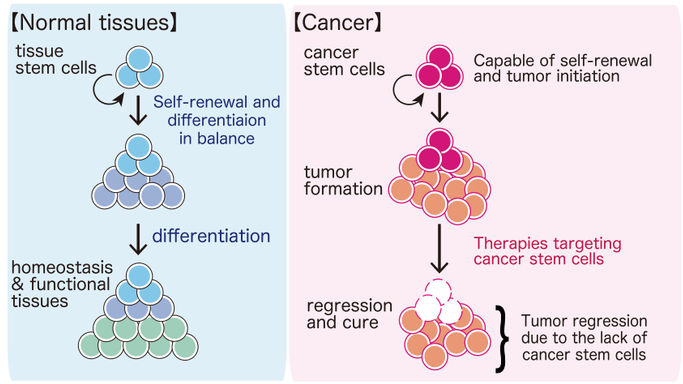
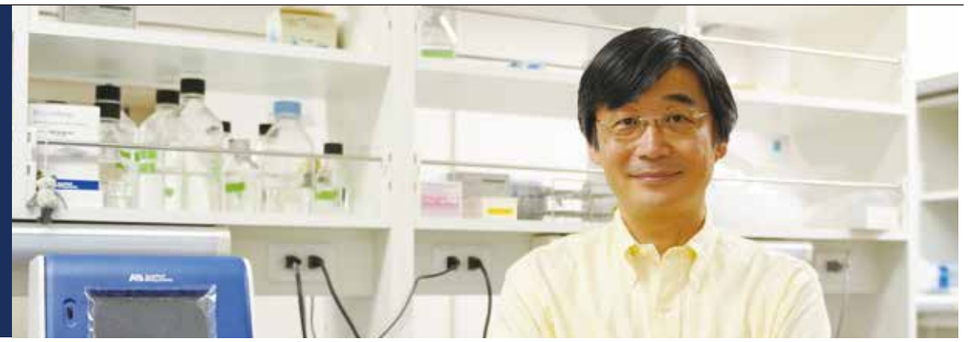
Stem cells in tissues and cancer



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.



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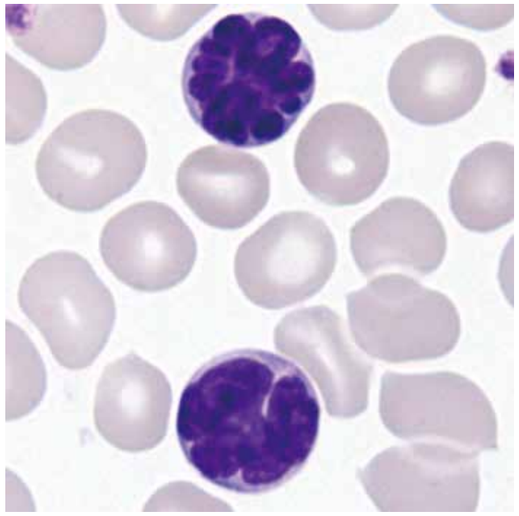
Lab. of Regulatory Information (Visiting)

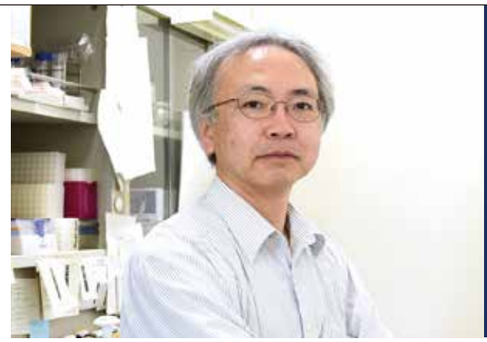
A human retrovirus, human T-cell leukemia virus type 1 (HTLV-1), is an etiological agent of adult T-cell leukemia (ATL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). There are 10 million HTLV-1 carriers throughout the world, and about 0.8 million in Japan. Kyushu area is an endemic area of HTLV-1, while a recent epidemiological survey showed that the number of HTLV-1 carriers in urban area was increased in the last 20 years. Therefore, HTLV-1 is still an important issue in this country. We are studying the molecular pathogenesis of HTLV-1 using clinical samples from the patients with ATL or HAM/TSP, and asymptomatic carriers.



ATL cells have a hyper lobulated nucleus, and are called "flower cells".

Lab. of Primate Model

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.



