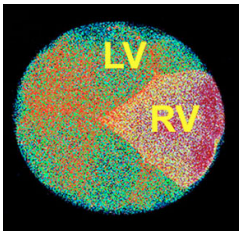
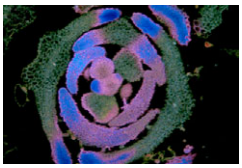


Left-right from the top

What mechanisms are responsible for asymmetric body patterning? To reach the top of the signalling cascade, Michael Levin and colleagues (p. 1657) have explored the role of the ion transporter H^+-V-ATPase (V-ATPase) in regulating left-right (LR) asymmetry. Using a loss-of-function drug screen, they show that a V-ATPase inhibitor induces heterotaxia (the abnormal arrangement of organs) in *Xenopus*, zebrafish and chick. How does V-ATPase affect asymmetry? V-ATPase has two basic functions: to regulate pH and to regulate the membrane potential. By independently manipulating these pharmacologically and in other ways, the authors demonstrate that both are involved in establishing LR asymmetry in *Xenopus*. V-ATP subunits are expressed very early in *Xenopus* development, upstream of other early LR determinants. The authors propose that during early cleavage stages, the asymmetric localisation of V-ATPase creates a membrane potential gradient and a pH gradient, which combine to activate a small charged morphogen, precipitating an asymmetrical genetic cascade. They discuss ways of testing this model in other species.

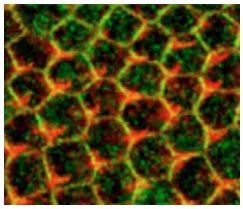


LEAFY feeds forwards

The meristem identity regulator LEAFY (LFY) is crucial for the switch from vegetative growth to flower development in plants. Two downstream targets of LFY are known in this pathway – *APETELA1* and *CAULIFLOWER* (*CAL*) – but the rest of the regulatory cascade is poorly understood. Doris Wagner recently identified five new LFY targets; now her group has found that one of these – LATE MERISTEM IDENTITY 1 (LMI1) – is a meristem identity regulator (p. 1673). *lmi1* mutants enhance the phenotype of a weak *lfy* mutant, abolishing *CAL* induction; moreover, LMI1 binds to the *CAL* promoter, indicating that LMI1 activates *CAL* directly. This interaction between LFY, LMI1 and CAL resembles a transcriptional network motif called a feed-forward loop: LFY activates LMI1, then both activate CAL. The authors explain how this feed-forward loop might ensure that the switch to reproductive development does not respond to transient environmental changes. LMI1 also has LFY-independent roles in leaf development and in leaflet and bract suppression; the authors suggest possible targets of this LMI1 function.

Chipping away at flowering

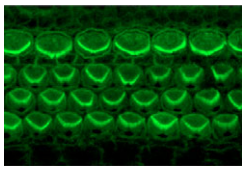
In another study about the switch to flowering (p. 1693), Lars Hennig and colleagues investigate the protein MULTICOPY SUPRESSOR OF IRA1 (MSI1). MSI1 is a component of the fertilization independent seed complex (FIS), which resembles the *Drosophila* Polycomb complex PRC2. The process of flowering is controlled by three main pathways that converge to regulate a protein called SOC1, which is repressed by the potent flowering inhibitor FLOWERING LOCUS C (FLC). First, the authors showed that MSI1 activates the floral transition: *msi1* mutants had a late flowering phenotype, and transgenic plants with increased MSI1 levels flowered early. Then, analysis of *msi1 soc1* double mutants demonstrated that MSI1 acts upstream of SOC1. But by what mechanism? Because FIS is involved in chromatin regulation, they investigated this using chromatin immunoprecipitation (ChIP) assays, and found that MSI1 is required for the H3K4 methylation and H3K9 acetylation of *SOC1* chromatin. Chromatin modifications are known to be involved in the regulation of *FLC*; now, the authors conclude that MSI1 regulates *SOC1* in a similar way.

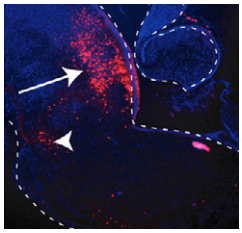


Planar polarity: novel functions and player

Two papers in this issue shed light on the establishment and functions of planar cell polarity (PCP). The PCP pathway, which regulates cell orientation within the plane of an epithelium, was first described in *Drosophila*: activated Frizzled (Fz) receptors trigger the redistribution of core group PCP proteins, which include Dishevelled (Dvl) and Flamingo (Fmi); these then specify the orientation of cells and associated bristles. Frank Laski and colleagues (see p. 1789) have identified a new component of the PCP pathway – a *Drosophila* homologue of the actin depolymerization factor cofilin called Twinstar (Tsr) – that they find is required for Fz and Fmi redistribution during PCP establishment. What does this tell us about the mechanisms that govern the redistribution of core proteins? The authors propose that Tsr-dependent actin reorganisation is triggered by a gradient of activated Fz across the cell, leading to the asymmetric accumulation of Fz and other core proteins that might be either stabilised by actin filaments or transported via an actin-dependent pathway. Asymmetric Fz then signals further reorganisation of actin filaments into future bristles. The authors discuss other factors that might be required for actin cytoskeleton reorganisation in PCP, including the small GTPase Rho.

The PCP pathway is conserved, and homologous pathways have been described in *Xenopus* (where it regulates convergent extension), in zebrafish, and recently in the mouse (where it orientates cochlea sensory hairs). On p. 1767, Anthony Wynshaw-Boris and colleagues show that in the mouse, Dvl homologues – Dvl1 and Dvl2 – regulate a coordinated lengthening and narrowing of the neural plate, which strongly resembles *Xenopus* convergent extension. Furthermore, the authors introduced into the mouse a *Dvl2* transgene carrying a point mutation identical to the *Dsh1* allele that abolishes the PCP pathway in the fly. Following this, Dvl2 was no longer able to regulate convergent extension or the polarity of cochlea sensory hair cells, demonstrating remarkable conservation between PCP in the fly and convergent extension in the mouse.





New dimensions for Shh

The mid/hindbrain is an excellent model for studying 3D tissue patterning, but although its anteroposterior (AP) patterning is well characterised, dorsoventral (DV) patterning is not. Now, Blaess et al. (p. 1799) have used conditional mutagenesis to investigate how sonic hedgehog (Shh) directs DV patterning. Shh has two signalling modes involving the Gli transcription factors: in Gli2A-mediated Shh signalling, Shh converts Gli2 into a transcriptional activator; and in Gli3R-mediated Shh signalling, Shh opposes the processing of Gli3 into a repressor. The authors conditionally removed all Shh signalling (by mutating the receptor *Smo*) or just Gli2A-mediated Shh signalling (by mutating *Gli2*) at E9.0 or at E11.5 in the mouse mid/hindbrain. Gli2A-mediated signalling was needed early on for ventral patterning and for the dorsal restriction of Gli3 transcription. Gli3R-mediated signalling was important throughout for the development of dorsal structures and before E11 for regulating growth by inhibiting apoptosis. Gli3R-mediated Shh signalling also regulated the expression of the AP organiser Fgf8, leading the authors to conclude that Shh coordinates the AP and DV patterning of the developing mid/hindbrain.

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