LEAP

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Lipid Molecules

Studies on Specific Activities and Functions of Lipid Molecules to Develop **Innovative Medical Technologies**

[Research and Development Objectives] Comprehensive elucidation of functional lipid which contributes to breakthrough medicines

Program Supervisor (PS)

YOKOYAMA Shinji

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Program Officer (PO)

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Lipids carry fundamental functions in living organisms as major components of biomembranes and energy-storage molecules. Numbers of their derivatives also play specific roles in regulating metabolism, immunity/inflammation, reproduction, circulation, neural network, etc, and are involved in pathogenesis of various disorders and diseases related to these systems. The objective of this research and development R&D area is to investigate novel biological functions of lipids and develop new technologies for their analysis, to elucidate molecular mechanism of lipid-associated various diseases, and finally to exploit novel developmental seeds for compounds and technologies to overcome these diseases, i.e. chemical compounds relevant to pre-clinical stage, target materials and reactions promising medical application in near future, or innovative diagnostic methods that may construct new clinical benefits, etc.

Lipid research has advanced along with numbers of discovery of new biological activities and exploitation of new analytic technologies. Therefore more innovative research and exploitation should also be necessary in order to accomplish the goal of this program and initiatively dispatch the novel results toward the world. It should be also important to gather ideas of researchers in various different fields and disciplines, such as the scientists in clinical medicine, pharmaceutical sciences, synthetic chemistry, biophysics and bioengineering, and information engineering, as well as those in lipid biology and biochemistry who have carried mainstream of lipid research. Broad viewpoints based on our interdisciplinary research team works will be indispensable for advancement of research and development in lipid research field to strengthen our international competitiveness.

We would like the program members to conduct their researches with practical translational outputs always in their mind. However, it does not necessarily mean that all the members are obliged to produce practical seeds within the term. We consider it is also important to promote fundamental basic studies that would possibly become the basis for generation of innovative technologies, diagnostics, and medicines only in not-remote future, for development and enforcement of international competitiveness of our lipid research. The research field of biological activities of lipids is continuously expanding, and this R&D area is expected to lead the world in innovative and explorative research in this field.

Because of expected medical application, target lipids are primarily set as the molecules originating in mammalian cells. However, the molecules closely related to human disorders and of nutritional importance may be included, such as omega-3 fatty acids and ceramide

R&D Area Advisors

ISHII Ken	Professor, The University of Tokyo
UESUGI Motonari	Professor, Kyoto University
OKADA Yasushi	Team Leader, RIKEN Center for Biosystems Dynamics Research
OGAWA Yoshihiro	Professor, Kyushu University
CHIBA Kenji	Fellow, Mitsubishi Tanabe Pharma Corporation
NISHIJIMA Masahiro	Professor Emeritus, Showa Pharmaceutical University
HANDA Tetsurou	Auditor, Kyoto Pharmaceutical University
FUKAMI Kiyoko	Professor, Tokyo University of Pharmacy and Life Sciences
FUKUSHIMA Daikichi	Director, Ono Medical Research Foundation, Foundation Chairman
NISHIMAKI-MOGAMI Tomoko	National Institute of Health Sciences

Started in 2015 ••• 1st period

Development of MULTUM-PALM and its application to cell membrane biology

UEDA Masahiro Professor, Graduate School of Frontier Biosciences, Osaka University

. . . 1st period

Elucidation of molecular mechanism of body surface barrier formation by lipids

KIHARA Akio

Professor, Faculty of Pharmaceutical Sciences, Hokkaido University

. . . 1st period

Chain length of fatty acids, elucidation of mechanisms of disease control and development of fundamentals toward medical evolution

SHIMANO Hitoshi Professor, Internal Medicine (Endocrinology and Metabolism), Faculty of Medicine, University of Tsukuba

. . . 1st period

Creation of a novel technology "Optolipidomics" to identify, control and observe functional lipids using light

> SETOU Mitsutoshi Director, International Mass Imaging Center, Hamamatsu University School of Medicine

