



Title of Project : Quality of lipids in biological systems

Makoto Arita
(RIKEN, Center for Integrative Medical Sciences, Team Leader)

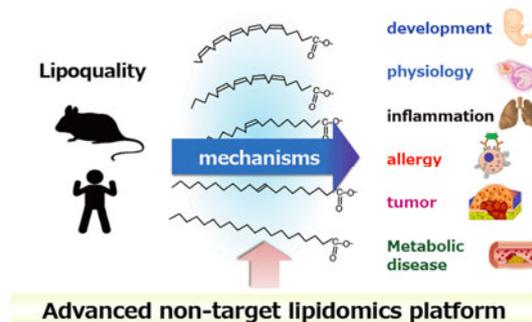
Research Project Number : 15H05897 Researcher Number : 80292952

【Purpose of the Research Project】

Lipids are recognized as extremely diversified molecules, however, the reason for this diversity of lipids is not fully understood. Precise determination of each molecular species of lipids, namely lipoquality (quality of lipids), becomes a prerequisite to understand their biological roles and potential links between lipid metabolisms and biological phenotypes. The purpose of this research project is to understand the functional roles of diverse lipid species in biology, especially focusing on the mechanisms in which specific quality of lipids are required to elicit biological functions.

【Content of the Research Project】

Lipids are a class of hydrophobic molecules that function as structural component of biological membrane, neutral lipids as a major form of energy storage, and lipid mediators as signaling molecules. Quality of lipids (lipoquality) largely affects these three major functions of lipids. For example, quality of membrane lipids and lipid microdomains regulate the function of proteins and thus modify cellular functions. Quality of neutral lipids affects energy homeostasis, and quality of fatty acids such as omega-3 and omega-6 series affects the mediator balance under physiological and/or pathophysiological conditions. Recent advances of mass spectrometry enabled the detailed study of metabolism, distribution and dynamics of individual class of lipids. In this project, we'll develop an advanced non-target lipidomics platform to comprehensively monitor and distinguish different quality of lipids, and thus try to understand how different quality of lipids and their unique metabolites are recognized by target proteins that could explain the biological significance of diverse lipid species in living systems.



【Expected Research Achievements and Scientific Significance】

Since lipids are water-insoluble molecules and are not the primary product of genome, it is still difficult to handle or control. Because of these specific properties, lipid research is lagging behind compared to other life science fields. Advanced mass spectrometry now enables the detailed analysis of lipids, and one of the goals of this project is to develop a hub of advanced non-target lipidomics platform within next 5 years. It is expected to identify novel bioactive lipids by using advanced lipidomics platform. Also visualization of lipid distribution by imaging technology and clarifying molecular interaction of lipids and membrane proteins will provide a new basis to understand the role of specific lipid-protein interaction in membrane biology. Since lipid balance is involved in various biological phenomena, we aim to elucidate how lipid homeostasis is maintained and how disruption of this homeostatic balance can initiate diseases.

【Key Words】

Lipoquality: Functional features of diverse lipid molecular species

【Term of Project】 FY2015-2019

【Budget Allocation】 1,180,100 Thousand Yen

【Homepage Address and Other Contact Information】

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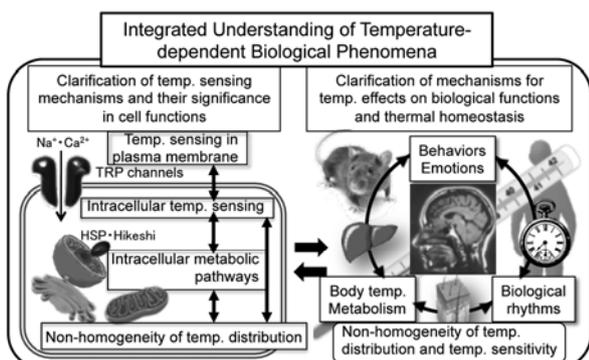
Title of Project : Integrative understanding of biological phenomena with temperature as a key theme

Makoto Tominaga
(National Institutes of Natural Sciences, Okazaki
Institute for Integrative Bioscience, Professor)

