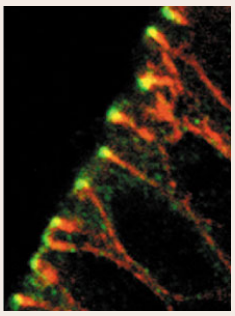
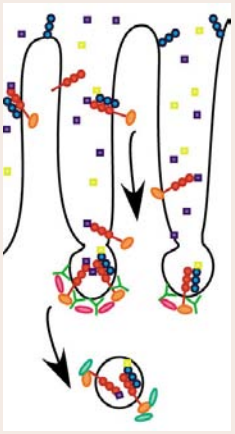
In this issue

by Jane Bradbury



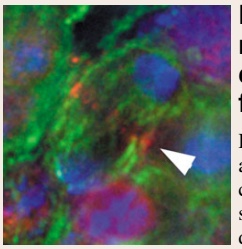
Shroom helps achieve closure

During neural tube closure, a crucial event in development of the brain and spinal cord, a flat sheet of epithelial cells is converted into a closed tube. As part of this process, a band of actin that encircles the tip of the columnar neuroectodermal cells contracts like a purse string, turning them into wedge-shaped cells. Jeffrey Hildebrand now reports that the actin-binding protein Shroom is a key regulator of this shape change (see p. 5191). Hildebrand shows that Shroom localizes to the apical tip of the adherens junctions of neuroectodermal cells in vivo and that expression of full-length Shroom or its C-terminal domain in polarized MDCK cells causes apical constriction by recruiting F-actin and myosin II to apical junctions. He goes on to show that myosin II accumulation is reduced at apical junctions in the neural tubes of *Shroom*-mutant mice. Thus, Shroom seems to act as a crucial determinant of epithelial cell shape during neural tube closure by influencing actomyosin distribution.



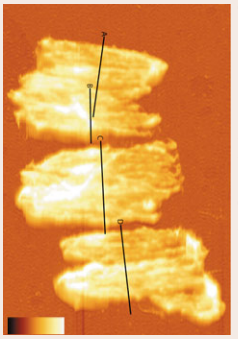
A Dab2 hand in development

The endocytosis of lipoprotein receptors, which mediate the uptake of many protein cargoes by cells, involves specific signals in the receptors. However, which proteins interact with these signals to mediate endocytosis is unclear. Meghan Maurer and Jonathan Cooper now report that endocytosis of the lipoprotein receptor megalin in mouse embryonic visceral endoderm (VE) cells requires Dab2, an adaptor protein that binds to megalin and to endocytic proteins (see p. 5345). Both megalin and Dab2 are expressed in the VE, a polarized epithelium that supplies nutrients to the early embryo. The authors show that endocytosis of megalin and its co-receptor cubilin is greatly reduced in $dab^{-/-}$ embryos, which arrest before gastrulation. Dab2 has two isoforms – p96 and p67 – and, by making isoform-specific knock-in mice, the authors show that p96 rescues endocytosis and embryonic development more efficiently than p67, which lacks endocytic-protein-binding sites. The authors propose that Dab2 p96 is indispensable in the VE as an adaptor for the endocytosis of megalin and other unidentified receptors that supply the embryo with proteins vital for development.