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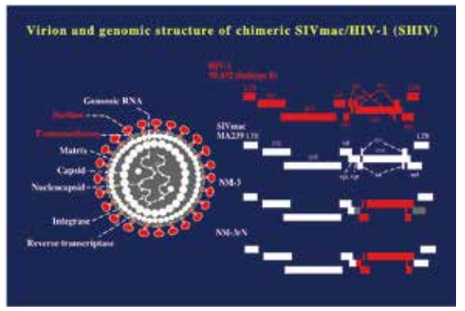

Virion and genomic structure of chimeric SIVmac/HIV-1 (SHIV).

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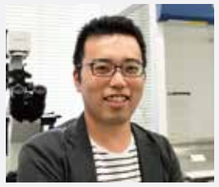
Topics

Lab. Of Immunology
(Inter-Organ Communication Research Team)

Although it is obvious that host physiology is adversely affected by cancers, the underlying mechanisms behind cancer's adverse effects on the host remain poorly understood. To tackle this, we study cancer-host interaction with the aid of mouse genetics, multi-omics analysis, and bioinformatics. We aim to develop novel therapeutics that can efficiently mitigate cancer's adverse effects on the host, thereby improving both patients' QOL and efficacy of currently available anti-cancer therapies.



Program-Specific Assoc. Prof.
Shinpei Kawaoka

Lab. of Systems Virology

Biological data is often high-dimensional, and therefore difficult to process, visualize, and analyze. The goal of my research is the discovery of new insights in biological data using bioinformatics approaches. Recent projects include the prediction of new regulators from thousands of gene expression samples (RNA-seq), and understanding the timing of epigenetic modifications from ChIP-seq data. Currently, I am developing a bioinformatics method for finding interesting genes in single-cell RNA-seq data.

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Lab. of Infectious Disease Model

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Our laboratory is focusing on intractable viruses such as human immunodeficiency virus, hepatitis C virus and human T-cell leukemia virus. These viruses share common similarities; disease development after long-term persistent infection, presence of unique mechanism for the immune evasion, and narrow and selective host range. Especially, the last one leads us to be incapable of employing small laboratory animals as immunocompetent models for viral infection. In this point of view, we have challenged these issues and established novel non-human primate models for the intractable viruses. With the use of the model animals, we would like to unravel the molecular and immunological mechanisms by which the viral persistency and disease onset are induced, and further challenge applied research regarding the development of vaccines and new therapeutics.

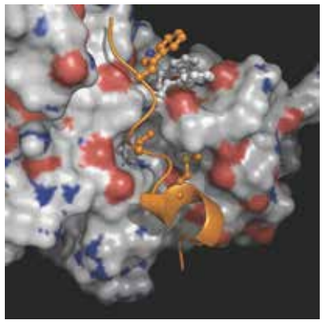


Figure 1 Interaction between HIV-1 Nef N-terminus and mu-1 subunit of adaptor protein-1

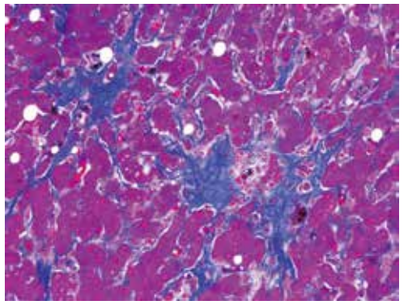


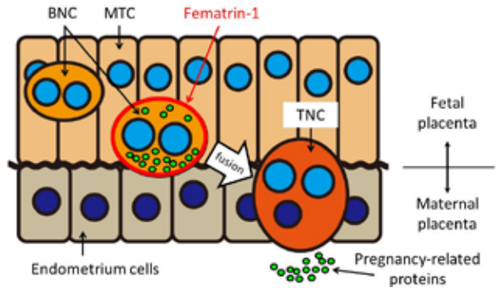
Figure 2 histopathological analysis of liver fibrosis in a tamarin persistently infected with GBV-B (Masson's trichrome staining)

Lab URL *https://akari-labo.jimdo.com/*

inFront

Lab. of Virus-Host Coevolution

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.



Fematrin-1, a bovine endogenous retrovirus K1-derived protein, is involved in the formation of trinucleate cells (TNC) appreared in bovine placenta. BNC: binucleate cells; MTC: mononucleate trophoblast cells.

