【Grant-in-Aid for Scientific Research(S)】

Integrated Science and Innovative Science (Comprehensive fields)

Title of Project : Molecular-anatomical research on multi-modal regulation of synaptic transmission in higher brain regions

Masahiko Watanabe
(Hokkaido University, Graduate School of Medicine, Professor)

Research Area : Neuroanatomy
Keyword : Molecular and cellular neuroscience

【Purpose and Background of the Research】

Principal neurons in higher brain regions receive and integrate an enormous number of synaptic inputs. The weight of individual synapses varies according to input- target-, activity- and state-dependent manners. The multi-modal regulatory mechanisms are the fundamental to functional CNS function. However, little is known to data except for activity-dependent regulatory mechanisms in the postsynapse.

In the present research project, I aim to figure out the molecular-anatomical architecture involved in these regulations. I will apply neuroanatomical, neurophysiological, and neurobehavioral techniques to gene-manipulated animals, and test three hypotheses as described below.

【Research Methods】

1. Input- and target-dependent regulations by postsynaptic TARPs. The hypothesis that synaptic numbers of AMPA receptors are regulated by TARP-mediated competition for postsynaptic 'slots' among GluR subtypes is tested here. To validate this hypothesis, I will examine effects of TARP knockout on synaptic expression of AMPA receptors in the hippocampus and striatum.

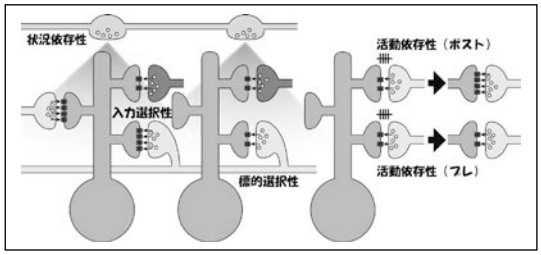

Fig 1 Signaling

2. Activity-dependent regulation by presynaptic VGluTs. The hypothesis that VGluT subtypes expressed in the presynapse is involved in activity-dependent modulation of synaptic efficacy is tested here.We will examine VGluTs at synapses in the cerebellum, amygdala and striatum to pursue the relationship of expressed VGuTs with the induction of short- and long-term synaptic plasticity.

3. Target-specificity of state-dependent regulation by neuromodulators. The hypothesis that target-specificity by neuromodulators is mediated by specific cell adhesion molecules between neuromodulatory fibers and target neurons is tested here. We will clarify it by examining the nigro-striatal dopaminegic, septo-hippocampal cholinergic, and CCK-projection systems.

【Expected Research Achievements and Scientific Significance】

Through the project, our understanding on multi-modal regulatory mechanisms for synaptic transmission will be greatly deepened.

【Publications Relevant to the Project】

・Yoshida T, Uchigashima M, Yamasaki M et al.: Unique inhibitory synapse with particularly rich endocannabinoid signaling machinery on pyramidal neurons in basal amygdaloid nucleus. **Proc. Natl. Acad. Sci. USA**. 108:3059-3064, 2011.
・Ichikawa R, Yamasaki M, Miyazaki T et al.: Developmental switching of perisomatic innervation from climbing fibers to basket cell fibers in cerebellar Purkinje cells. **J. Neurosci.** 31:16916-16927, 2011.

【Term of Project】 FY2012-2016

【Budget Allocation】 167,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.hucc.hokudai.ac.jp/~e20704/
watamasa@med.hokudai.ac.jp