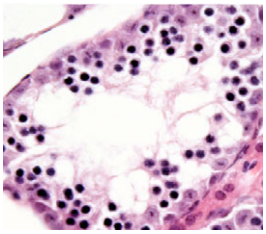
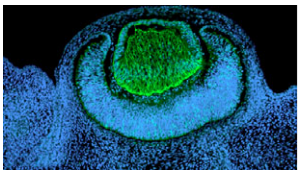


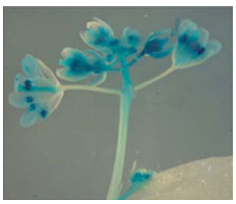
Akts of stem cell self-renewal

The self-renewing ability of stem cells is crucial in many developmental contexts; however, the mechanisms that regulate the switch between proliferation and differentiation are poorly understood. Spermatogonial stem cells (SSCs) provide an excellent model in which to study self-renewal as large numbers of stem cells can be expanded in culture and the markers that characterise these cells are well defined. On p. 1853, Shinohara and colleagues reveal a crucial role for the phosphoinositide-3 kinase (PI3K)-Akt pathway in mouse SSC self-renewal. Glial cell line-derived neurotrophic factor (GDNF) has previously been shown to regulate the self-renewal of SSCs in culture via downstream signals that have yet to be fully elucidated. Now these authors show that Akt is phosphorylated in the presence of GDNF and that this activated Akt can maintain SSC self-renewal in culture for several months; this self-renewal capacity can be inhibited by a chemical inhibitor of PI3K. Whether these insights can be applied to other tissue-specific stem cells remains to be determined.



Eyeing-up Wnt-independent pygopus

Pygopus – a core component of the canonical Wnt-signalling pathway – plays a crucial role in development and disease. Its essential transcriptional co-activator activity is mediated through its interaction with β-catenin, Tcf, Bcl9 and Hyrax. In *Xenopus*, Pygopus 2 (Pygo2) orthologues regulate the expression of eye markers. Surprisingly though, it has been suggested that this activity operates independently of the Wnt pathway. Richard Lang and co-workers (p. 1873) now show that lens development in mice depends on Pygo2-mediated regulation of the transcription factor Pax6. They further show that Pygo2 function, in this setting, is Wnt-independent. By conditionally deleting *Pygo2* in certain tissues in mice where it is normally expressed – the ocular mesenchyme and the presumptive lens ectoderm (PLE) – these researchers show that Pax6 expression is reduced in the PLE and a small lens subsequently develops. Interestingly, they find that Pygo1 is dispensable for lens development. Future work should uncover the pathway in which Pygo2 operates during lens development and reveal whether Pygo2 has other Wnt-independent roles.

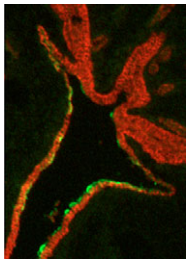


Flowering: silencing gets complex

At least four genetic pathways regulate flowering time in *Arabidopsis*. The establishment and maintenance of gene expression patterns, in part through chromatin modification events, contributes to the coordination of complex genetic networks and thus to the control of flowering. The ATP-dependent chromatin remodelling complex SWR1C – which catalyses H2A replacement with the H2AZ variant – has been characterised in yeast and mammals, and recent studies have hinted that SWR1C homologues also exist in plants. Now Choi et al. (p. 1931) provide further evidence of this with their study of potential *Arabidopsis* SWR1C homologues, such as AtSWC6 and SUF3. They show that mutations in these genes generate similar phenotypes, such as extra petals and early flowering. Furthermore, these proteins form a complex and both AtSWC6 and SUF3 bind to the promoter of the floral repressor *FLOWERING LOCUS C*. Together, these findings show that an SWR1C-like complex is likely to exist in *Arabidopsis* that regulates diverse aspects of plant development, and not just flowering.

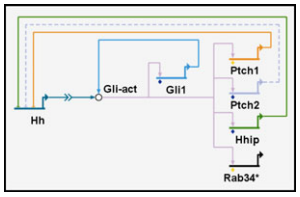
Neurons in a spindle over division

In the mammalian cortex, cell-fate choices are determined by the orientation of the mitotic spindle. Previous studies have shown that when the mitotic spindle of a cell orientates parallel to the apical surface of the neural tube, two progenitor cells are generated, but when it orientates perpendicularly, a neuron and a progenitor are produced in a stem cell mode of division. Whether these findings can be extrapolated to cell divisions in the rest of the nervous system, particularly in the spinal cord, is unknown. Using a novel, time-lapse imaging assay, Kate Storey and co-workers now reveal (p. 1943) that in the chick spinal cord the mitotic spindle orientation does not correlate with a switch from progenitor-only to neuron plus progenitor-generating divisions. However, it does distinguish stem cell modes from terminal modes of division that produce only neurons. The birth of neurons from stem cell divisions is captured for the first time and, surprisingly, the relationship between spindle orientation and cellular identity appears different in the spinal cord as compared with the cortex.



Subdividing the urinary tract: a tail of buds

Kidney-filtered waste products are excreted from the body via the urinary tract, which comprises the intra-renal collecting system and the ureter. These structurally and functionally distinct tissues derive from the ureteric bud (UB). Now Doris Herzlinger and co-workers report that two mesenchymal cell populations – the nephrogenic mesenchyme and the tailbud-derived mesoderm (TBM) – surround the UB, and that the ureter develops as a consequence of the distal UB's close association specifically with the TBM (p. 1967). Their fate-mapping studies in the chick show that BMP4 secreted from the TBM induces ureter morphogenesis and can do so when expressed ectopically in regions of the UB normally fated to develop into the intra-renal collecting system, revealing the multipotent nature of the proximal UB. The authors suggest that the complex morphogenetic processes required to bring the TBM into close contact with the UB might contribute to the high incidence of human congenital defects that occur at this junction between the kidney and the ureter.



Targeting the targets of Hedgehog

Sonic hedgehog (Shh) is secreted during neural tube (NT) development from the notochord to specify different progenitors in a concentration-dependent manner through the activity of activator (GliA) and repressor (GliR) forms of the Gli proteins. Andrew McMahon's group – using a combined genetic and bioinformatics approach to identify novel Gli targets during NT patterning – now suggest on p. 1977 that, surprisingly, GliA and GliR differ in their selection of target binding sites. Gli1-directed chromatin immunoprecipitation products were screened against genomic tiling arrays of putative Hedgehog targets (predicted from transcriptional profiling studies) to reveal both known and novel Shh-Gli targets, such as *Nkx2.2* and *Rab34*, respectively. These targets were then validated by bioinformatics, expression studies in cell culture and transgenic experiments. Along the way, the authors have developed an algorithm that improves current in silico target prediction methods and the authors suggest that their approach could expand our understanding of transcriptional regulation in other developmental settings.