Assoc. Prof.
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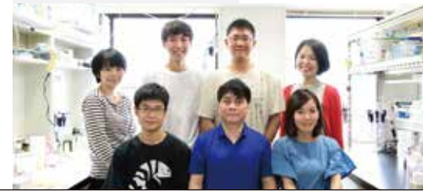
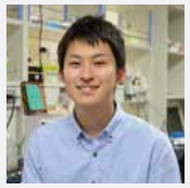


Lab URL *https://paleovirology.jimdo.com/*

Topics

Laboratory of Immune Regulation

As we live in 24-hour cycle of day and night, the immune system shows active and resting phases during the course of day. We found that a hormone controls the diurnal change of immune functions. We aim to reveal the mechanism how irregular life style and unblanced hormonal production, often seen in modern society, cause immune dysfunction and chronic inflammation, to propose better ways of clinical treatments.



Research Fellow
Shimba Akihiro

Lab. of Experimental Immunology (visiting)

There are more than 80 medically recognized autoimmune diseases and the incidence of these diseases and inflammatory immune diseases such as atopic dermatitis, pollen allergy, food allergy and inflammatory bowel disease has been increasing. However, in most cases, etiology and pathogenesis are not totally clear and therapeutics remain empiric. Thus, it is urgent to find therapeutic targets and develop a novel method for controlling excessive immune responses. So far, I have mainly focused on the activation of the innate immune system, but in my future study here, I would like to highlight the acquired immune system and develop next-generation immunoregulatory method through especially “regulatory T cell” research. Personal motivation is being a strong driving force to this direction as well.

Program-Specific Assoc.Prof.
Masataka Asagiri

Non-human Primate Experimental Facility

The center runs BSL-3 NHP facilities and has been accommodating various researches from all over Japan as a Joint Usage/Research Center for fusion of advanced technologies and innovative approaches to viral infections and life science. Facility veterinarians and other staffs support researchers by doing daily animal care and use and facility management. By March 2012, a new BSL-2 facility is constructed and one of BSL-3 facility is renovated. The center is expected to grow in use and popularity.

Reproductive Engineering Team

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

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.

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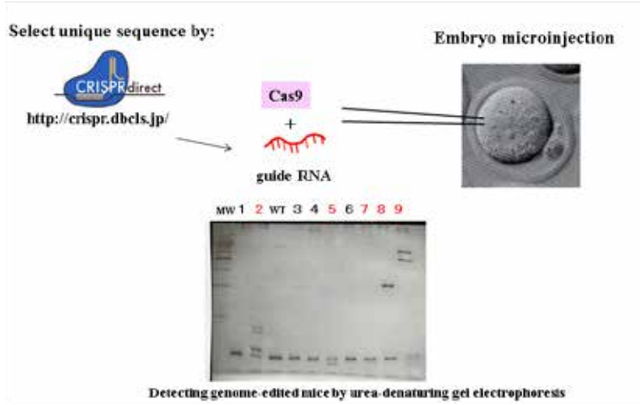
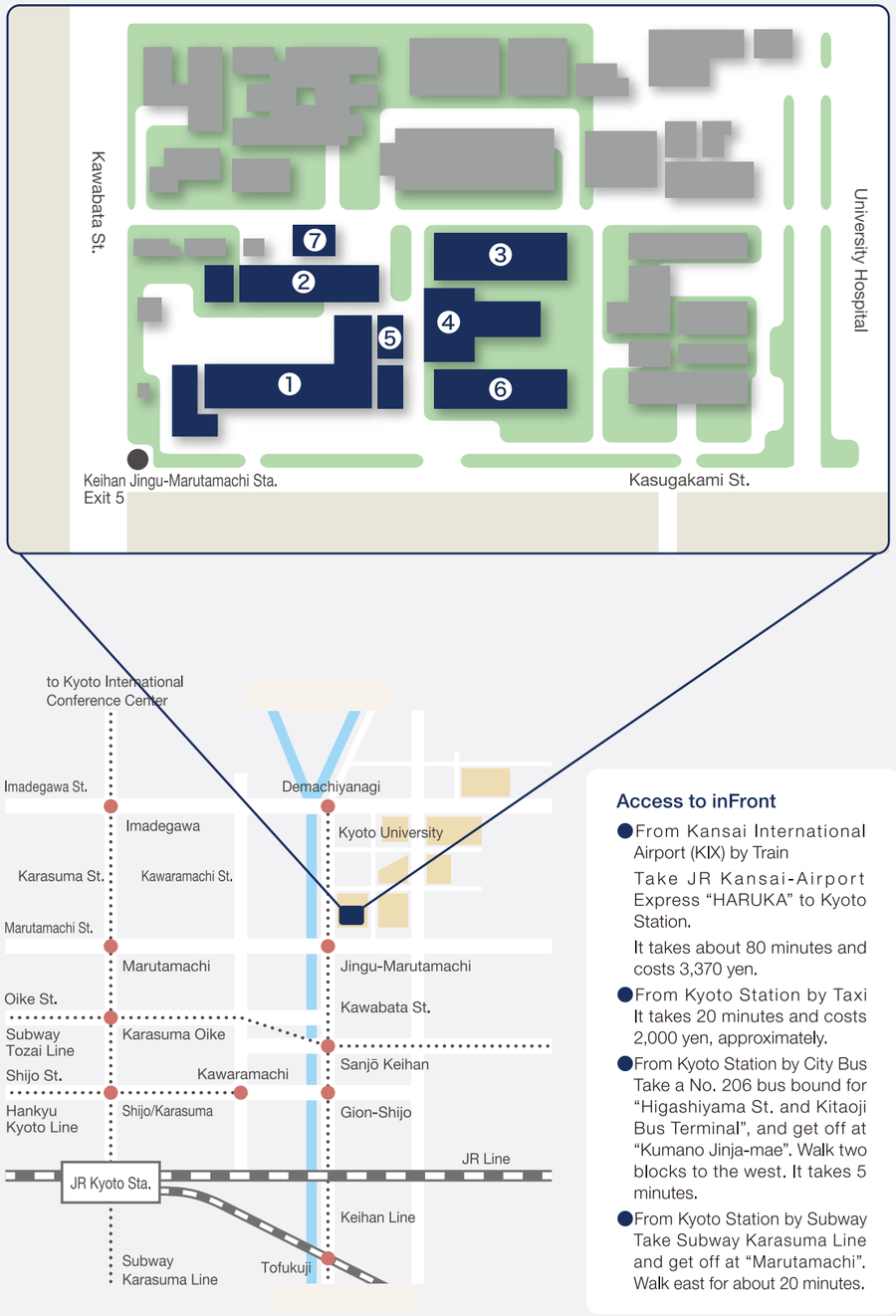


