

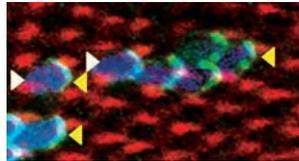
### Facing the complexities of jaw development

During craniofacial development, the lower jaw skeleton is derived from cephalic neural crest cells that are present in the mandibular region of the first pharyngeal arch. To investigate how mandibular identity is specified, Ruest et al. analysed mandibular development in endothelin-A receptor (*Ednra*) null mouse embryos, which are born with severe craniofacial defects (see p. 4413). The researchers report that most of the lower jaw structures in *Ednra*<sup>-/-</sup> embryos are homeotically transformed into upper jaw structures, which are similar changes to those seen in mice lacking two downstream effectors of *Ednra* signalling – the distal-less homeobox genes *Dlx5* and *Dlx6*. These structural changes are preceded by disrupted gene expression in the mandibular arch, except for in one region possibly involved in lower incisor development. Thus, suggest the researchers, establishing mandibular identity requires both *Ednra*-dependent and -independent signalling pathways.



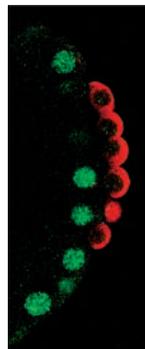
### Localising planar cell polarity

The establishment of planar cell polarity (PCP) – the polarisation of epithelial cells within the plane of the epithelium – is central to the development of many animal organs. To understand how the multiprotein complexes that establish PCP in the *Drosophila* eye are localised, Das et al. have studied flies mutant for such PCP proteins (see p. 4467). They report that, by driving the membrane association of Diego (Dgo), the Wnt receptor Frizzled (Fz) maintains the apical localisation of Flamingo (Fmi), which controls the apical localisation of other PCP factors, including Fz. In this way, a positive-feedback loop is established that controls the initial uniform apical localisation of PCP multiprotein complexes. Later during development, PCP proteins become localised to opposite sides of the cells and, because Dgo is redundant to Prickle (Pk) and Strabismus (Stbm) in maintaining Fmi localisation, the authors speculate that Fz/Dgo and Stbm/Pk maintain Fmi localisation in the R3 and R4 photoreceptors, respectively.



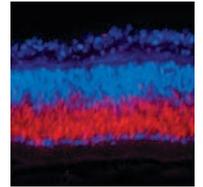
### A fertile migration

Primordial germ cells (PGCs) often migrate long distances through animal embryos to the future gonad, guided by attractive and repulsive cues from surrounding somatic cells. On p. 4545, Hanyu-Nakamura and co-workers investigate how the lipid phosphate phosphatases Wunen (Wun) and Wun2 control PGC (pole cell) survival and migration in *Drosophila*. Somatic expressed Wun and Wun2 are known to provide a repulsive cue for pole cell migration and to reduce their viability when overexpressed. But this new research shows that maternal Wun2 promotes pole cell survival in a cell-autonomous manner, and that this survival is dependent on the balance between the activity of Wun and Wun2 in somatic cells and Wun2 in pole cells. The researchers suggest that somatic Wun and Wun2 direct pole cell migration by depleting an extracellular substrate that is essential for pole cell survival, and speculate that similar mechanisms may act in other developmental processes.



### New retina anyone?

Untreated retinal detachment inevitably causes blindness in humans. However, birds, fish and urodele amphibians are luckier – they can regenerate their retinas. On p. 4607, Spence and co-workers investigate this process in chick embryos. They describe how two modes of retinal regeneration – transdifferentiation of retina pigmented epithelium (RPE) and activation of stem/progenitor cells in the ciliary body and ciliary marginal zone (CB/CMZ) – are both stimulated by Fibroblast growth factor 2 (Fgf2). In addition, they show that ectopic expression of Sonic hedgehog (Shh) stimulates regeneration from the CB/CMZ in the absence of Fgf2, and that Shh-induced regeneration requires Fgf signalling. By contrast, ectopic *Shh* expression inhibits retinal regeneration via RPE transdifferentiation, indicating that Shh is involved in RPE maintenance. Spence et al. conclude that the hedgehog pathway is an important modulator of both types of retinal regeneration.



### HOXA13 and BMPs link limbs

Although many of the genes involved in limb development have been identified, little is known about their transcriptional regulation. On p. 4581, Knosp and co-workers report that HOXA13, a transcription factor whose absence causes developmental defects in mammalian digits and interdigital tissue, controls distal limb morphogenesis by directly regulating the expression of bone morphogenetic proteins (BMPs) 2 and 7. The researchers show first that *Bmp2*, *Bmp7* and *Hoxa13* are co-expressed during normal mouse limb development, and that absence of functional HOXA13 reduces *Bmp2* and *Bmp7* expression in the affected limb tissues. Then, they identify and characterise enhancer regions in *Bmp2* and *Bmp7* that interact with the HOXA13 DNA-binding domain in vitro and in vivo. Finally, they show that exogenously applied BMP2 or BMP7 partly rescues the *Hoxa13* mutant limb phenotype. These results thus identify an important mechanistic link between two well-characterised families of developmental factors.



### Gasping for air

Early embryos get the oxygen they need for metabolism by diffusion. After gastrulation, however, efficient oxygen delivery requires a cardiovascular system. On p. 4623, Ramírez-Bergeron and colleagues use a mouse embryonic stem (ES) cell culture system to show that hypoxic responses are important for establishing the early mesoderm and its differentiation into haemangioblasts – bipotential precursors of endothelial and haematopoietic cells. They report that hypoxia accelerates the expression of Brachyury (a mesoderm-patterning gene), BMP4 (a mesoderm-promoting growth factor) and FLK1 (the receptor for vascular endothelial growth factor and a marker for haemangioblasts). This response depends on hypoxia inducible factor (HIF), as ES cells null for the HIF subunit aryl hydrocarbon receptor nuclear translocator (ARNT) produce fewer FLK1<sup>+</sup> cells in normoxic and hypoxic conditions. The researchers conclude that ineffective responses to hypoxia underlie the previously observed failure of *Arnt*<sup>-/-</sup> embryos to form a functional cardiovascular system.

