DANDRITE
Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

AARHUS UNIVERSITY

# Virtual DANDRITE Lecture

## Thursday 17 December 2020

**11.00 – 12.00**

**Online via Zoom**

Please find Zoom link via the Outlook calendar invitation. If you have not received this, please write an e-mail to Kathrine: kh@dandrite.au.dk


## Atsushi Sugie

Associate Professor at the Brain Research Institute,
Niigata University,
Japan


## Elucidation of the molecular mechanisms of neural circuit maintenance via synapse

The nervous system has the remarkable ability to adapt and respond to various stimuli. Such neural adjustment is largely acquired through plasticity at the synapses. The active zone (AZ) is the region at the presynaptic membrane that mediates neurotransmitter release and is composed of a dense collection of conserved scaffold proteins. We found that Drosophila photoreceptor AZs undergo molecular remodeling *in vivo* after prolonged exposure to natural ambient light. In these conditions, we observed that the number of AZs containing the CAST/ELKS family protein Bruchpilot was reduced in the photoreceptor axons. Further, DLiprin-α (Liprin-α/Syd-2) and Rab3-interacting molecule (RIM)-binding protein were delocalized from the AZs. In contrast, the localization of DSyd-1 (mSyd-1/Syd-1) and of the voltage-gated calcium channel Cacophony appeared unmodified. The modulation of the photoreceptor AZ was regulated by neural activity in the postsynaptic neurons via a feedback circuit. In search of the molecular effectors of this feedback loop, we found that the divergent canonical Wnt pathway promotes AZ reorganization via microtubule destabilization. These data revealed that AZs undergo reversible remodeling *in vivo* and the molecular machinery that regulates this process (Sugie et al., *Neuron* 2015 ; Sugie et al., *J. Vis. Ex.* 2017).

Individual neurons grow and migrate during development, locating their appropriate target and forming functional neural circuits. Although they cannot be regenerated, the neurons in a circuit could be maintained for a lifetime, implying that specific mechanisms exist to maintain the long-term health and integrity of the nervous system. This is in contrast to somatic cells, which are constantly replaced. If the inter-neuronal communication mechanism for maintaining cell health gets disrupted, it could cause irreversible functional deterioration of neural circuits, leading to aging, or neurodegenerative diseases and mental disorders. However, the molecular mechanism underlying the intercellular communication keeping neuronal circuits healthy is still barely understood. Using the Drosophila photoreceptor as a good model to address this question, we are currently investigating how specific pre- and postsynapses interact during degeneration and are digesting whether the neuronal activity, the divergent canonical WNT pathway, and autophagy systems are responsible for intercellular communication to keep neuron healthy.