Introductory Remarks to Symposium 10

Membrane trafficking processes and presynaptic proteostasis

Marijn Kuijpers and Anna Karpova, Nijmegen (Netherlands) and Magdeburg

The molecular makeup of synapses is extraordinarily complex, and their distance from the cell body, where most protein synthesis occurs, can be enormous. Because neurons are both postmitotic and long-lived, maintaining the integrity of their proteome is of particular importance. Several hundred different proteins can be found in forebrain synapses and this complex proteome creates a unique situation with respect to the molecular dynamics of protein exchange, in particular at the presynapse. How protein turnover is regulated in axons and axon terminals, and whether this occurs locally (i.e. at the synapse) or in the soma is a key cell biological question. Currently there is a surprising paucity of data on necessities for, and mechanisms of protein replacement at presynapses. Gaps in our knowledge concern: which degradative pathways are involved, how different pathways contribute to the presynaptic proteome, which signals direct proteins into a given pathway, how proteins are sorted for certain degradative mechanisms, how synaptic activity affects degradation, how cross-talk is regulated, and which presynaptic sensor mechanisms identify protein 'damage'.

In this symposium we will look at the specific contribution of autophagy and axonal trafficking to axonal and presynaptic proteostasis and discuss how presynaptic function and plasticity is regulated by autophagy. Mechanisms that couple autophagosome biogenesis to synaptic activity will be presented (Daniel Colon-Ramos). We will discuss how non-canonical functions of autophagosomes (e.g. signalling) impact presynaptic development, maintenance and function (Natalia Kononenko). Autophagosomes fuse with late endosomes to undergo robust retrograde transport and the resulting amphisomes serve as signaling and sorting platforms while trafficking in a retrograde direction to the cell soma (Anna Karpova). We will also address defects in anterograde axonal transport in the neurodegenerative disorder Hereditary Spastic Paraplegia (Vranda Garg). Finally, loss of neuronal autophagy causes the selective accumulation of tubular Endoplasmic Reticulum (ER) in axons under physiological conditions, resulting in increased excitatory neurotransmission as a consequence of elevated calcium release from ER stores (Marijn Kuijpers).
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Symposium 10

Thursday, March 23, 2023
11:00 - 13:00, Lecture Hall 104

Chairs: Marijn Kuijpers and Anna Karpova, Nijmegen (Netherlands) and Magdeburg

11:00 **Opening Remarks**

11:05 Daniel Colon-Ramos, New Haven, USA
MECHANISMS OF LOCAL SYNAPTIC AUTOPHAGY VIA TRAFFICKING OF ATG-9 (S10-1)

11:30 Natalia Kononenko, Cologne
SURVIVAL-INDEPENDENT ROLES OF NEURONAL AUTOPHAGY (S10-2)

11:55 Anna Karpova, Magdeburg
AMPHISOME BIOGENESIS, TRAFFICKING AND SIGNALING AT PRESYNAPTIC BOUTONS (S10-3)

12:20 Vranda Garg, Goettingen
DEFECTIVE AXONAL TRANSPORTATION OF A CONTACT SITE PROTEIN CAUSING NEURODEGENERATION IN ZEBRAFISH (S10-4)

12:35 Marijn Kuijpers, Nijmegen, The Netherlands
AUTOPHAGY CONTROLS ER CALCIUM STORES TO REGULATE NEUROTRANSMISSION (S10-5)