Research Project Number : 15H05927 Researcher Number : 90260041

【Purpose of the Research Project】

Temperature affects various physiological functions and is one of the most important factors in homeostasis. This research project concerns two subgroups, ‘temperature sensing’ and ‘temperature-responding systems’, and seeks to integrate our understanding of temperature-dependent biological phenomena with the development of techniques that detect and regulate local temperatures in cells and organs with high resolution and precision. In this project we will clarify: 1) How temperature-sensing mechanisms in the plasma membrane and in cells work together to allow precise temperature detection; 2) How temperature is sensed and integrated in temperature-dependent physiological responses that include regulation of body temperature, metabolism, biological rhythms and animal behaviors; and 3) What are the mechanisms and physiological functions of spatiotemporal non-homogeneity of temperature distribution and detection.



Conceptual diagram of thermal biology research

【Content of the Research Project】

This inter-disciplinary research project will investigate temperature-sensing mechanisms and their involvement across a wide range of biological responses and from molecular to whole organism levels. The project will consider two subgroups, ‘A01: temperature sensing’ and ‘A02: temperature-responding systems’ to clearly address the questions of how temperature is sensed and how temperature is related to biological functions, respectively.

‘A01: temperature sensing’ addresses temperature sensing mechanisms by focusing on plasma membrane molecules, intracellular molecules and intracellular metabolic pathways. ‘A01’ also seeks to develop ways to detect and regulate local temperatures at a cellular level, which would facilitate future temperature-sensing research. ‘A02: temperature-responding systems’ will focus on the neural circuits that integrate information concerning ambient temperature sensation, the effects of temperature on metabolic functions and biological rhythms, and mechanisms involved in emotion formation. ‘A02’ also clarifies crosstalk between temperature-responding systems by developing methods to detect and regulate local temperatures in organs. Comprehensive collaborations among the research groups will further enhance the progress of each research project.

【Expected Research Achievements and Scientific Significance】

Research that fosters an integrated understanding of temperature-dependent biological phenomena would create a novel discipline, ‘thermal biology’, which would contribute to progress in life science. Furthermore, this project could also lead to a novel concept wherein ‘temperature’ as a physical quantity could be viewed as an element of new signaling mechanisms.

【Key Words】

Thermal biology: a science in which mechanisms of temperature sensation and their involvement in physiological functions are investigated.

【Term of Project】 FY2015-2019

【Budget Allocation】 1,171,000 Thousand Yen

【Homepage Address and Other Contact Information】

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Title of Project : Chromosome Orchestration System

Katsuhiko Shirahige
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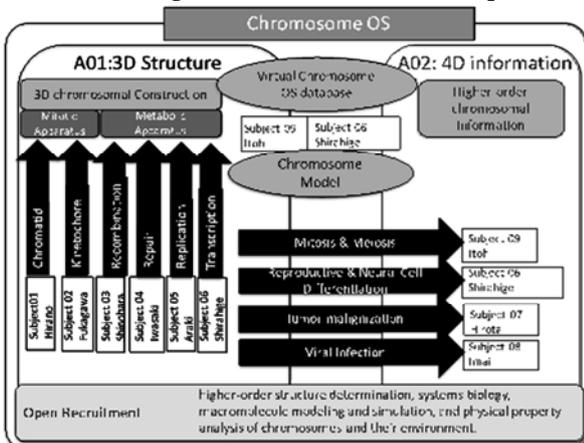
Research Project Number : 15H05970 Researcher Number : 90273854

【Purpose of the Research Project】

Chromosomes play a fundamental role in many biological processes. Previous research efforts have advanced our understanding of specific chromosomal events, such as DNA transcription, replication, recombination, partitioning, and epigenetic modification. One of the major future challenges in chromosome biology will be to provide an overall framework of how these individual activities are orchestrated and coordinated to maximize their effects in a variety of biological processes that evolve over time. In this project, we will elucidate the overarching coordinating mechanism that enables a whole set of chromosomes to act as a single functional entity, in both space and time, a new concept that we term “chromosome orchestration system (OS).” For this purpose, we will investigate (i) the mechanisms that determine three-dimensional (3D) chromosome architecture; and (ii) the processes that integrate four-dimensional (4D, i.e., 3D plus time) information transmission. New scientific knowledge gained from this project will further expand the horizon of drug discovery, regenerative medicine, and other life sciences in Japan.

