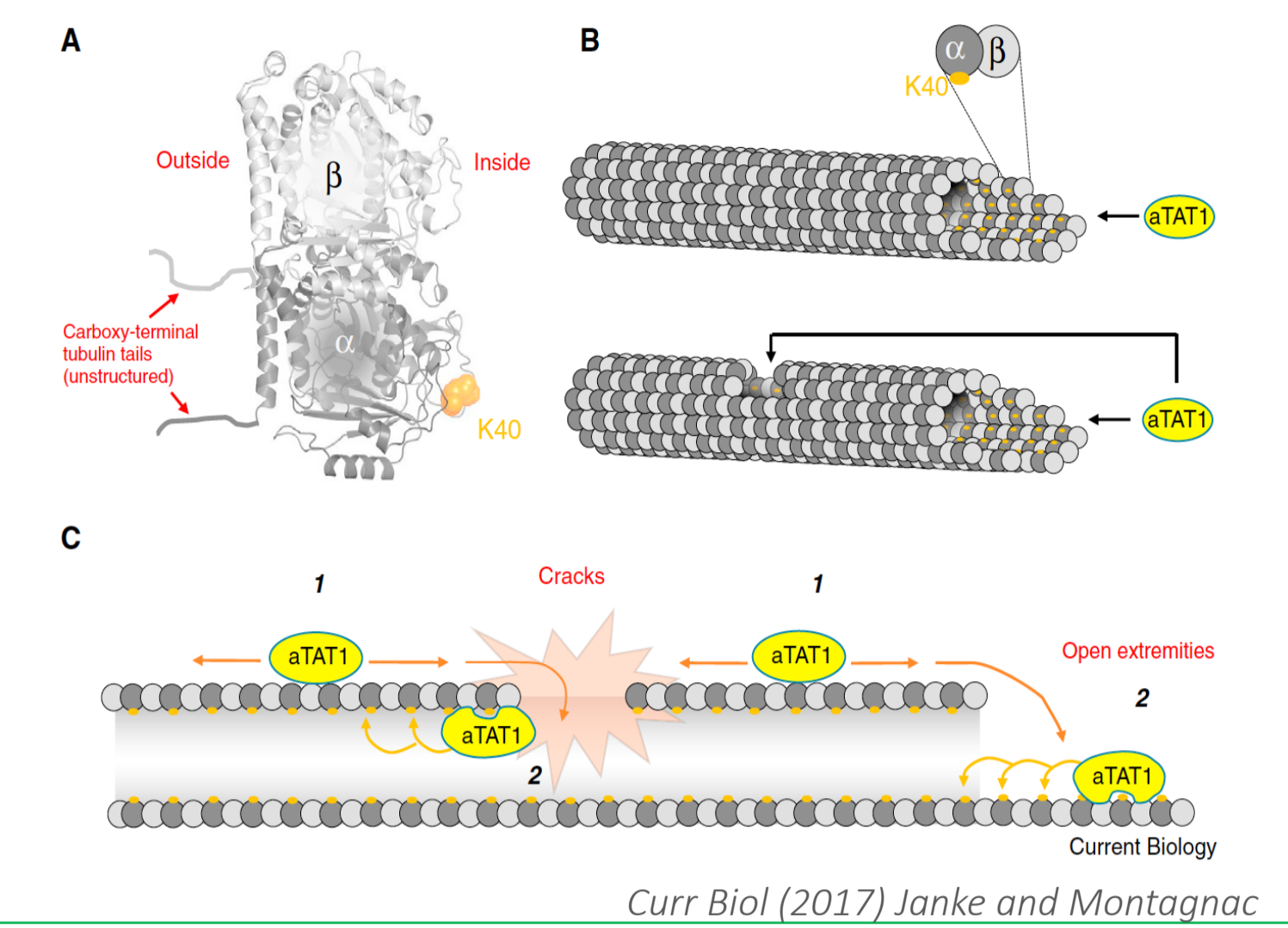


ATAT1-enriched vesicles promote microtubule acetylation via axonal transport

Morelli G¹, Even A², Broix L¹, Turchetto S¹, Weil M², Laurent Nguyen¹

Introduction

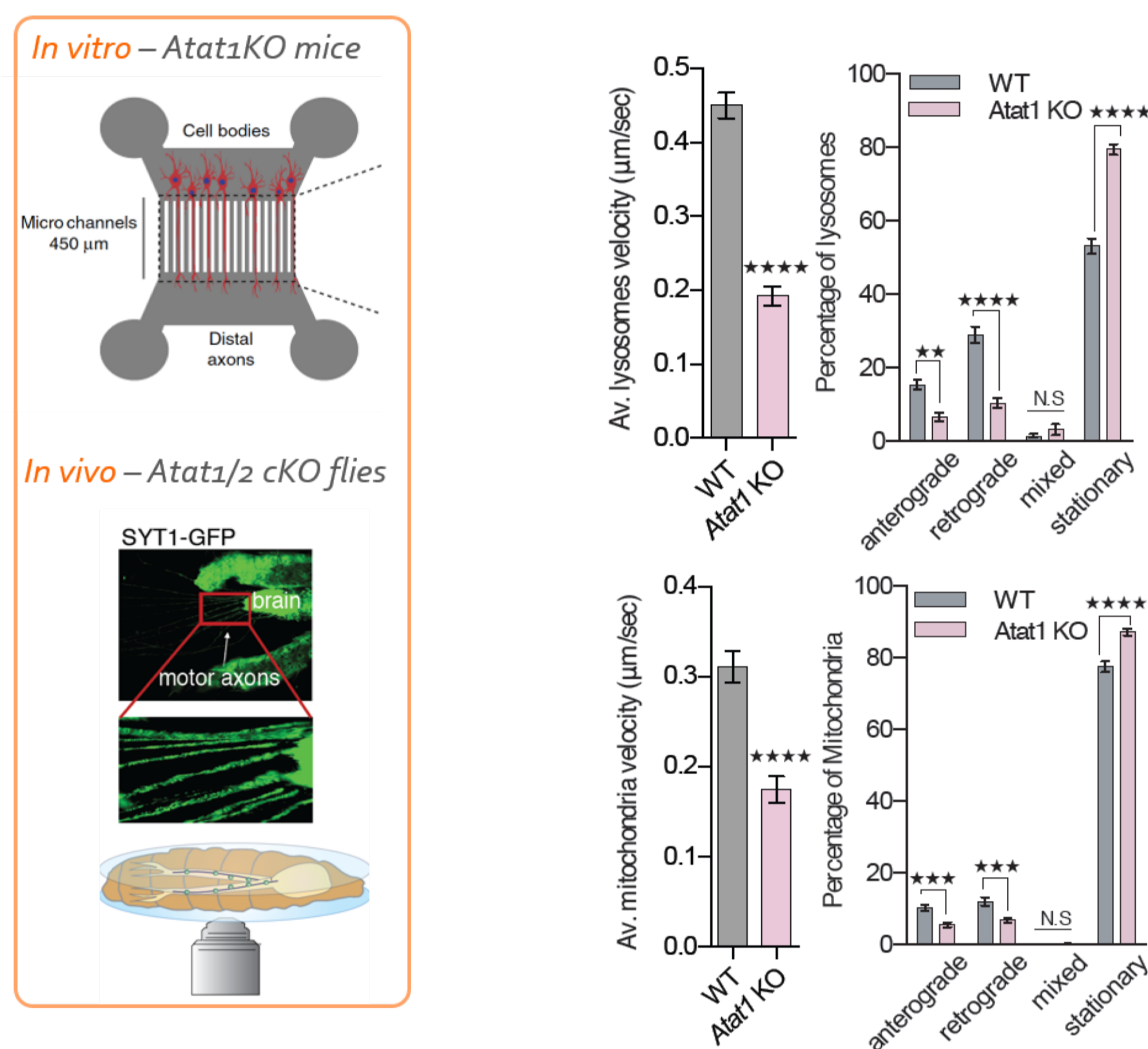
Neurons are polarized cells, structurally and functionally divided into somatodendritic and axonal compartments. Axons are often long and characterized by intense bidirectional microtubule (MT)-dependent transport of cargos to control critical functions, including cell survival and neurotransmission. Post-translational modifications (PTMs) of MTs have been suggested to modulate axonal transport. The acetylation of α -tubulin in MTs is driven by the α -tubulin N-acetyltransferase 1 (ATAT1). Recent *in vitro* experiments performed with recombinant ATAT1 have suggested that it can enter the lumen of MTs from their extremities and/or lateral imperfection and passively diffuses to promote acetylation of α -tubulin K40 residues. However, it remains unclear how ATAT1 reaches and acetylates MTs in living cells. In order to decipher how ATAT1 promotes the MT acetylation in neurons, we combined cell free assays with cellular and molecular analyses of cultured mouse cortical neurons and motoneurons of *Drosophila larva in vivo*.



