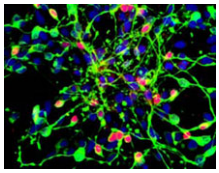
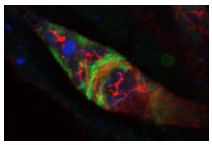


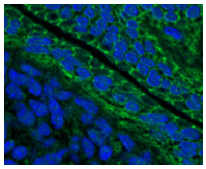
Oligodendrocyte differentiation: human ES cells take it slow

Damage to myelin, a membrane sheath that encases axons and speeds up nerve impulse transmission, is linked to certain CNS disorders, such as multiple sclerosis and spinal cord injury. On p. 1443, Su-Chun Zhang and colleagues now report progress in generating oligodendrocytes – the cells that produce myelin in the CNS – from human embryonic stem cells (hESCs), opening up new avenues for both basic and clinical research. Mouse embryonic stem cells (mESCs) can be efficiently differentiated into oligodendrocytes, but this is not the case for hESCs. The authors show that, as with mESCs, treating hESCs with sonic hedgehog induces oligodendrocyte differentiation by triggering the activation of a conserved transcription factor cascade. But in hESCs, this process takes around 14 weeks; in mESCs, it takes just two. In addition, the mitogen FGF2, which promotes oligodendrocyte differentiation in mESCs, stalls it in hESC-derived cultures. Thus, a conserved transcriptional network appears to underlie oligodendrocyte differentiation in human cells, but this network is probably regulated in different ways among species.



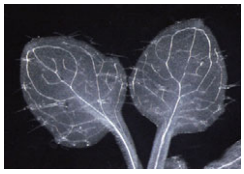
Insulin signals for control of germline stem cell divisions

The cell cycle of stem cells is tightly controlled so that they can divide throughout life and respond to challenges such as injury and starvation. Defects in this control could result in abnormal tissue maintenance or cancer. Now, Hannele Ruohola-Baker and co-workers analyse cell division in *Drosophila* germline stem cells (GSCs) and reveal that the cell cycle regulator Dacapo is suppressed by microRNAs (miRNAs); in turn, the miRNAs might be controlled by insulin (p. 1497). This group has previously shown that the miRNA pathway regulates Dacapo in GSCs. Here, the authors demonstrate that several miRNAs can target the *dacapo* 3′ UTR directly, and that mutations in these miRNAs lead to abnormal GSC divisions. The *dacapo* 3′ UTR also responds to insulin receptor (InR), but not to TGF-β, signalling (two pathways known to regulate GCS divisions), and InR-deficient GSCs display defects resembling those of miRNA pathway mutants. Based on these and other findings, the authors propose that insulin regulates the division of GSCs through miRNAs and Dacapo.



Vangl2 keeps on trac(t)

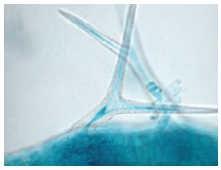
Female reproductive tract (FRT) development in vertebrates is controlled by Wnts, but little is known about the different intracellular pathways involved. Now, Alysia vandenBerg and David Sassoon describe how non-canonical Wnt signalling through a core member of the planar cell polarity (PCP) signalling pathway, vang-like 2 (Vangl2), is involved in this process (p. 1559). They report that *loop-tail* mice, which carry a *Vangl2* mutation (*Vangl2*^{Lp}), have FRT defects at birth that resemble those of *Wnt7a* mutants. Their findings show that the polarity of uterine epithelial cells in *Vangl2*^{Lp} mice is abnormal, with defective cytoskeletal actin polarisation and mislocalised scribble 1 – an apicobasal polarity protein. As *Vangl2*^{Lp} mutants die at birth, the researchers grafted FRTs from mutants into normal mice to study the later effects of this mutation. They found that the initial defects worsen over two weeks and that *Wnt7a* levels are reduced in both homozygous and heterozygous grafted *Vangl2*^{Lp} FRTs, indicating that Vangl2 acts dominantly in the FRT. From their findings, the authors conclude that both canonical and non-canonical Wnt signalling participate in FRT development.

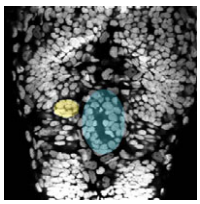


Trafficking cellular insights from plant vascular development

In this issue of *Development*, two papers exploit the genetic tractability of the model plant *Arabidopsis thaliana* to investigate plant vascular development, and by doing so shed new light on processes that are of general importance to multicellular life. In the first study (see p. 1529), Naramoto et al. investigate the role of VAN3 in the formation of a continuous leaf vasculature and report that both its subcellular localisation and activity are regulated by phosphoinositide (PI) signalling. VAN3 is an ARF GTPase-activating (ARF-GAP) protein, a family of proteins that regulate multiple cellular processes, including endocytosis and secretion, through their roles in vesicle transport and protein trafficking. Consistent with it functioning in the post-Golgi transport pathway, VAN3, the authors report, localises to subdomains of the trans-Golgi network (TGN). Through genetic interaction studies and yeast two-hybrid screening, they identify two novel regulators of VAN3 localisation: CVP2, an inositol polyphosphate 5′ phosphatase, and VAN3-binding protein (VAB). CVP2, they show, regulates VAN3 localisation to the TGN by regulating cellular PI levels, whereas VAB helps to recruit VAN3 to PI-enriched TGN subdomains. PIs also control the ARF-GAP activity of VAN3, leading the researchers to propose that they have a dual role in regulating the subcellular distribution and enzymatic activity of VAN3. Future work should identify whether VAN3 is also involved in polar auxin transport.

In the second study, Pascal Genschik and colleagues turned to *Arabidopsis* development to shed light on the activity of the ubiquitin protein ligase APC/C (p. 1475), which is important for DNA replication and cell division but which surprisingly remains active in post-mitotic vertebrate cells, such as neurons. The researchers report that APC/C also remains active in most post-mitotic *Arabidopsis* cells, and that reduced APC/C activity in mutant plants results in developmental defects. These defects include disturbed vein patterning in the cotyledon (the first leaf of a germinating seed) and increased vascular tissue, indicating that APC/C functions in vascular development and organisation. Although the role of PIs in vesicular trafficking and the post-mitotic functions of APC/C now await further investigation, these two studies illustrate the power of diverse model systems for biological research.





Nodal fishes out brain asymmetries

Left-right asymmetries in the nervous system are common among animals, and their importance is obvious in phenomena such as human language processing, which occurs mainly in the brain's left hemisphere. Now, Myriam Roussigné and colleagues reveal that Nodal signalling regulates asymmetric neurogenesis in zebrafish (p. 1549). The elaboration of asymmetries between the bilateral habenular nuclei, a group of nuclei located in the diencephalon, largely depends on the parapineal, a nucleus that sits on the brain's left side owing to unilateral, left-sided Nodal signalling. Here, the authors identify the chemokine receptor gene *cxcr4b* as an early marker of habenular neurons. They show that neurogenesis begins earlier in the left than in the right habenula, and that this asymmetry is independent of the parapineal. Disrupting the asymmetric activity of Nodal, however, leads to the symmetric onset of habenular neurogenesis. These results indicate that asymmetric Nodal signalling acts not just to bias the laterality of the parapineal but also has an early role in asymmetric habenular neurogenesis.