IN BRIEF

APOPTOSIS

BID, BIM, and PUMA are essential for activation of the BAX- and BAK-dependent cell death program

Ren, D. *et al. Science* **330**, 1390–1393 (2010)

The release of cytochrome *c* from mitochondria is crucial for apoptosis and is regulated by homo-oligomers of the pro-apoptotic proteins BAX and BCL-2 homologous antagonist or killer (BAK). It is not clear how activation of BAX and BAK is controlled, and how BCL-2 homology 3 (BH3)-only proteins of the BCL-2 family are involved in this process. Ren *et al.* show that the BH3-only proteins BH3-interacting domain death agonist (BID), BCL-2-interacting mediator of cell death (BIM; also known as BCL2L11) and PUMA are essential for homo-oligomerization of BAX and BAK and for the initiation of apoptosis in response to several stimuli. The triple-knockout mice show similar developmental defects to those observed upon loss of BAX and BAK, and cannot respond to death signals despite the presence of other BH3-only factors. Thus, these proteins might directly activate BAX and BAK rather than indirectly act through interactions with anti-apoptotic BCL-2 proteins.

CYTOSKELETON

An invasive podosome-like structure promotes fusion pore formation during myoblast fusion

Sens, K. L. *et al. J. Cell Biol.* **191**, 1013–1027 (2010)

The formation of multinucleated myotubes in *Drosophila melanogaster* involves fusion between mononucleated muscle founder cells and fusion-competent myoblasts (FCMs), and Sens *et al.* identify a new podosome-like structure that mediates this process. The authors show that filamentous actin foci localize to FCMs and protrude, by several finger-like projections, into the apposing founder cell, creating a 'dimple'. Wiskott–Aldrich syndrome protein (WASP) and SCAR complexes carry out redundant roles in the formation of these actin foci, but only WASP is required for efficient invasion; by contrast, SCAR mediates the formation of a thin sheath of actin along the founder cell membrane. The WASP-mediated invasion of the actin foci into the founder cell seems to be needed to initiate the formation of a single-channel fusion pore between the two fusing muscle cells, a hallmark of a membrane fusion event.

CELL SIGNALLING

Primary cilium-dependent and -independent Hedgehog signaling inhibits $p16^{INK4A}$

Bishop, C. L. *et al. Mol. Cell* **40**, 533–547 (2010)

Primary mammalian cells undergo replicative senescence after repeated passage, and this is often associated with induction of the tumour suppressor p16 (also known as CDKN2A). To identify new regulators of p16 expression, Bishop *et al.* conducted a genome-wide short interfering RNA screen and found that Hedgehog signalling represses p16 through binding of the Hedgehog effector GLI2 to the p16 promoter. To investigate the relationship between Hedgehog signalling and p16, the authors studied primary cilia — which harbour components of the Hedgehog signalling pathway and, for unknown reasons, are found at low levels in cultured cells. Hedgehog signalling is active in cells with primary cilia, and cells at a higher passage number have fewer primary cilia. Furthermore, depletion of p16 increases cilia formation in cultured cells. Thus, Hedgehog signalling inhibits p16 expression and this might regulate the formation of primary cilia and the onset of replicative senescence.