Started in 2015 1st period

Elucidation of the mechanism of the hijacking of host lipids by pathogens and its application to pharmaceutical development

HANADA Kentaro Director, Department of Biochemistry & Cell Biology, National Institute of Infectious Diseases

Started in 2016 2nd period

Understanding disease mechanisms based on glucosylated lipid functions

KAMIGUCHI Hirovuki

Deputy Director, RIKEN Center for Brain Science

Started in 2016 2nd period

Development of innovative technology for structure-based drug design targeting prostanoid receptor

KOBAYASHI-SHIMIZU Takuya Professor, Department of Medical Chemistry, Kansai Medical University

Started in 2016 2nd period

Elucidation of metabolic control by oxysterols and disease molecular mechanism

> SATO Ryuichiro Professor, Graduate School of Agricultural and Life Sciences, The University of Tokyo

Started in 2016 ••• 2nd period Creation of a novel approach for drug development by elucidation of the regulation mechanism of cell migration with S1P transporters

> NISHI Tsuyoshi Associate Professor, ISIR, Osaka University

Development of novel anti-infective drugs targeting lipid metabolism YAMASAKI Sho Professor, Research Institute for Microbial Diseas Osaka University Started in 2017 . . . 3rd period Innovative research by control and visualization of cellular membrane phospholipids SHINDOU Hideo Vice Project Leader, National Center for Global Health and Medicine (NCGM) Started in 2017 ••• 3rd period Elucidation of roles and functions of bioactive lipids underlying stress-related dysfunctions and foundation of novel technology platforms for bioactive lipid-targeting clinical applications FURUYASHIKI Tomoyuki Professor, Graduate School of Medicine, Kobe University Started in 2017 . . . 3rd period Elucidation of disease mechanism and study of drug discovery targeted for oxidized lipids YAMADA Kenichi Professor, Faculty of Pharmaceutical Sciences, Kyushu University . . . 1st period Development of milieu-lipidomics platform for grasping metabolic crosstalk between host and intestinal bacteria **IKEDA Kazutaka** Deputy Team Leader, Laboratory for Metabolomics, RIKEN Center for Integrative Medical Sciences (IMS) Started in 2015 ••• 1st period Elucidation of roles of lipids in the epithelial-mesenchymal transition **IKENOUCHI Junichi** Professor, Faculty of Sciences, Kyushu University Started in 2015 1st period Control of functional lipids using optogenetics **UEDA Yoshibumi** Specially Appointed Researcher, Department of General Systems Studies, Graduate School of Arts and Sciences, The University of Tokyo Started in 2015 ••• 1st period The role of lipid in the exosome derived from the inflammatory cancer **KOTANI Ai** Professor, Institute of Medical Science, Tokai University Started in 2015 1st period

Started in 2016

2nd period

Development of basic technologies for medical application based on oxidized phospholipid-derived bioactive fatty acids

KONO Nozomu

Associate Professor, Graduate School of Pharmaceutical Sciences, The University of Tokyo

