IN BRIEF

CELL DEATH

Membrane binding by tBid initiates an ordered series of events culminating in membrane permeabilization by Bax

Lovell, J. F. *et al. Cell* 12 Dec 2008 (doi:10.1016/j.cell.2008.11.010)

The role of BCL-2-family proteins in mitochondrial outer membrane permeabilization (MOMP) has been unclear. To gain insight, Lovell *et al.* used fluorescently labelled proteins in an *in vitro* system to reconstitute MOMP and simultaneously measure protein–protein and protein–membrane interactions in real time. This approach revealed an ordered series of events that are required for MOMP: truncated BID (tBID) binds to mitochondrial membranes, where it associates with the pro-apoptotic protein BAX, causing its oligomerization and integration into the membrane, which leads to MOMP. The anti-apoptotic protein BCL-XL inhibits MOMP by binding to and sequestering membrane-bound tBID. In turn, pro-apoptotic BAD releases tBID from BCL-XL, thereby restoring binding of tBID to BAX and BAX-mediated MOMP.

ORGANELLE DYNAMICS

Mitofusin 2 tethers endoplasmic reticulum to mitochondria

Martins de Brito, O. & Scorrano, L. *Nature* **456**, 605–610 (2008)

The interaction between mitochondria and the endoplasmic reticulum (ER) has important functions in Ca^{2+} signalling and other cellular processes, but the underlying molecular mechanisms have been unknown. Martins de Brito and Scorrano now show that the dynamin-related protein mitofusin 2 (MFN2), which is mutated in the inherited motor neuropathy Charcot–Marie–Tooth type IIa (CMTIIa), is enriched at contact sites between mitochondria and the ER. MFN2 on the ER bridges the two organelles by interacting with MFN2 and mitofusin 1 on the surface of mitochondria. Ablation or silencing of MFN2 disrupts ER morphology and reduces the efficiency of mitochondrial uptake of Ca^{2+} released from the ER. These findings also point to a role for the ER and its interaction with mitochondria in the pathogenesis of CMTIIa.

PROTEIN FOLDING

Real-time redox measurements during endoplasmic reticulum stress reveal interlinked protein folding functions

Merksamer, P. I. *et al. Cell* **35**, 933–947 (2008)

The accumulation of misfolded proteins (endoplasmic reticulum (ER) stress) triggers the unfolded protein response (UPR), which initiates events to restore protein homeostasis in the ER. However, when and how quickly normal protein folding is restored is unknown, as it is difficult to measure unfolded protein levels directly in living cells. By predicting that ER stress and the UPR affect the redox state in the normally oxidizing ER lumen, the authors created separate redox-sensitive and UPR-sensitive fluorescent probes to measure the redox state in the ER and UPR activity, respectively, in single cells. Indeed, different types of ER stress affected protein oxidation and revealed functional links between the ER's protein folding, modification and quality control systems.