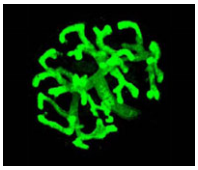
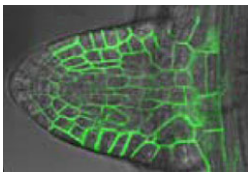


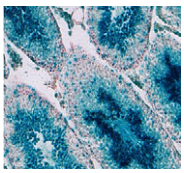
Semaphorin applies brakes to branching morphogenesis

Semaphorins are secreted signals that function during diverse developmental events, from axon guidance to angiogenesis. Although the plexin A family of semaphorin receptors has been well characterised, less is known about the B-type plexins, particularly their roles in organogenesis. Now Korostylev et al. have discovered that the Sema4d-plexin B1 ligand-receptor pair negatively regulates branching morphogenesis during kidney development by RhoA-ROCK pathway activation (see p. 3333). By analysing the expression of this pair in developing organs, the authors found that plexin B1 and Sema4d are expressed in epithelial and mesenchymal compartments, respectively, implicating them in the epithelial-mesenchymal interactions that occur during organogenesis. Next, in cultured mouse embryonic kidneys, they found that exogenously applied Sema4d reduces ureteric branching and activates RhoA. However, when they blocked the RhoA-ROCK pathway, Sema4d stimulated ureteric branching. From these findings, the authors conclude that RhoA-ROCK signalling acts as an endogenous brake on plexin B1-triggered, branch-promoting signalling through a function that is distinct from ROCK's maintenance of the cytoskeletal structure of the ureteric tree.



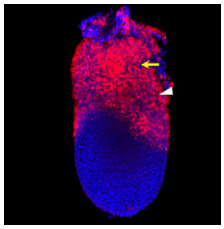
PGPs ration auxins for export

Auxins, a family of plant hormones, are powerful regulators of plant development and growth that need to be actively transported into and out of cells. Here, Jiří Friml and colleagues report that the two auxin export systems, the phosphoglycoprotein (PGP) and the PIN protein systems, although independent, cooperate during *Arabidopsis* developmental patterning, and they propose a new model in which PGPs function partly by rationing the auxin that is available for PINs to directionally transport (see p. 3345). In the *Arabidopsis* embryo, PINs localise to polarised patches at the plasma membrane. The authors now show that PGPs are dispersed throughout the plasma membrane of embryonic tissue. Their mutant analysis reveals, among other findings, that the two systems function synergistically in the spatial patterning of the auxin response in embryos and roots. It is here, the authors propose, that PGPs regulate auxin flow both by directly interacting with PINs and by generally exporting auxin from cells, thus limiting the auxin that is available for directional transport.



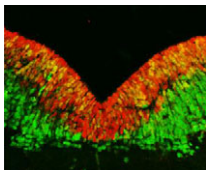
No Cdk2 for 1 in embryogenesis

The mammalian cell cycle machinery contains multiple cyclin-dependent kinases (Cdks) that are thought to have specific functions. For example, Cdk1 is proposed to be essential for mitotic entry and exit, whereas Cdk2 drives cells through the G1–S phase transition. Yet, surprisingly, Cdk1 can partially compensate for Cdk2 loss, even though Cdk2 remains essential for meiosis. Now, on p. 3389, Ande Satyanarayana and colleagues demonstrate that Cdk2 cannot compensate for the lack of Cdk1 during mouse embryogenesis, even when expressed from a *Cdk1* promoter. They report that *Cdk1* deletion leads to early embryonic death, as does substituting *Cdk2* for both copies of *Cdk1* to eliminate differences in the timing of expression. Conversely, $Cdk2^{-/-}$ mice in which one *Cdk1* copy is replaced by *Cdk2* are sterile, showing that *Cdk1*-driven *Cdk2* expression cannot rescue the $Cdk2^{-/-}$ meiotic defect. The mitotic function of Cdk2, however, is not affected. These results confirm that Cdk1 is essential for mammalian development and highlight the functional differences amongst mammalian Cdks.



Dishing up blood from ES cells

The primitive erythroid (PrE) lineage is the first mammalian blood cell lineage to form – in the embryonic yolk sac from its hemangioblast precursor – but little is known about the signals that specify it, or how it is regulated (primitive erythropoiesis occurs for just 48 hours). Gordon Keller and colleagues now employ an ES cell differentiation approach (see p. 3447) to investigate the involvement of Wnt and Notch signalling in PrE specification. By inducing genes and by assaying transcriptional activity and differentiation markers in ES cells, they have discovered that canonical Wnt signalling, together with Notch pathway inhibition by Numb, is required for an in vitro hemangioblast equivalent to differentiate specifically into the PrE lineage. By contrast, Notch signalling inhibits primitive erythropoiesis by upregulating Wnt pathway inhibitors. Of particular interest, the authors report, is the rapid downregulation of Wnt signalling, which suggests that just a short period of Wnt activity is required to establish the PrE fate, which might in turn underlie the transient nature of primitive erythropoiesis.



Dopaminergic neurogenesis expands with Otx2

Dopaminergic neurons in the ventral midbrain (VM), also known as mesencephalic dopaminergic (mesDA) neurons, control voluntary movements, and their degeneration is associated with Parkinson's disease (PD). In the course of brain development, the establishment of correct VM progenitor domain identity depends on the transcription factor Otx2, but is Otx2 important for mesDA neurogenesis? The answer, as Daniela Omodei and co-workers report on p. 3459, is yes. By analysing mouse mutants that conditionally overexpress *Otx2* in the mesencephalon, the authors reveal that too much Otx2 leads to selectively increased mesDA progenitor proliferation and to the expansion of the mesDA progenitor domain. This occurs in a dosage-dependent and anteroposteriorly graded manner. Conversely, lack of Otx2 dramatically reduces mesDA progenitor proliferation and causes early cell cycle exit. The authors also show that Otx2 controls mesDA progenitor proliferation via the canonical Wnt pathway and promotes progenitor differentiation by inducing an intricate transcription factor cascade. These findings flag Otx2 as a potential target for future cell-replacement therapies for PD.

IN JOURNAL OF CELL SCIENCE

STRA8 – no commitment-phobe

Successful meiosis in male and female gonads, and normal spermatogenesis, depend on *Stra8* (stimulated by retinoic acid 8); however, its role in normal male meiosis has been largely unexplored. In *J. Cell Sci.*, Manuel Mark and colleagues now investigate STRA8 function in mouse male germ-cell development. The authors find that *Stra8*-null male germ cells engage in premeiotic replication and commit to meiotic synapsis and recombination, but that synapsis is subsequently disrupted, probably by defects in chromosome pairing. By contrast, in female mice STRA8 is required by germ cells to initiate meiosis. Interestingly, mutant spermatocytes undergo premature chromosome condensation and entry into meiotic metaphase, which suggests that they retain some characteristics of mitotic cells. From these data, the authors propose that STRA8 is required for spermatocytes to progress through the early stages of meiotic prophase (notably homologous-chromosome pairing), and is involved in regulating the switch from a mitotic pattern of cell division to the meiotic pattern.

Mark, M. et al. (2008). STRA8-deficient spermatocytes initiate, but fail to complete, meiosis and undergo premature chromosome condensation. *J. Cell Sci.* 121, 3233-3242.