

Virtual DANDRITE Seminar

Thursday 3 September 2020
15.00 – 16.00

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



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Drosophila Rab2 controls lysosome biogenesis and drives axonal transport of dense core vesicles and lysosomal organelles

The evolutionary conserved family of Rab ('Ras-related in brain') GTPases are master regulators of intracellular membranous trafficking. I will present our work on *Drosophila* Rab2, for which we have demonstrated an important role in lysosome biogenesis, and in axonal traffic of dense core vesicles and endolysosomal organelles. We find that Rab2 is recruited to late endosomal membranes, where it controls the fusion of lysosomal-associated membrane protein (LAMP)-containing vesicular carriers of biosynthetic material to late endosomes. Rab2 also promotes fusion of lysosomes to late endosomes, and fusion of autophagosomes to the endolysosomal pathway. These results suggest that *Drosophila* Rab2, by controlling the major heterotypic fusion processes at the late endosome, is a crucial regulator of the endolysosomal and autophagic pathways. The second part of the talk will address the role of Rab2 in the nervous system more specifically. We find that expression of *Drosophila* Rab2 is enriched in the somata of long-axon, high-capacity peptidergic neurons. Live imaging of axons in peripheral nerves demonstrates that Rab2 plays a critical role in the bidirectional fast axonal transport of DCVs, endosomes and lysosomal organelles. Active Rab2 is present at DCVs undergoing axonal transport, and proximity-dependent biotinylation indicates that Rab2 associates with the Kinesin-3/unc-104 motor protein *in situ*. Similar to Rab2, the lysosomal motility factor Arl8 is also needed for axonal transport of DCVs and co-localizes with DCV cargo markers. However, unlike Rab2, Arl8 is also critical for the DCVs to exit from cell bodies into axons. Our results, together with those of others, reveal several parallels between the regulation of biogenesis and motility of DCVs and lysosomes, implying a possible evolutionary relationship between these organelles.