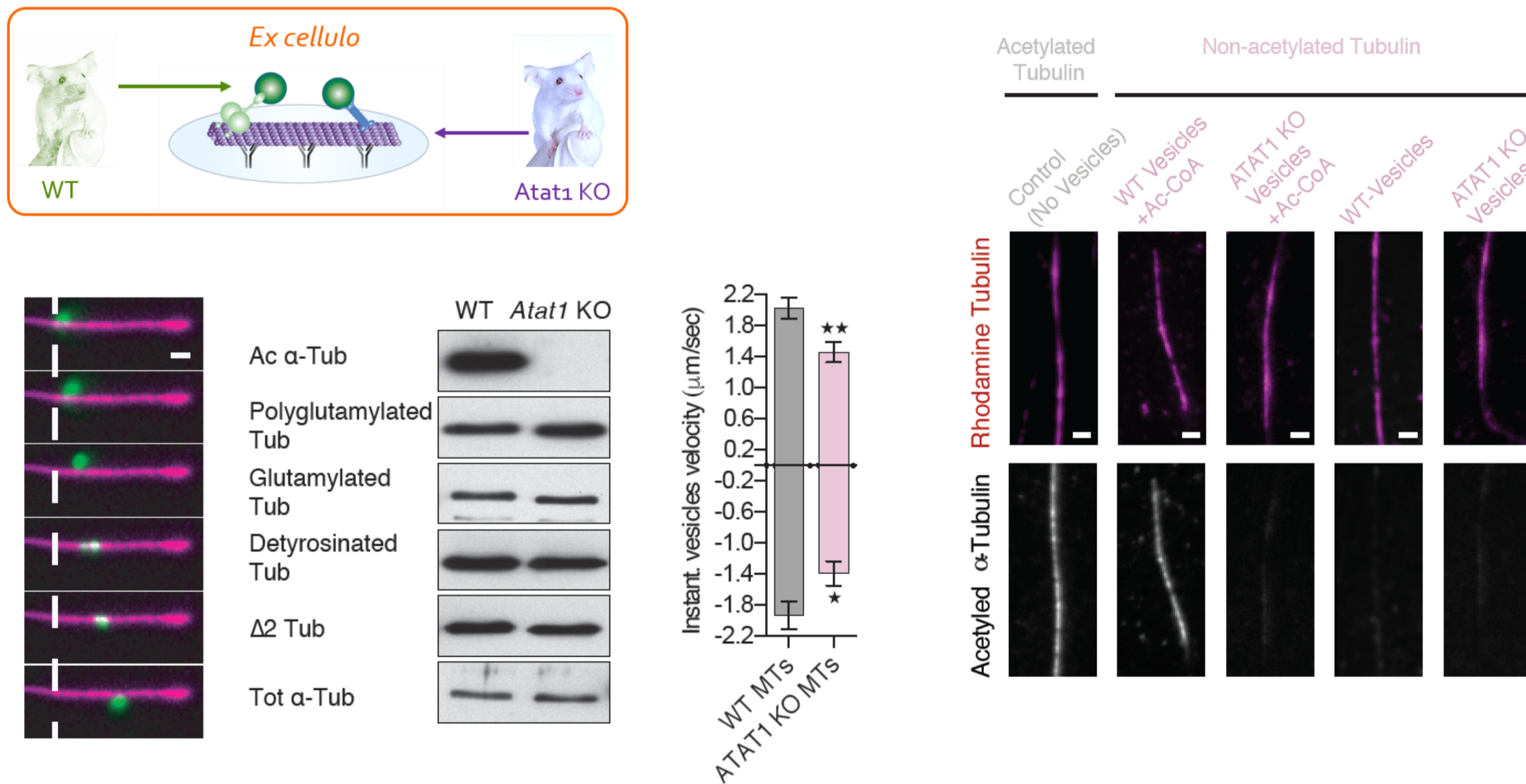
Curr Biol (2017) Janke and Montagnac

Results

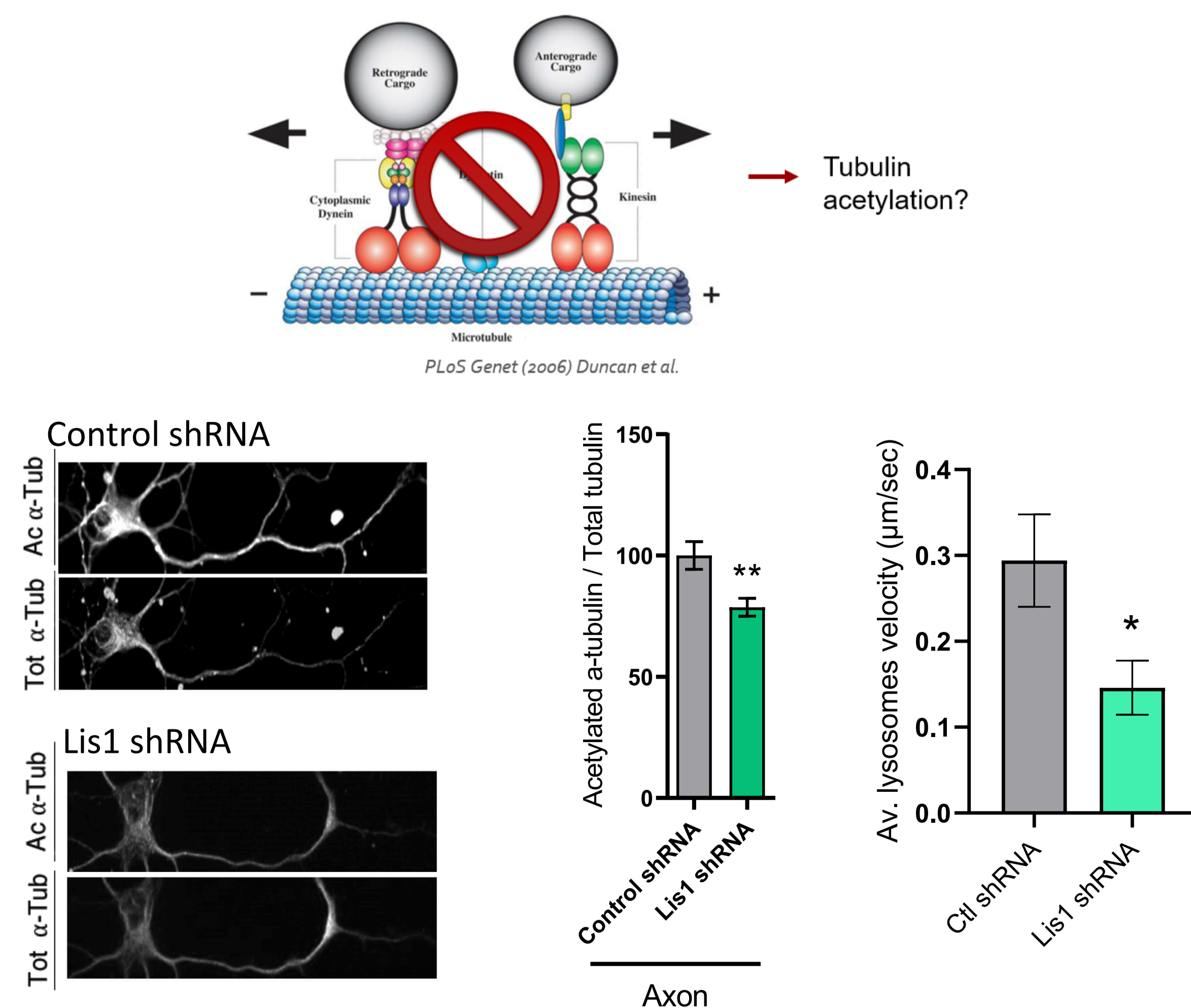
1. DEPLETION OF ATAT1 IMPAIRS AXONAL TRANSPORT OF ORGANELLES IN CORTICAL NEURONS AND MOTONEURONS OF DROSOPHILA



