(NIPS)

Department of Molecular and Cellular Physiology

The Division of Biophysics and Neurobiology (Prof. KUBO, Yoshihiro and Assoc. Prof. TATEYAMA, Michihiro) aims to clarify the mechanisms of ion channels, receptors, and G proteins, which are key elements of the nervous system. The Division approaches structure-function relationships and structural dynamics of the elements through biophysical analyses with the electrophysiological and optical techniques in in vitro expression systems.)

The Division of Structural Biology (Material-Life Boundary Research Group, Exploratory Research Center on Life and Living Systems (ExCELLS)) (Project Prof. MURATA, Kazuyoshi) strives to elucidate the functions of biomolecular complexes from a structural perspective. The Division uses a cryo-electron microscope to perform structural analyses of biomolecular complexes. In addition, electron tomography and serial block-face scanning electron microscopy (SBF-SEM) is used for morphological and structural analyses of intracellular biomolecular complexes.

The Division of Neural Development & Regeneration (Adjunct Division, Adjunct Prof. SAWAMOTO, Kazunobu) studies the mechanism whereby neurons and glial cells are generated during brain development and regeneration after brain injury. The Division also tries to stimulate these regeneration processes.

Department of Homeostatic Regulation

The Division of Cell Structure (Prof. FURUSE, Mikio and Assoc. Prof. IZUMI, Yasushi) focuses on the molecular basis of cell-cell junctions involved in epithelial barrier function and passive transfer via paracellular pathways. In addition to basic analysis using cultured epithelial cells, the Division is proceeding with individual-level analysis using genetically modified mice and Drosophila in conjunction with techniques in the fields of cell biology and physiology.

The Division of Cardiocirculatory Signaling (Cardiocirculatory Dynamism Research Group of the ExCELLS) (Prof. NISHIDA, Motohiro and Project Prof. NISHIMURA, Akiyuki) aims to clarify the mechanism that controls the cardiovascular adaptation or maladaptation to hemodynamic load. Specifically, it strives to elucidate the molecular mechanism of cardiovascular homeostasis from the viewpoint of signal transduction by using a wide range of techniques, including creation of model mice for human cardiovascular disease, measurement of cardiovascular functions using isolated organs, signal transduction analysis using primary cultured cardiomyocytes, and in situ imaging of post-translational protein modification based on chemical principles.

The Division of Molecular Neuroimmunology (Prof. MURAKAMI, Masaaki and Project Assoc.Prof. HASEBE, Rie) has been analyzing tissue-specific autoimmune diseases and found two novel concepts. One is the gateway reflex, which is a novel mechanism of neuroimmune interactions, and the other is the IL-6 amplifier, which is a fundamental mechanism of inflammation in nonimmune cells including tissue-specific cells. The IL-6 amplifier is activated by the simultaneous activation of STAT3 and NF-kB followed by the excessive activation of NF-kB. As for the gateway reflex, six types have been reported so far. Environmental and artificial stimulations, including gravity, electrical stimulation, pain, stress, light, and inflammation in joints, activate specific neural

pathways, which induce activation of the IL-6 amplifier at specific blood vessels of target organs, particularly those with blood barriers, such as the central nervous system. Activation of the IL-6 amplifier accumulates autoreactive CD4+ T cells in the blood around the specific blood vessels, resulting in the development of tissue-specific inflammatory diseases. The lab is investigating details about the neural pathways for the six as well as searching for new gateway reflexes.)

The Division of Ultrastructural Research (Adjunct Division) (Adjunct Prof. OHNO, Nobuhiko) aims to clarify the molecular backgrounds of structural and functional changes in the nervous system in myelin diseases. To this end, the Division uses imaging techniques such as 3-dimensional microstructure analysis involving microtome-integrated serial block-face scanning electron microscopy (SBF-SEM). In addition, by combining such imaging techniques with cultured models and genetically modified animals, the Division is elucidating the mechanisms of dynamic changes in organelles (e.g., mitochondria) in the nervous system and developing technologies to control these changes.

Department of Fundamental Neuroscience

In the Division of Multicellular Circuit Dynamics (Prof. WAKE, Hiroaki), we mainly use two-photon microscopy to visualize the structure and function of neurons and glial cells in the mouse brain under awake conditions and extract their activities in physiological and pathological conditions. Furthermore, we are using holographic microscopy to manipulate neurons and glial cells activity with high spatiotemporal resolution based on this activity information.)

The Division of Homeostatic Development (Assoc. Prof. NARUSHIMA, Madoka) focuses on the remodeling of neuronal circuits during the developmental and injury recovery periods. In particular, they are involved in the following: 1) electrophysiological analysis of synaptic transmission and receptor functions; (2) analysis of plastic changes in the functions of the inhibitory neurotransmitters GABA and glycine, especially from the viewpoint of the intracellular regulation mechanism for chloride ion concentration; and (3) use of in vivo multiphoton laser microscopy to determine the morphological and behavioral changes in neuronal circuits during the developmental period and in various disease states, and the contribution of glial cells to these changes.

The Division of Visual Information Processing (Prof. YOSHIMURA, Yumiko) characterizes the neural circuits of the visual cortex and elucidates the mechanisms underlying the experience-dependent development of the cortex. To this end, cortical slices and anesthetized and conscious mice are analyzed with the combined use of local laser light stimulation and electrophysiological and Ca^{2+} imaging techniques.

The Division of Biophotonics (Biophotonics Research Group of the ExCELLS) (Prof. NEMOTO, Tomomi and Assoc. Prof. ENOKI, Ryosuke) advances the development and application of cutting-edge imaging devices, including in vivo two-photon microscopes, multi-beam scanning-type two-photon microscopes, and two-photon super-resolution microscopes. The Division also conducts research in the field of chronobiology, for instance utilizing imaging techniques to examine the neuroscientific basis of circadian rhythms.

