
When less is more: logistics of axonal transport by Kinesin-2

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Bobra,
Gadgil,
Barbora *et al.*, in prep

Girotra, Singh,
Kulkarni *et al.*, 2017,
Traffic

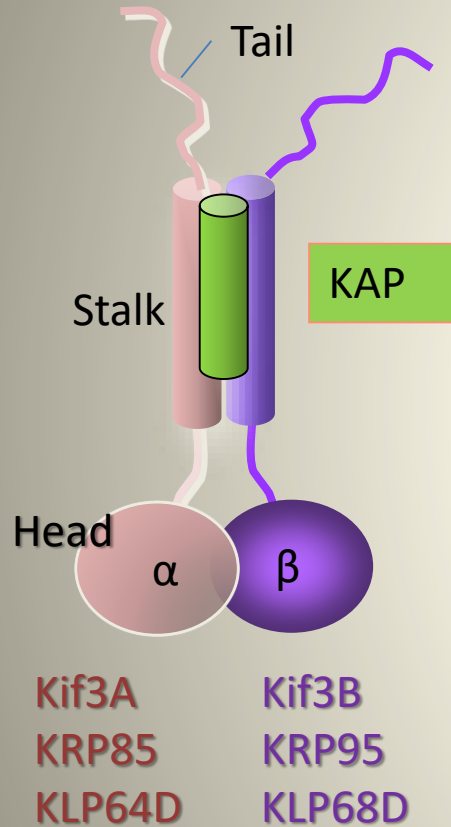
Jana, Jain *et al.*,
2016, in revision

Sadananda, Hamid *et al.*, 2012, Traffic

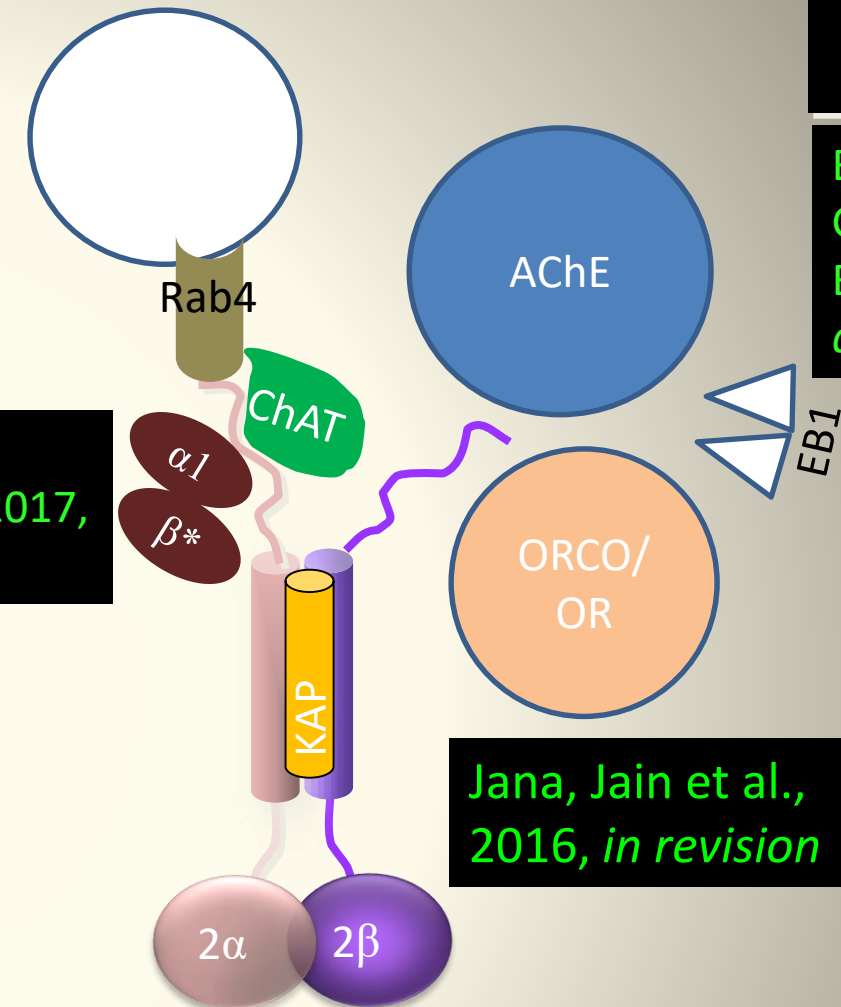
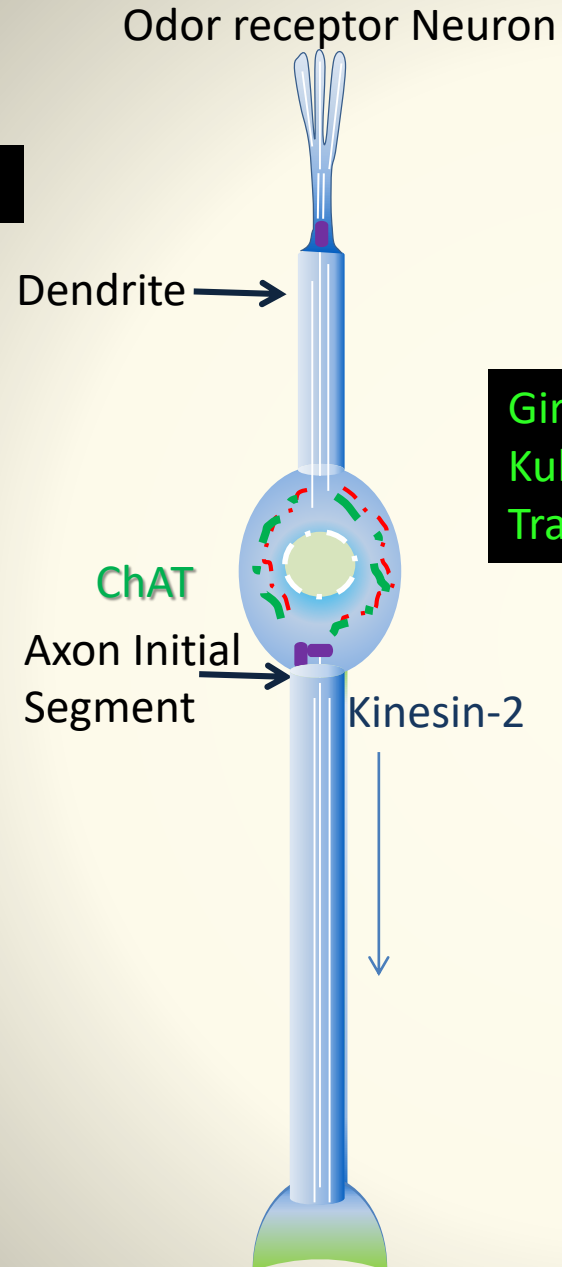
Dey *et al.*, 2017, Cell Reports

