IMS

RIKEN
Since 1917

RIKEN Center for

Integrative Medical Sciences

Stratified medicine for a healthy long-lived society. Creation of a research platform for new biomedical science.

Director
Kazuhiko Yamamoto

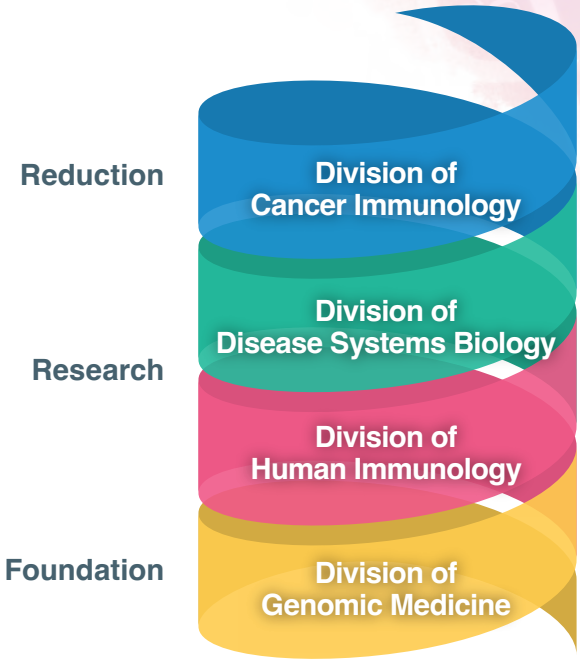
Japan is facing urgent health issues, such as lifestyle-related diseases, various cancers and brain-function disorders, in an increasingly aging society. It has become apparent that the human immune system not only relates to autoimmune diseases, infectious diseases and allergies, but also to many other age-related disorders. It is now thought that disease onset is caused by highly complex combinations of environmental stresses and body reactions, in addition to genomic variations, in each individual.

At the RIKEN Center for Integrative Medical Sciences (IMS), we aim to clarify the pathogenic mechanisms underlying human diseases and to translate this knowledge into novel therapies for the benefit of society. IMS will tackle various research questions to expound the functions of the human genome and immune system. IMS research is based on the concept of disease as a dynamic body system interacting with environmental stresses. We will create a research platform to clarify the processes that maintain or disrupt body homeostasis and then transfer that knowledge into the creation of new therapies and medicines.

In particular, IMS will strengthen its genome and immunology research platforms through new inputs from functional genomics research, with special emphasis on gene expression networks such as the FANTOM project. Based on this new research platform, IMS will integrate the knowledge of both human genome function and immune system, and lead cutting edge science to solve the problems of various diseases.

IMS will promote comprehensive multi-layered analysis of the genome, epigenome, proteins, lipids, cells, organs and individuals. IMS will statistically and computationally analyze the vast amounts of these advanced complex data. The results will be translated, as applicable, to hospitals and other medical institutions. In addition, IMS will develop a research platform for human immunology. With this platform, results obtained from mouse and other experimental animal models are translated to humans, and disease mechanisms identified from human research will be recapitulated in mouse models and cell culture systems. Using this combination of technologies, IMS will expand the research field for next-generation cancer immunology.

In collaboration with domestic and international research institutions and industries, IMS will create a research platform that contributes to the next generation of medical science and to a healthy long-lived society in Japan.



Young Chief Investigator Program

Nurturing young researchers who will be the future leaders of multidisciplinary strategic research

The Young Chief Investigator (YCI) program provides a seven-year career path for selected young investigators to carry out independent multidisciplinary research in a host laboratory at IMS. They are expected to pioneer new research fields and create novel scientific possibilities in these fields by integrating their own research with the existing research at IMS.

Director

Kazuhiko Yamamoto

Deputy Directors

Haruhiko Koseki

Harukazu Suzuki

Hiroshi Ohno

Senior Advisors

Shizuo Akira

Advisory Council

Division of Genomic Medicine

- Lab. for Transcriptome Technology
- Lab. for Cellular Function Conversion Technology
- Lab. for Genome Information Analysis
- Lab. for Applied Computational Genomics
- Lab. for Large-Scale Biomedical Data Technology
- Lab. for Advanced Genomics Circuit
- Lab. for Comprehensive Genomic Analysis
- RIKEN-IFOM Joint Lab. for Cancer Genomics
- Lab. for Genotyping Development
- Lab. for Statistical and Translational Genetics
- Lab. for Pharmacogenomics
- Lab. for Cardiovascular Genomics and Informatics
- Lab. for Systems Genetics
- Lab. for Functional Non-coding Genomics
- Lab. for Retrotransposon Dynamics