Completed

Started in 2017 • • • Started in 2015 ••• 1st period . . . 2nd period 3rd period Functional analysis on cholesterol Development and application of the Mechanisms of lipid dynamics on plasma metabolizing enzyme that defines a novel phosphatidylinositol-specific membranes and their application T cell subset and the clinical application nucleic acid drug for disease control SUZUKI Jun **TAKAHASHI Hayato** SUIZU Futoshi Professor, Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University Assistant Professor, Department of Dermatology, Keio University School of Medicine Associate Professor, Institute for Genetic Medicine, Hokkaido University Started in 2017 . . . Started in 2016 . . . 2nd period . . . 3rd period 1st period Unraveling a novel metabolic system Molecular mechanism and The molecular mechanism that regulates orchestrated by a metabolic sensor physiological role of PI4P-driven cellular signaling pathways through toward development of therapeutics lipid countertransport system organelle-specific lipid domains SEKIYA Motohiro **NAKATSU** Fubito TAGUCHI Tomohiko Associate Professor, Department of Internal Medicine, Endocrinology and Metabolism, Tsukuba University Associate Professor, Department of Neurochemistry and Molecular Cell Biology, Graduate School of Medical and Dental Sciences, Niigata University Professor, Graduate School of Life Sciences, Tohoku University Started in 2017 . . . 1st period Started in 2016 2nd period . . . 3rd period Development of vibrational Understanding pathogenic mechanisms Dissecting intracellular phospholipid microspectroscopy to determine lipid of skin diseases by focusing on traffic for understanding mitochondrial polyphosphoinositide metabolism species in live tissues derived from patients functional integrity NAKAMURA Yoshikazu NAGASHIMA Yu **TAMURA** Yasushi Assistant Professor, Department of Neurology, School of Medicine, The University of Tokyo Associate Professor, Faculty of Science and Technology, Tokyo University of Science Professor, Faculty of Science, Yamagata University Started in 2017 Started in 2016 ••• 2nd period ••• 3rd period . . . 1st period Development of enzymatic fluorometric assays Development of molecular tools for for quantifying phospholipids, sphingolipids and acylglycerols and for evaluating Palmitoylation-dependent regulations the clarification of metabolism and of membrane receptors in synapses molecular interaction of glycolipids asymmetrical distribution of membrane lipids HAYASHI Takashi **HIRAI Go MORITA Shin-ya** Section Chief, National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP) Professor, Graduate School of Pharmaceutical Science, Kyushu University Associate Professor, Shiga University of Medical Science Started in 2017 . . . 1st period Started in 2016 . . . 2nd period . . . 3rd period Identification of functional lipid Elucidation of the molecular mechanism Identification of lipid metabolites metabolites to control purinergic of dietary lipids-mediated reproductive controlling physiological function of the chemical transmission, and the molecular dysfunction to develop novel drugs and uterus mechanism-based drug discovery research treatments for infertility **HIROTA Yasushi MIYAJI** Takaaki YAMANASHI Yoshihide Lecturer, Department of Obstetrics and Gynecology, Graduate School of Medicine, The University of Tokyo Research Professor, Advanced Science Research Center, Okayama University Assistant Professor, Department of Pharmacy, the University of Tokyo Hospital Started in 2016 Started in 2015 . . . 2nd period 1st period Development of novel Physiological and pathological microsystems for highly sensitive roles of cholesterol in primary cilia analysis of lipid transport proteins **MIYAMOTO Tatsuo** WATANABE Rikiya Associate Professor, Research Institute for Radiation Biology and Medicine, Hiroshima University Chief Scientist, Molecular Physiology Laboratory, RIKEN 1st period Started in 2017 • • • 3rd period . . . Elucidation of the immune-metabolic-Functional elucidation of bioactive regeneration systems network linked by alkenyl-type lysophospholipids fatty acids YAMAMOTO Kei **OISHI Yumiko** Associate Professor, Graduate School of Technology, Industrial and Social Science, Tokushima University Professor, Department of Biochemistry & Molecular Biology, Nippon Medical School Started in 2016 ••• 2nd period Started in 2017 • • • 3rd period Understanding lipid-related orphan Characterization of the early steps G protein-coupled receptors using activating GPCR mutations of high-density lipoprotein (HDL) formation **INOUE** Asuka **KIMURA** Yasuhisa Associate Professor, Graduate School of Pharmaceutical Sciences, Tohoku University Assistant Professor, Graduate School of Agriculture, Kyoto University Started in 2016 2nd period Started in 2017 • • • 3rd period Development of novel treatment The clarification of lipid-mediated strategies by regulating functional mechanisms in the inflammatory lipids involved in the pathogenesis of and repairing process after stroke pulmonary hypertension SHICHITA Takashi Project Leader, Stroke Renaissance Project, Tokyo Metropolitan Institute of Medical Science **ENDO** Jin Assistant Professor, Department of Cardiology,

CREST/PRIME

Aging

Immunological Memory

Multi-Sensing

Anti-infectives

Proteostasis

Early Life Stage

Adaptation / repair Impa

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Keio University School of Medicine