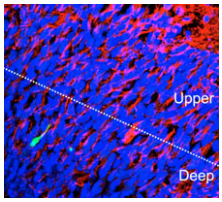
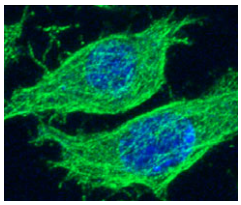


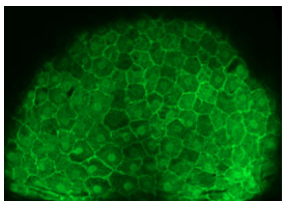
Neural progenitor divisions up to Par

The balance between proliferative (self-renewing) and differentiative division of neural progenitor cells during development determines the final size of the different brain regions, but what regulates this balance? On p. 11, Magdalena Götz and colleagues reveal that the cell polarity Par-complex proteins play a key role in this important balancing act. During neurogenesis in the mouse brain, ventricular zone (VZ) progenitors enlarge the progenitor pool through proliferative division but subventricular zone (SVZ) progenitors mainly divide differentiatively to form neurons. In VZ progenitors only, Par-complex proteins are enriched at the apical surface. The researchers now show that the amount of endogenous Par-complex proteins decreases in parallel with the number of cortical progenitors during development. Overexpression of Par proteins, they report, increases the number of Pax6^{+} self-renewing progenitors in vivo and in vitro by selectively promoting symmetric proliferative cell division; knockdown of Par3 has the opposite effect. Thus, the researchers conclude, Par-complex proteins regulate the balance between proliferation and differentiation in the developing cerebral cortex.



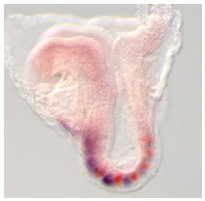
Motor protein zips up dorsal closure

During dorsal closure (DC) in *Drosophila* embryos, actin-rich filopodia extended by the leading edge cells of two epithelial sheets make transient cell-cell contacts that allow the sheets to 'zipper' together and form permanent cell-adhesion structures. Now, Susan Parkhurst and co-workers reveal that the *Drosophila* myosin XV homolog Sisyphus facilitates these processes (see p. 53). Sisyphus – an actin-based motor protein – contains a microtubule-binding MyTH4 domain and a cargo-binding FERM domain. The researchers show that Sisyphus is expressed at high levels in the leading edge cells and in their filopodia during the zippering phase of DC. RNAi knockdown of Sisyphus, they report, disrupts the correct alignment of cells on opposing sides of the fusing epithelial sheets and the adhesion of cells in the final zippering phase. They also identify several putative Sisyphus cargos, including DE-cadherin (which is involved in filopodia-mediated adhesion) and several microtubule-linked proteins. Overall, the researchers propose that Sisyphus regulates filopodia dynamics during DC by coordinating actin and microtubule cytoskeleton components.



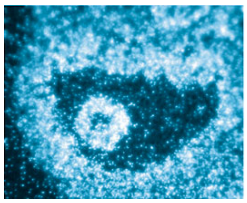
Calcium signals early asymmetry

Although vertebrates look bilaterally symmetrical, their internal organs are placed asymmetrically. In some organisms, Ca^{2+} signalling and cilia function in the embryonic node have been implicated in the establishment of this left-right (LR) asymmetry. Now, Schneider and colleagues report that Ca^{2+} fluxes also have a conserved function in LR patterning before node formation (see p. 75). In zebrafish embryos, Kuppfer's Vesicle (KV), which is derived from the dorsal forerunner cells (DFCs), is homologous to the node in mice and chicks. The researchers show that endogenous Ca^{2+} is released in the DFC region after the onset of gastrulation but before KV and cilia formation. The inhibition of this early Ca^{2+} release, the researchers report, disrupts KV formation, which alters the expression of asymmetric markers and the asymmetric placement of internal organs. Other experiments indicate that β-catenin inhibition is the target of this early Ca^{2+} signalling. Finally, the researchers identify DFC-like cells in *Xenopus* embryos and provide evidence that early Ca^{2+} signalling is a conserved feature of LR patterning.



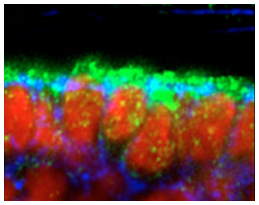
Segmentation clock: Wnt3a out of time?

According to the 'clock and wavefront' model of somitogenesis, a segmentation clock driven by oscillations of Notch, Fgf and Wnt signalling in the presomitic mesoderm (PSM) is translated into a periodic array of somites at the so-called wavefront. Wnt3a/β-catenin signalling is widely believed to be a component of this clock, but on p. 85, Terry Yamaguchi and colleagues surprisingly suggest otherwise. To study Wnt3a's role in somite segmentation, the researchers introduced conditional loss- and gain-of-function β-catenin alleles into mice. Their findings show that although Wnt3a is necessary for the clock gene oscillations that occur during somitogenesis, Wnt3a/β-catenin signalling does not function as an integral component of the segmentation clock because small, irregular and abnormally located somites do develop in the absence of β-catenin and cycling clock gene expression. From their results, the researchers conclude that Wnt3a/β-catenin signalling has a permissive, rather than an instructive, role in the oscillation of clock genes, and that it controls somite boundary formation by regulating the anteroposterior position of segment boundary-determining genes.



Egging on cell communication

The development of mammalian oocytes is supported by cumulus cells in the ovarian follicle. At the same time, oocytes actively regulate follicular development. John Eppig and co-workers now provide new insights into this bidirectional communication by reporting that oocyte-derived factors – specifically BMP15 and GDF9 – promote the biosynthesis of cholesterol in mouse cumulus cells (see p. 111). The researchers show that transcripts that encode cholesterol biosynthesis enzymes are downregulated in *Bmp15*$^{-/-}$ and *Bmp15*$^{-/-}$/*Gdf9*$^{+/-}$ double mutant mouse cumulus cells before the preovulatory surge of luteinizing hormone, and are also downregulated in wild-type cumulus cells that are out of contact with oocytes. Oocytes, they report, express very low levels of these transcripts compared with cumulus cells and, in the absence of cumulus cells, produce very little cholesterol. Together, these results uncover an unexpected role for cumulus cells – the synthesis of cholesterol for the oocyte – and reveal that BMP15 regulates mouse follicular development before the luteinizing hormone surge.



mRNA transport stems from structure

The subcellular localisation of mRNA transcripts during development can play a key role in the control of patterning and differentiation. In *Drosophila* embryos, the mRNAs of some developmental genes, such as *wingless*, are localised by their active transport along microtubules by the dynein complex. Now, on p. 133, Henry Krause and co-workers identify a consensus motif for the transport of RNA to the apical cytoplasm of fly embryos. By using an embryo microinjection assay, the researchers identify an element (WLE3) in the 3'UTR of *wingless* mRNA that is necessary and sufficient for the apical transport of *wingless* mRNA in preblastoderm *Drosophila melanogaster* embryos. By examining *wingless* mRNA sequences in other *Drosophila* species, the researchers show that WLE3 has a highly conserved stem-loop structure. Mutagenic analysis, however, indicates that only a few key residues, base pairs and bulges in WLE3 are required for its activity. These essential features are also present in other apical localization elements and might, therefore, define the first consensus motif for apical RNA transport.

Jane Bradbury