Division of Human Immunology

- Lab. for Autoimmune Diseases
- Lab. for Human Immunogenetics
- Lab. for Lymphocyte Differentiation
- Lab. for Transcriptional Regulation
- Lab. for Immune Cell Systems
- Lab. for Innate Immune Systems
- Lab. for Immune Homeostasis
- Lab. for Cytokine Regulation
- Lab. for Immunological Memory
- Lab. for Inflammatory Immune Metabolism
- Infectious Diseases Research Unit

Division of Disease Systems Biology

- Lab. for Developmental Genetics
- Lab. for Intestinal Ecosystem
- Lab. for Integrative Genomics
- Lab. for Mucosal Immunity
- Lab. for Gut Homeostasis
- Lab. for Skin Homeostasis
- Lab. for Tissue Dynamics
- Lab. for Integrated Cellular Systems
- Lab. for Metabolomics
- Lab. for Microbiome Sciences
- Lab. for Metabolic Networks
- Lab. for Epigenome Inheritance
- Lab.for Symbiotic Microbiome Sciences
- Drug Discovery Antibody Platform Unit

Division of Cancer Immunology

- Lab. for Medical Science Mathematics
- Lab. for Cancer Genomics
- Lab. for Immunotherapy
- Lab. for Human Disease Models
- Lab. for Cancer Invasion and Metastasis
- aAVC Drug Translational Unit

RIKEN Hakubi Research Team

- Genome Immunobiology RIKEN Hakubi Research Team

Young Chief Investigator Program

- YCI Lab. for Immunological Transcriptomics
- Proteome Homeostasis Research Unit

- Office of the Center Director

Division of Genomic Medicine

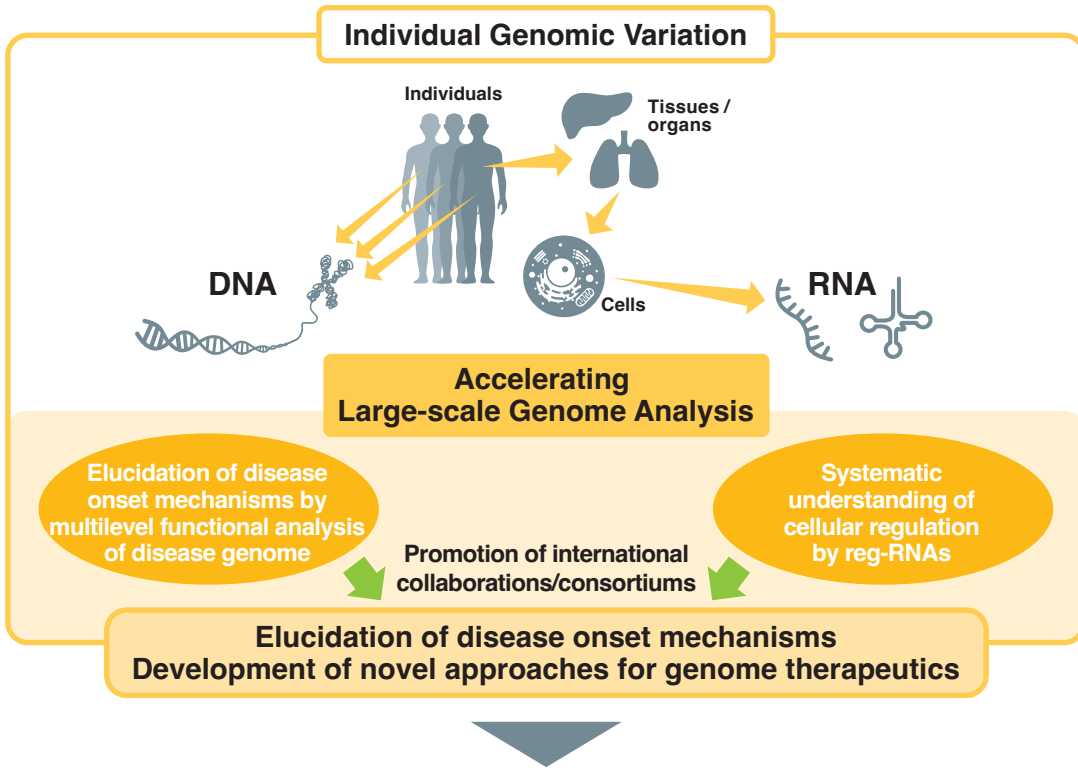
Elucidating causal genetic factors in disease onset

