Individual Differences

Understanding the mechanisms of sex and individual differences and advancing prediction technology

Research and Development Objectives

Towards elucidating and predicting sex and individual differences and intrapersonal changes — A departure from the conventional practice of medical care based on patient averages

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The manifestations of various symptoms of our diseases and health conditions vary not only between the sexes and between individuals, but also even within the same person at different stages of life. Significant individual differences are also sometimes observed in the effects and side effects of medicines and other drugs. Following the experience of the new coronavirus infection (COVID-19), the public interest in sex and individual differences has urgently increased. However, current medical and health research is mainly based on population averages, and the medical care that many people receive is not always optimized for the individual. The first step approaching to the issues is to understand the mechanisms of gender and individual differences in specific symptoms, diseases, and health conditions at the molecular level. Based on this information, new treatment and prevention methods need to be developed that are optimized for the individual, such as precise stratification for specific diseases and the development of predictive models at the individual level.
In this research and development area, basic and clinical medical researchers, experimental biologists, epidemiologists, computer scientists and mathematicians, as well as measurement and information technology researchers, will work closely together, combining latest knowledge and technologies from different fields to integrate and analyze multi-level data at the molecular, cellular, tissue, organ, individual and population levels.
The project aims to elucidate the mechanisms by which individual and sex differences in health and disease, as well as changes within the same individual, are generated, and to develop optimal treatment and prevention technologies for individuals by constructing accurate stratification of pathological states and predictive models at the individual level.

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AMED-CREST Started in 2024 — 1st period

Understanding the molecular basis governing individual differences of health-span and developing aging-prediction technology

ISHITANI Tohru
Professor, Research Institute for Microbial Diseases, Osaka University

There are individual and sex differences in lifespan and healthspan, making it difficult to measure the degree of aging or remaining lifespan based on age alone. In this study, we aim to understand the molecular mechanisms underlying individual and sex differences in lifespan and healthspan and to create aging prediction technology by conducting data-driven research that complements humans and ultra-rapid aging animals. In addition, by discovering quantitative aging markers and anti-aging molecules, we aim to create personalized medical technology seeds that can detect signs of aging in individual humans and extend healthspan.

Elucidation and control of the cellular microenvironment that produces sex and individual differences through deep learning

SHIMAMURA Teppei
Professor, Medical Research Laboratory, Institute of Integrated Research, Institute of Science Tokyo

This research develops an analytical platform using deep learning and next-generation small molecule inhibition technologies to analyze multi-scale, multi-modal data related to sex and individual differences. By elucidating differences in cellular states and microenvironments, their determinants, and possibilities for personalized therapies, we aim to accelerate disease research discovery and verification. We will validate the platform using osteoarthritis and intractable gastrointestinal cancers as targets, aiming to develop new treatments and prognosis prediction models that consider sex and individual differences, ultimately contributing to the realization of personalized medicine.

Multi-omics analysis for elucidating the difference between maternal and paternal genetic traits and its application to the prediction of obesity and diabetes

SUZUKI Yutaka
Professor, Graduate School of Frontier Sciences, The University of Tokyo

We aim to gain a deep understanding of the molecular mechanisms underlying sex differences, individual differences, and intra-individual changes, which will serve as the basis for future medical applications and prediction of unaffected diseases.
We will make full use of biological samples and genome data accumulated at BioBank Japan and Tohoku Medical Megabank Organization, the most representative biobanks in Japan.
We will conduct an intensive and precise multi-omics analysis of umbilical cord blood as an example of tissue in which newborns begin to express their own genes for the first time, we will attempt to elucidate the diversity of sex differences in genetic traits.

Development of predictive models and novel therapies based on sex and individual differences for cardiovascular disease

MIYAGAWA Shigeru
Professor, Graduate School of Medicine, Osaka University

Cardiovascular disease is one of the leading causes of death in Japan, with its progression being profoundly affected by sex and individual variability. Our objective is to develop predictive models for cardiovascular diseases, mainly heart failure and aortic aneurysm, through the integration of multi-omics analysis of tissue and blood samples, lifestyle data, clinical data, and the latest artificial intelligence technology, as well as a data distribution platform capable of distributed federated learning. We also aspire to develop novel therapeutic strategies by elucidating the underlying pathological mechanisms through comprehensive omics analysis.

Integrated understanding of sex-dependent biomodulation mechanisms associated with the interaction of circadian and seasonal rhythms and application to prediction technology

YASUO Shinobu
Professor, Faculty of Agriculture, Kyushu University

Mood and physical conditions in humans are regulated by interactions between circadian rhythms, seasonal rhythms, and menstrual rhythms in menstruating women. However, the interactions among multi-scale rhythms still need to be clarified. A series of our studies, a collaborative effort between experimental and mathematical researchers, aims to elucidate the interaction mechanisms underlying sex-dependent multi-scale rhythms and search for biomarkers to evaluate the interactions. Our goal is to develop a technology that can predict multi-scale-rhythm-associated symptoms such as winter depression and premenstrual syndrome.

PRIME Started in 2024 — 1st period

The realization of preemptive medicine through the elucidation of cardiovascular complex disease systems driven by the integration of static and dynamic omics

ITO Kaoru
Team Leader, RIKEN Center for Integrative Medical Sciences

Cardiovascular complex diseases are complicated conditions that arise from intricate interactions between genetic and environmental factors, with significant influences from individual and sex differences. In this research project, we will integrate dynamic omics data with pioneering artificial intelligence, alongside genomic and clinical information, to achieve a comprehensive understanding of these individual and sex differences in disease. Simultaneously, we will establish and validate methods for stratifying disease risk in individuals who have not yet developed the disease. Ultimately, our goal is to build and implement a precision medicine system that proposes preventive measures tailored to various stages, from health to pre-disease and disease onset.

