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### Poster Abstract

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#### **Rab3GAP-Rab18 module: a novel regulator of autolysosome maturation**

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Autophagy is an evolutionarily conserved lysosomal degradation pathway in eukaryotes. During this process, dispensable or aberrant organelles are sequestered into double-membrane vesicles, called autophagosomes that eventually fuse with lysosomes. Inside the newly formed autolysosomal lumen, the cargo is degraded and the resulting monomers are subsequently recycled. Thus, this process is essential for cellular homeostasis and autophagy dysfunction is linked to several diseases such as neurodegeneration, cancer and aging. Autophagosome-lysosome fusion is a key step of autophagy, however our knowledge about its genetic regulation is still limited. During the autophagic process, the cellular endomembrane system undergoes extensive transformation. Small GTPases of the Rab protein family are major regulators of membrane dynamics. The nucleotide bound state of Rab proteins is dependent of several cofactors, including the activator GEFs (guanine nucleotide exchange factor) and inactivator GAPs (GTPase-activating protein). Our research focuses on the Rab3GAP2 protein that forms a heterodimeric complex with Rab3GAP1. Rab3GAP1/2 complex is multi-modal Rab cofactor as on one hand it can function as a GAP for Rab3, but on the other, it can also act as a GEF for Rab18. In our study using *Drosophila melanogaster*, we found that the loss of Rab3GAP2 inhibits autophagic degradation. In addition, we showed that loss of Rab3GAP2 leads to the severe alteration of lysosome morphology and function leading to autophagosome accumulation. We also found that knocking-down Rab18 inhibits autophagy in a similar way to Rab3GAP2. Finally, we found that aged Rab3GAP2 mutants show neuromuscular disorders, which is a wellknown hallmark of autophagy defect. Taken together our results suggest that Rab3GAP-Rab18 module acts as a novel regulator of autolysosome maturation.