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ORGANELLE DYNAMICS

Getting in touch

> a novel membrane contact site between mitochondria and lysosome-like vacuoles

Membrane-bound organelles of the secretory pathway are interconnected through endocytic vesicles that facilitate the exchange of lipids, proteins and metabolites. In yeast, the endoplasmic reticulum (ER) is connected to mitochondria through the ER–mitochondria encounter structure (ERMES), which has been implicated in lipid biogenesis and transfer. Now, two studies in *Developmental Cell* report a novel membrane contact site between mitochondria and lysosome-like vacuoles in yeast, and reveal a physical and metabolic link between mitochondria and the endocytic compartment.

Using electron microscopy, both groups observed that vacuolar and mitochondrial membranes that are in close proximity form contacts. However, the membranes did not fuse, and the organelles maintained their separate identity; thus, they termed this membrane contact site vacuole and mitochondria patch (vCLAMP).

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To identify the components of the vCLAMP, Hönscher *et al.* overexpressed components of the HOPS (homotypic fusion and vacuole protein sorting) tethering complex, which mediates endosome–lysosome fusion. They noted that the numbers of contact sites between vacuoles and mitochondria increased when the HOPS subunit Vps39 was overexpressed, which suggests that it promotes vCLAMP formation. Moreover, both groups demonstrated that GFP-tagged Vps39 accumulates at vCLAMPs, which is consistent with a role for this protein at these junctions. Hönscher *et al.* found that the location of Vps39 at vCLAMPs was independent of the HOPS complex but required the RAB7-like GTPase Ypt7, which binds to Vps39 and is needed for fusion events at the lysosome-like vacuole.

Importantly, Elbaz-Alon *et al.* showed that genetic ablation of Vps39 (leading to a loss of vCLAMPs) increased the number of ERMES foci, whereas the loss of ERMES enhanced vCLAMP formation. Elbaz-Alon *et al.* found that deletion of both contact sites resulted in a lethal phenotype. These findings indicate that ERMESs and vCLAMPs are co-regulated and that at least one contact site between these organelles is required to maintain cellular function. Moreover, Elbaz-Alon *et al.* found that ion and amino acid transporters colocalize at vCLAMPs, which implies that these contact sites might have a role in interorganelle transport.

Hönscher *et al.* went on to show that, under respiratory growth conditions, vCLAMP formation was reduced, whereas the number of ERMES foci was increased, suggesting that these contact sites are reciprocally regulated in response to metabolic cues. Consistent with this, the phosphorylation status of Vps39 was altered in response to changes in the carbon source in the growth medium, and vCLAMP formation was inhibited in cells expressing a phosphomimetic form of Vps39.

Finally, Elbaz-Alon *et al.* established that vCLAMPs have a role in phospholipid transport, and they propose that this junction functions as an alternative route for the transport of small molecules in the absence of ERMES.

In summary, the identification of this novel contact site between mitochondria and vacuoles highlights the complexity of interorganellar crosstalk. Further studies are required to fully unravel the composition and function of vCLAMP and to elucidate the mechanism governing the co-regulation of contact site formation between mitochondria and the endocytic compartment in response to the changing physiological requirements of the cell.

Andrea Du Toit

ORIGINAL RESEARCH PAPERS Hönscher, C. *et al.* Cellular metabolism regulates contact sites between vacuoles and mitochondria. *Dev. Cell* **30**, 86–94 (2014) | Elbaz-Alon, Y. *et al.* A dynamic interface between vacuoles and mitochondria in yeast. *Dev. Cell* **30**, 95–102 (2014)
FURTHER READING Rowland, A. A. & Voeltz, G. K. Endoplasmic reticulum–mitochondria contacts: function of the junction. *Nature Rev. Mol. Cell Biol.* **13**, 607–625 (2012)