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

AARHUS UNIVERSITY

DANDRITE Lecture

Thursday 27 April 2023

13.00 – 14.00

Building 1262 room 101

Bartholins Allé 2, 8000 Aarhus C

Volker Haucke

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How the presynapse forms and functions

Nervous system function relies on the polarized architecture of neurons, established by directional transport of pre- and postsynaptic cargoes. While delivery of postsynaptic components depends on the secretory pathway, the identity of the membrane compartment(s) that supply presynaptic active zone (AZ) and synaptic vesicle (SV) proteins is largely unknown. I will discuss our recent advances in our understanding of how key components of the presynaptic machinery for neurotransmitter release are transported and assembled focussing on our recent studies in genome-engineered human induced pluripotent stem cell-derived neurons and in Drosophila larvae. Specifically, I will focus on the composition and cell biological identity of the axonal transport vesicles that shuttle key components of neurotransmission to nascent synapses and on machinery for axonal transport and its control by signaling lipids. These studies reveal an unexpected function for a lysosome-related organelle as the basic building block for presynaptic biogenesis.

In the second part of my talk I will discuss the question how exocytosis and endocytosis are balanced to maintain presynaptic membrane homeostasis. In most recent work we have found that the SV calcium sensor Synaptotagmin 1 couples exocytic SV fusion to the endocytic retrieval of SV membranes by promoting the local activity-dependent formation of the signaling lipid phosphatidylinositol 4,5-bisphosphate [PI(4,5)P2] at presynaptic sites. Interference with this mechanism impairs SV membrane retrieval but not exocytic SV fusion. Our findings demonstrate that local Synaptotagmin 1-induced lipid signaling couples SV exocytosis in central nervous system neurons.

Host: Poul Henning Jensen