Single nucleotide resolution analysis and prediction of gene regulatory elements by saturation mutagenesis MPRA

INOUE Fumitaka
Associate Professor, WPI-ASHBi, Kyoto University

Genetic factors responsible for diseases, individual differences, and evolution are more likely to be found in gene regulatory elements in the non-coding genome, rather than in coding regions. In this project, we utilize the Massively Parallel Reporter Assay (MPRA), which enables us to characterize enhancer functions in a high-throughput manner and at single-nucleotide resolution, to predict the effects of single nucleotide variants on gene regulation. Through this approach, we aim to understand the molecular mechanisms underlying diseases and individual differences.

Space-time proteomics with single-cell resolution enabled by next-generation proteome sequencer

KANAO Eisuke
Assistant Professor, Graduate School of Pharmaceutical Sciences, Kyoto University

This research aims to completely renovate bottom-up proteomics technologies from the perspective of separation science and materials chemistry, developing a "next-generation" proteome sequencer. Furthermore, this technology will be applied for time-lapse analysis of single cells and spatial proteomics. Based on these technologies, we will capture the proteome changes during early development with unprecedented resolution as the first step toward understanding the mechanisms of sex and individual differences.

Investigating individual differences by human population-scale cell culture and time-series multi-omics

KOJIMA Shohei
Special Postdoctoral Researcher, RIKEN Center for Integrative Medical Sciences

I will employ a miniaturized human population cell culture system to conduct time-series multi-omics analyses and statistical genetics. This approach aims to unravel the complex human genetics and biology underlying the emergence of human phenotypic differences that cannot be understood by snapshot research. This work will bridge the gap between real-world studies in biobanks and laboratory-based mechanistic research, and generate basic research data that forms the foundation for improved disease prediction and precision medicine.

Study for individual differences of A-to-I RNA editing

SAKURAI Masayuki
Associate Professor, Research Institute for Biomedical Sciences,Tokyo University of Science

A-to-I RNA editing has the same effect as base substitution or mutation from A to G, but is a change in genetic information that is not described in the genomic information. It is highly possible that unexplained individual and sex differences may result from differences in editing, which in turn may include differences that affect cancer incidence, disease incidence, life span, and health. This project aims to clarify this, to accumulate information on A-to-I RNA editing sites, and to construct an editome database.

Study of development of prediction platforms for progression of lung cancers based on differential omics backgrounds among sex and individual differences

SUZUKI Ayako
Associate Professor, Graduate School of Frontier Sciences, The University of Tokyo

This study aims to develop a predictive platform of lung cancer progression by integrating spatial omics techniques, human lung organoids and gene expression network analytical methods. We will measure the omics background of cells that reflect individual differences, as well as their responses to endogenous and exogenous stress stimuli. We will analyze detailed information of aberrant differentiation statuses of lung cancer cells at omics levels and utilize it for prediction of lung cancer progression.

Development of functional connectivity analysis method using deep learning and estimation of individual traits and neuropsychiatric disorders

CHIKAZOE Junichi
Team Leader, Araya Inc., R & D Department

This research aims to establish new analytical methods for resting-state fMRI data to develop objective indicators for diagnosing mental disorders. We will use multilayer perceptrons and Transformer models to examine functional connections between brain regions and construct individual characteristic estimation models. Additionally, we will create diagnostic algorithms for neuropsychiatric disorders using data from the AMED Brain/MINDS Beyond project. We particularly focus on methods for utilizing deep learning in biological data with limited sample sizes.

Mechanisms underlying heart failure pathogenesis through the lens of inter-individual variability of hematopoietic clonal divergence

NAKAYAMA Yukiteru
Assistant Professor, the University of Tokyo

Persistent inflammation following the immune response against external cardiac stress underlies incident heart failure. We have recently reported that heart failure induces the phenotypic modulation of hematopoietic stem cells, immmature cells that all types of blood cells originate from. We hypothesize that individual differences of immune response at the level of hemaotopoietic stem cells would determine inter-individual variability in risks of incident heart failure. We will analyze the differences in bone marrow niches as well.

Understanding the impact of differential sex chromosome states on cellular phenotypes

YOKOBAYASHI Shihori
RIKEN ECL Team Leader, RIKEN Center for Integrative Medical Sciences

The sex chromosome composition in the human genome is typically the XX type in females and the XY type in males, and one X chromosome in females is epigenetically silenced to compensate for the differences in gene dosage. In this study, I aim to understand sex differences at a cellular level by elucidating the impact of sex chromosome composition or conversion/instability in the X-chromosome epigenome status on cellular phenotypes and functions.

Precision stratified treatment based on individual differences due to retrotransposon-based insertion polymorphisms

YOSHIMI Akihide
Chief, Division of Cancer RNA Research, National Cancer Center Research Institute

Transpossable elements (TEs), also known as jumping genes, are known to make up about 46% of the human genome. In this project, we aim to investigate the impact of individual differences due to TE insertion polymorphisms on treatment outcomes and prognosis of cancer patients, and to refine prognosis and treatment response prediction systems by identifying new biomarkers. Additionally, by elucidating the mechanisms of expression, we aim to develop treatment methods and propose stratified treatments based on individual differences in TE insertion polymorphisms.