Kulkarni *et al.*, 2017, FASEB J

Doodhi *et al.*, 2009, 2012

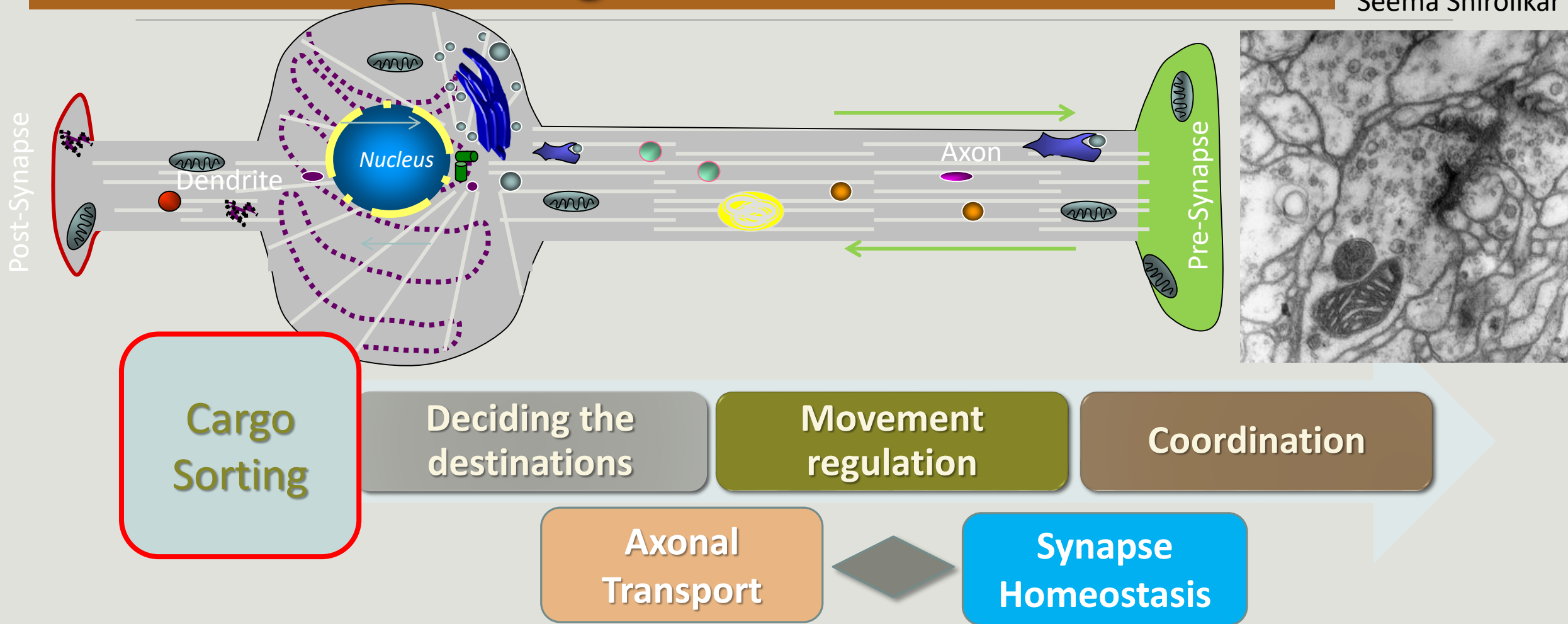


Kinesin-2

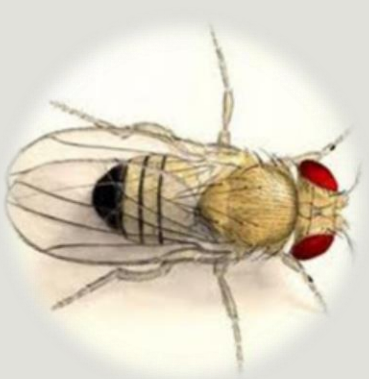


Axonal Transport – Complex Logistics and Function

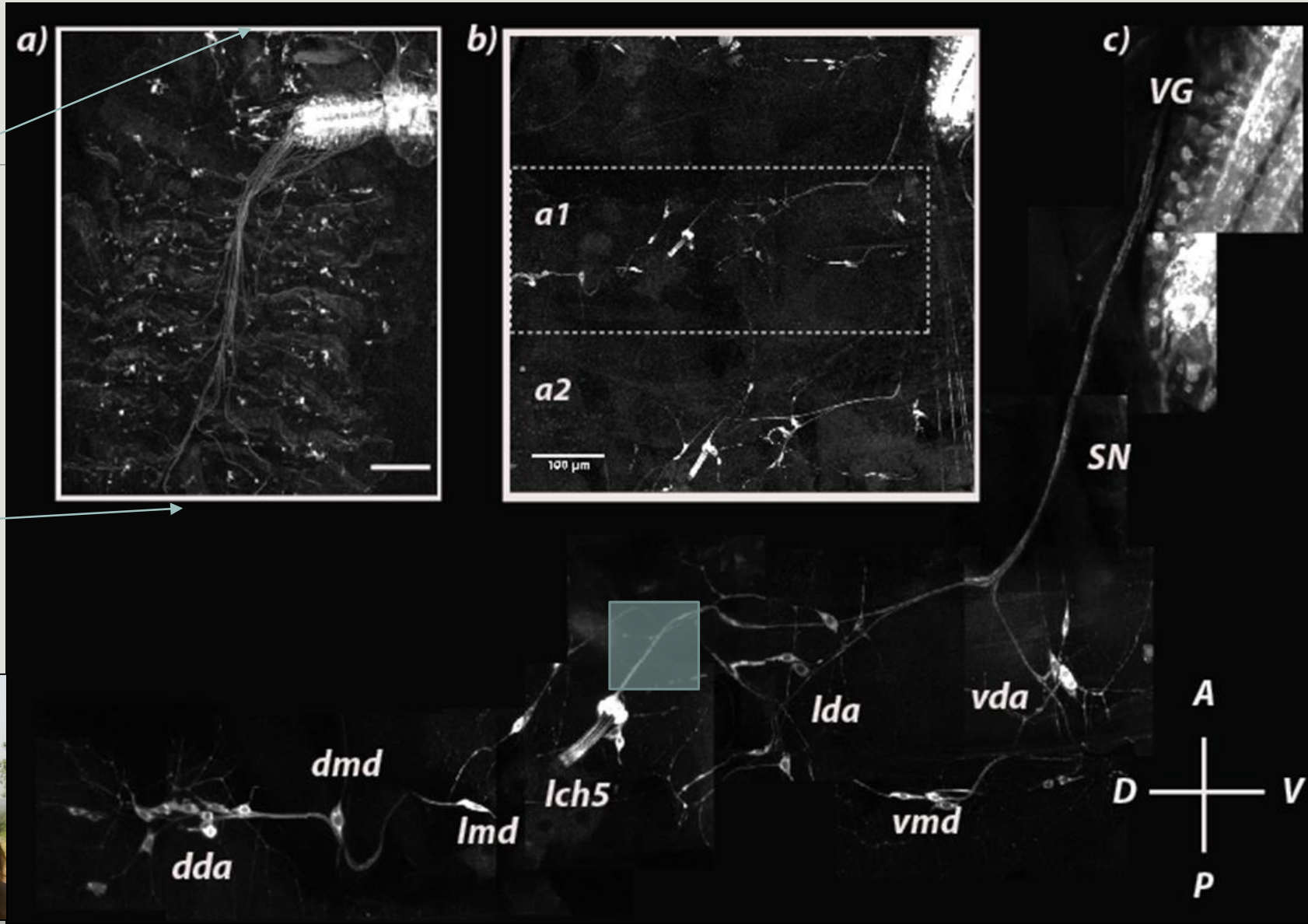
Seema Shirolikar



Nervous system *Drosophila* larva



Aparna Sadanada



Segmental Nerve – Transverse Section

Motor Axons

Sensory axon

Mitochondria



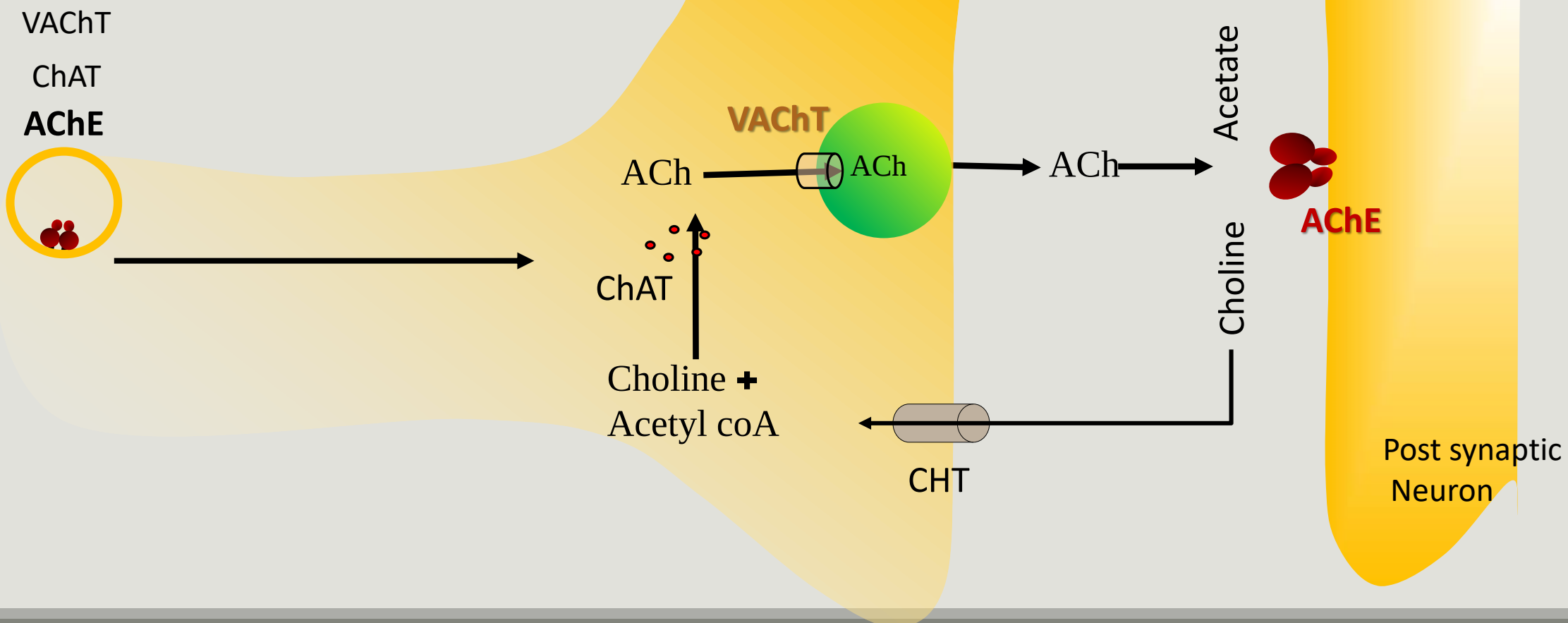
1 μ m



Cholinergic cycle

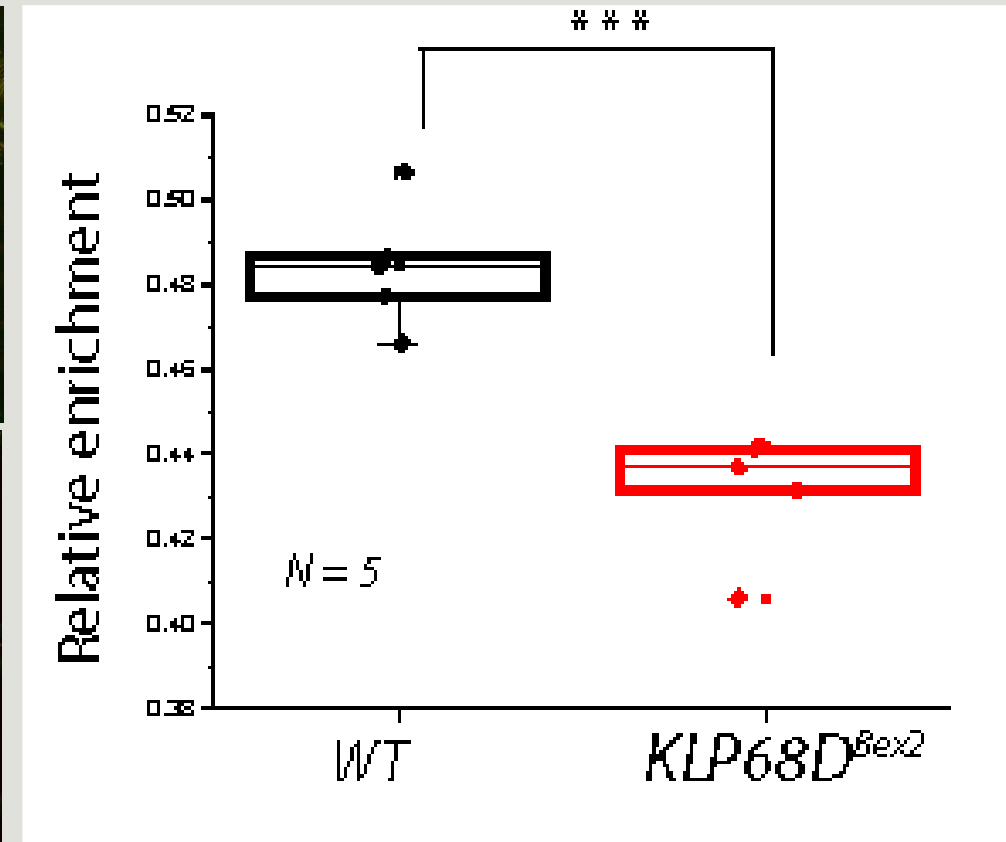
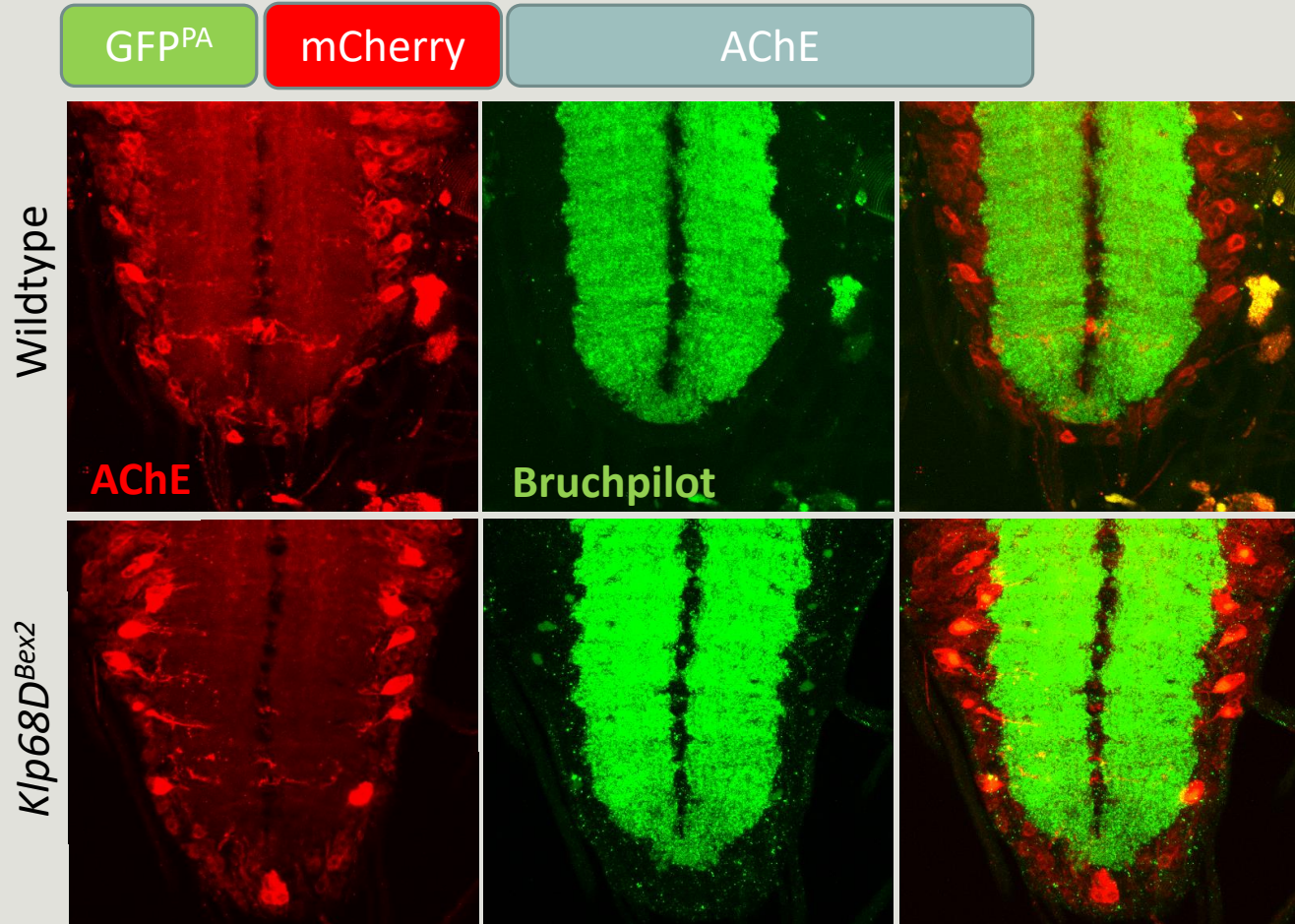
Anuttama Kulkarni

