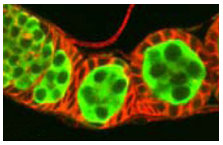
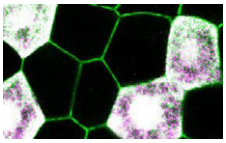


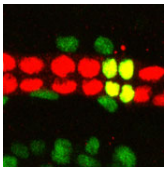
Cell cycle crucial for stem cell maintenance

Stem cell maintenance involves both intrinsic factors produced by the stem cells and extrinsic factors produced by their microenvironment. Dahua Chen and colleagues have been investigating the poorly understood intrinsic mechanisms that repress the differentiation of germline stem cells (GSCs) in *Drosophila* and now report that the proper control of cell mitosis is essential for stem cell maintenance (see p. 4133). The researchers first show that the *eff* gene, which encodes an E2 ubiquitin-conjugating enzyme (Eff), is essential for GSC maintenance. Eff, they report, interacts with the anaphase-promoting complex/cyclosome, a multisubunit E3 ligase that targets mitotic regulators for degradation during the cell cycle. Furthermore, the expression of a stable form of the mitotic regulator Cyclin A results in the loss of GSCs. Thus, the researchers suggest, Eff-mediated degradation of Cyclin A (and probably other mitotic cyclins) is essential for GSC maintenance in *Drosophila* and, because the regulation of mitotic cyclins is evolutionarily conserved, a similar mechanism might maintain stem cells in mammals.



Not so negative: inhibitors expand Wnt range

Members of the Wnt family of secreted signalling proteins play many crucial roles during embryonic development. Wnt signalling is negatively regulated by secreted Frizzled-related proteins (sFRPs), which bind to Wnts extracellularly, but now, on p. 4083, Yusuke Mii and Masanori Taira report that the sFRPs Frzb and Crescent (Cres) can expand the signalling range of Wnts by enhancing their diffusion. By microinjecting mRNAs for tagged versions of Wnt8, Wnt11, Frzb or Cres into *Xenopus* embryos, the researchers show that Wnts do not diffuse effectively, whereas sFRPs spread widely. However, they report, the expression of an sFRP and a tagged Wnt in the same blastomere or in separate oocytes that are then co-cultured promotes Wnt diffusion. Most importantly, Wnt8 conveyed by sFRPs activates Wnt signalling at a distance from its source in vitro and in vivo, even though sFRPs usually act as Wnt inhibitors. Overall, these results provide new insights into how the range of Wnt signalling is regulated in vertebrates.

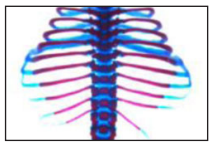


Sanpodo notches up asymmetric divisions

The generation of cell-type diversity in multicellular organisms involves asymmetric cell division. During such divisions in *Drosophila*, Notch signalling in one daughter cell induces its acquisition of the 'A' fate; antagonism of Notch signalling by the cell-fate determinant Numb in the other daughter cell induces the 'B' fate. Although Numb is expressed in other cells in which Notch regulates developmental decisions, Numb inhibits Notch signalling only during asymmetric divisions, but why? On p. 4089, James Skeath and colleagues answer this long-standing question by showing that the transmembrane protein Sanpodo (Spdo), which is only expressed in asymmetrically dividing cells, plays a dual role in regulating Notch signalling during asymmetric divisions. Their loss-of-function and misexpression studies demonstrate that Numb converts Spdo from an activator to an inhibitor of Notch signalling. Thus, in 'B' daughter cells, which express *spdo*, *numb* and *Notch*, Spdo inhibits Notch signalling, whereas it amplifies Notch signalling in 'A' daughter cells, which do not express *numb*, thereby ensuring the faithful execution of asymmetric divisions.

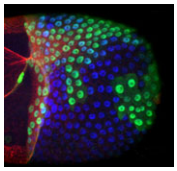
Patched through to lipid trafficking

Hedgehog (Hh) signalling regulates growth and differentiation in many vertebrate and invertebrate tissues. Central to the Hh signalling pathway is the repression of Smoothened (Smo) signalling (which regulates the transcription factor Cubitus interruptus) by the transmembrane receptor Patched (Ptc) when Hh is absent. Now, Suzanne Eaton and colleagues report that, in *Drosophila* wing discs, Ptc uses lipids derived from Lipophorin, a lipoprotein particle with which Hh associates, to regulate Smo signalling (see p. 4111). The researchers show that *Drosophila* Ptc, which resembles the lipid-trafficking protein Niemann-Pick type C-1, recruits internalised Lipophorin to Ptc-positive endosomes. A sterol-sensing domain in Ptc, they report, regulates trafficking of both lipids and Smo from this compartment. Furthermore, Ptc uses lipids derived from Lipophorin to destabilise Smo on basolateral membranes. The researchers suggest, therefore, that Ptc normally regulates Smo degradation by changing the lipid composition of the endosomes through which Smo passes and that Hh might signal, in part, by influencing how Ptc utilises the lipids in Lipophorin.



Telling tails of Cdx2 function

The vertebrate homeodomain transcription factors Cdx1, Cdx2 and Cdx4 play essential roles in anteroposterior vertebral patterning through the regulation of Hox gene expression. Cdx2 might also be involved in axial elongation, but the early lethality of *Cdx2*-null mice has precluded a full examination of this potential role. Now, by using the Cre-loxP system to generate a conditional *Cdx2* allele, Joanne Savory and co-workers provide new insights into how Cdx2 regulates posterior development in mice (see p. 4099). First, they show that the loss of Cdx2 in post-implantation embryos results in axial truncation. Then, they show that this phenotype is associated with the reduced expression of genes encoding several key players in axial elongation. Finally, they use chromatin immunoprecipitation to show that three of these genes (*T*, *Wnt3a* and *Cyp26a1*) are direct Cdx2 targets. Based on these results, the researchers propose a model for posterior embryonic development in mice in which Cdx2 coordinates axial elongation and somite patterning through Hox-independent and Hox-dependent pathways, respectively.



A fateful balancing act on Tramtrack

During organ morphogenesis, cells coordinate their behaviours in both time and space, but how do they achieve this complex feat? On p. 4187, Michael Boyle and Celeste Berg reveal that, during *Drosophila* egg chamber development, the transcription factor Tramtrack69 (TTK69) interacts with Notch and the insect steroid hormone Ecdysone to coordinate cellular behaviours temporally and spatially. Fly egg chambers, which mature through 14 stages, contain a single oocyte covered with columnar follicle cells, which later form dorsal appendages (DAs; protrusions that facilitate gas exchange). The researchers show that TTK69 and Notch form a mutually repressive feedback loop, and that an Ecdysone-mediated switch from Notch to TTK69 expression regulates the fates and shapes of the columnar follicle cells at stage 10B. Later in development, TTK69 controls DA tube volume. These and other results, suggest the authors, support a model for the regulation of egg chamber development in which spatially restricted co-factors work with TTK69 to define appropriate responses to a globally available temporal signal.

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