【Grant-in-Aid for Transformative Research Areas（B）】

Section III

Title of Project： Next-generation non-invasive biological deep-tissue manipulation by biomolecular engineering and low physical energy logistics

INOUE Keiichi
(The University of Tokyo, The Institute for Solid State Physics, Associate Professor)

Number of Research Area：20B301　Researcher Number：90467001

【Purpose of the Research Project】

The aim of this research area is to develop new molecular tools (receiver molecules) that can sense three types of low-physical energy (photothermal, ultrasonic, and magnetic) and to create new biological manipulation methods using state-of-the-art low-physical energy logistics methods, instead of conventional biological manipulation methods using electrical stimulation, medication, and optogenetics. This is expected to create a new research field for minimally invasive and site-specific biological manipulation at the cellular level including deep tissues without the introduction of instruments into the body.

【Content of the Research Project】

Higher animals have a network of nerves throughout their bodies, and, especially, the human brain is composed of tens of billions of neurons. Our emotions, memories, and behaviors are controlled by the sophisticated neural activity generated by these networks. Numerous studies using electrical stimulation, morphological observation, and medication stimulation have revealed the mechanisms of neural activity at the molecular level. Recently, the advent of optogenetics, which uses light-dependent ion transport proteins, enabled us to manipulate the activity of individual circuits with an extremely high spatiotemporal resolution to investigate the role of higher-order neural activity.

However, non-invasive manipulation of neural circuits deep in the body of large animals such as humans is still difficult and remains a major obstacle to a complete understanding of neural networks.

In this research area, we aim to realize a non-invasive manipulation method of deep neural circuits, which has been difficult to achieve with existing methods, by focusing on three types of low-physical energy: photothermal, ultrasonic, and magnetic energies. For this aim, we develop novel molecular tools (receiver molecules) that can sense these low-physical energies and regulate the activity of ion channels, enabling us to genetically make all cell types responsive to low-physical energies. In addition, we advocate the concept of "low-physical energy logistics," which integrates the manipulation of living organisms by low-physical energy, and establish a method to freely deliver various low-physical energies to any part of the body. This will allow us to manipulate receiver molecules in the body with high spatiotemporal precision and to propose new experimental research methods to understand the physiological roles and mechanisms of neural activity in deep tissues.

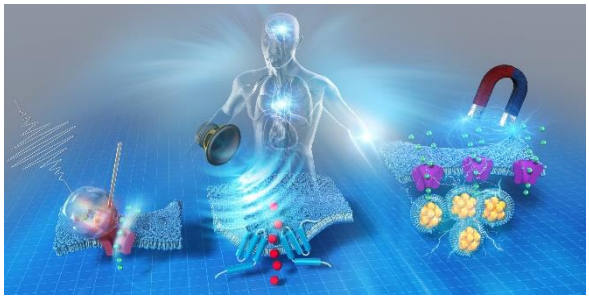

Figure. The image of low-energy manipulation

【Expected Research Achievements and Scientific Significance】

By developing a number of molecular systems in this research area based on our original concept, we will be able to provide a great deal of insight into the relationship between protein response to external stimuli and functional expression. In addition, the attempt to systematize knowledge and technology subdivided by physical energy is expected to provide not only a bridge to apply cutting-edge technology of each field to others, but also to integrate physical energy technology, create new technology, and understand the essential interaction between physical energy and living matters. In the application of brain science, it is expected to realize a completely stress-free research method in which neural activity of higher animals under free behavior can be directly manipulated from the outside. In the future, the application of the technology developed in this area to medical treatment is expected to lead to the creation of therapies that are extremely patient-friendly and do not require the introduction of devices into the body.

【Key Words】

Receiver molecule: an active molecular system that senses three types of low-physical energy with high sensitivity and controls the opening and closing of ion channels accordingly.

Low-physical energy logistics: new physical concepts and methodologies to deliver low-physical energy into the deep tissue with high efficiency, precision, and spatio- temporal resolution to manipulate receiver molecules

【Term of Project】 FY2020-2022

【Budget Allocation】 121,900 Thousand Yen

【Homepage Address and Other Contact Information】

https://low-energy-manipulation.com/
low-energy-manipulation@issp.u-tokyo.ac.jp