Our DNA contains all the necessary information to start and maintain life, yet we are far from unraveling the complexity of the human genome. Understanding *how* and *when* genes are regulated in a wide variety of human cells and *how* genetic variants across individuals lead to differences in susceptibility of disease are necessary not only to define healthy and disease states, but also to elucidate causal genetic factors in disease onset. Defining regulatory features together with genetic variants across individuals will greatly enhance personalized medicine and the development of effective therapies.

In the Division of Genomic Medicine, we aim to investigate the entirety of the human genome by studying the gene regulatory features, including expression and function of coding and non-coding RNAs, dynamic changes of chromatin states, and their physical associations to one another. The Division focuses on developing genomic technologies and building analytical tools to reconstruct gene regulatory networks controlling human development, aging and disease onset. The Division also investigates the human genome by Genome Wide Association Studies (GWAS) based on targeted- and whole-genome sequencing to newly identify genetic variants associated with diseases and clinical phenotypes. The Division strives to integrate regulatory features with disease-associated polymorphisms, specifically found in non-coding regions, to elucidate causal drivers of disease through advanced statistics and AI algorithms.

Resolving the complexity of the human genome cannot be achieved by a single lab or division; it requires international collaborative efforts. In the Division, we spearhead the FANTOM consortium that aims towards the complete functional categorization of regulatory RNAs and their associations to chromatin – with the goal to create the world's first regulatory RNA catalog. The Division also co-leads the international Human Cell Atlas project, which envisions to map the molecular programs and spatial features of all human cells at single cell resolution.

The principles of the Division include: Innovation in genomic technology, Excellence in analytical algorithms, Value in integrative and scalable databases, and Promotion of a collaborative research environment. Through these principles and team efforts, we strive to unravel the complexity of the human genome in order to crack the inner workings of human physiology and to develop therapeutic solutions for all diseases and individuals.



We will develop new methods for genome-based drug discovery and produce supporting evidence for the realization of genomic medicine

Division of Human Immunology

Development of research platforms for human immunology, elucidation of the principles of the immune system

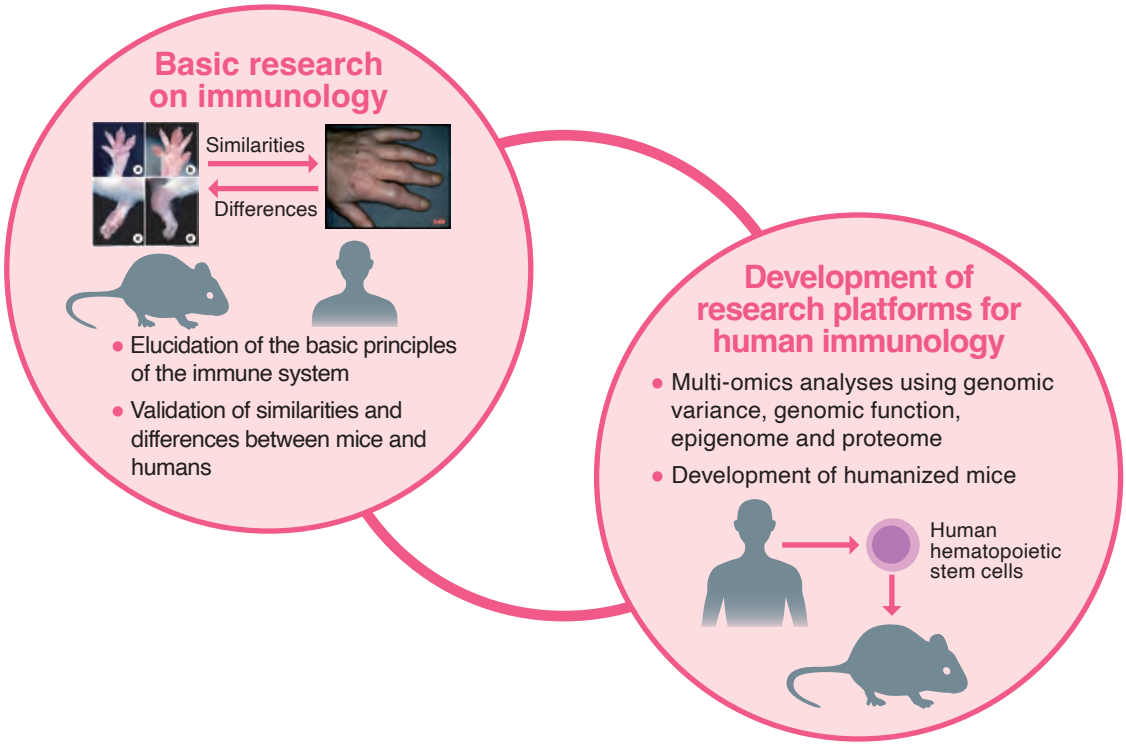
The immune system normally protects our body. However, once it collapses, the immune system can lead to various diseases — autoimmune diseases such as rheumatoid arthritis and vasculitis, allergic diseases such as asthma, and immunodeficiencies such as those manifested by opportunistic infections.

