

Detailed Status Information

Manuscript #	29-01-2019-ADV-eLife-45631
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Submission Date	31st Jan 19
Current Stage	Waiting for full submission/resubmission
Title	Vps8 overexpression inhibits HOPS-dependent trafficking routes by outcompeting Vps41/Lt 
Manuscript Type	Research Advance
Corresponding Author	Prof. Gábor Juhász (Biological Research Centre of the Hungarian Academy of Sciences)
Contributing Authors	Mr. Péter Lőrincz , Ms. Lili A. Kenéz , Ms. Sarolta Tóth , Ms. Viktória Kiss , Ágnes Varga , Dr. Tamás Csizmadia , Zsófia Simon-Vecsei 
Group Authorship	None of the authors are group authors or consortia.
Abstract	Two related multisubunit tethering complexes promote endolysosomal trafficking in all eukaryotes: Rab5-binding CORVET that is believed to be transformed into Rab7-binding HOPS. We have recently identified miniCORVET (Lőrincz et al, 2016a), containing Drosophila Vps8 and three shared core proteins, which is required for endosome maturation upstream of HOPS in highly endocytic cells. Here we show that Vps8 overexpression inhibits HOPS-dependent trafficking routes including late endosome maturation, autophagosome-lysosome fusion, crinophagy and lysosome-related organelle formation. Mechanistically, Vps8 overexpression abolishes the late endosomal localization of HOPS-specific Vps41/Lt and decreases the amount of assembled HOPS. Proper ratio of Vps8 to Vps41 is thus critical because Vps8 negatively regulates HOPS by outcompeting Vps41. Endosomal recruitment of miniCORVET or HOPS specific subunits requires proper complex assembly, and Vps8/miniCORVET is dispensable for autophagy and crinophagy. These together indicate that pre-assembled complexes are independently recruited to target membranes in Drosophila rather than being transformed during vesicle maturation.
Impact Statement	Our previous and present data indicate that pre-assembled tethering complexes miniCORVET and HOPS are recruited to target membranes independent of each other.
Reviewing Editor	Assigned
Suggest a Senior Editor	Randy Schekman (Howard Hughes Medical Institute, University of California, Berkeley), Vivek Malhotra (The Barcelona Institute of Science and Technology)
Senior Editor to Exclude	Ivan Dikic (Goethe University Frankfurt)
Suggestions from the Board of Reviewing Editors	Noboru Mizushima (The University of Tokyo) - BRE, Hong Zhang (Institute of Biophysics, Chinese Academy of Sciences) - BRE
Author Reviewer Suggestions to Include	Helmut Krämer (University of Texas Southwestern Medical Center), Alexey Merz (University of Washington School of Medicine)
Author Reviewer Suggestions to Exclude	Eric Baehrecke (University of Massachusetts Medical School), Nava Segev (UIC)
Keywords/Other Research Organisms	HOPS, CORVET, autophagy, endocytosis, crinophagy, tethering 
Major Subject Area(s)	Cell Biology, Developmental Biology
Research Organism(s)	<i>D. melanogaster</i>
Competing Interests	No competing interests declared
Funding	No Funders The funders had no role in study design, data collection and interpretation, or the decision to submit the work for publication.
Data Availability	Data Availability: All data generated or analysed during this study are included in the manuscript and supporting files. N/A
Ethics	Human Subjects: No Animal Experimentation: No
Previous Interactions	MiniCORVET is a Vps8-containing early endosomal tether in Drosophila. Corresponding author: Gábor Juhász
Dual-Use Research	No
Permissions	Have you reproduced or modified any part of an article that has been previously published or submitted to another journal? No

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Submission incomplete	29th Jan 19