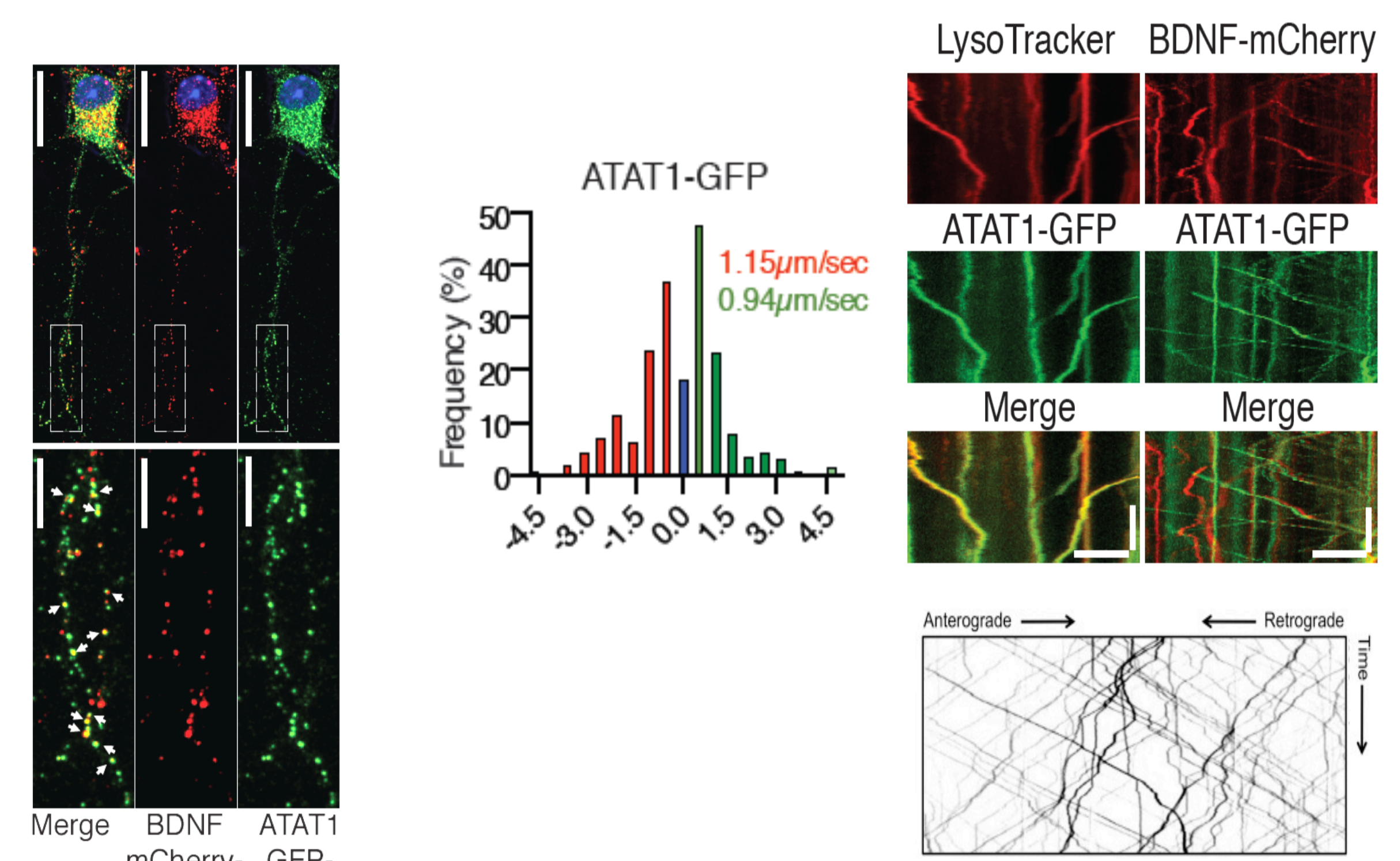
2. MOTILE VESICLES PROMOTE MICROTUBULE ACETYLATION



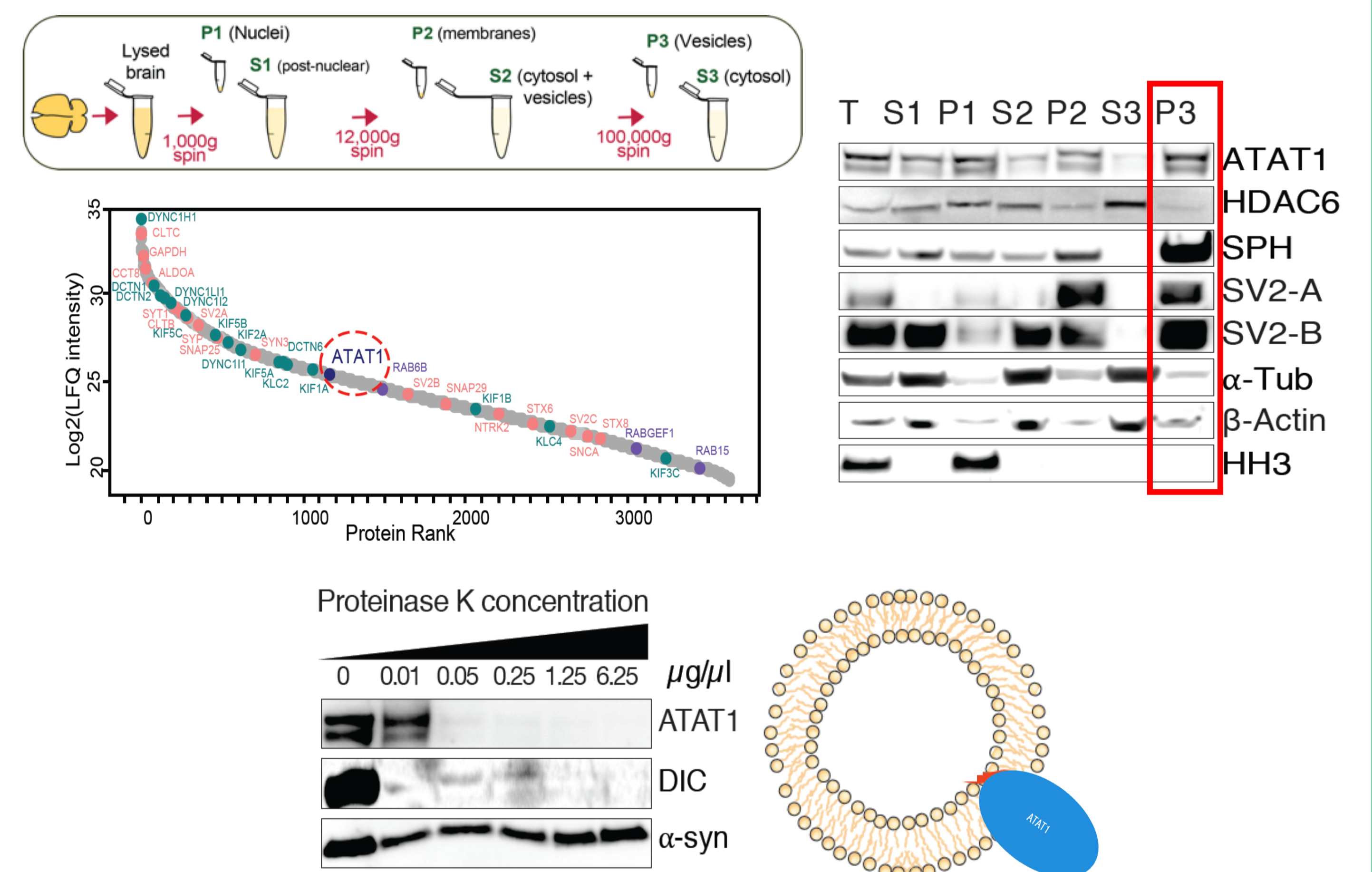
3. BLOCKADE OF MT-DEPENDENT TRANSPORT IMPAIRS TUBULIN ACETYLATION



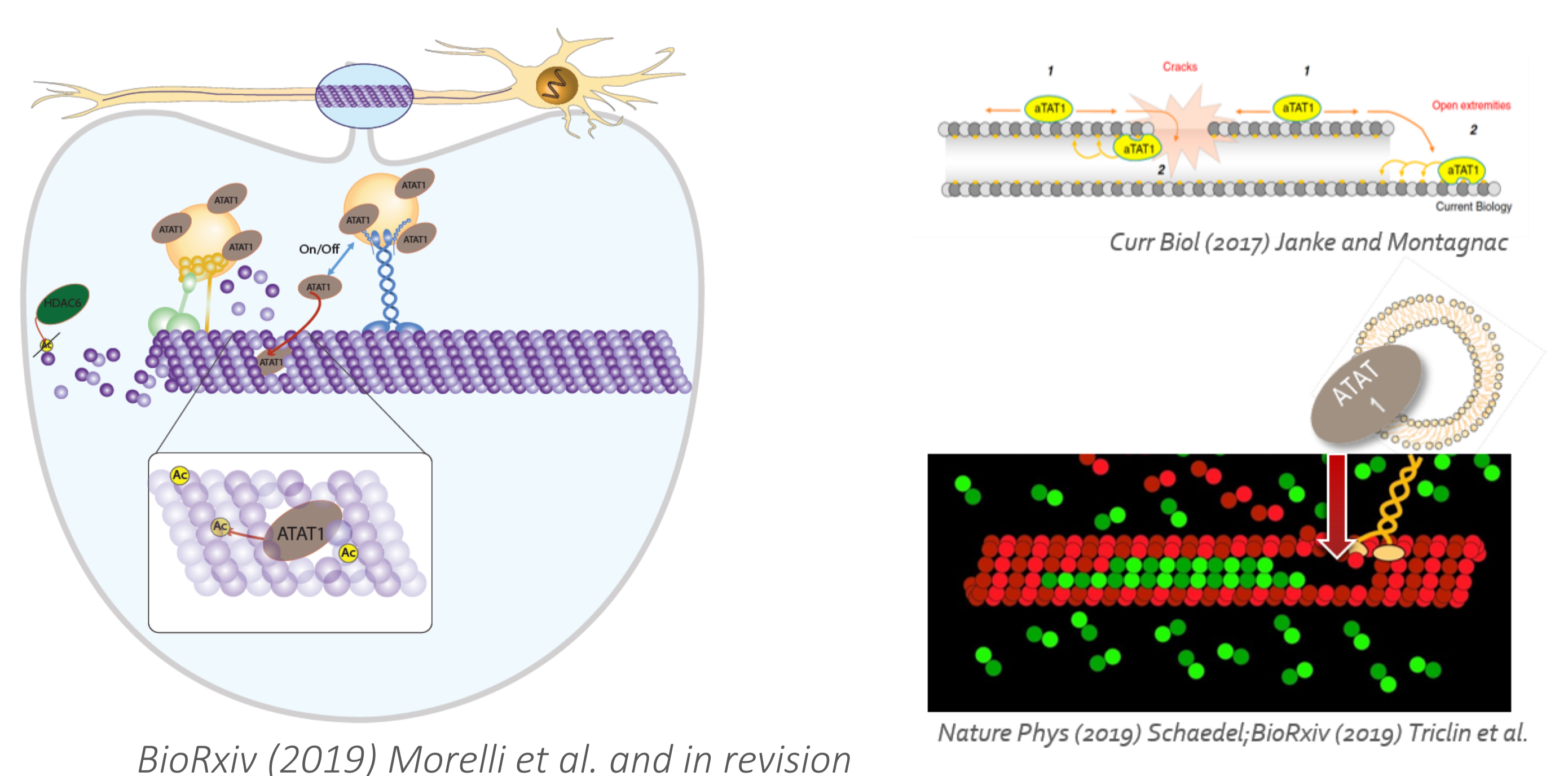
4. VESICULAR ATAT1 IS TRANSPORTED IN AXONS



5. ATAT1 IS ENRICHED AT THE EXTERNAL SURFACE OF MOTILE VESICLES



WORKING MODEL



BioRxiv (2019) Morelli et al. and in revision

Nature Phys (2019) Schaedel; BioRxiv (2019) Triclin et al.

Conclusions

Our work unveils the existence of a predominant pool of ATAT1 at the cytosolic side of motile vesicles, whose active transport promotes acetylation of α -tubulin in MTs. Therefore, we propose that the transport of ATAT1-enriched vesicles is the main driver of axonal MT acetylation.