RIKEN Center for Integrative Medical Sciences
Stratified medicine for a healthy long-lived society. Creation of a research platform for new biomedical science.

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 Science (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. 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 mathematically 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 the healthy long-lived society in Japan.

Director
Tadashi Yamamoto

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.
Elucidation of disease onset mechanisms originating from the genome

The genetic information in the genome is the blueprint of life, and it is important to know how the genes are regulated to understand the conditions of a wide variety of different cells, tissues and organs, therefore defining their “Healthy” and “Disease” states.

In our division, we will expand our current research platform for genome analysis and technology development for gene expression network analysis (omics). As a result, we will be able to elucidate the processes of disease onset based on the human genome and strengthen the platform for the development of novel genome therapeutics and genomic medicine.

To comprehensively understand unknown functions of the genome, we need to understand the basic functions of cells by functional genomics approaches. To do this, we will perform large-scale analyses of gene expression and function in various human cell types, including analyses of regulatory RNAs (non-coding RNAs with functions). Furthermore, we will develop technologies to comprehensively analyze and understand the unexplored functions of the genome. Also, based on the high-precision human genomic data and disease-related genetic polymorphisms that have been accumulated, we will integrate the gene expression databases of various human cells and tissues (e.g., transcriptome databases such as FANTOM, epigenome databases), perform statistical genomic analyses using human genome associated “big data” and elucidate disease onset mechanisms by multilevel functional analyses.

To accelerate large-scale genome analysis, joining international collaborative research efforts is necessary. In the international project “FANTOM”, presided over by our division, we are promoting the identification and functional analysis of regulatory RNAs with the aim to create the world’s first regulatory RNA catalog. We are also playing a central role in Asia in the international “Human Cell Atlas” collaborative project, which aims to map the characteristics and location information of all human cells.

Based on our comprehensive research efforts, we aim to develop novel approaches for genome therapeutics to provide the finest medical strategies for all individuals.

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

Translation of disease processes

Validation of disease-related genes

Outside the body

Environmental factors (dryness, bacteria, nutrition, mental stress)

Neuronal system

Endocrine system

Immune system

Outside the body

External barrier (skin, gut, bronchial pathway)

Inside the body

Disease status

Non-disease status

Genetic factors

Aging factors

Division of Disease Systems Biology

Haruhiko Koseki

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