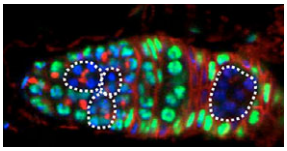
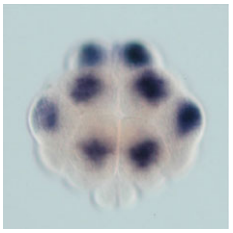


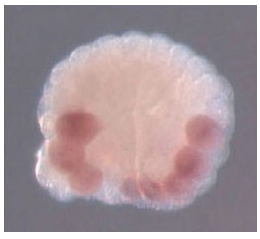
Stonewalling stem cell differentiation

Organisms have to maintain appropriate numbers of various stem cells. Too few can cause infertility or defective tissue regeneration; too many may increase the risk of cancer development. Stem cells are maintained mainly by preventing the expression of differentiation factors – sometimes this occurs through chromatin-mediated transcriptional repression. Maines and co-workers now report that epigenetic control mediated by the DNA-associated protein Stonewall (Stwl) maintains female germline stem cells (GSCs) in *Drosophila* (see p. 1471). The researchers show that clones of *stwl*$^{-}$ GSCs are lost by differentiation and that overexpression of *stwl* causes an expansion of GSCs. Because *stwl* mutants act as suppressors of variegation (genes that prevent patchy gene silencing within tissues), they propose that Stwl is involved in chromatin-dependent gene repression. Finally, they show that Stwl represses the expression of many genes, some of which contain putative binding sites for Pumilio, a translation inhibitor that, together with Nanos, represses the translation of key differentiation factors in GSCs. Thus, the researchers conclude, two overlapping mechanisms block GSC differentiation.



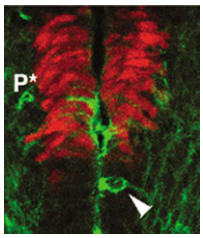
Asymmetric cell division: fateful FGF antagonism

Asymmetric cell division during embryogenesis contributes to cell diversity by generating daughter cells that adopt distinct developmental fates. Little is known about how many of these asymmetric divisions are regulated, but two papers in this issue suggest that FGF signalling plus an ectoderm-derived signal control asymmetric division and the specification of notochord/neural precursors in ascidian embryos. In these embryos, two pairs of mother cells give rise to neural and notochord precursors. Daughter cells in which ERK is activated develop into notochord cells, whereas the others develop into neural cells. But FGF and its receptor, which activate ERK, are widely distributed in the mother cells and surrounding vegetal cells, so how is an asymmetric cue generated? On p. 1491, Picco and colleagues show that the segregation of notochord and neural fates in *Ciona* embryos is an intrinsic property of the mother cells that is acquired through their interaction with ectoderm precursors. This interaction is mediated by the ephrin-Eph signalling system, which is better known for its roles in axon guidance and cell adhesion. The inhibition of ephrin-Eph signalling causes symmetric cell division and generates only notochord precursors, the researchers report. The ephrin-Eph signal attenuates ERK activation in the neural-fated daughter cell. Thus, a directional ephrin-Eph signal from the ectoderm polarises the notochord/neural mother cell and asymmetrically modulates ERK activation and fate specification in the daughter cells. On p. 1509, Kim and colleagues examine the specification of notochord/neural precursors and of mesenchyme/muscle precursors in another ascidian, *Halocynthia roretzi*. They find that a directional FGF signal alone determines the asymmetric division of the muscle/mesenchyme mother cells, but that an FGF antagonising signal from the neighbouring ectoderm controls the polarity of the notochord/neural mother cells. This signal suppresses FGF signal transduction in the neural-fated daughter cell and the expression of *FoxA*, which encodes an essential transcription factor for notochord formation. Together, these two papers provide strong evidence for a new mechanism by which FGF signalling, in combination with an antagonising signal from the ectoderm, controls asymmetric cell division and cell fate specification during ascidian notochord/neural development.



Ripple effect in somite patterning

Segmental structures in vertebrates (the ribs, for example) develop from embryonic structures called somites – blocks of mesodermal cells that periodically bud off from the unsegmented presomitic mesoderm (PSM). Somite formation and the establishment of their rostro-caudal pattern require the transcription factor Mesp2. Now, Morimoto and colleagues reveal that negative regulation of Mesp2 by Ripply2, a putative transcriptional co-repressor, is required to establish rostro-caudal patterning within mouse somites (see p. 1561). Expression of *Ripply2*, the researchers report, is downregulated in *Mesp2*-null mice. Furthermore, Mesp2 binds to the *Ripply2* gene enhancer, indicating that *Ripply2* is a direct target of Mesp2. Unexpectedly, given that *Mesp2*-null embryos fail to segment and have an extended caudal compartment in their PSM, *Ripply2*-null embryos have a rostralized phenotype because of prolonged Mesp2 expression. This and other findings suggest that Mesp2 activates *Ripply2* but that Ripply2 negatively regulates *Mesp2*. This negative-feedback loop, the authors propose, is an essential component of the regulatory network that establishes rostro-caudal patterning within somites.



Molecular code breaking in the CNS

During the development of the mammalian CNS, multipotent progenitors generate the three major neural cell lineages (neurons, oligodendrocytes and astrocytes) at specific times and places. But what coordinates the generation of these cell types? On p. 1617, Sugimori and co-workers suggest that the combined action of two classes of transcription factors holds the answer. The researchers use in vitro (rat neurosphere assay) and in vivo (genetic and gene expression studies in mice) approaches to examine neurogenesis and oligogenesis in the developing ventral spinal cord. They report that Pax6, Olig2 and Nkx2.2 – transcription factors that specify the positional identity of the multipotent progenitors – are also involved in the timing of neural cell differentiation. These 'patterning factors' do this, the researchers show, by modulating the activities of proneural (Ngn1, Ngn2, Ngn3 and Mash1) and inhibitory (Id1 and Hes1) helix-loop-helix transcription factors. Thus, they propose, these two classes of transcription factors form a molecular code that controls the spatiotemporal pattern of neuro/gliogenesis.

Fishy mechanism for left-right asymmetry

During gastulation, Nodal signalling on the left side of the ventral node establishes the left-right (LR) axis of the embryo, which controls the position of the internal organs. In mouse embryos, polycystic kidney disease 2 (*Pkd2*), which encodes the Ca^{2+}-activated channel polycystin 2 (PC2), is thought to activate left-side-specific *Nodal* transcription. Now, Schottenfeld and colleagues reveal that LR patterning in zebrafish embryos also requires *pkd2* but that here, *pkd2* restricts expression of the *nodal* gene *southpaw* (*spaw*) to the left half of the embryo (see p. 1605). They show that *curly up* (the zebrafish ortholog of *Pkd2*) mutants have LR defects in organ positioning that resemble human heterotaxia. But, whereas there is no activation of *Nodal* in the lateral plate mesoderm of mouse *Pkd*$^{-/-}$ embryos, *spaw* is bilaterally activated in *curly up* embryos, they report. Thus, although PC2 is involved in LR patterning in both zebrafish and mouse embryos, its function in this process might not be conserved, a result that calls into question the so-called two-cilia hypothesis for LR axis formation.

Jane Bradbury