Seminar/Talk

Role of adhesion molecule neuroligin-1 in synaptogenesis probed by single molecule imaging & regulation of tyrosine phosphorylation

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Host: Harald Janovjak

To gain insight into the molecular mechanisms by which early neuronal connections mature into excitatory or inhibitory synapses, we are examining the dynamics, nanoscale organization, and signaling mechanisms associated with the adhesion molecule neuroligin-1 (Nlg1).

We recently developed a highly sensitive labeling strategy relying on fluorophore-conjugated monomeric streptavidin to target Nlg1 carrying a short, enzymatically biotinylated tag. Using super-resolution imaging techniques including uPAINT, STED and dSTORM, we demonstrate specific labeling of Nlg1 at synapses in both dissociated neurons and organotypic slices, with reduced steric hindrance and absence of cross-linking compared to multivalent probes. We are also developing a simulator of single molecule dynamics which allows us to quantitatively interpret our live cell imaging experiments (SPT, FRAP, FCS). Finally, we demonstrate an important role of Nlg1 phosphorylation in synapse specification, focusing on a unique intracellular tyrosine residue (Y782) located in the gephyrin-binding motif (Giannone et al., Cell Reports 2013). Strikingly, optogenetic phosphorylation of Nlg1 using a photoactivatable tyrosine kinase, induces the formation of new dendritic spines (Letellier et al., submitted).

Recent references:

Chamma et al., Nature Protocols 2017; Chamma et al., Nature Comms 2016 ; Garcia et al., PNAS 2015 ; Letellier et al., Nature Neurosci 2014 ; Czöndör et al., Nature Comms, 2013 ; Giannone et al., Cell Rep 2013.

Friday, March 31, 2017 10:00am - 11:00am
Mondi Seminar Room 2, Central Building

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