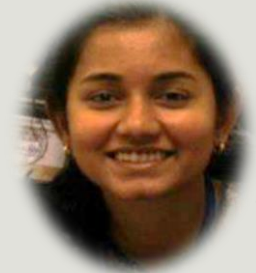
Cell body



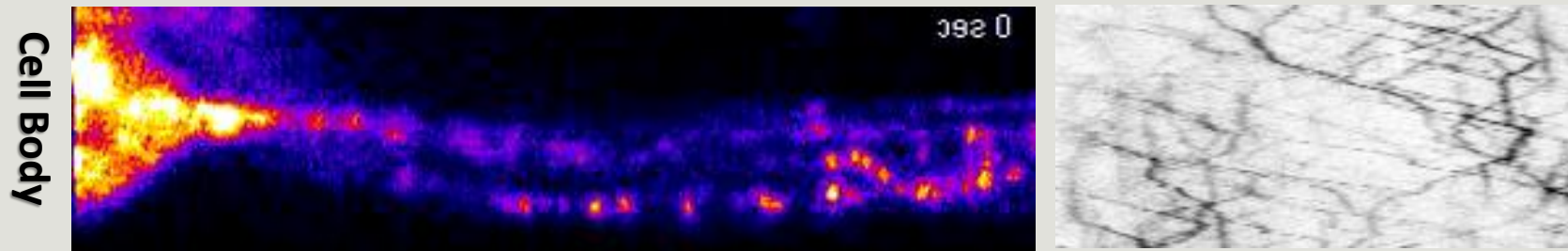
KLP68D (Kinesin-2 β) is necessary for GPAC-AChE localization to the neuropil

chaGal4>GPAC-AChE

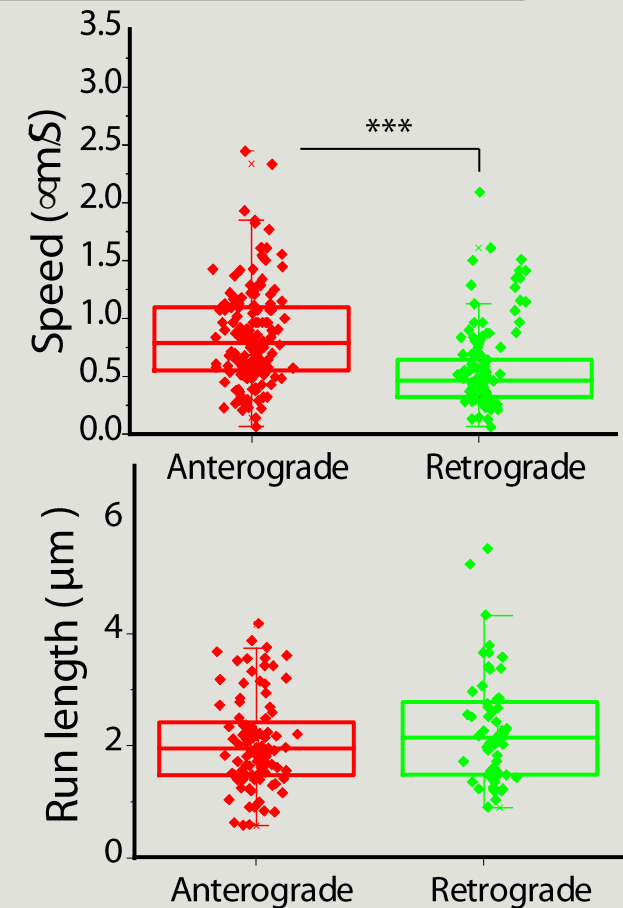
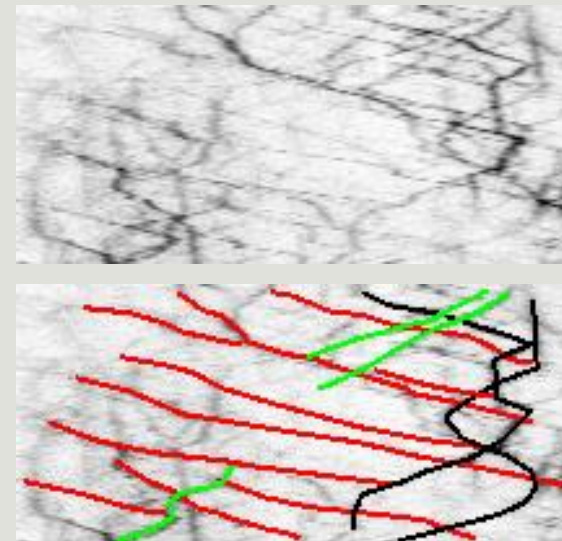
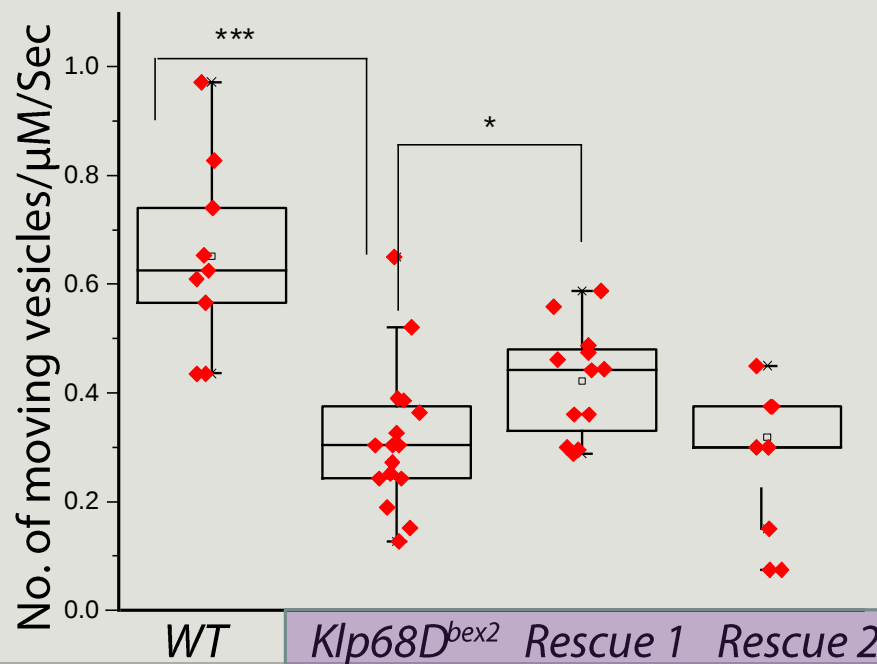
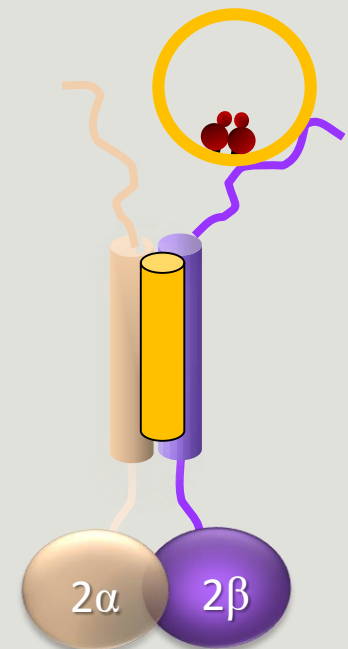




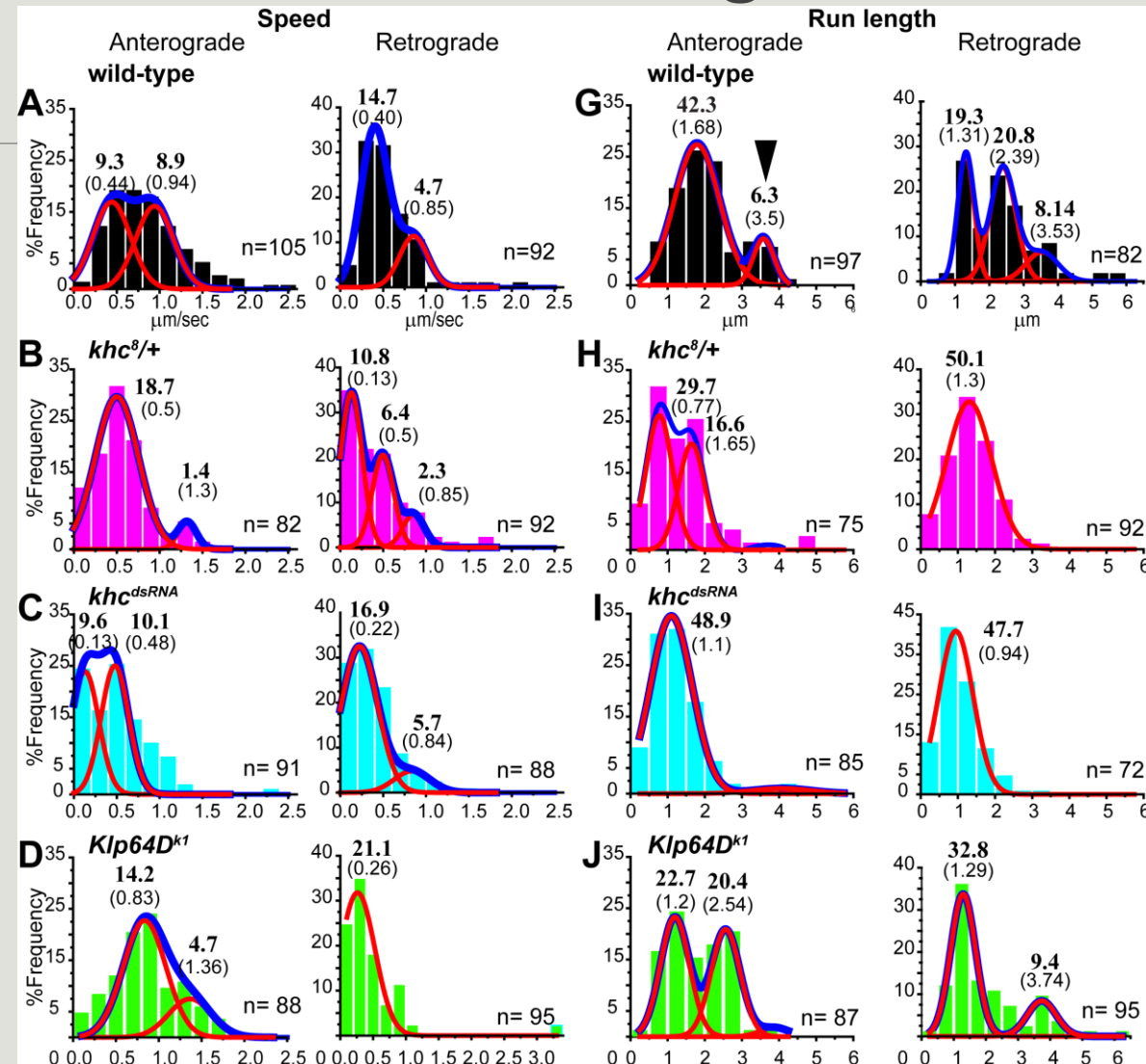
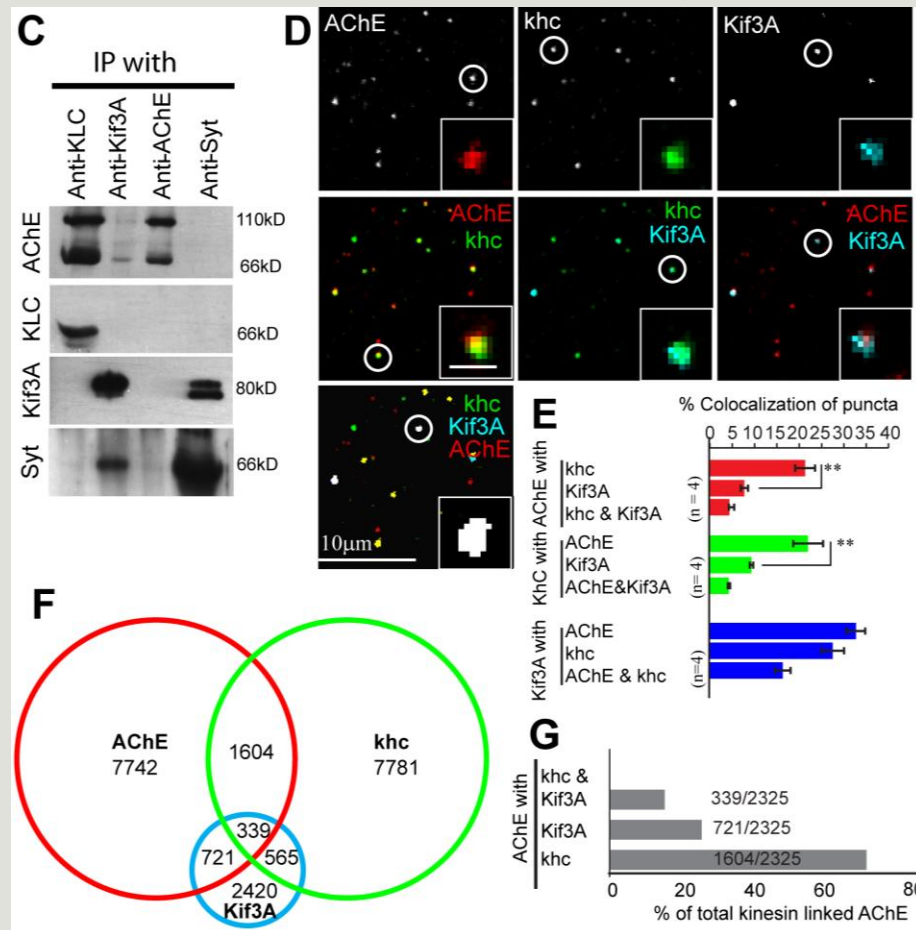
GPAC-AChE transport in the axons



