Elucidation of the Principles of Formation and Function of the Brain Neural Network and Creation of Control Technologies

[Research and Development Objectives]
Clarification of the control mechanisms of neural circuit operation and its formation

Program Supervisor (PS)
Seiji Ozawa
Professor, Takasaki University of Health and Welfare

This R&D area aims to elucidate the molecular and cellular mechanisms of the generation, development, and regeneration of the brain neural network; to investigate how neural networks composed of a variety of elements in individual brain areas work and express their specific functions; and to clarify how the brain works as a coherent system by integrating the activities of these local networks. On the basis of such research, it also aims to create technologies for controlling the process of formation and activities of the brain neural network.

Specific approaches may include elucidation of the molecular mechanisms of development, differentiation, regeneration, target recognition, and migration of neurons (components of neural networks) and glial cells that significantly influence neural network formation and functions; elucidation of the mode of neural network activities by combining new technologies, such as visualization of specific neurons with the use of specific expression molecules and fluorescent proteins, simultaneous recording of activities of many neurons, and local stimulation with a caged compound; research to clarify the relationship of higher order brain functions with synaptic events through the combination of research at the network and system levels in model animals and research on the regulatory mechanism of synaptic transmission at the molecular and cellular levels; elucidation of the mechanism of neural network reorganization at the critical period or after brain damage; and creation of technologies for intervention in its process.
The brain combines sensory information from multiple systems including vision, smell, taste, hearing, and somatosensation, to control behavior. However, the mechanisms behind the comparison and integration of different sensory modalities are not well understood. To address this issue, we will utilize the brain of the fruit fly Drosophila, a convenient model organism for visualizing and manipulating neurons at the single-cell level. By systematically analyzing the brain regions that integrate signals sent from different sensory centers, and by combining diverse experimental techniques to reveal the functions of identified neural circuits, we aim to reveal the processes underlying integration of sensory information.

The cerebral cortex is composed of several tens of billions of neurons and is divided into tens of areas. Each area is further divided into many smaller modules, i.e., functional neural circuits. In this project, we will investigate the structure and function of unitary functional circuits in the cerebral cortex, using in vivo two-photon calcium imaging with single-cell resolution. We will explore how the unitary circuits develop and work, and elucidate the basic architecture of functional neural circuits in the cerebral cortex.

The critical role of the hippocampus in long-term memory formation has been well established. Mossy fibers in the hippocampus extend from granule cells to form specialized synapses with the dendrites of CA3 pyramidal neurons and a variety of inhibitory interneurons. This interconnection of excitatory and inhibitory neurons regulates neuronal activities. We will focus on the roles of the cell adhesion molecules and their associated protein afaadin to elucidate the molecular and cellular mechanisms of (1) target cell recognition, (2) synapse formation, and (3) neuronal plasticity in these hippocampal mossy-fiber synapses. Our results will contribute to the understanding of molecular mechanisms in the formation of neuronal circuits and to the development of novel strategies for treatment of neuronal diseases.