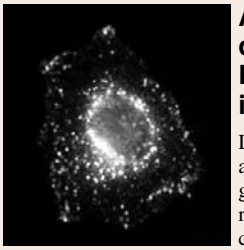
Ploughing the right cytokinetic furrow

During cytokinesis, an actin-based cleavage furrow separates the dividing cells. The furrow must be accurately positioned relative to the microtubule spindle but how this is achieved is unclear. On p. 5381, Robert Saint and colleagues report that in *Drosophila* cells, a Rho-family GTPase-activating protein (RhoGAP) called Tumbleweed (Tum/RacGAP50C) acts as a furrow-positioning signal by linking anaphase microtubules to the assembly of the cytokinetic furrow at the cortex. The authors show that, in *Drosophila* embryos, cells that lack Tum do not form furrows and fail to localize key cytokinetic components correctly, including the Rho guanine-nucleotide-exchange factor (RhoGEF) Pebble (Pbl). Pbl is thought to initiate changes in Rho activity at the cell equator that culminate in furrow formation. Disruption of the Pbl-interacting domain of Tum also prevents furrow formation but not localization of Tum to the microtubules near where the furrow should form. The authors conclude that Tum is required early in cytokinesis in *Drosophila* and that the interaction between Tum and Pbl forms an essential link between the mitotic spindle and formation of the cleavage furrow.



Taking the lid off focal adhesions

Cells adhere to the extracellular matrix through focal adhesions (FAs). These act as anchors for the intracellular stress fibres that generate the force necessary for cell migration and also function as signalling centres through which extracellular signals are transduced by integrin molecules. On p. 5315, Clemens Franz and Daniel Müller use fluorescence microscopy and atomic force microscopy (AFM) to reveal the ultrastructure of FAs for the first time. To gain access to the FAs, the authors 'de-roofed' fibroblast cells expressing YFP-linked paxillin, a cytoskeletal protein present in FAs, by using gentle sonication to remove the upper surface of the cell and its intracellular organelles. They then used fluorescence microscopy to identify FAs before examining them by AFM, which allows high-resolution analysis of cellular structures under near-physiological conditions. Their work provides detailed insights into the 3D arrangement of microfilaments in FAs, the height and volume of FAs, and the localization of paxillin in the membrane-proximal part of the FA.



Arrestin' new details about LPA_1 internalization

Lysophosphatidic acid (LPA) evokes growth-factor-like responses in many cells through three related LPA receptors. Like many receptors, these can be internalized by endocytosis but the full details of their regulation are unclear. Harish Radhakrishna and colleagues now shed light on key aspects of this, in particular the involvement of cholesterol (see p. 5291). The authors show that both clathrin and the adaptor protein β-arrestin are required for endocytosis of the LPA_1 receptor and that β-arrestin, which targets many receptors to clathrin-coated pits, attenuates LPA signaling. In addition, they demonstrate that depletion of membrane cholesterol in HeLa cells inhibits LPA signalling, recruitment of β-arrestin to the membrane, and the subsequent endocytosis of LPA_1. Finally, they show that LPA_1 localizes to cholesterol-rich microdomains upon ligand stimulation. These results provide new insights into the link between clathrin-mediated endocytic events and cholesterol-dependent processes at the plasma membrane. They also reveal an important aspect of the regulation of LPA_1, namely that cholesterol is required for its association with β-arrestin prior to its clathrin-dependent endocytosis.

Development in press

Oogenesis enhanced by cell death

In species from nematodes to humans, many healthy, developing oocytes die around the pachytene stage of meiosis. Why and how this happens is not known. Now, in a paper published in *Development*, Boag and co-workers report that a conserved ribonucleoprotein (RNP) complex regulates germline apoptosis in *Caenorhabditis elegans*. They identify a germline RNA-binding protein, CAR-1 (for cytokinesis/apoptosis/RNA binding), and show that it associates with the RNA helicase CGH-1 in an RNA-dependent manner within a germline RNP complex. This interaction is conserved in *Drosophila* oocytes. RNAi-mediated knockdown of CAR-1 in nematodes increases oocyte apoptosis, as does CGH-1 depletion. Unexpectedly, if apoptosis is prevented in worms that have reduced *car-1* expression, defects in oogenesis lead to gonad failure. The researchers conclude that CAR-1 has a conserved role in oogenesis and propose that germline apoptosis enhances the formation of functional oocytes.

Boag, P. R., Nakamura, A. and Blackwell, T. K. (2005). A conserved RNA-protein complex component involved in physiological germline apoptosis regulation in *C. elegans*. *Development* **132**, 4975-4986