Cell Body



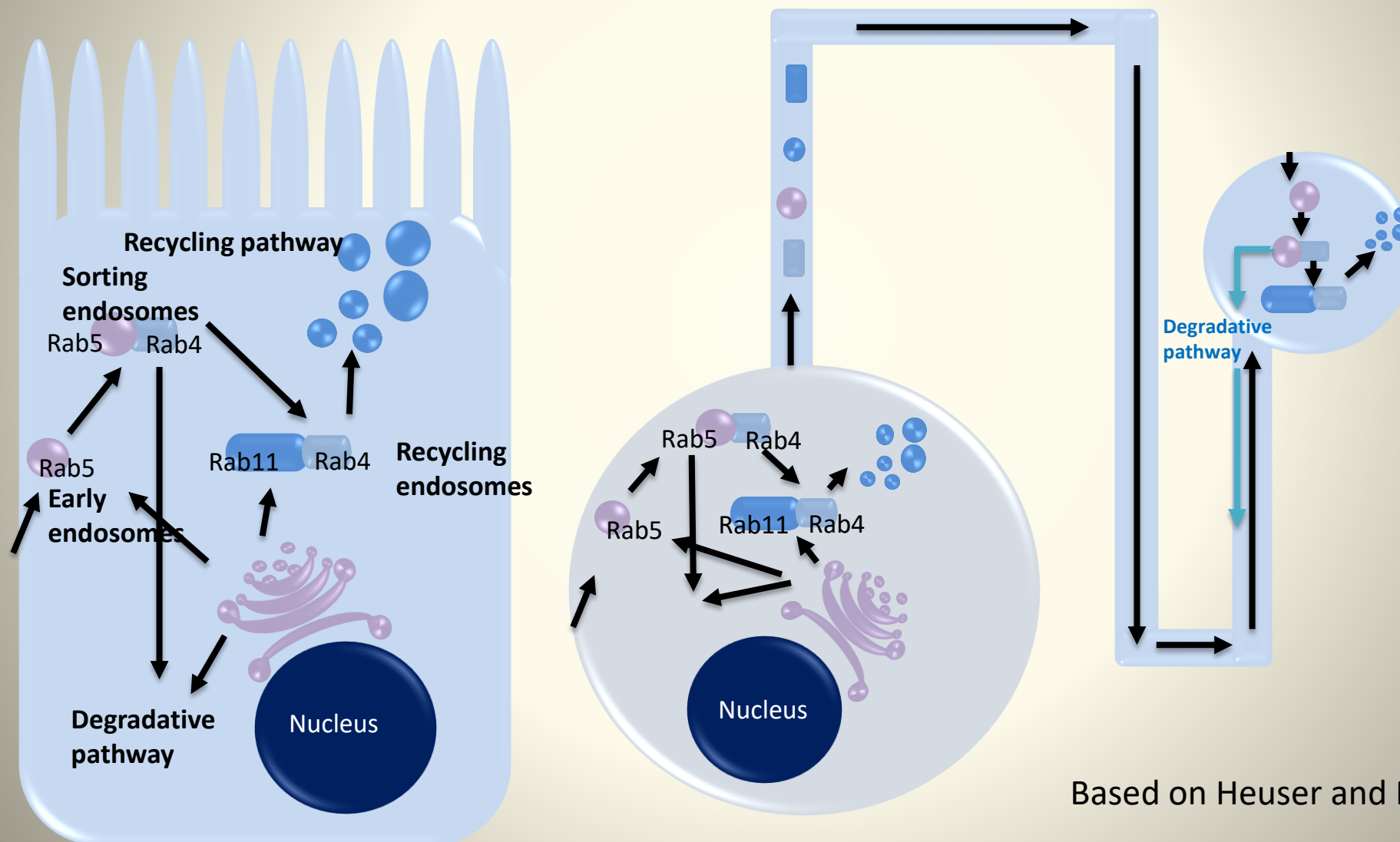
Kinesin-1 and 2 together steer the AChE containing vesicles towards the synapse





Geometry of cells defines localization and trafficking of endosomal sorting machinery

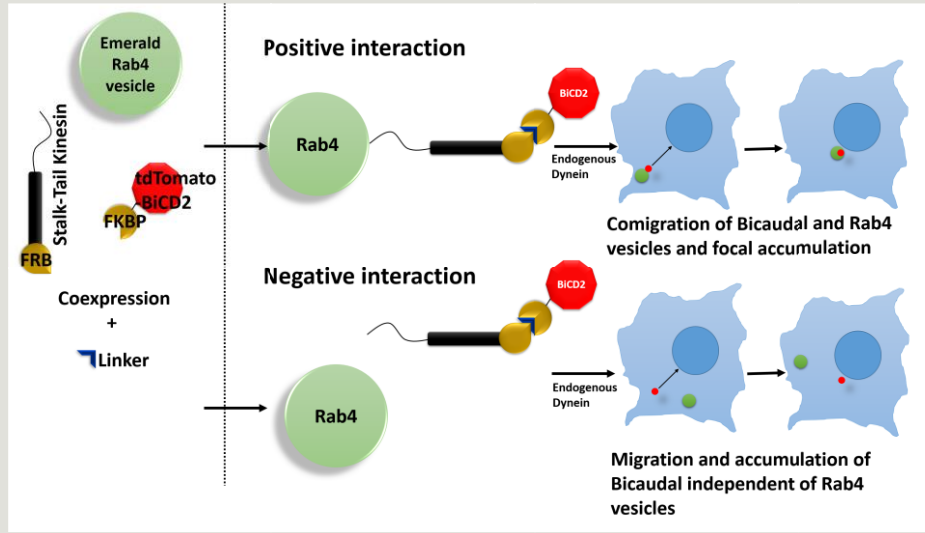
Swagata Dey



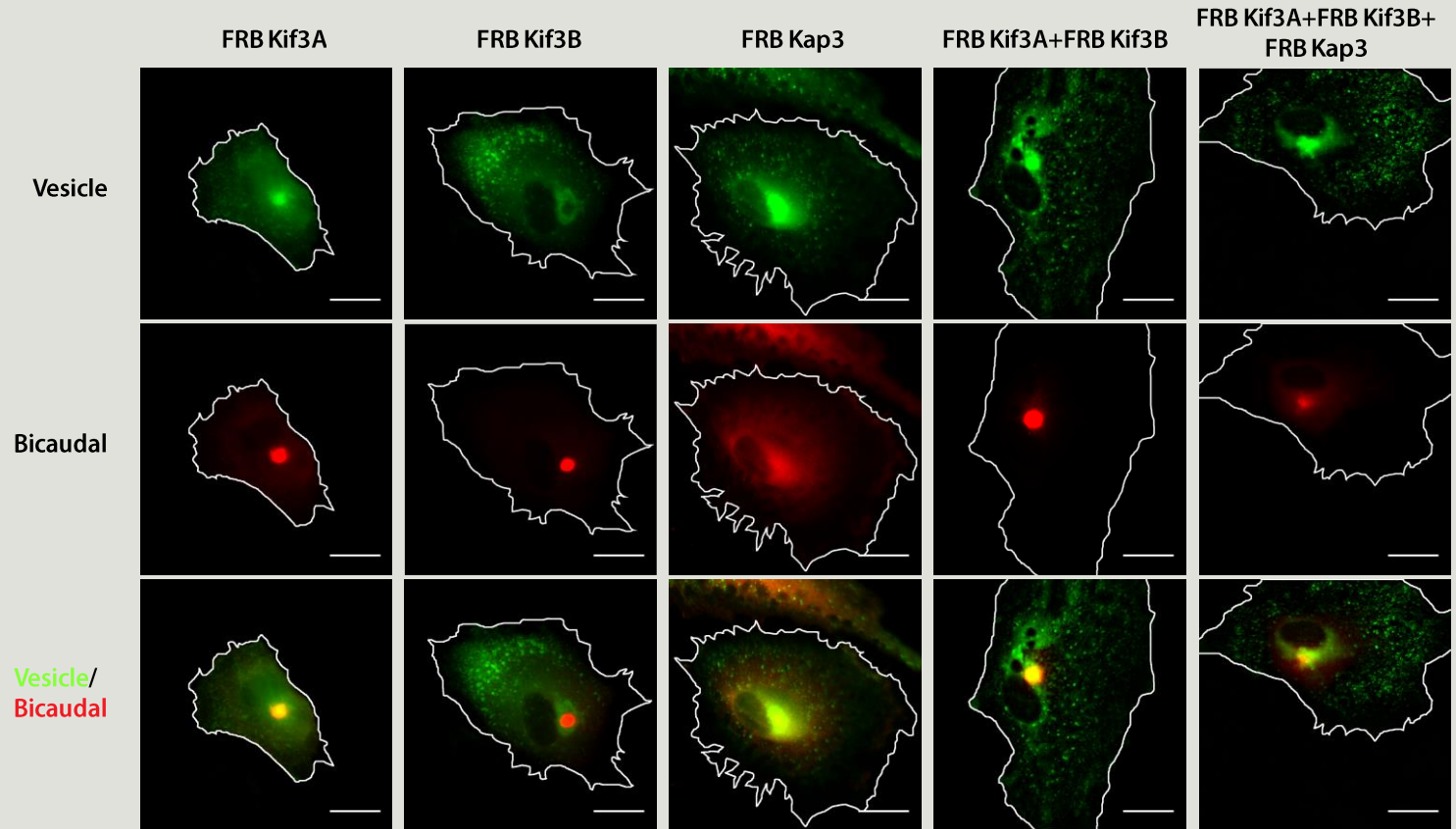
Based on Heuser and Reese, JCB 1973



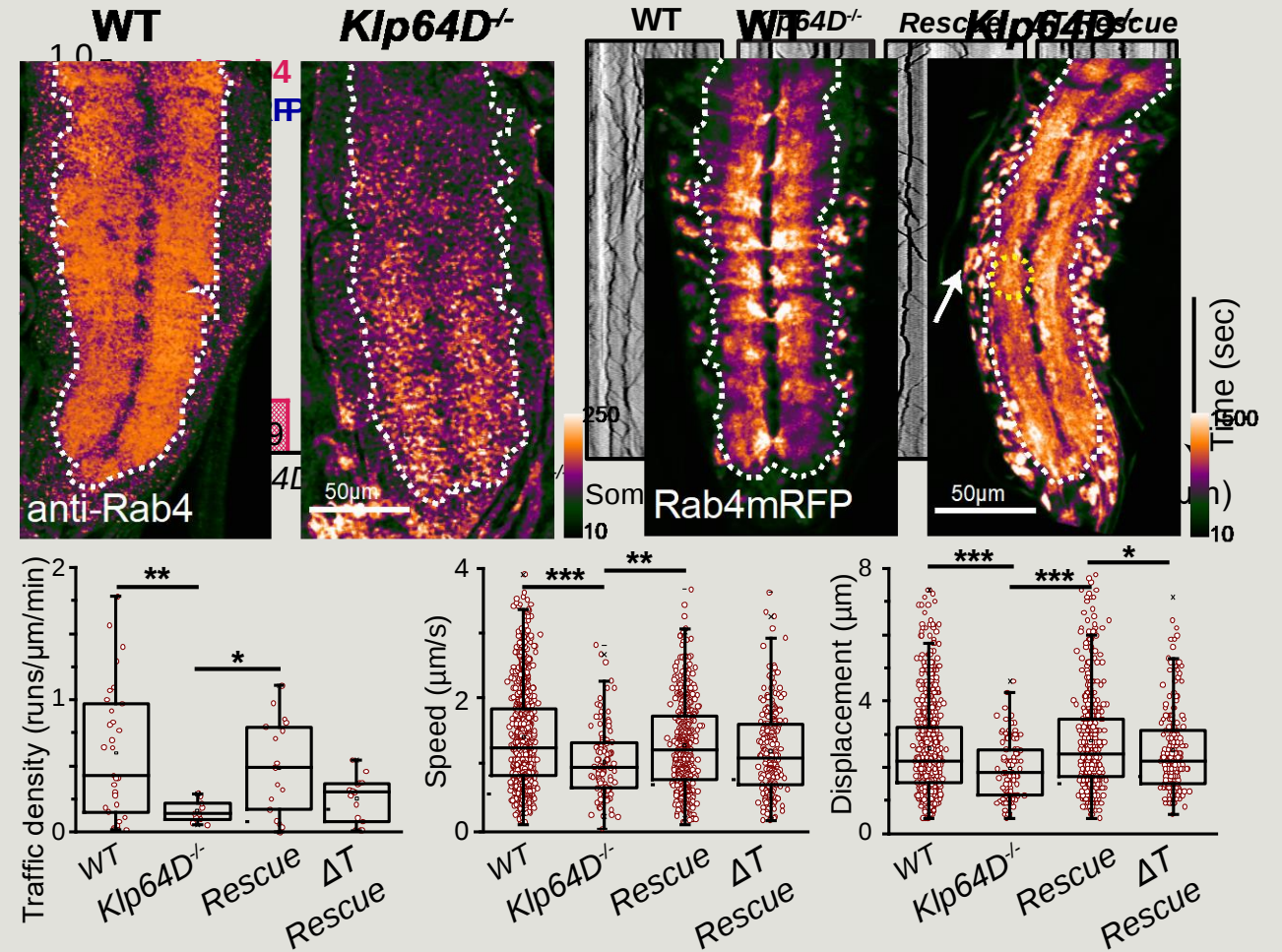
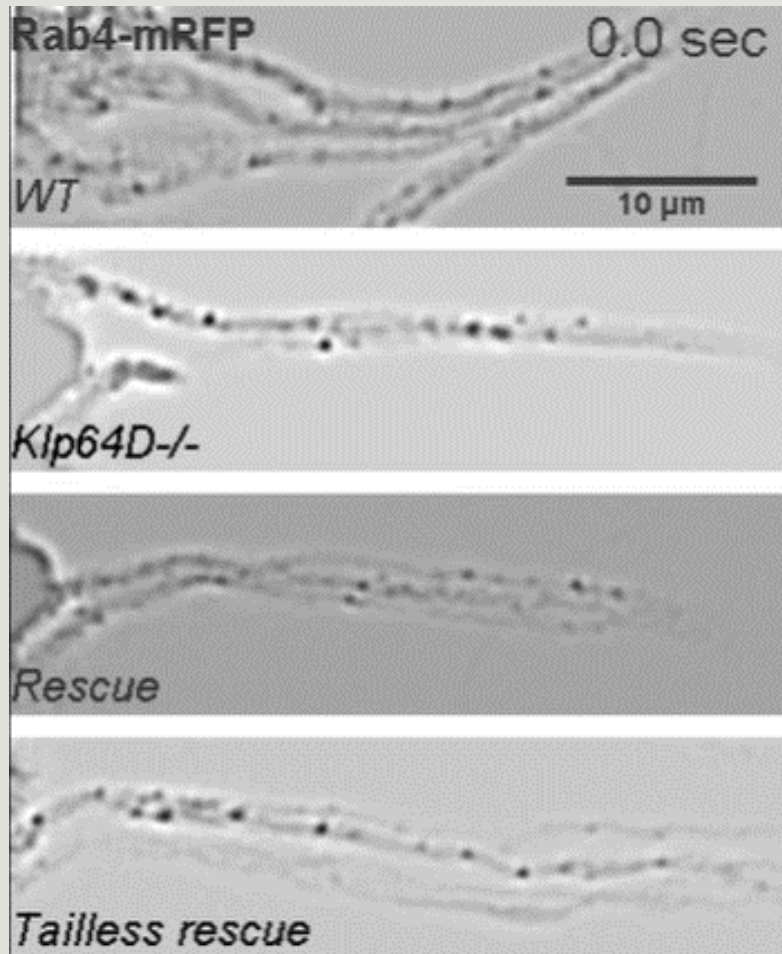
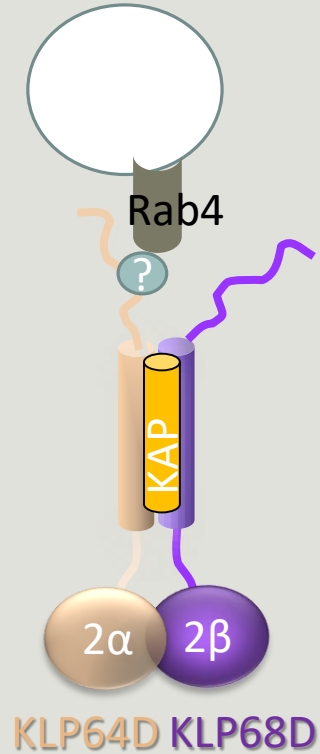
Rab4 binds to the Kinesin-2 α tail and Kif13



