

# Homeostasis

Innovation for Ideal Medical Treatment Based on the Understanding of Maintenance, Change and Breakdown Mechanisms of Homeostasis among Interacting Organ Systems



## [Research and Development Objectives]

Integrated clarification of the maintenance and change mechanisms of dynamic homeostasis in the body and creation of technology to understand and regulate complex dynamic homeostasis to achieve preventive medicine, appropriate diagnosis and treatment

Program Supervisor (PS)

**NAGAI Ryozo**

President, Jichi Medical University

The objective of this R&D area is to comprehend the process from birth to demise, which takes place in the individual, from the view of a dynamic homeostatic mechanism and to elucidate the mechanisms as to how the individual adapts and changes in reaction to internal and external stresses in a spatio-temporal and cross-sectional manner. The dynamic homeostatic mechanism is operated via a high-order network consisting of the nervous, immune, endocrine, circulatory, and other systems. Furthermore, we aim to understand various diseases, including lifestyle diseases, as deviations from or breakdown of a "homeodynamic" state, constituting a ground for the development of preventive technologies that predict and control such deviation.

Particularly in recent years, technologies such as development of cell-specific genetically modified animals and cell separation technologies have made great progress and they have triggered major changes in life science and medicine. Expectations are to gain a better understanding of mechanisms of homeostasis and adaptations to various stressors, which function through interactions between different cells, systems, and organs. Furthermore, advances in life science and clinical medicine that control these mechanisms are needed. Specifically:

1. How complex functional networks behave interdependently in order to maintain homeostasis in response to external and internal stresses will be elucidated. These networks correlate among multiple organs, such as between parenchyma cells and interstitial cells, among organs as well as among the systems like the nervous, immune, endocrine, circulatory and others. In particular, humoral factors, neurotransmission, immunocytes, and interstitial cells that are involved in the maintenance and dysfunction of homeostasis need to be identified. These findings are needed to develop technologies that can be used to control homeostasis.

2. Researchers are expected to elucidate the phases of sequential and dynamic changes that take place in an individual's homeostatic mechanism during the life stages through birth, growth, development, and aging. Technologies that enable early detection of the subtle symptoms of these phases, as well as those to control them, are to be developed.

3. This R&D area involves research aiming at elucidation of the mechanisms in onset and progression of organ dysfunction resulting from internal and external factors, the biological defense mechanisms against stresses and injuries and healing mechanisms. Furthermore, we aim to develop technologies that will assist in the diagnosis and treatment of human patients. We will apply results of basic research for examination in clinical cases as much as possible, and investigate the potential of medical care where multiple medical departments cooperate based on new concepts of pathology.

4. We aim at the establishment of highly reliable methods to control these networks, based on multilateral understanding of the dynamic interactions between these complex networks. To achieving this goal, we will work to promote simulation technologies and theoretical computational science research that would make these technologies possible.

Through this research, we will elucidate previously unknown molecular, cellular, and networking mechanisms and develop new medical technologies based on these understandings.

## R&D Area Advisors

|                          |   |
|--------------------------|---|
| <b>IRIKI Atsushi</b>     | Team Leader, RIKEN Center for Biosystems Dynamics Research                                |
| <b>OHSHIMA Etsuo</b>     | Representative Director and President & CEO, Kyowa Pharma Chemical Co., Ltd.              |
| <b>KANGAWA Kenji</b>     | Emeritus Director General, National Cerebral and Cardiovascular Center Research Institute |
| <b>KOJIMA Itaru</b>      | Professor, Gunma University   |
| <b>SAKAGUCHI Shimon</b>  | Professor, Osaka University   |
| <b>SAKATA Tsuneaki</b>   | Senior Fellow, Shionogi & Co., Ltd.   |
| <b>SUNAGAWA Kenji</b>    | Director, Circulatory System Research Foundation  |
| <b>NAKAO Kazuwa</b>      | Professor (Special Appointment), Kyoto University   |
| <b>NAGASE Miki</b>       | Professor, Kyorin University  |
| <b>NABESHIMA Yo-ichi</b> | Director, IBRI, Foundation for Biomedical Research and Innovation at Kobe                 |
| <b>MOCHIZUKI Atsushi</b> | Professor, Institute for Frontier Life and Medical Sciences, Kyoto University             |