Our strategy for developing genome-edited mice using CRISPR-Cas9 system.

Lab URL ***https://www2.infront.kyoto-u.ac.jp/an/newpage1.html***

Map & Access



Access to inFront

- From Kansai International Airport (KIX) by Train
  Take JR Kansai-Airport Express “HARUKA” to Kyoto Station.
  It takes about 80 minutes and costs 3,370 yen.
- 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.

❶ South Research Bldg. No.1 Institute for Frontier Life and Medical Sciences Bldg. No.1

- Lab. of Tumor Viruses
- Lab. of Molecular and Cellular Biology
- Lab. of Biomaterials
- Lab. of Tissue Stem Cell Biology
- Lab. of Immunology
- Lab. of Tissue Regeneration
- Lab. of Organ and Tissue Reconstruction
- Lab. of Developmental Epigenome
- Lab. of Embryonic Stem Cell Research
- Lab. of Integrative Biological Science
- Lab. of Experimental Immunology
- Lab. of Nano Bioprocess
- Lab. of Developmental Systems
- Lab. of Stem Cell Genetics
- Lab. of Cell Fate Dynamics and Therapeutics
- Administration Office

❷ Institute for Frontier Life and Medical Sciences Bldg. No.2

- Lab. of Molecular Genetics
- Lab. of Virus Control
- Lab. of Tumor Viruses
- Lab. of Cell Regulation
- Lab. of Immune Regulation
- 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 Virus-Host Coevolution

❸ Institute for Frontier Life and Medical Sciences Bldg. No.3 (under renovation)

❹ Institute for Frontier Life and Medical Sciences Bldg. No.4

- Lab. of Immune Regulation
- Center for Animal Experiments

❺ Institute for Frontier Life and Medical Sciences Bldg. No.5

- Lab. of Embryonic Stem Cell Research
- Lab. of Integrative Biological Science
- Lab. of Biomechanics
- Lab. of Developmental Systems
- Lab. of Cell Fate Dynamics and Therapeutics

❻ Molecular Biology Research Bldg.

- Lab. of RNA Viruses
- Lab. of Ultrastructural Virology
- Lab. of Biomechanics
- Lab. of Systems Virology
- Lab. of Primate Model
- Reproductive Engineering Team
- Non-human Primate Experimental Facility

❼ Institute for Frontier Life and Medical Sciences North Research Bldg.

- Lab. of Molecular Genetics
- Lab. of Infectious Disease Model