To develop comprehensive remedies for immune-related diseases, it is essential to fully understand the human immune system. Current immunological research has been established based on the studies of mouse and other experimental animal models. Indeed, there exists basic and common principle mechanisms between mice and humans; however, the precise structures of their two immune systems are different. Thus, there are various difficulties when we transfer the research results from mice to humans.

With the aim of promoting research on human diseases, the Division of Human Immunology will establish research platforms to compare humans and mice, and validate the similarities and differences between them.

We will also strive to elucidate the unsolved basic principles of the immune system and transfer that knowledge to human immunology. To understand the human immune system, we must continue our challenges on the central questions in immunology by using experimental model animals, cell cultures and other experimental tools.

In addition, we will develop “humanized mice” that recapitulate the human immune system in mice. Humanized mice will allow us to efficiently test the hypotheses derived from experiments. Through the research platforms we develop, we will contribute to the expansion of human immunology.



We will develop a research platform for human immunology

Division of Disease Systems Biology

Environment versus body — Understanding disease as a dynamic system Creation of a new research field

The human body normally maintains homeostasis, and thus we are not easily affected by environmental disturbances. However, disruption of this homeostatic balance can trigger various diseases, often very serious ones.

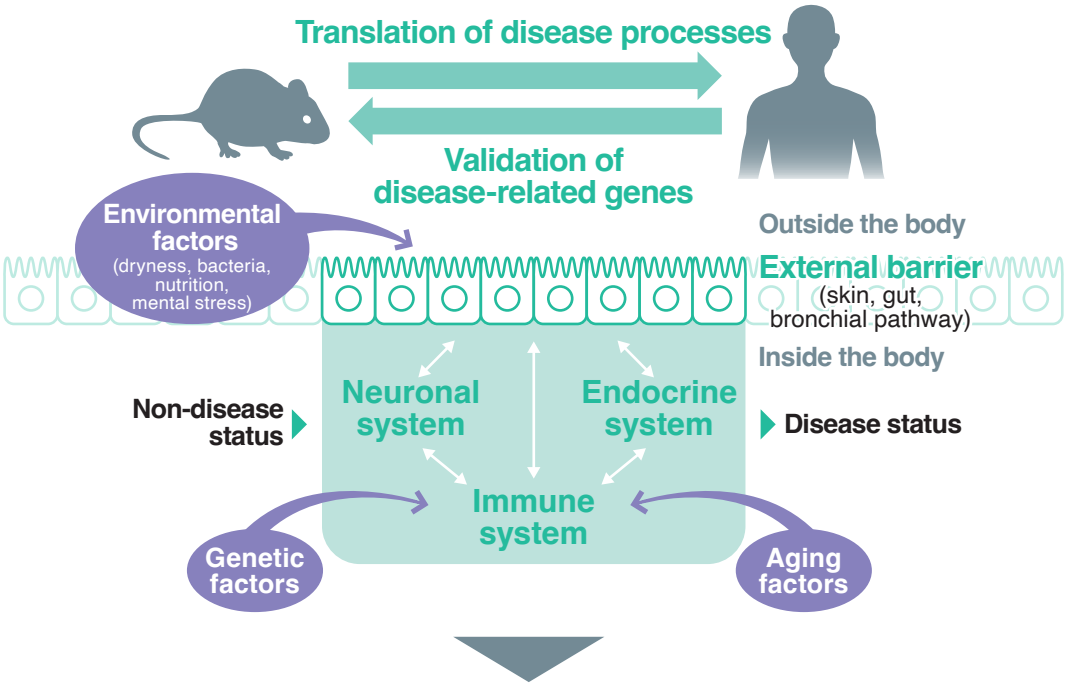
IMS aims to elucidate how homeostasis is maintained and how its disruption causes disease. The knowledge generated here will be combined with insights gained from genomic research, which continues to identify genetic and epigenetic diversity and consequently disease susceptibility, in human. Using this integrated approach, IMS will spearhead the development of personalized preventive medicine and therapeutics.