【Content of the Research Project】

The main goal of this project is to describe the mechanisms that regulate the functional unity of the chromosomes (chromosome OS) by thoroughly examining the structural relationship between, and the hierarchy of, individual chromosomal functions. To this end, this project is composed of two groups of researchers, one focusing on the 3D structure and the other on 4D information processing (Figure 1). In order to develop a complete understanding of the chromosomal plasticity

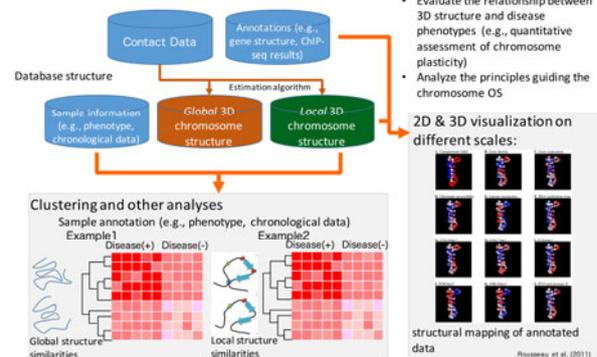


and functional coordination, the 3D Group will combine molecular devices that mediate individual chromosomal functions and attempt to reconstitute large-scale 3D structures in vitro.

The 4D Group, on the other hand, will explore the dynamic, time-dependent processes for 3D chromosomal structure change during the cell cycle, meiosis, differentiation, stress response, and pathogenesis. The Group will further identify the decoding machinery that converts structural alterations into biologically relevant information. While the activities of these two groups will be closely related and mutually complementary for the most part, there will be several topics that are addressed from different perspectives. As a common methodological basis, a chromosome OS information platform and a chromosome model will be developed.

【Expected Research Achievements and Scientific Significance】

We will create the chromosome OS information platform in this project, a knowledge-based



systematic annotation and visualization tool for documenting and explaining chromosomal behaviors in dynamic cellular processes (Figure 2). This tool will help clarify the molecular basis for chromosomal integrity and will enhance our understanding of the pathogenesis of chromosome-linked diseases. We will also create a computer-based model that simulates multiple chromosomal functions. This model will have the potential for future application to a variety of fields including disease control and animal breeding.

【Key Words】

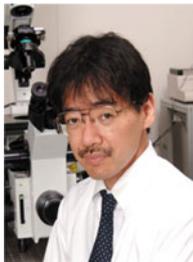
Metabolic network
Expression of genetic function
Chromosome construction, function, and partitioning

【Term of Project】 FY2015-2019

【Budget Allocation】 1,146,200 Thousand Yen

【Homepage Address and Other Contact Information】

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kshirahi@iam.u-tokyo.ac.jp



Title of Project : Resonance Biology for Innovative Bioimaging

Atsushi Miyawaki
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Research Project Number : 15H05947 Researcher Number : 80251445

【Purpose of the Research Project】

Using phenomenal behaviors in the coupling between electromagnetic waves and transition dipole moments of molecules, in the research project “Resonance Bio,” we develop new technologies that revolutionize bioimaging. This project is a collaborative effort principally by (bio)chemists who design molecules and optical physicists who control electromagnetic waves, and is creating a critical mass for technological innovations in bioimaging. Our technologies are expected to resonate in a variety of research communities to catalyze a paradigm shift in our understanding of disease development.

【Content of the Research Project】

Given the project’s liberal environment, all the members will have a chance to share several critical problems confronting current bioimaging. Although subject to change, examples include “What are the forthcoming techniques for super-resolution and deep imaging?”, “How should we investigate stress, an ambiguous phenomenon, both intensively and extensively?”, “How can we zoom in on and out of a biological structure at diverse spatial scales?”, “How should we cope with terabyte image data?”, and “What are the theoretical and practical dimensions of bioimaging?”.

While this project focuses on the interaction between light and molecules, it may also incorporate technologies from other areas, such as those that employ electrons and

sound. In addition, non-life scientists are highly welcome. For example, software contests sponsored by this project are expected to motivate general programmers to take the plunge into bioimaging. We will actively disseminate information on the progress and achievements of this project worldwide through our publications and the Web. Our efforts will hopefully speed up the progress of many life sciences in Japan as we address the growing needs of those fields.