Emerald Rab4

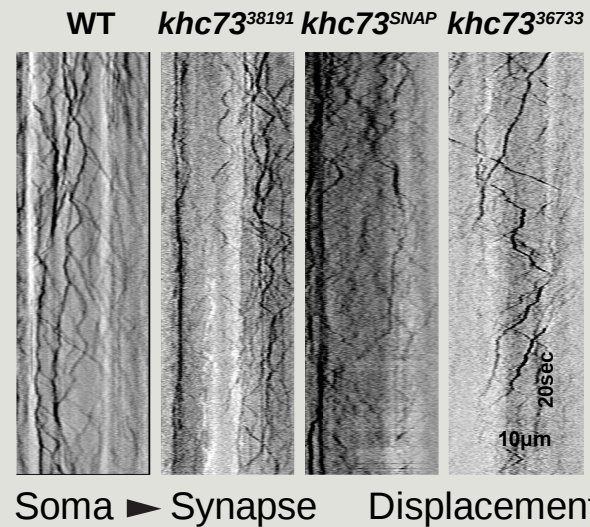
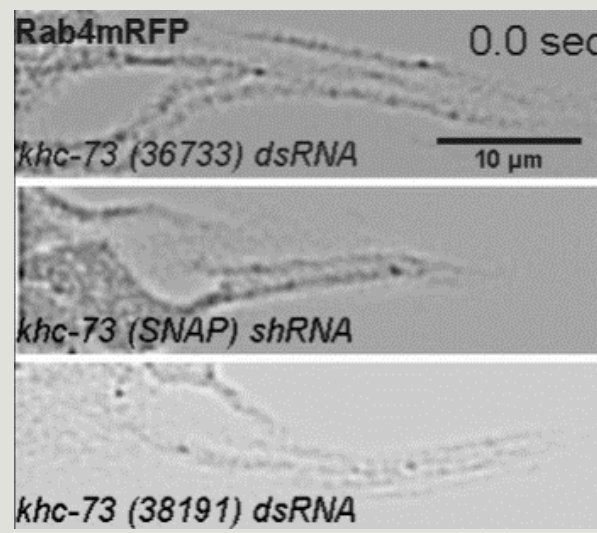
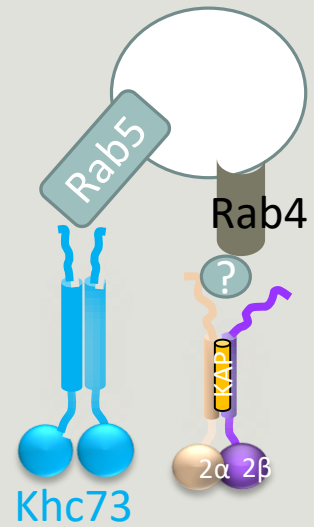
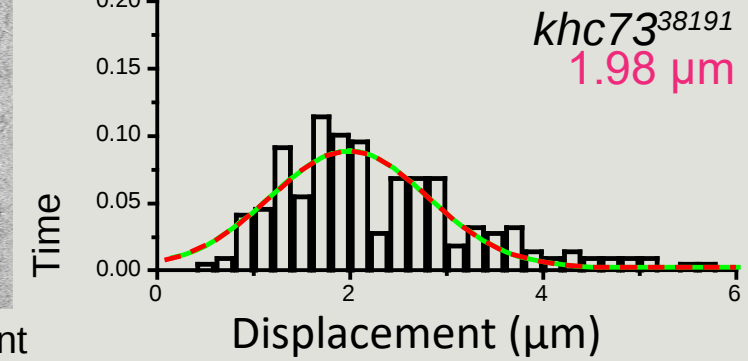
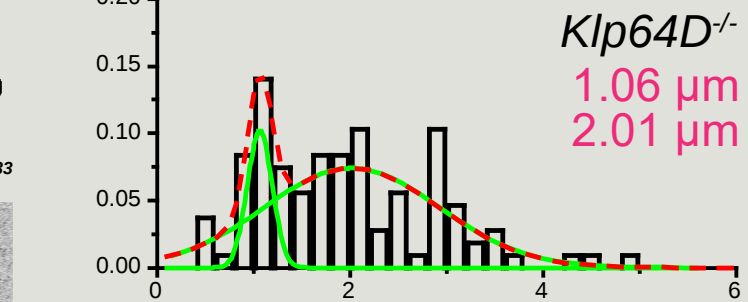
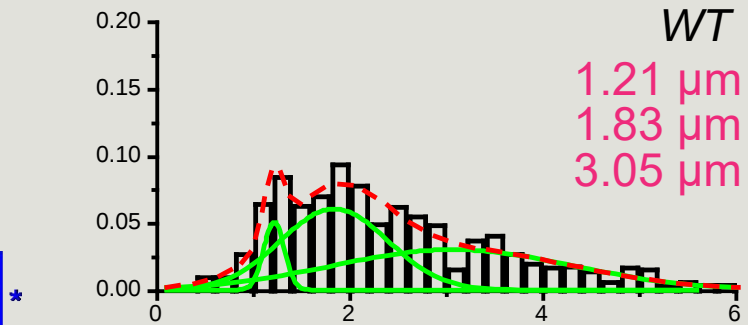
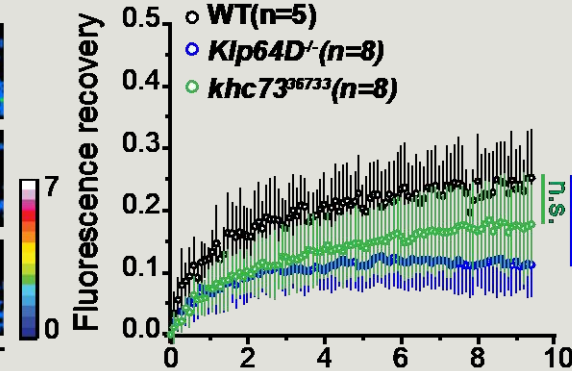
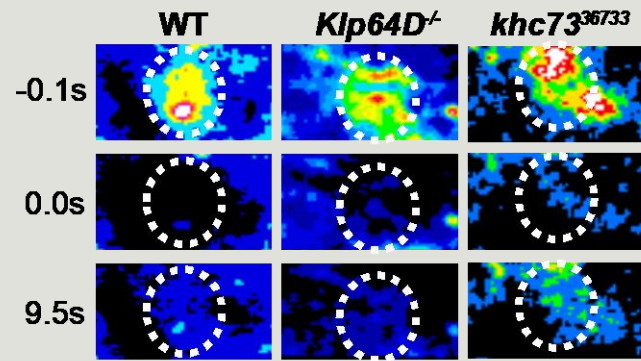
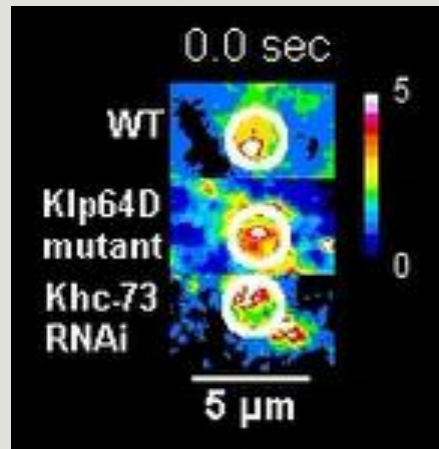


Lack of Kinesin-2 α tail reduces the anterograde bias of Rab4-associated vesicle transport in axons





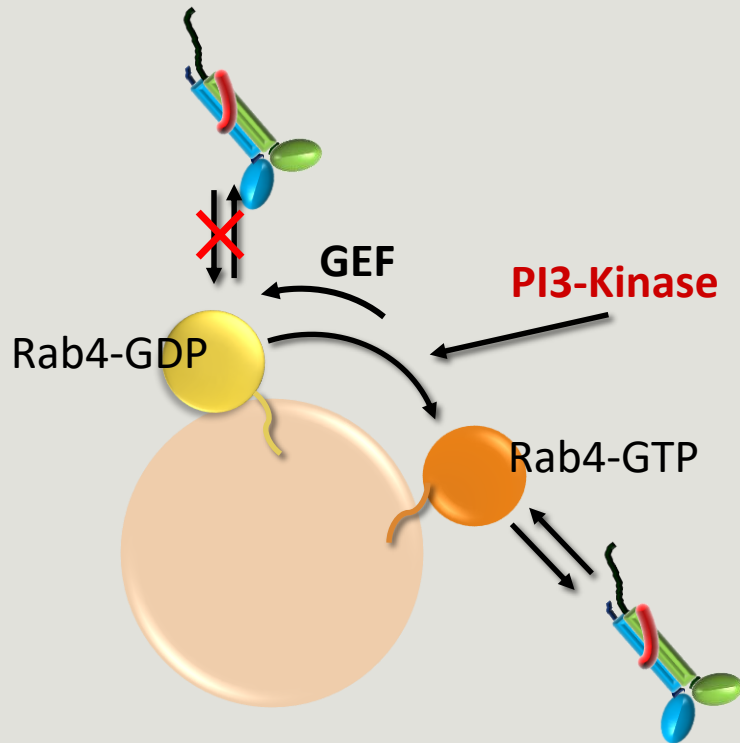
Kinesin-3 orthologue, Khc73, contributes longer runs of Rab4-associated vesicles in axons