External environmental stress is initially blocked at the external body barrier, the boundaries inside and outside of the body such as the skin, gut or bronchial pathway. The external body barrier not only absorbs daily environmental changes, but it also functions to maintain homeostasis inside the body. However, when environmental changes are so rapid and damage the external barrier, pathogens can enter the body causing immune signals to activate the body defense system.

Under long-term environmental stresses, prolonged immune activation causes chronic inflammation. In this circumstance, links between the immune system, neuronal system and endocrine system can lead to diseases such as diabetes, cardiovascular disease, and other life style-related diseases, in various body organs. Not only external environmental factors, but also a complex combination of internal factors can also affect disease onset. Individual genomic differences (genetic factors) and various age-related body changes (aging factors) affect the balance of body homeostasis.

Thus, to understand the complicated process of disease onset, it is necessary to generate an integrated model based on systematic analyses on multiple levels, from the genome, molecules, cells, tissues, and organs to the whole body.

Focusing on interaction between the body and the environment, the Division of Disease Systems Biology aims to elucidate the mechanisms of chronic inflammation. We will challenge the measurement and collection of data on multiple levels and, based on this integrated data, we will promote the technical development of modeling and simulation tools, thus creating a new research field. By comparing human clinical data and mouse experimental data, we will elucidate the processes of disease onset.



We will elucidate the regulation of homeostasis and disease onset as a dynamic living system

Division of Cancer Immunology

Explore novel principles of the immune system, focusing on tumor cells

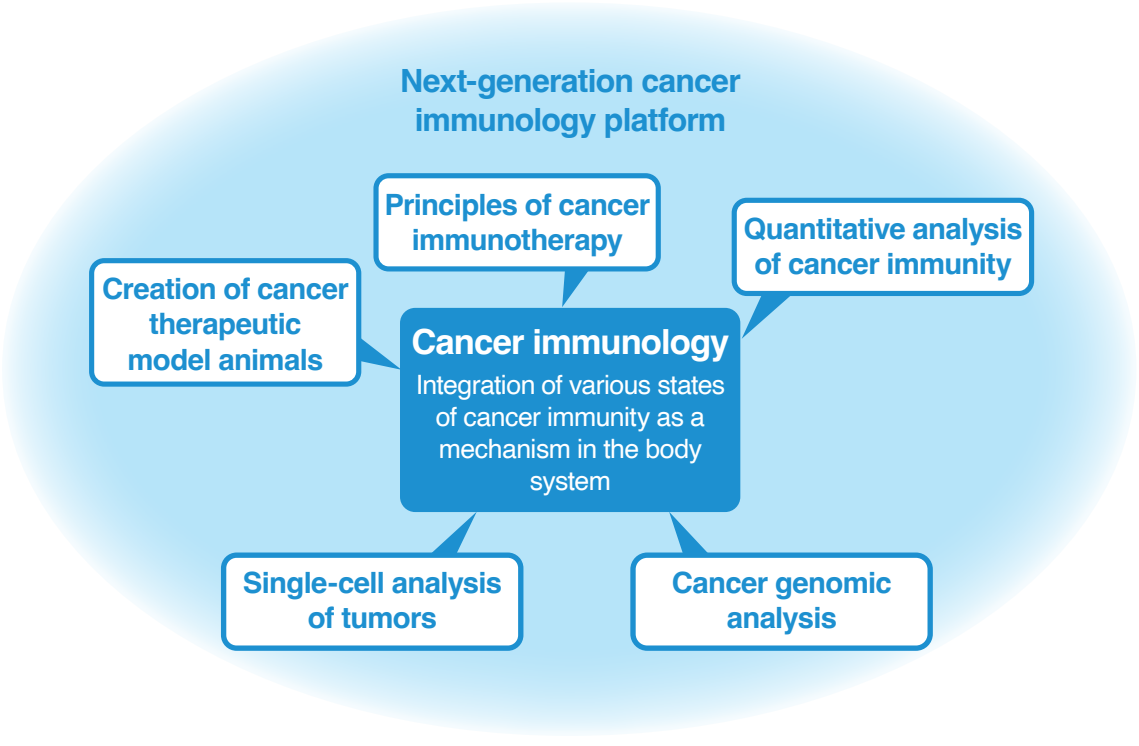
Normal cells become cancerous through the accumulation of mutations. Our division will elucidate the relationships between tumor cells, genomic functions and the immune system, and will develop next-generation immunotherapies for the complete cure of cancer.

