ASHBi SEMINAR

Development of structure-guided synapse organizers for neural circuit control

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Date Monday, 29 July 2024

Time 16:00 − 17:00 [JST]

Venue Conference Room
(B1F, Faculty of Medicine Bldg. B)

*Register via the right QR code

Abstract

Neuronal synapses are the specialized connections in neural circuits to constitute the sites where information is transmitted between neurons. Dynamic structural changes in synapses such as formation, maintenance, and reorganization at any time are characteristic features, and a group of molecules called synaptic organizers play an important role in this process. Disruption of these process is associated with various neurological and psychiatric disorders, so-called "synaptic diseases". One of the dynamic changes in synaptic organizers that have been reported that the cell adhesion-type synaptic organizers, neuroligins and neurexins (Nrxs) are subjected to sequent proteolytic cleavages by several enzymes and act in an inhibitory effect on synapse formation and maintenance (Suzuki et al., Neuron 76(2):410-422 (2012)). Another dynamic change in synapses is the rapid synapse formation and maturation by the new class of the synapse organizers, the extracellular scaffold adhesion-type synaptic organizers (ESPs: Extracellular Scaffolding Proteins) such as cbln1 that simultaneously binds to presynaptic Nrxs and postsynaptic delta-type glutamate receptors (GluDs). To extend the function of cbln1 to be the universal excitatory synapse connector, neuronal pentraxin 1 (NPTX1), an ESP that binds to AMPA-type glutamine receptors (GluAs) was fused with cbln1 and the artificial synaptic connector CPTX was designed based on the structural information. CPTX administration to mice models of cerebellar ataxia, Alzheimer's disease, and spinal cord injury has demonstrated the improvement of the behavioural abnormalities by rapid induction of synapse formation (Suzuki et al., Science 69(6507):eabb4853 (2020)). We are further studying the structure of synaptic molecules and binders to develop the next generation synapse connectors. In this seminar, I will also talk about the recent development of synaptic connectors for more specific target based on structural information and in situ structural analysis using cryo-EM/ET, and introduce the Bio2Q project, which studies the molecular mechanisms of multi-organ connections.

Organizer : Graduate School of Medicine Institute for the Advanced Study of Human Biology (WPI-ASHBi)

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