Control of lysosomal biogenesis and Notch-dependent tissue patterning by components of the TFEB-V-ATPase axis in Drosophila melanogaster

In vertebrates, TFEB (transcription factor EB) and MITF (microphthalmia-associated transcription factor) family of basic Helix-Loop-Helix (bHLH) transcription factors regulates both lysosomal function and organ development. However, it is not clear whether these 2 processes are interconnected. Here, we show that Mitf, the single TFEB and MITF ortholog in Drosophila, controls expression of vacuolar-type H^+-ATPase pump (V-ATPase) subunits. Remarkably, we also find that expression of Vha16-1 and Vha13, encoding 2 key components of V-ATPase, is patterned in the wing imaginal disc. In particular, Vha16-1 expression follows differentiation of proneural regions of the disc. These regions, that will form sensory organs in the adult, appear to possess a distinctive endo-lysosomal compartment and Notch (N) localization. Modulation of Mitf activity in the disc in vivo alters endo-lysosomal function and disrupts proneural patterning. Similar to our findings in Drosophila, in human breast epithelial cells we observe that impairment of the Vha16-1 human ortholog ATP6V0C changes the size and function of the endo-lysosomal compartment and that depletion of TFEB reduces ligand-independent N signaling activity. Our data suggest that lysosomal-associated functions regulated by the TFEB-V-ATPase axis might play a conserved role in shaping cell fate.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Regulatory Genomics, IFOM the FIRC Institute of Molecular Oncology
Contributors: Tognon, E., Kobia, F., Busi, I., Fumagalli, A., De Masi, F., Vaccari, T.
Number of pages: 16
Pages: 499-514
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Autophagy
Volume: 12
Issue number: 3
ISSN (Print): 1554-8627
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 7.07 SJR 4.197 SNIP 1.859
Web of Science (2017): Impact factor 11.1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 5.69 SJR 3.066 SNIP 1.424
Web of Science (2016): Impact factor 8.593
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 6.01 SJR 3.816 SNIP 1.958
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 5.44 SJR 3.583 SNIP 1.768
Web of Science (2014): Impact factor 11.753
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 5.2 SJR 3.361 SNIP 1.635
Web of Science (2013): Impact factor 11.423
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 5.15 SJR 2.91 SNIP 1.197
Web of Science (2012): Impact factor 12.042
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 4.75 SJR 3.141 SNIP 1.119
Web of Science (2011): Impact factor 7.453
BFI (2010): BFI-level 2