RESEARCH HIGHLIGHTS

Asymmetric division masters apoptosis

Asymmetric cell division can produce one daughter cell that undergoes programmed cell death but it is unclear whether it is functionally linked to apoptosis. In *Caenorhabditis elegans*, a neuroblast division produces the neurosecretory motoneuron and a sister cell that is destined to die. Julia Hatzold and Barbara Conradt (*PLoS Biol.* **6,** e84; 2008) have shown that asymmetric division of this neuroblast is required for the subsequent death of the sister cell and that three proteins regulating spindle positioning in the neuroblast also control programmed cell death in this lineage. Two of these proteins were previously linked to asymmetric division in other organisms: in *Drosophila melanogaster*, the homologue of ces-1/snail regulates Inscuteable expression, a protein required for asymmetric division; in *Volvox carteri,* the homologue of Dnj-11, a DNA J-domain-containing protein, controls asymmetric division. These findings suggest that the same factors could control asymmetric division and apoptosis in a wide range of organisms. NLB

BBS proteins take on migration

Bardlet-Biedl syndrome (BBS) is a ciliopathy associated with characteristic facial patterns and a disorder of the enteric nervous system; however, the underlying cause of these defects is unknown. Tabin *et al.* (*Proc. Natl Acad. Sci USA* **105,** 6714–6719; 2008) report that BBS patients, as well as mouse and zebrafish models of BBS, show similar mid-face and cranial features and that neural crest cell (NCC) migration is impaired in fish lacking BBS proteins. This is consistent with the known migration of NCCs from the brain to form cranial and facial structures, as well as NCC movement to the intestine where they regulate gastrointestinal motility and secretion. BBS proteins were previously linked to Wnt and Shh signalling through their ciliary role and these two pathways also regulate NCC migration. In the new study, modulation of Wnt signalling partially rescued NCC migration defects observed in fish. Thus, BBS proteins affect cell migration, and these results also indicate that defects associated with ciliopathies may originate from a wider range of cellular and developmental processes than previously thought. NLB

Collective migration in morphogenesis

The mammalian mammary gland undergoes branching morphogenesis during both puberty and cycles of pregnancy and lactation. Zena Werb and colleagues (*Dev. Cell* **14**, 570–581; 2008) have used time-lapse microscopy to follow this process in three dimensions using organotypic cultures, and show that this is driven by a new type of collective cell migration. By following both myoepithelial cells and luminal cells, they observed that new ducts emerge from a multilayered epithelium, and myoepithelial cells constrain duct elongation. Luminal cells migrate collectively, but continue to intermingle and do not form protrusions. Although tissue architecture remains, single cells are only partially polarized, suggestive of a 'morphologically active' epithelial state. Through inhibitor studies, they show that each stage has distinct requirements: proliferation, Rac and MLCK initiate the formation of new ducts, whereas ROCK later restores the bilayered epithelium. By comparing epithelium organization *in vivo* during puberty or in a hyperplasia, they propose that a common mechanism drives the initiation of breast cancers. AS

Histone deacetylases repair DNA

Histone deacetylases regulate chromatin architecture and transcription. As HDAC3 is required for embryonic development, Scott Hiebert and colleagues (*Molecular Cell* **30,** 61–72; 2008) have generated conditional knockout mouse embryonic fibroblasts (MEFs). They report that increased acetylation of histone H4 at Lys 5, 12 and 16 and, H3 at Lys 9 and 14 occurs at the expense of H3K9 trimethylation. Approximately 200 genes, mainly associated with signalling and metabolism, were either up- or downregulated. HDAC3 ablation in cell lines is known to cause loss of H3S10 phosphorylation, mitotic arrest and catastrophe; surprisingly, the knockout MEFs progressed through mitosis with only a slight decrease in H3 phosphorylation, although the authors recapitulate the published effects by deriving an immortalized cell line from the knockout MEFs. HDAC-null MEFs do show cell-cycle delays, probably due to S-phase checkpoint activation by DNA damage: the DNA double-stranded break marker γ-H2AX formed more foci with or without exogenous damage, whereas p53 was slightly induced and the transcriptional co-repressor Kap1 and replication protein MCM2 were hyperphosphorylated. Furthermore, comet assays suggested that DNA repair was inefficient. SAHA and TSA, inhibitors of class I HDACs, in clinical trials as chemotherapeutics and known to induce DNA damage, as well as siRNAs against HDAC1 and 2 produced similar effects. Thus, perturbations in chromatin assembly due to the loss of class I deacetylases may affect the DNA damage response, although the mechanistic details of this connection remain to be elucidated. BP

Vaccinia mimics apoptotic body

The prototype poxvirus *Vaccinia* mimics apoptotic bodies, enabling host-cell infection through macropinocytosis. Mercer and Helenius (*Science* **320**, 531–535; 2008) found that mature viruses (MVs) induced formation of spherical membrane blebs, which retracted coincident with viral entry. To investigate the relationship between blebbing and infection, the authors selectively inhibited known components in the macropinocytosis pathway. Interestingly, they found that activation of p21-activating kinase (PAK1) and its regulatory partner Rac1 was essential for both membrane blebbing and MV infection. Debris from apoptotic cells is subjected to macropinocytosis, dependent on the surface-exposed lipid phosphatidylserine (PS). The authors showed that selectively masking PS at the MV membrane had no effect on MV binding to the cell surface but was sufficient to inhibit membrane blebbing and MV infection. Macropinocytosis and apoptotic mimicry may enable *Vaccinia* to avoid immune detection. This work will provide new avenues for targeting antivirals to prevent host-cell infection by poxviruses. AJ

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