Joint KJELDGAARD & DANDRITE Lecture

Thursday 25 September 2014 at 11.30 - 13.00
iNANO Aud. (building 1593-012), Aarhus University
Gustav Wieds Vej 14, 8000 Aarhus C
Sandwiches outside the iNANO Aud. from 11.30, lecture start at 12.00


A Joint Kjeldgaard & DANDRITE Lecture

Reinhard Jahn
Department of Neurobiology,
Max-Planck-Institute for Biophysical Chemistry,
Göttingen, Germany

Molecular machines governing exocytosis of synaptic vesicles

Neurotransmitter release from presynaptic nerve endings is mediated by Ca^{2+} -dependent exocytosis of synaptic vesicles. During the past years, the molecular steps mediating exocytotic membrane fusion have been unraveled although a lot of open question remain. Fusion is carried out by the SNARE proteins synaptobrevin/VAMP, syntaxin 1, and SNAP-25. Upon membrane contact, the vesicular SNARE synaptobrevin forms complexes with the plasma membrane-resident SNAREs SNAP-25 and syntaxin 1. Complex formation proceeds from the N-terminal end towards the C-terminal membrane anchors, thus pulling the membranes together and initiating fusion ("zipper" hypothesis of SNARE function). The steps of SNARE assembly are controlled both by members of conserved protein families such as the SM- and CATCHR-proteins, and they are tightly controlled by specialist proteins responsible for calcium regulation such as the calcium sensor synaptotagmin and complexins.

In our own work, we have focused on understanding the mechanisms of SNARE assembly and SNARE-induced fusion using structural and biochemical approaches and in-vitro fusion reactions with native and artificial membranes. Our recent results lend strong support to the zipper hypothesis, showing that during SNARE complex formation the helical bundle extends into the membrane and that only few SNARE complexes may suffice for effective fusion of bilayers. Furthermore, we have studied intermediate states of the SNARE-dependent fusion pathway involving techniques such as cryo-electron microscopy, resulting in novel insights into the structure of fusion intermediates.

In addition, we have investigated the interactions of the calcium sensor synaptotagmin 1 with SNAREs and with membranes. Our results lend support to the view that the interactions with membranes that are primarily of electrostatic nature are indeed crucial for synaptotagmins function in regulating exocytosis. Currently we believe that the calcium-dependent formation of a cross-link between the vesicle and the plasma membrane may play a central role in activating the SNARE proteins.

Host: Ernst-Martin Füchtbauer, Section for Molecular Cell and Developmental Biology,
Dept. Molecular Biology and Genetics, Aarhus University

The lecture will be followed by a chalk-board session for PhD students (in the iNANO Aud.)

The Kjeldgaard Lecture Series is organised by
Dept. Molecular Biology and Genetics
www.mbg.au.dk/lectures

AARHUS UNIVERSITY

The DANDRITE Seminar Series is organised by
Danish Research Institute of Translational Neuroscience
www.dandrite.au.dk/seminar