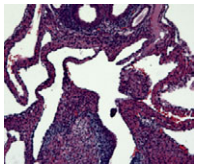
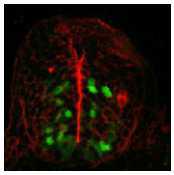
PANning for AG

In flowers, the conserved transcription factor AGAMOUS (AG) is important for reproductive organ development and for terminating stem cell maintenance, but how is its own activation controlled? Now, on p. 1613, Jan Lohmann and co-workers reveal that the bZIP transcription factor PERIANTHIA (PAN) directly regulates *AG* in *Arabidopsis*. The researchers show that PAN binds to a highly conserved *AG* enhancer motif and is required for in vivo *AG* enhancer activity. *AG* expression levels usually do not change in *pan* mutants, indicating that other factors redundantly regulate *AG* expression, but they decrease when *pan* mutants are grown in shorter days, demonstrating that the regulatory circuitry of *AG* senses environmental influences. Conversely, in *ag* mutants, *PAN* expression continues for too long, suggesting that a negative-feedback loop exists between the two factors. A second study by Das, Meyerowitz and colleagues corroborates the role of PAN in regulating *AG* (see p. 1605). Based on their findings, the authors of both studies propose that PAN directly regulates *AG* expression as part of a redundant regulatory network.



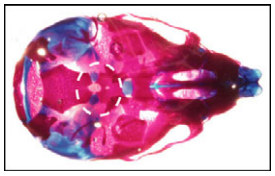
Sh(h)aping the heart's blueprint

Malformations of the atrial septum, which separates the two heart atria, are common human congenital heart defects, but the molecular mechanisms that orchestrate septation are unknown. On p. 1761, Ivan Moskowitz and co-workers investigate the relationship between cardiac progenitor (CP) specification and atrial septation in mice and find that sonic hedgehog (Shh) signalling specifies CPs for the septum outside of the atrium. The researchers report that hedgehog (Hh) signalling specifically marks CPs for the atrial septum and pulmonary artery and show, using genetic inducible fate mapping, that Hh-receiving CPs migrate from the second heart field into the atrium. CPs made unresponsive to Hh signalling migrate normally into the atrium, but populate the atrial walls rather than the septum. Conversely, constitutively activating Hh signalling leads to an enlarged septum. These findings indicate that Hh-mediated CP subspecification establishes a blueprint for septation. Finally, by demonstrating that removing Shh from pulmonary endoderm causes septal defects, the authors implicate respiratory tissue in cardiac patterning, and propose that cardiac septa and the respiratory apparatus might have co-evolved.



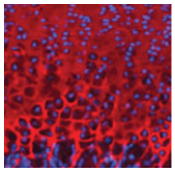
Sugar-coated stop signs for neurons

Proper neuronal migration is crucial for vertebrate nervous system development, but how do neurons know when to stop migrating? Hitoshi Okamoto and colleagues now shed light on this question and report that some neuronal progenitors in zebrafish fail to stop migrating at their normal position when a sugar called fucose is not synthesized correctly (see p. 1653). By screening for mutants in which vagus motor nuclei do not form properly, the authors isolated the *towhead* mutant and found that *towhead* encodes GDP-mannose 4,6, dehydratase (GMDS), a key enzyme in the fucosylation pathway. Accordingly, the authors detected fewer fucosylated glycans than normal in *towhead* mutant embryos, but although fucosylation has been reported to regulate Notch signalling, this signalling pathway is not altered in *towhead* mutants. The authors also demonstrate that, for correct migration, GMDS is not required in vagus motor neuron progenitors, but instead in the surrounding epithelial cells. They propose, therefore, that fucosylated glycans on epithelial cells prevent migrating vagus motor neuron progenitors from overshooting their target.



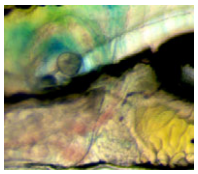
Sonic hedgehog enhanced from a distance

Sonic hedgehog (Shh) signalling is a key player in vertebrate development, patterning structures ranging from the nervous system to the limb. It is also crucial for the morphogenesis of the epithelial lining of the mouth and of the respiratory and gut tubes in mice. Here, on p. 1665, Toshihiko Shiroishi and co-workers identify long-range enhancers that regulate regional *Shh* expression in the epithelial lining and demonstrate their developmental function. By comparing genomic sequences across mammals and teleost fish, the authors identify three conserved non-coding sequences (CNCSs) upstream of the *Shh* coding region, which together recapitulate *Shh* expression in the epithelial lining of the oral cavity, pharynx, lung and gut. To examine the function of CNCSs in vivo, the researchers deleted the one that drives pharyngeal *Shh* expression and report that this results in the severe underdevelopment of pharyngeal structures, such as the soft palate. These results indicate that the three long-range *Shh* enhancers partition the epithelial lining into three domains and are required for proper epithelial morphogenesis.



Sulphated proteoglycans meshing to the bone?

Heparan sulphate proteoglycans (HSPGs) and chondroitin sulphate proteoglycans (CSPGs) are major components of the extracellular matrix (ECM), but whereas HSPGs regulate various developmental signalling pathways, including hedgehog (Hh) signalling, the function of CSPGs is less clear. In their study of mouse endochondral bone formation on p. 1697, Nancy Schwartz and colleagues now demonstrate for the first time that CSPGs modulate Indian hedgehog (Ihh) signalling. The researchers show that chondroitin sulphate chains (CSCs) are under-sulphated in brachymorphic (*bm*) mutant mice, whereas heparan sulphate chains are normal. To investigate CSPG function, they analysed *bm* limb growth plates (tissue growth areas near the end of long bones), where they detected diminished Ihh signalling, an abnormal, aggregated distribution of Ihh, and decreased chondrocyte proliferation. Using biochemical assays, the authors show that Ihh binds CSCs directly; in addition, Ihh co-immunoprecipitates with the CSPG aggrecan. Based on these and other data, the researchers speculate that HSPGs and CSPGs can function together to establish morphogen gradients and thus modulate Hh signalling in the developing growth plate.



seahorse separates motility and sidedness

Defects in motile cilia, cell surface organelles found in tissues such as the epithelial lining of the lungs, are linked to numerous diseases, including chronic respiratory disorders and disturbances in left-right (L/R) asymmetry, but what role does ciliary motility play in these diseases? On p. 1621, Serluca, Burdine and colleagues report that two mutations in the zebrafish *seahorse* gene, which encodes the leucine-rich repeat-containing protein Lrrc6l, disrupt ciliary motility and cause pronephric cysts, but rarely result in L/R patterning defects. The mutations do not affect pronephric patterning or overall cilia structure, but disrupt ciliary motility in the pronephros and the neural tube. However, their effect on fluid flow in Kupffer's vesicle (KV), a ciliated structure important for L/R asymmetry, is weaker and variable, and changes in KV fluid flow do not correlate well with L/R phenotypes. In addition, a previously reported *seahorse* mutation is known to cause pronephric cysts without disrupting ciliary motility. Thus, the authors suggest that the functions of *seahorse* in ciliary motility and in downstream cilia-related phenotypes are separate.