Utilization of the immune system to treat human cancer is called “cancer immunotherapy”, and various cancer immunotherapies have been proposed. Many types of immune cells cooperate in the human body and consist of two types of immune reactions: innate immunity that preexists in our body and adaptive immunity that must be acquired. It is known that highly effective immunotherapies activate multiple types of immune cells. IMS has developed a novel immunotherapy, aAVC, that activates both the innate and adaptive immune systems.

IMS has also developed an experimental mouse model that recapitulates human leukemia. Using this mouse model, we analyzed the characteristics of “leukemic stem cells”, and developed a novel cancer therapy. We also developed a novel cancer immunotherapy using human iPS cells. In addition, IMS has identified tumor-specific genomic sequences and translated these findings to improve clinical diagnosis.

However, there are still many unsolved fundamental questions in cancer immunology, such as pathogenesis of malignancy, the relationship between cancer stem cells and cancerous tissues, and the mechanisms of cancer immune evasion.

The Division of Cancer Immunology will create research platforms for cancer genomic analysis and develop experimental mouse models for cancer therapeutics. We will conduct single-cell analysis of gene expression in tumors that promote understanding of tumor cells. Studies will include the analysis of interactions between tumor cells and immune cells. Through these diversified approaches, we aim to explore the fundamental principles of cancer immunology that lead to breakthroughs towards novel therapeutics.



We will promote research for the establishment of novel therapeutics

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https://www.ims.riken.jp/english/

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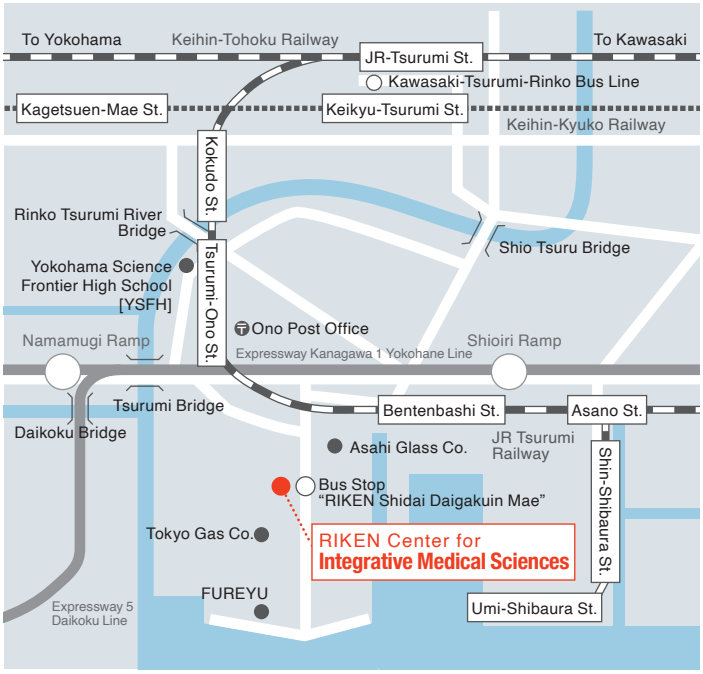
Access

- **By Bus**
  Take the #08 bus (bound for Fureyu) from Platform 8 at the East Exit of Tsurumi Station (also accessible from the West Exit of Keikyu Tsurumi Station) and get off at the RIKEN Shidai Daigakuin Mae bus stop. The institute is across the street.
- **By Train**
  A 15-minute walk from JR Tsurumi-Ono Station on the JR Tsurumi Line, which is directly accessible by transfer at JR Tsurumi Station.
- **By Taxi**
  Use the taxi stand at the East Exit of JR Tsurumi Station or the West Exit of Keikyu Tsurumi Station.



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