Started in 2012 ... 1st period

Holistic investigation of the inter-organ communication systems responsible for metabolic homeostasis and disorders

**KATAGIRI Hideki**  
Professor, Tohoku University Graduate School of Medicine

Started in 2012 ... 1st period

Elucidating the pathophysiology of senescence-associated homeostatic disorders and its control

**HARA Eiji**  
Professor, Research Institute for Microbial Diseases, Osaka University

Started in 2012 ... 1st period

Discovering therapies for intractable diseases through the identification and characterization of gut microbiota

**HONDA Kenya**  
Professor, Keio University School of Medicine

Started in 2012 ... 1st period

Mechanisms of homeostatic maintenance by quorum control of the tissue in whole body

**MIURA Masayuki**  
Professor, Graduate School of Pharmaceutical Sciences, The University of Tokyo

Started in 2012 ... 1st period

Study of autophagy toward development of therapy for disorders caused by hypernutrition

**YOSHIMORI Tamotsu**  
Professor, Graduate School of Frontier Biosciences, Osaka University

Started in 2013 ... 2nd period

A challenge to reveal dynamic properties in circadian sleep-wake homeostasis

**UEDA Hiroki**  
Professor, Graduate school of Medicine, The University of Tokyo

Started in 2013 ... 2nd period

Clarifying and controlling the pathology of lifestyle diseases caused by alteration of homeostatic maintenance based on tissue repair

**OIKE Yuichi**  
Professor, Graduate School of Medical Sciences, Kumamoto University

Started in 2013 ... 2nd period

Homeostatic regulation by bones through the inter-organ metabolic network

**SATO Shingo**  
Junior Associate Professor, Tokyo Medical and Dental University, Graduate School of Medical and Dental Sciences

Started in 2013 ... 2nd period

Identification of novel scavenging system in organisms and its therapeutic application

**MIYAZAKI Toru**  
Professor, Faculty of Medicine, The University of Tokyo

Started in 2013 ... 2nd period

Understanding homeostatic mechanisms maintained by the cardio-osteo-renal network and interconnecting blood vessels

**MOCHIZUKI Naoki**  
Director General, National Cerebral and Cardiovascular Center Research Institute

Started in 2014 ... 3rd period

Regulatory mechanism underlying tissue fibrosis induced through local cell-cell interaction and systemic organ network and its medical applications

**OGAWA Yoshihiro**  
Professor, Graduate School of Medical Sciences, Kyushu University

Started in 2014 ... 3rd period

Phosphatostasis and phosphatopathy: pathophysiology of the inter-organ network maintaining phosphate homeostasis

**KURO-O Makoto**  
Professor, Center for Molecular Medicine, Jichi Medical University

Started in 2014 ... 3rd period

Homeostatic regulation and dysregulation of neural stem cells under physiological and pathological challenges

**GOTOH Yukiko**  
Professor, Graduate School of Pharmaceutical Sciences, The University of Tokyo / Principal Investigator, International Research Center for Neurointelligence (IRCIN), The University of Tokyo

Started in 2014 ... 3rd period

A novel approach to drug discovery through receptor activity modification

**SHINDO Takayuki**  
Professor, Faculty of Medicine, Shinshu University

Started in 2014 ... 3rd period

Understanding the autonomic nervous system underlying the gut-brain axis: with a view to exploring higher-order homeostatic mechanisms

**TAKAHASHI Yoshiko**  
Deputy Executive Vice-President, Professor, Graduate School of Science, Kyoto University

Started in 2014 ... 3rd period

Investigation of energy metabolism and immune system based on the association with autonomic nerve and peptides

**NAKAZATO Masamitsu**  
Professor, Department of Internal Medicine, University of Miyazaki

Started in 2014 ... 3rd period

Signal transduction systems responsible for tissue, organismal and transgenerational homeostasis

**NISHIDA Eisuke**  
Director, RIKEN Center for Biosystems Dynamics Research

※: The names of the position, institution and organization are as of the end of the R&D pursuit area year.