【Expected Research Achievements and Scientific Significance】

Advances in dissemination will make it easy to standardize bioimaging techniques to meet biologists’ demands and desires. This is expected to activate the bioimaging industry that handles dyes, microscopy systems, and software. Bioimaging technologies developed in this project will be spread into the industrial world, such as the pharmaceutical industry, and will improve quality of life.

【Key Words】

Bioimaging, light microscopy, image processing, fluorescent protein

【Term of Project】 FY2015-2019

【Budget Allocation】 1,198,000 Thousand Yen

【Homepage Address and Other Contact Information】

<http://reso.m.ehime-u.ac.jp>



Title of Project : Discovery of the logic that establishes the 3D structure of organisms

Shigeru Kondo
(Osaka University, Graduate School of Frontier Biosciences,
Professor)

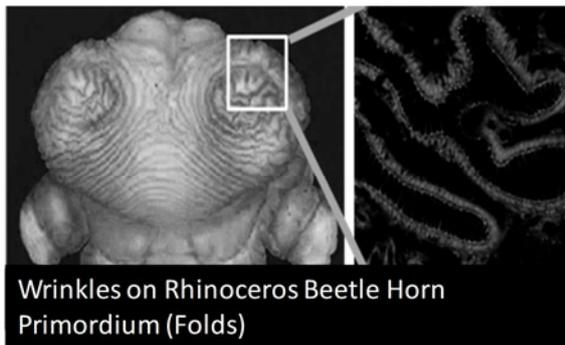
Research Project Number : 15H05856 Researcher Number : 10252503

【Purpose of the Research Project】

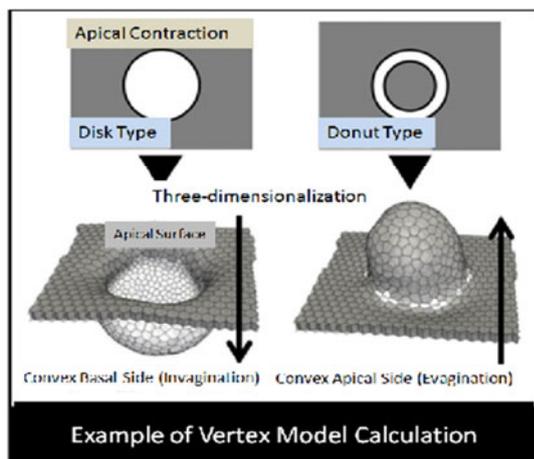
In this research project, we approach morphological phenomena that cannot be understood without an explicit awareness of "three-dimensionality (3D)". Our aim is to explain the logics governing the creation of the three-dimensional form of living beings.

【Content of the Research Project】

There are two characteristics of this research project: (1) specialized research subjects in 3D morphogenesis; and (2) the integration of mathematical science.



In the above picture of a rhinoceros beetle's horn primordium, a complex folded structure can be seen, but it is hard to correlate it with the completed form. To start, the creation of the elegant structure of the completed form in its fully-folded state can be considered all but impossible. From a mathematical perspective, it is difficult to answer the question, "In the real world, which doesn't allow for anything but a



kolimited amount of expansion and contraction, how can an arbitrarily complex shape be folded out of the planar surface of a primordium?" Nevertheless, as long as one cannot answer the question posed by this spatial structure, one cannot truly know how organisms get their 3D form. Conversely, if one understood how to fold such complicated 3D shapes, then one could create any given shape.

Additionally, some of the research subjects we are working on include the 3D transformation of fish somites, chiral torsion in the hindgut of *Drosophila*, in vitro cultivation of epithelial cells showing 3D morphogenesis, and the 3D transformations occurring in the cell layer during neural tube formation in amphibian embryos.

If one uses an appropriate calculation system like a 3D vertex model, one can calculate the way in which forces generated in one section of the cell sheet transform the morphogenetic fields. If we combine this system with experimental data and extend it mathematically, then complete explanations of complex 3D structures such as that of the treehopper will no longer be mere dreams.

