



P-115

A new relationship between miniCORVET and HOPS tethering complexes

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Lysosomal degradation plays an important role in maintaining cellular homeostasis by sequestering and degrading extracellular (endocytosis) and intracellular (autophagy) cargo in eukaryotic cells. Cargo containing vesicles mature into lysosomes which requires several fusion steps. During vesicle fusions tethering factors bind GTP bound Rab proteins and tether target membranes.

Two related multisubunit tethering complexes have been identified in the endocytotic and autophagic pathways in yeast. In general HOPS promotes the fusion of Rab7 positive late endosomes and autophagosomes with the vacuole, whereas CORVET tethers Rab5 positive early endosomes. Both are composed of six subunits, sharing 4 class C subunits. Two Rab-binding complex specific proteins are located on the opposing ends (Vps41 and Vps39 in HOPS, Vps8 and Vps3 in CORVET, respectively). We have recently identified miniCORVET which contains only one Rab5-binding complex specific Vps (Vps8) and three class C proteins in *Drosophila*.

Although they share similar structure and experiments made on yeast suggest that CORVET and HOPS can be transformed into each other via intermediate complexes, their interplay is incompletely understood.

The goal of our research was to examine the relationship of these complexes by overexpressing the Rab binding subunits in different fruit fly tissues. Surprisingly, the overexpression miniCORVET specific Vps8 could block all HOPS dependent processes but the overexpression of the HOPS specific Vps41 did not prevent the function of miniCORVET. Mechanistically, Vps8 overexpression abolishes the late endosomal localization of HOPS-specific Vps41 and decreases the amount of assembled HOPS. Based on these results we suggest that Vps8 can displace Vps41 from the class C core, pointing to a competition between the specific subunits. Our data – challenging the current model of CORVET/HOPS formation – give novel insights into the interplay and functions of these tethering complexes.