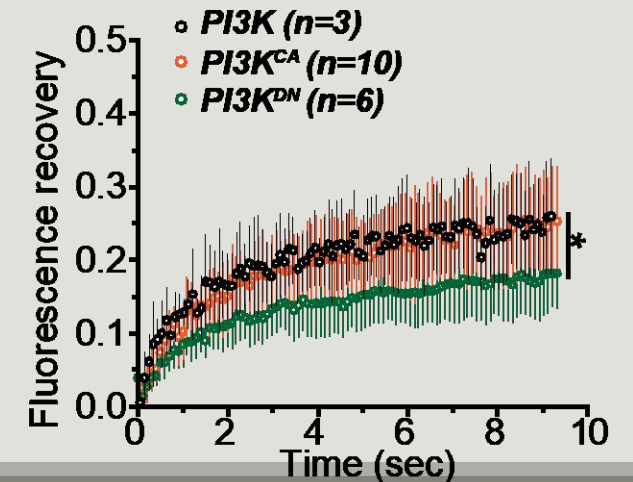
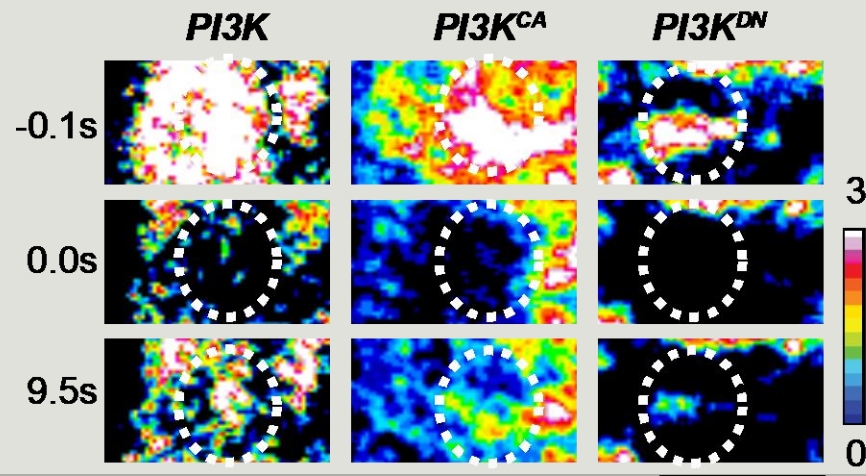
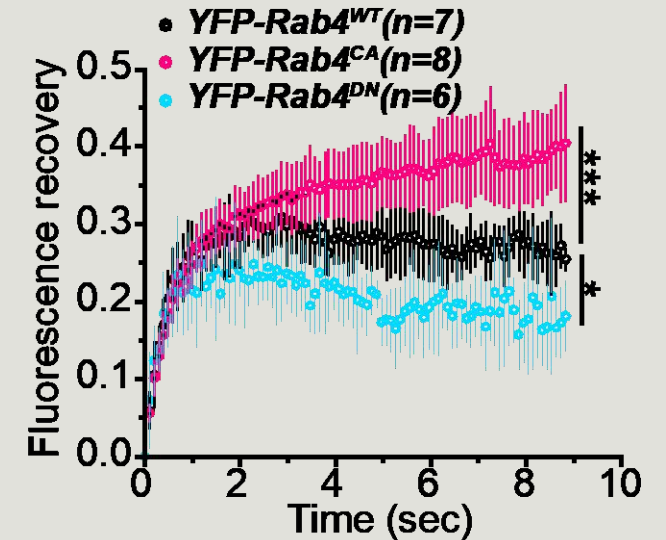
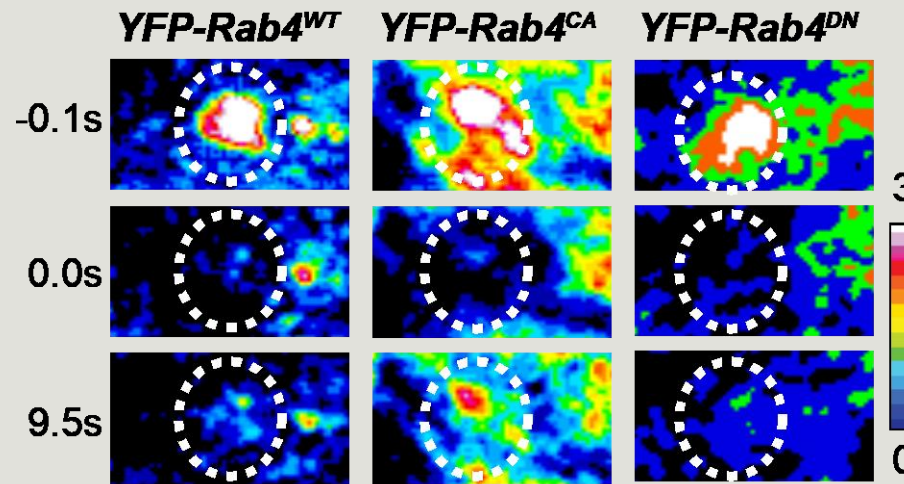


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Rab4 activation induces transport of associated vesicles towards synapse



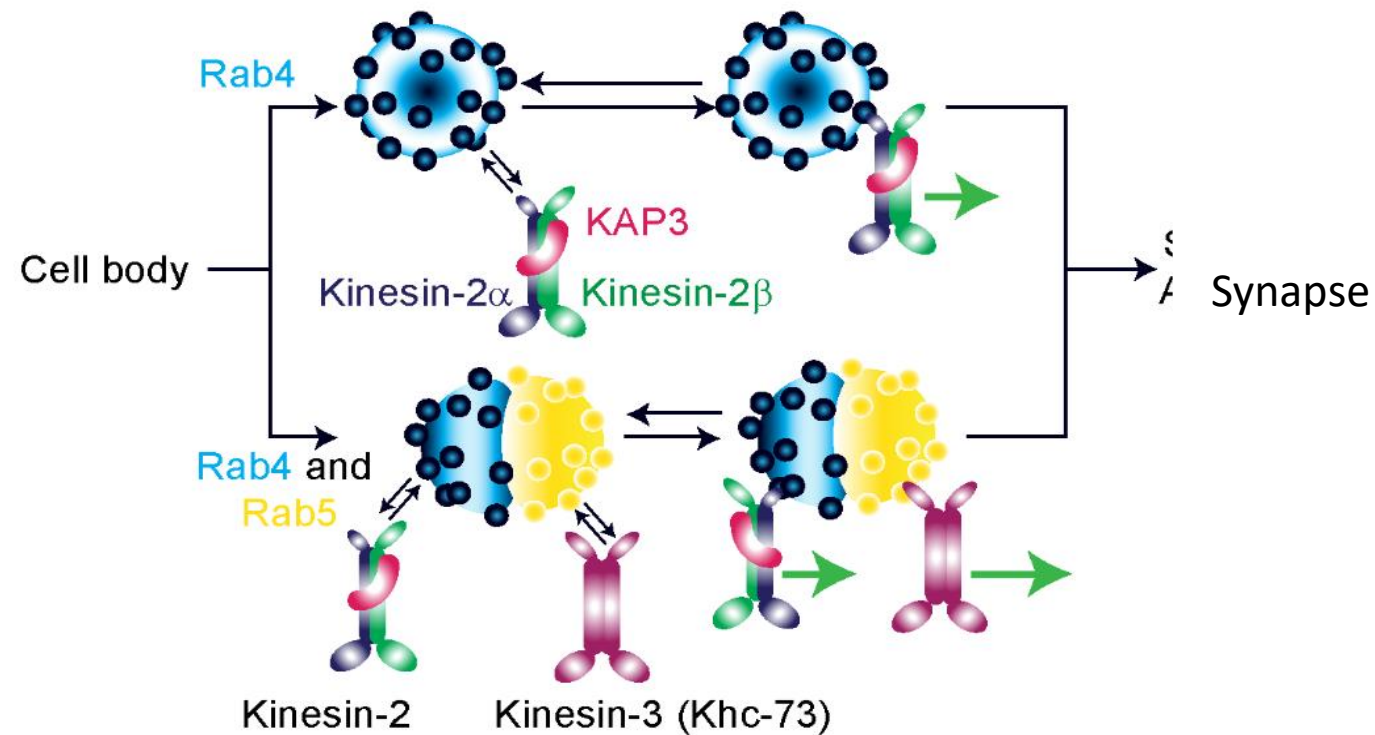
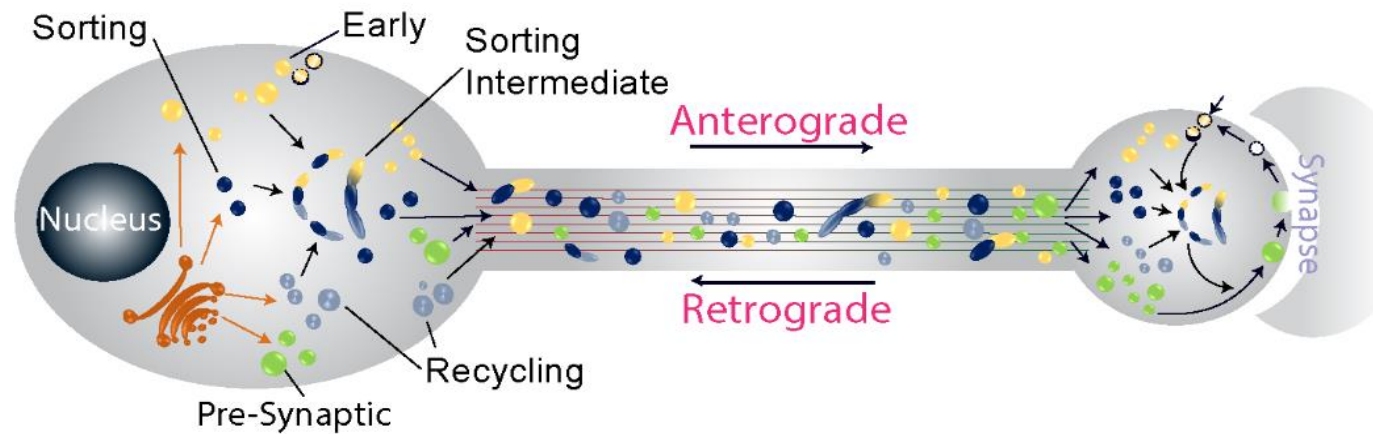
Imamura et.al. 2003, JCS





