

## **Seminar**

### **Insulin and Vps34-mediated PI(3)P signalling regulates endosomal flux underlying developmental synaptic remodelling via Rab4**

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Rab4GTPase, required for endosomal sorting and trafficking, is implicated in synaptic atrophy and dementia in *Drosophila* and humans, respectively. To uncover the underlying mechanism, we studied the correlation between Rab4 vesicle transport in axons and episodic remodelling of synapses in the central nervous system (CNS) of *Drosophila* larvae. It revealed that synapse-bound traffic of Rab4 vesicles and presynaptic enrichment of Rab4 increases during the programmed contraction of synapses in the CNS. This coincides with activation of insulin and Vps34-mediated signalling that elevates phosphatidylinositol-3-phosphate [PI(3)P] levels on Rab4 vesicles. Increased PI(3)P levels recruit PX-domain-containing motor, Klp98A, accelerating the synapse-directed traffic which subsequently increased presynaptic enrichment of Rab4. These findings elucidate the molecular mechanism that regulates developmental synaptic plasticity in the CNS via insulin signalling and directed axonal transport of endosomes.

***Friday, Oct 24<sup>th</sup> 2025***

***11:30 Hrs (Tea / Coffee 11:15 Hrs)***

***Auditorium, TIFRH***