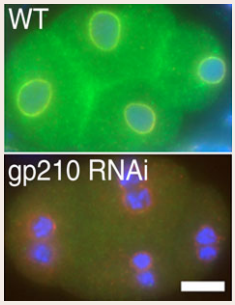
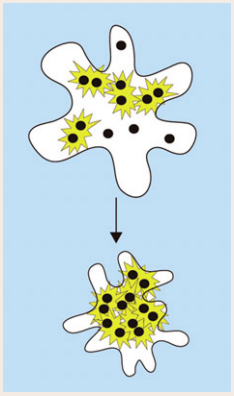
In this issue



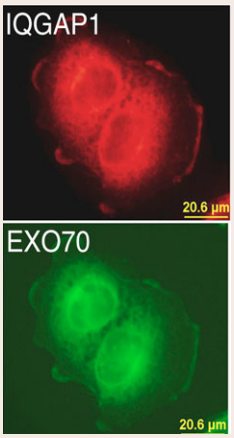
gp210 breaks it down

In animal cells, the nuclear envelope is broken down and then rebuilt during every cycle of mitosis. During breakdown, multiple components of the envelope – including nuclear pore complexes, the nuclear lamina and nuclear membranes – are dismantled, but how is this process controlled? On page 317, Iain Mattaj and colleagues show that gp210, a transmembrane protein in the nuclear pore complex, is necessary for nuclear envelope breakdown. The authors show that, in early-stage *C. elegans* embryos, the nuclear lamina cannot depolymerise when gp210 is knocked down or mutated, which gives rise to daughter cells with twinned nuclei. Moreover, antibodies that target gp210 inhibit the breakdown of *Xenopus* nuclear envelopes in vitro. The authors show that antibody binding reduces phosphorylation of the C-terminal domain of gp210, without altering its localisation or interfering with normal nuclear import. Knocking down cyclin-B–cdc2 (the kinase that is thought to phosphorylate gp210 during mitosis) mimics the phenotype of gp210 depletion in *C. elegans*. Therefore, the authors propose, phosphorylation of gp210 by cyclin-B–cdc2 may trigger breakdown of the nuclear envelope. Their results shed light on a key early step in mitosis.



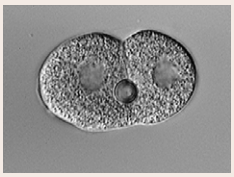
Death by shrinkage

Cell condensation is a hallmark of apoptosis. This decrease in volume – which occurs during both the intrinsic and extrinsic apoptotic pathways – is thought to result from the efflux of chloride ions, and subsequently water, from the cell. The importance of cell condensation in the apoptotic program remains unclear – is it a by-product of other processes, or a necessary step on the path to apoptosis? On page 290, Harald Sontheimer and colleagues explore mechanisms of cell condensation in human glioma cells. The authors show that DIDS, an inhibitor of chloride channels, stops cells from shrinking and consequently blocks apoptosis by either pathway. The authors go on to show that glioma cells can be induced to shrink by hyperosmotic shock; importantly, this shrinkage triggers apoptosis, even without additional death stimuli. The authors propose that cell condensation might trigger apoptosis by bringing auto-activating enzymes and cell-surface receptors into closer proximity. These results identify cell condensation as a key effector step in apoptosis.



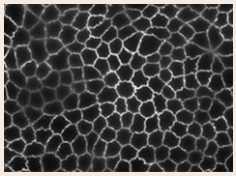
Polarized growth: IQGAP1 shows the way

During migration, exocytic vesicles fuse with the cell's leading edge to enable directional growth. This polarized secretion is thought to be promoted by the exocyst complex – which tethers vesicles to the plasma membrane – and by septin proteins that associate with the exocyst. However, little is known about how the process is regulated. Now, Mahasin Osman and colleagues (p. 391) propose that the actin-modulating protein IQGAP1 activates polarised secretion. Using co-immunoprecipitation, the authors show that the N-terminal region of IQGAP1 binds the exocyst-septin complex directly in pancreatic β-cells. This interaction is disrupted by the expression of the GTPase CDC42, which is known to bind the C-terminal region of IQGAP1. Moreover, CDC42 also inhibits IQGAP1-mediated insulin secretion. The authors propose, therefore, that IQGAP1 regulates exocytosis by switching between two conformations: CDC42-bound (secretion off) and exocyst-bound (secretion on). The authors go on to demonstrate that IQGAP1 promotes protein synthesis and interacts with the ER translocon. These results implicate IQGAP1 as a major regulator of cell migration and growth.