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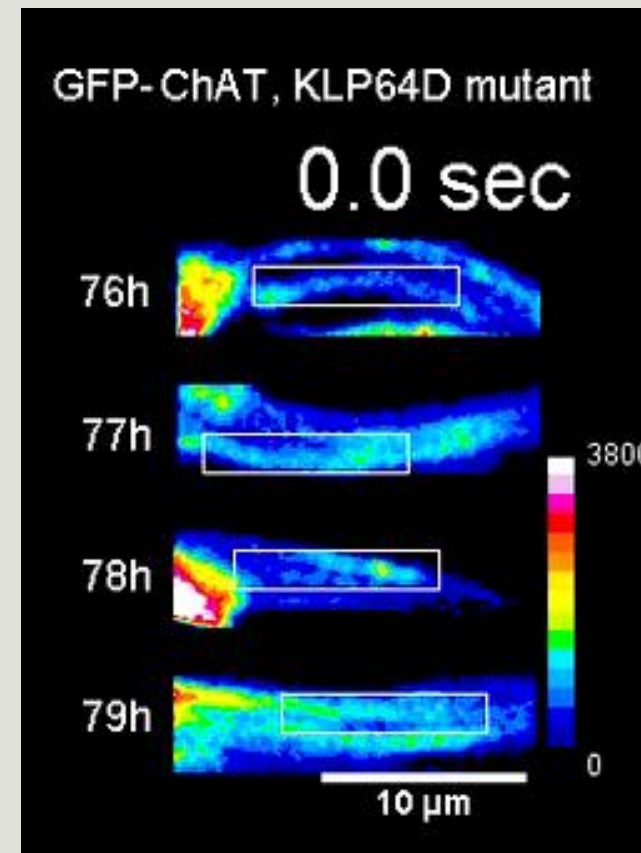
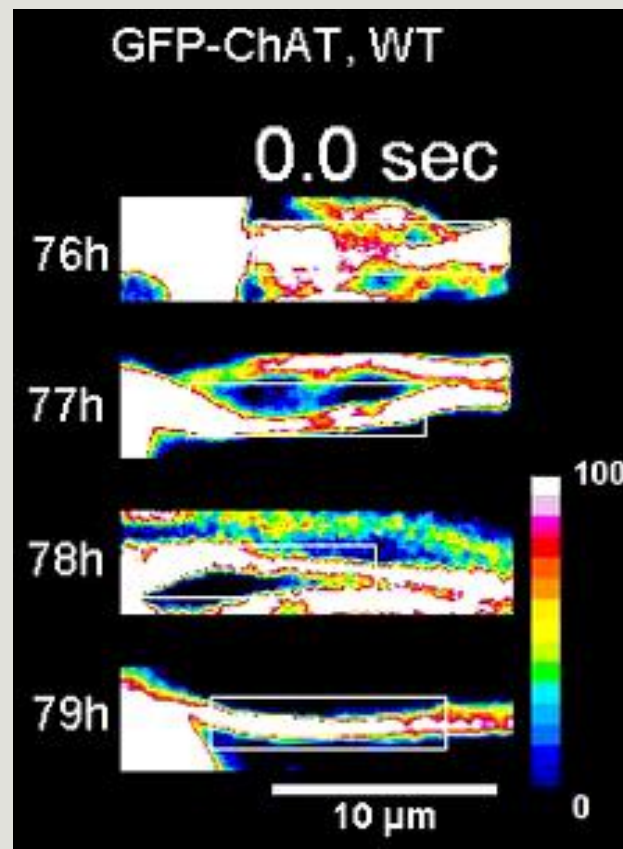
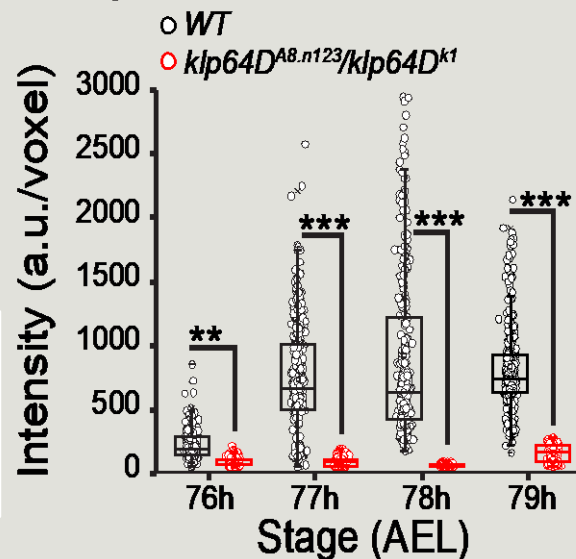
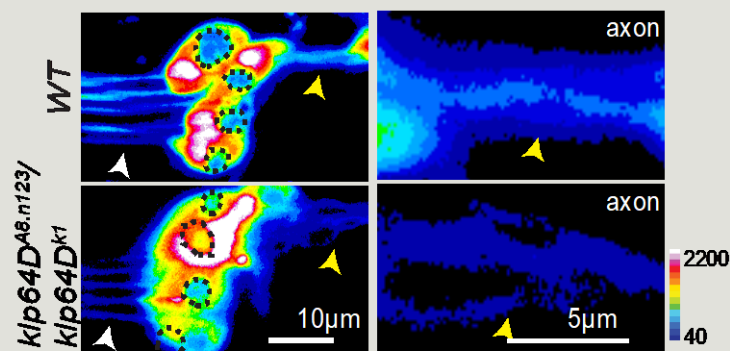
Endosomal Traffic in a Neuron



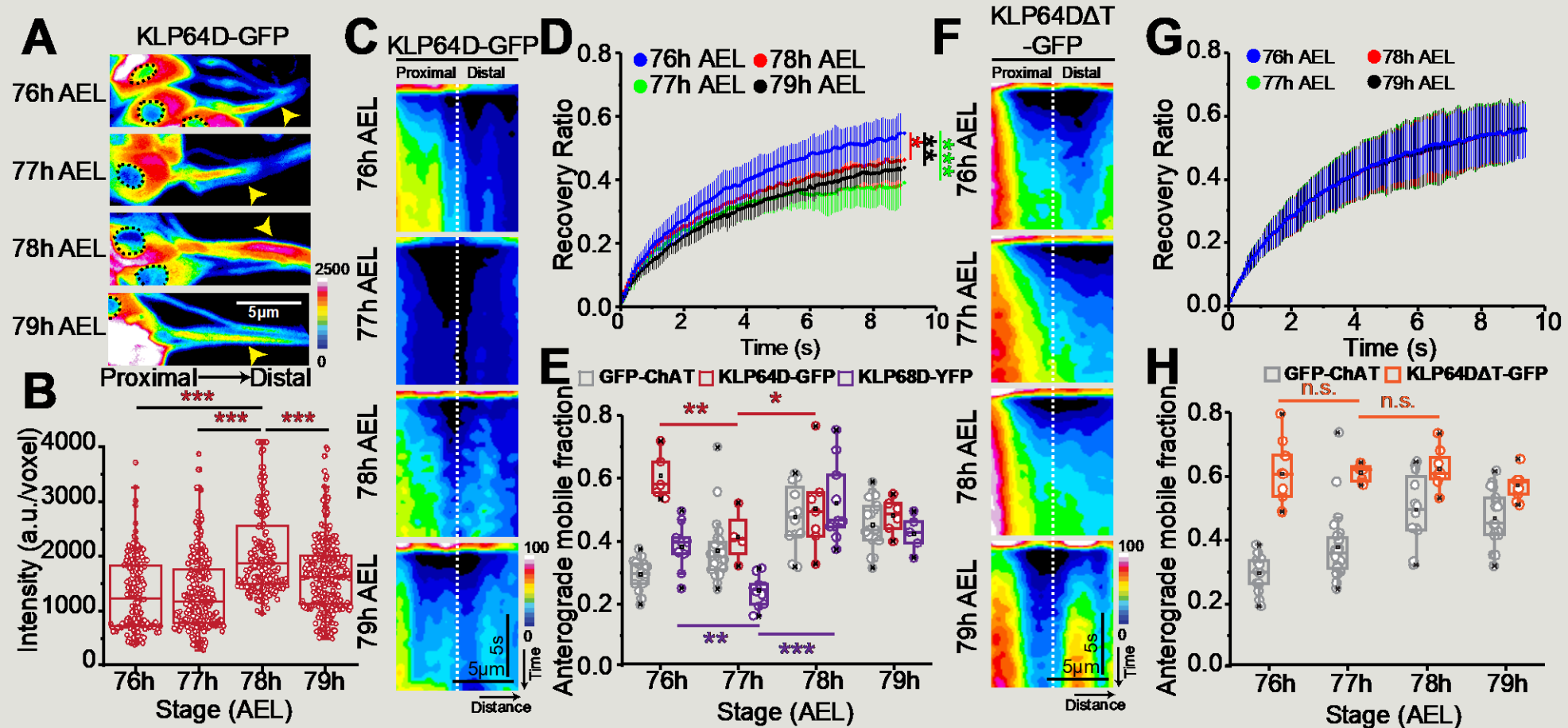


Swagata Dey

Kineisn-2 is also required for the anterograde movement of ChAT in axon



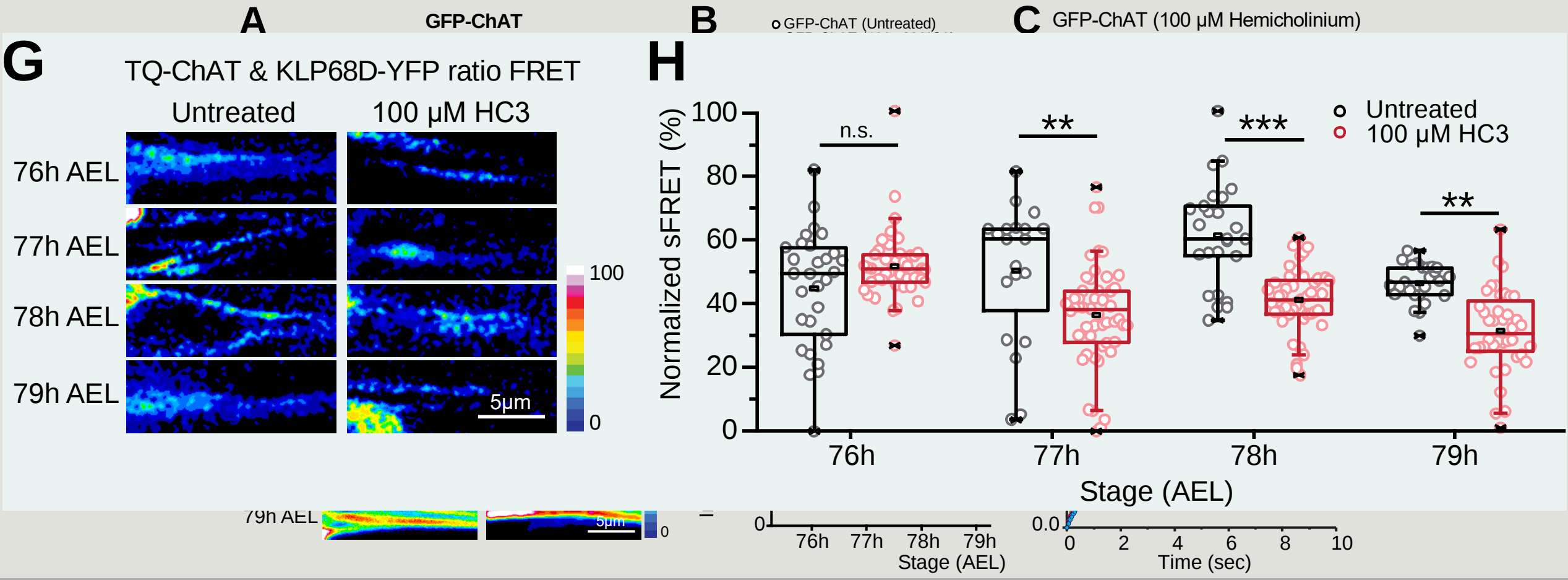
The motor flux in axon also increases in an episodic manner as that of ChAT



