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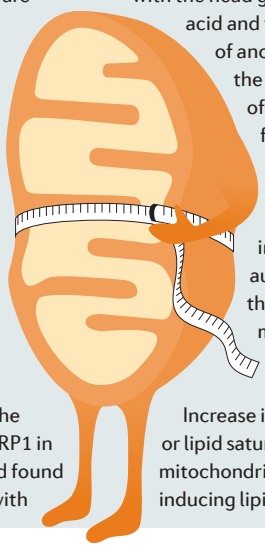
ORGANELLE DYNAMICS

Sizing mitochondria with phospholipids

Mitochondria undergo cycles of fusion and fission, which serve as an adaptation to the metabolic needs of the cell, but how exactly these events are regulated remains elusive. Focusing on mitochondrial fission, Adachi *et al.* reveal that the lipid composition of the mitochondrial membrane influences these dynamic changes of mitochondrial morphology.

Dynamin-related protein 1 (DRP1) is a GTPase that constricts mitochondrial membranes during fission. As dynamin, a closely related protein, is known to bind to lipids, the authors explored the lipid-binding properties of DRP1 in an *in vitro* liposome assay, and found that it specifically interacts with phosphatidic acid species that contain long saturated acyl chains. Further analysis revealed that DRP1 can interact with the head group of phosphatidic acid and the saturated acyl chains of another lipid, and that the simultaneous binding of both is important for DRP1–membrane interactions.



Vicky summersby/NPG

To investigate the relevance of these interactions *in vivo*, the authors manipulated the composition of mitochondrial membrane lipids in mouse embryonic fibroblasts. Increase in phosphatidic acid or lipid saturation resulted in mitochondrial elongation, whereas inducing lipid desaturation promoted mitochondrial fragmentation. Notably, lipid desaturation counteracted the effects of the increase in phosphatidic acid levels, indicating that saturated acyl chains and phosphatidic acid are both needed to regulate the activity of DRP1 in mitochondrial fission; further experiments revealed that these interactions inhibit the GTPase activity of DRP1.

> “saturated acyl chains and phosphatidic acid … regulate the activity of DRP1”

Finally, DRP1 was found to directly interact with mitochondrial phospholipase D, an enzyme that produces phosphatidic acid, suggesting that this might drive localized inactivation of fission machinery. As phosphatidic acid also promotes the activity of the fusion machinery, this study highlights the more general role of phosphatidic acid synthesis in modulating mitochondrial fusion and fission cycles.

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ORIGINAL ARTICLE Adachi, Y. *et al.* Coincident phosphatidic acid interaction restrains Drp1 in mitochondrial division. *Mol. Cell* **63**, 1034–1043 (2016)

FURTHER READING Westermann, B. Mitochondrial fusion and fission in cell life and death. *Nat. Rev. Mol. Cell Biol.* **11**, 872–884 (2010)