Cytokinesis: furrows without a spindle

The formation of a cleavage furrow on the cell surface is the first step in cytokinesis, the final act in mitosis. The orientation of the mitotic spindle determines where the cleavage furrow will form, but which spindle component controls this process? Classical experiments conducted in the 1960s and 1970s – in which cell division was monitored in echinoderm eggs that had been enucleated or forced into a doughnut shape – suggested that astral microtubules control the site of furrowing. However, more recent work in *C. elegans* and cultured cells implicates the central spindle as the main determinant of the furrow site. Now, George von Dassow and colleagues (p. 306) recapitulate a series of early experiments, using cells in early *C. elegans* embryos. By visualising membrane invagination and contractile ring formation (using GFP-labelled myosin), the authors show that cleavage furrows can form in doughnut-shaped cells, even when the central spindle is abolished by knocking down the microtubule-associated protein SPD-1. Surprisingly, anucleate cells are also capable of furrow formation. However, cytokinesis often fails to complete when the central spindle is perturbed or mislocated. These data indicate that astral microtubules and the central spindle are both important for successful cell division, and shed light on the longstanding question of how cytokinesis is controlled.



Tight junctions: pores for thought

Tight junctions act as intercellular glue, providing a seal between epithelial cells that restricts the paracellular movement of molecules. However, the epithelium is permeable to certain solutes, which pass through small pores within tight junctions. Although tight-junction proteins such as the claudins have been implicated in pore formation, little is understood about pore structure or the regulation of transepithelial permeability. On page 298, James Anderson and colleagues describe the size and abundance of small tight-junction pores in five different epithelial cell lines and in pig ileum. By measuring the permeability of epithelia to polyethylene glycol oligomers of diverse sizes, the authors show that the pore size (4 Å radius) is similar for all the tested cell lines, but that the abundance of pores – and their apparent density within junctions – differs widely. Moreover, pore size is unaffected by overexpressing claudin-2, although pore number is increased. These results suggest that epithelial permeability – for small uncharged solutes at least – may be predominantly regulated by the abundance of small tight-junction pores.

Development in press

Par-sing the regulatory circuitry of oocyte polarity

In *Drosophila* oocytes, polarization of the microtubule cytoskeleton localizes the maternal RNAs that subsequently specify the anteroposterior (AP) and dorsoventral axes, but how is cytoskeletal polarity established and regulated? In a paper published in *Development*, Ai-Guo Tian and Wu-Min Deng report that the tumour suppressor Lethal (2) giant larvae (Lgl) and atypical protein kinase C (aPKC) play important roles in regulating microtubule polarity and in setting up the AP axis in *Drosophila* oocytes. They show that the loss of *lgl* in germline cells disrupts the normal localization of oocyte polarity markers. Restriction of Lgl activity to the posterior of the oocyte by anterior aPKC (which phosphorylates and inactivates Lgl) is also needed for the correct localisation of these markers, they report. Furthermore, active Lgl regulates the posterior enrichment of Par-1, a serine/threonine kinase that controls microtubule polarity in *Drosophila* oocytes. Together, these results indicate that a regulatory circuit that involves Lgl and its phosphorylation by aPKC establishes oocyte polarity.

Tian, A.-G. and Deng, W.-M. (2008). Lgl and its phosphorylation by aPKC regulate oocyte polarity formation in *Drosophila*. *Development* **135**, 463-471.