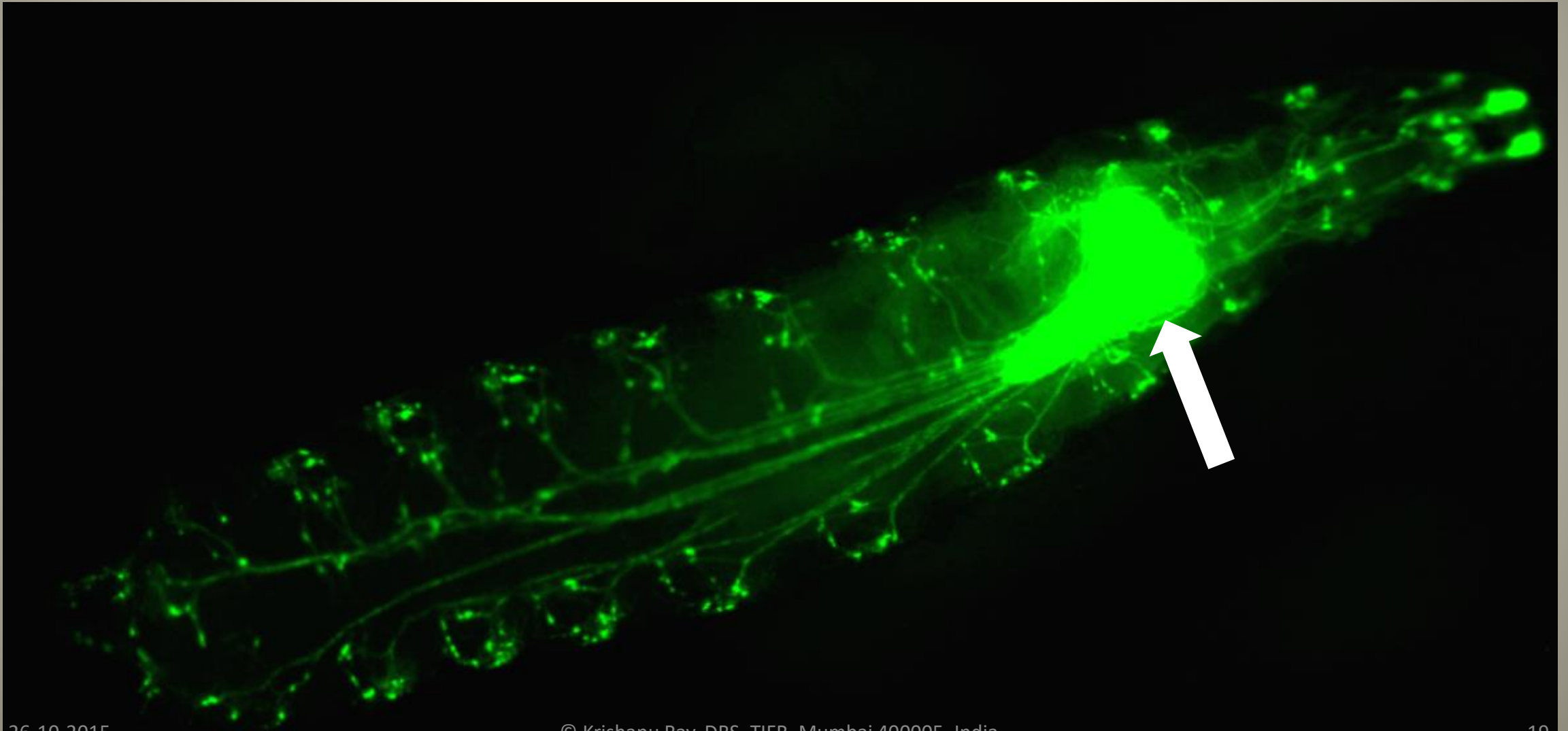


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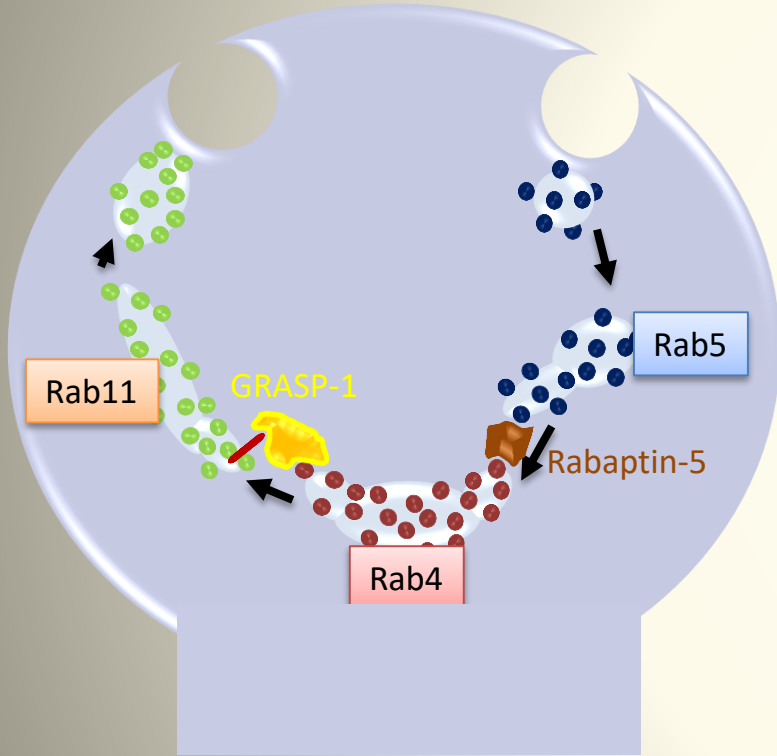
Cholinergic activity regulates episodic flow of ChAT towards the synapse



Cholinergic nervous system of a *Drosophila* larva

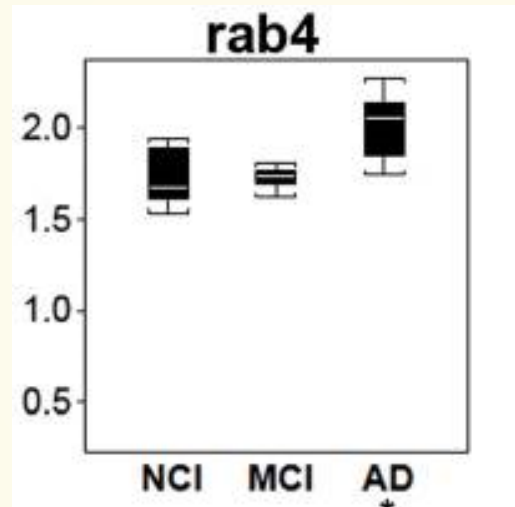


Rab4 balances membrane and cargo in early and recycling endosomes



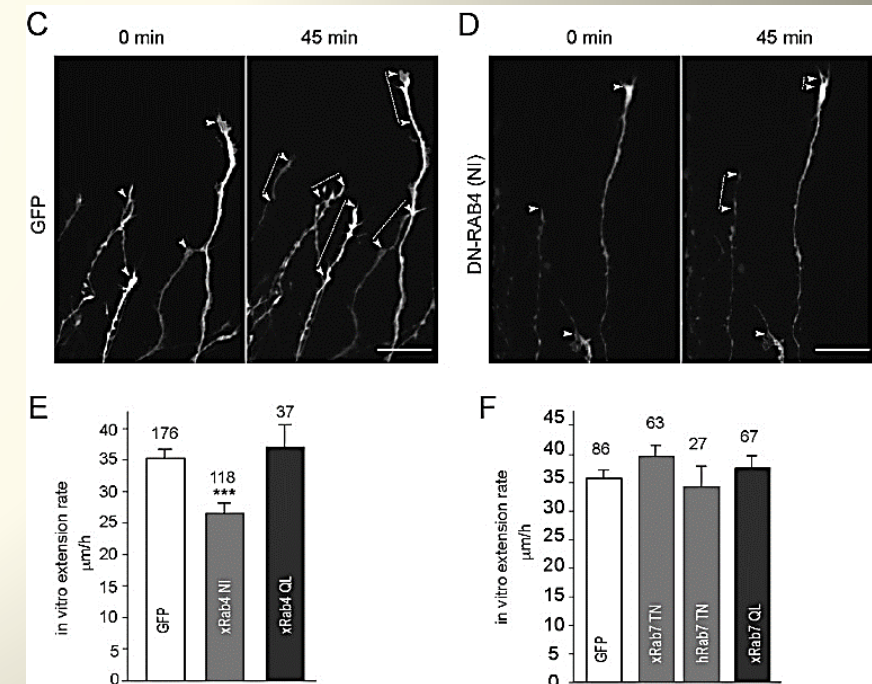
Adapted from:
Hoogenraad et.al. Plos Biol. 2010
Pavlos et.al. Small GTPases 2011

Rab4 overexpression correlated with
Alzheimer's Disease



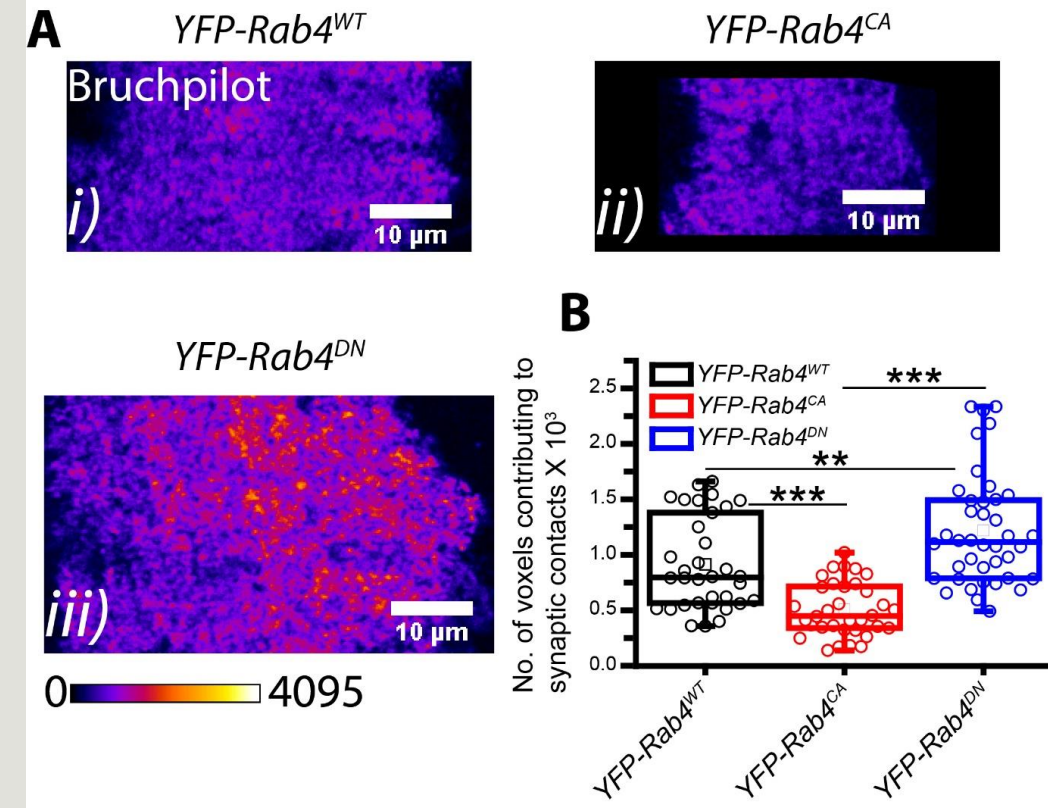
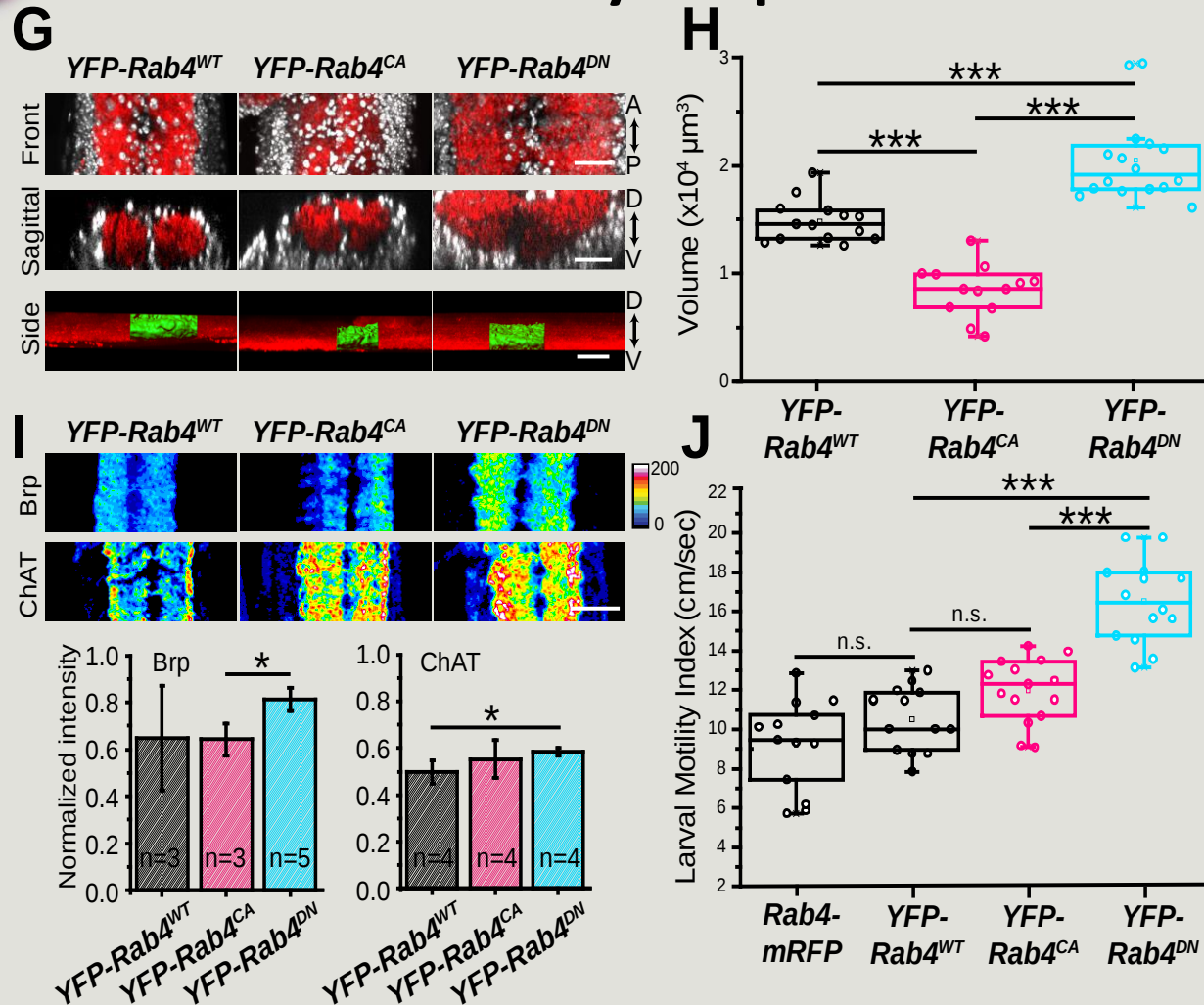
Ginsberg et.al. J. Chem.
Neuroana. 2011

Rab4 is essential for extension of growth cone



Falk et.al. J. Neurosci. 2014

Loss of Rab4-associated vesicle transport in axons enhances synapse assembly



Dipti Rai

Thanks for your patience..😊

Kinesin-2 projects:

- Swagata Dey, Anuttama Kulkarni, Zoheb Ahmed, Dipti Rai, Ayan Barbora, Rajarshi Sil, Pranali Patil and Priya Dutta

Spermatogenesis:

- Pankaj Dubey, Sameer Gupta, Chetanchanda Joshi, Purna Gadre and Tushna Kappor.

Laser Plasma:

- M. Krishnamurthy, DNAP, TIFR

TEM Facility:

- S. Shirolikar and Lalit Borde

Collaborators: Y. Khan (Sophia College), S. Mazumdar (DCS, TIFR), M. Krishnamurthy (DNAP, TIFR), and D. Panda (IIT-B)

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