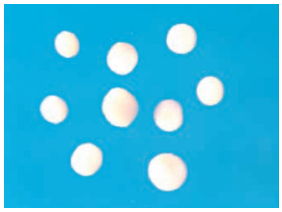
In this issue

Xrx1: proliferation in the neural plate

Posterior cells of the *Xenopus* neural plate undergo neurogenesis at the end of gastrulation, whereas cells of the anterior region continue to proliferate and differentiate at a later stage. Unlike posterior neurogenesis, the factors that regulate proliferation and differentiation of the anterior neuroectoderm are poorly understood. Now, on p. 5143, Andreazzoli and co-workers report that the homeobox gene *Xrx1*, which functions during eye and anterior brain development, is a crucial regulator of the balance between proliferation and neurogenesis of the anterior neuroectoderm. Activated by chordin and hedgehog signalling, *Xrx1* is expressed over the whole anterior neural plate and promotes proliferation by repressing the cell-cycle inhibitor p27Xic1. Xrx1 also activates two anti-neurogenic transcription factors, Xhairy2 and Zic2, and, in so doing, represses several genes associated with neurogenesis.

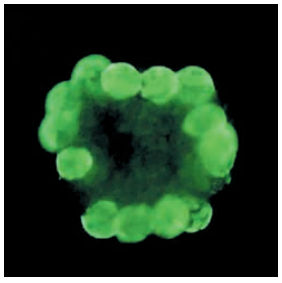


Recycling developmental tools during regeneration

Han et al. shed new light on the interplay between mechanisms of development and of regeneration (see p. 5123). The genes *Msx1* and *Msx2* are implicated in early development of the mouse limb, but their roles during limb regeneration have not previously been characterised. Ken Muneoka's lab has shown before that *Msx1* is expressed during digit tip regeneration in fetal and neonatal mice, and, by using *Msx1* mutants, they now demonstrate that *Msx1* is required for this regeneration response. Using a novel in vitro system, they demonstrate that exogenous Bmp4, a protein essential for digit regeneration, rescues the *Msx1* mutant phenotype. They also report that endogenous Bmp4 is regulated by the combined activities of Msx1 and Msx2, and that this regulation may be mediated by the transcriptional regulator Runx2.

macho-1 mesenchyme in ascidian embryos

Conserved signalling pathways can induce different outcomes in different developmental contexts. In the ascidian vegetal hemisphere, notochord and mesenchyme are induced in the anterior and posterior margins, respectively, by the same fibroblast growth factor (FGF). To become mesenchyme, the posterior blastomeres must inherit posterior-vegetal cytoplasm from the egg. Kobayashi and co-workers used gain- and loss-of-function experiments to demonstrate that the action of the posterior-vegetal egg cytoplasm is due to maternal mRNA encoding the putative transcription factor and muscle determinant Macho-1 (see p. 5179). Expression of *macho-1* is both necessary and sufficient to determine the mesenchymal fate of the posterior vegetal hemisphere; in its absence, notochord is induced. Kobayashi et al. suggest that Macho-1 acts upstream of the transcriptional repressor Snail, which suppresses notochord induction by suppressing the transcription factor Brachury.

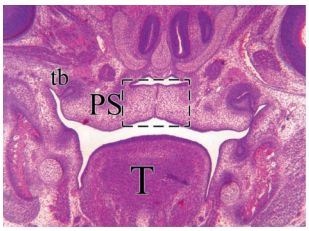


Enhancer swaps in fly and worm

Several developmental genes display remarkably conserved expression patterns between distantly related organisms. Little is known about the conservation of mechanisms that control gene expression, but it is perhaps surprising that enhancer sequences diverge relatively rapidly. On p. 5133, Ruvinsky and Ruvkun test whether enhancers from the fly can drive expression in homologous cell types in the worm. Approximately 90% of fly enhancers are unable to function in the worm, indicating that the binding sites of fly enhancer sequences and worm transcription factors have diverged too far for proper recognition to take place. The authors suggest that expression patterns are not conserved by preserving enhancer function, but by co-evolution among members of transcription initiation complexes, thus preserving the cohesive interactions between enhancers and their binding factors.

A crucial player in craniofacial development

Cranial neural crest (CNC) cells contribute extensively to structures of the head and neck, including the palate and the calvaria (the upper part of the cranium that surrounds the brain), but the regulation of CNC cell fate during cranial development is not well understood. Members of the transforming growth factor β (TGFβ) superfamily are believed to have important regulatory roles during the development of the palate and calvaria. The TGFβ type II receptor (TGFβIIR) is expressed in CNC-derived cells during palatogenesis, as well as in the CNC-derived dura mater, the dense fibrous membrane that provides inductive signals to the developing calvaria. By using a conditional mutant, Ito et al. (see p. 5269) show that loss of *Tgfbr2* expression in CNC cells results in palatal and calvaria defects caused by a lack of cell proliferation in CNC-derivatives of the palatal mesenchyme and dura mater. Intriguingly, the expression patterns of the transcription factor Msx1 and cell cycle regulator cyclin D1 are abnormal in *Tgfbr2* conditional mutants, raising the possibility that TGFβ signalling interacts with these to control CNC cell proliferation.



Flow dynamics and genetic determinism

Several known genes are crucial for blood vessel growth and differentiation but the cues that shape the architecture of the vascular system are still unclear. On p. 5281, Isogai and colleagues examine the influence of blood flow dynamics on the patterning of blood vessels that develop in the vertebrate trunk. Following observations of zebrafish embryos that express green fluorescent protein throughout the vascular network, the authors describe a two-step process of angiogenesis in which primary sprouts emerge from the dorsal aorta and secondary sprouts arise from the posterior cardinal vein. The authors used *silent heart* mutant embryos, which have hearts that do not beat, to show that circulatory flow dynamics do not affect the development of the primary network and have little influence on the patterning of the secondary network. Importantly however, their results support the idea that circulatory flow does affect the patterning of interconnections between the primary and the secondary networks, consistent with the notion that the architecture of the vascular system is orchestrated by the interplay between 'hard-wired' anatomy and flow dynamics.