Department of System Neuroscience

The Division of Behavioral Development (Prof. ISODA, Masaki, Project Assoc. Prof. TOMATSU, Saeka) aims to clarify the neural basis of social cognitive functions via studies of system neuroscience using primates. To this end, the Division conducts integrated analyses combining behavioral, electrophysiological, and neuropharmacological techniques, and also utilizes neuroanatomical methods and selectively manipulates neural circuits using viral vectors.

The Division of Neural Dynamics (Prof. KITAJO, Keiichi) aims to unveil the functional roles of diverse neural dynamics in brain information processing. In particular, experiments involving the non-invasive measurement of human ectroencephalogram and brain stimulation are used in conjunction with data analysis (nonlinear dynamics, network analysis, statistical machine learning methods, etc.) to model the information-processing mechanisms of the human brain and thereby clarify pathological conditions and individual characteristics.

The Division of Sensory and Cognitive Brain Mapping (Prof. TAKEMURA, Hiromasa) aims to investigate structure-function relationship in the human brain primarily based on neuroimaging methods. Specifically, the Division combines structural neuroimaging (diffusion and quantitative MRI) and functional neuroimaging (functional MRI) to investigate brain structure and function, in order to perform comparisons between human and animal brains as well as evaluate consequence of disorders)

Supportive Center for Brain Research

The Section of Multiphoton Neuroimaging (Assoc. Prof. MURAKOSHI, Hideji) explores cell functions by imaging cell morphology, signal transduction, and molecular interactions using unique two-photon microscopy techniques and two-photon fluorescence resonance energy transfer (FRET) microscopy. In addition to state-of-the-art optical technology, the Section develops novel fluorescent proteins and photoresponsive protein molecules. By combining these technologies with the patch clamp method, the Section aims to elucidate the functions of nerve cells and cultured cells.

The Section of Electron Microscopy (Prof. FURUSE, Mikio and Assoc. Prof. KUBOTA, Yoshiyuki) has introduced a microtome-integrated scanning electron microscope (SBF-SEM) for conducting connectomics analyses. With this device, the Section automatically captures several hundred to a thousand sequential electron microscope images a day and reconstructs them into 3D models. In addition, local neural networks in the cerebral cortex are analyzed using wide-area electron microscope image datasets and correlative light-electron microscopy, the latter of which seamlessly combines *in vivo* imaging by a two-photon microscope and an automated tape-collecting ultramicrotome (ATUM)-SEM.

The Section of Brain Function Information (Project Prof. FUKUNAGA, Masaki and Adjunct Prof. INUI, Koji) supports neuroimaging studies in humans and monkeys using high-field (3T and 7T) MRI, and promotes research on brain functional and structural analysis. Research areas in this section include basic research using MRI, technical development, and mathematical analysis of large multicenter clinical neuroimaging studies. The Section also supports the analysis of data obtained by collaborative projects involving magnetoencephalography (MEG) measurements conducted through academic year 2021, with the goal of advancing the evaluation of

human brain functions.

The Section of Cellular Electrophysiology (Prof. YOSHIMURA, Yumiko) explores the structures and dynamic control of neural circuits and the action and control mechanisms of synaptic transmission by applying an electrophysiological method (patch clamp technique) to different brain areas (e.g., cerebral cortex, basal ganglia and cerebellum), mainly using sample slices. The Section also aims to elucidate the developmental mechanisms of brain and nervous system diseases and to develop novel treatment methods by performing pathological analyses of mice with gene mutations related to these diseases. In this Section, Assist. Professors OTSUKA, Takeshi and SATAKE, Shin'Ichiro will mainly promote the joint research project.

Center for Genetic Analysis of Behavior

The Section of Viral Vector Development (Prof. ISODA, Masaki and Assoc. Prof. KOBAYASHI, Kenta) develops high-quality and high-performance virus vectors that can be applied to: i) analysis of the neural basis of higher brain functions using model animals such as primates and rodents, and ii) pathological analysis of mental and neurological diseases. In addition, it serves as a central hub for providing viral vectors in response to requests from other laboratories. Through such efforts, the Section actively promotes joint research.

The Section of Multilayer Physiology, (Prof. NISHIJIMA, Kazutoshi) promotes collaborative research for the evaluation of behaviors related to emotions, learning and memories, and for the recordings and analysis of neural (single-unit, local field potential, etc.) and muscular activities in an awake state.

Research Enhancement Strategy Office and Section of Advanced Research Support

The Research Enhancement Strategy Office and the Section of Advanced Research Support (Project Assoc. Prof. MARUYAMA, Megumi) promotes efforts to establish a new NIPS research strategy based on surveys of domestic and international research trends, and provides administrative support services as a hub for local and international research communities. The Office and Section are also engaged in interdisciplinary joint research on deepening the relationship between science and society. This research includes the field of neuroethics, which deals with the ethical and social issues that accompany the development of neuroscience research.

Center for Animal Resources and Collaborative Study

The Center for Animal Resources and Collaborative Study develops experimental animals (including mice, rats, rabbits, and monkeys) based on their characteristics (e.g., genetic recombination) and analyzes their phenotypes (physiological functions such as behavior, electrical activity, metabolism, etc.) from the perspectives of veterinary medicine and laboratory animal sciences. In addition, the Center develops strain preservation techniques and husbandry practices that are suitable for different animal species to improve the quality of animal experiments and animal welfare.