【Expected Research Achievements and Scientific Significance】

The extremely complicated structure of the treehopper helmet, like the horns of the rhinoceros beetle and the wings of insects, is formed from the folding of a cell sheet. Therefore, with a better understanding of the relationship between folding structures and 3D form, one can certainly claim to understand the mechanisms of the formation of the 3D shape of most insects and crustaceans. This is one of the primary goals of developmental biology.

【Key Words】 Three-dimensional form, Cell sheet, Origami theory

【Term of Project】 FY 2015-2019

【Budget Allocation】 1,102,300 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.3d-logic.jp/>



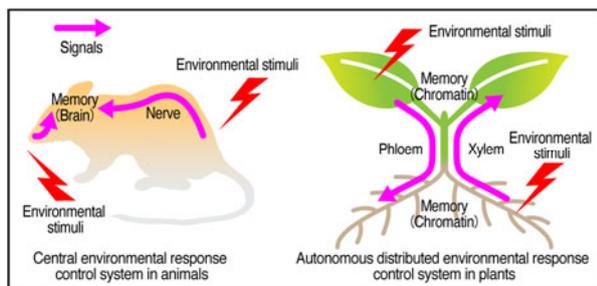
Title of Project : Integrative system of autonomous environmental signal recognition and memorization for plant plasticity

Toshinori Kinoshita
(Nagoya University, Institute of Transformative Bio-Molecules, Professor)

Research Project Number : 15H05955 Researcher Number : 50271101

【Purpose of the Research Project】

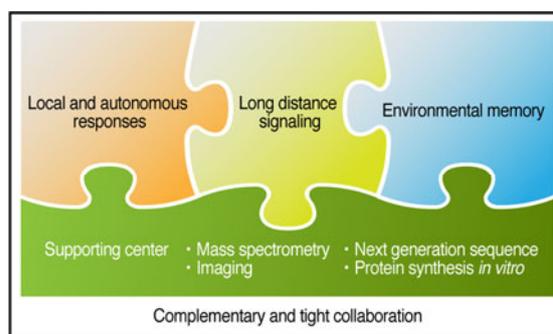
In contrast to mobile animals which seek environments suitable for survival, in order to respond rapidly to diverse environmental changes, immobile plants have evolved an “autonomous distributed environmental response control system” to control incoming signals via a systemic information transmission system while carrying out an autonomous environmental response, the control of which is distributed by groups of cells and tissues. For this type of control via autonomous distribution, in addition to local stimulus receptor sites and an autonomous response system, there ought to exist a system for the spatiotemporal integration of the local response. However, these molecular species are virtually undescribed. We aim to clarify our current understanding of plants’ dynamic environmental response control systems.



【Content of the Research Project】

In this area of research, researchers concentrating in the many diverse fields of plant science, by promoting the integration of hereto considered distinct areas of research such as “local and autonomous responses”, “long distance signaling”, and “environmental memory” in a coordinated manner, will be able to clarify our current understanding of the dynamic environmental response control system as a whole. In particular, it is thought that reconsideration of the system of fibrovascular bundles (merely regarded in textbooks as the organ which transports water and nutrients) in regards to environmental signals as the site of long distance signal transmission, could overturn conventional concepts regarding plant signal transmission. In addition, as plants lack brains, we believe that analysis of DNA, histone modifications, and changes in the dynamic state of chromatin

within the nucleus (referred to as epigenetic regulation) will provide evidence that plants are endowed with distributed memory control systems which respond to environmental stimuli.



【Expected Research Achievements and Scientific Significance】

Hereto, a group that has researched plant environmental responses from the aspect of long distance signaling transmission and memory data processing systems is internationally unprecedented, and we hope that our area of research, which has greatly advanced the environmental response research field as an innovative field of research, will also strengthen our contribution to our nation’s exceptional rise in scientific standards. In addition, through the establishment of both collaborative research positions at John Innes Centre · the Sainsbury Laboratory (UK) and Stanford University (USA) where cutting-edge plant research is being promoted, and a close-knit international research network, we hope that our area of research will help to usher forth a new tide of global research.

【Key Words】

Local and autonomous responses, Long distance signaling, Environmental memory

【Term of Project】 FY2015-2019

【Budget Allocation】 1,184,500 Thousand Yen

【Homepage Address and Other Contact Information】

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