Nature Reviews Molecular Cell Biology | Published online 23 Jan 2018; doi:10.1038/nrm.2018.4

MITOCHONDRIA

The needless PINK1

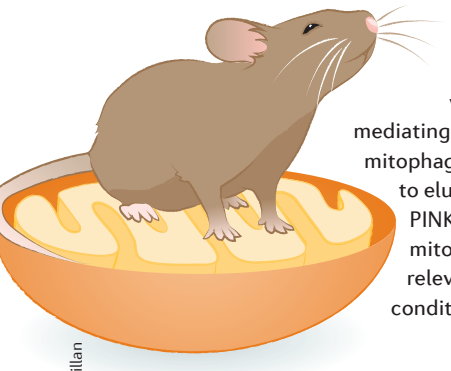
The mechanisms of mitophagy — the removal of mitochondria by selective autophagy — have been recently elucidated. A key pathway to mitochondrial clearance involves activation of PTEN-induced kinase 1 (PINK1) and the E3 ubiquitin-protein ligase parkin. This pathway has attracted much attention as mutations in parkin and PINK1 are linked to early-onset of Parkinson disease. However, the extent to which PINK1 contributes to mammalian mitophagy *in vivo* remains unclear. McWilliams *et al.* now report that in mouse tissues with high metabolic demand, mitophagy occurs independently of PINK1.

To study the function of PINK1 *in vivo*, the authors used mice that express a fluorescent reporter that enables the visualization of mitophagy and mitochondrial architecture in tissues (*mito*-QC reporter mice); these mice were either wild type or knockout for *Pink1*.

The authors first analysed mouse brains, as neural tissue has a very high energy demand, which depends on the maintenance of mitochondrial homeostasis. Moreover, previous studies showed that low-level, basal (constitutive) mitophagy occurs in this tissue. Although in cell cultures PINK1 is not detectable unless mitochondria are depolarized, PINK1 was found to be present in all regions of the central nervous system in normal physiological conditions. Interestingly, when comparing brain sections from *Pink1* wild type and knockout *mito*-QC mice, basal mitophagy was indistinguishable in neurons (including those relevant to Parkinson disease) and in non-neuronal cell types, indicating that the loss of PINK1 does not perturb basal neuronal mitophagy *in vivo*. The lack of detectable differences in basal mitophagy between PINK1-deficient and wild type cells was extended to other metabolically active tissues, including the liver, retina and pancreas. Thus, although there is some variability in the levels of mitophagy between cell types and tissues, PINK1 is dispensable for basal mitophagy in a variety of tissues.

These findings indicate that even though PINK1 is present, its physiological role in basal conditions is unclear and is not the major driver of mitophagy in this state. They also suggest that the function of PINK1 is cell-type and context dependent, with distinct pathways mediating basal and stress-induced mitophagy. Further work is needed to elucidate the mechanisms of PINK1-independent mitophagy *in vivo* and their relevance to pathological conditions.

Kim Baumann



V. Summersby/Macmillan Publishers Limited

ORIGINAL ARTICLE McWilliams, T. G. *et al.* Basal mitophagy occurs independently of PINK1 in mouse tissues of high-metabolic demand. *Cell Met.* https://doi.org/10.10316/j.cmet.2017.12.008 (2018)

FURTHER READING Harper, J. W., Ordureau, A. & Heo, J.-M. Building and decoding ubiquitin chains for mitophagy. *Nat. Rev. Mol. Cell Biol.* https://doi.org/10.1038/nrm.2017.129 (2018)