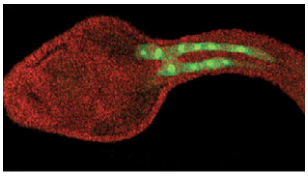
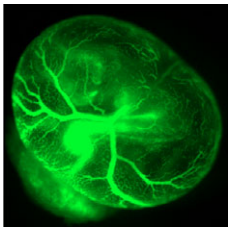
## Why mice have muzzles and birds have beaks

Although the faces of vertebrate embryos look remarkably similar at early stages of development, they rapidly adopt species-specific characteristics. But how is regional specification of the face achieved? The answer, suggest Brugmann and colleagues on p. 3283, is Wnt signalling. Using transgenic Wnt reporter embryos, the researchers show that domains of Wnt-responsive cells in the developing mouse face correspond to the facial prominences (for example, the characteristic muzzle) that develop later. These domains of Wnt responsiveness, the researchers note, generally coincide with areas where there is marked cell proliferation. Furthermore, they report, genetic or biochemical disruption of Wnt signalling in mouse embryos produces animals with unusually wide-set eyes and flattened midfaces. Similar investigations in chick embryos reveal that Wnt signalling is an evolutionarily conserved mechanism that determines facial features by regulating differential craniofacial growth. In other words, the radically different facial features of vertebrates might all be explained by species-specific, regional variations in Wnt signalling during craniofacial development.



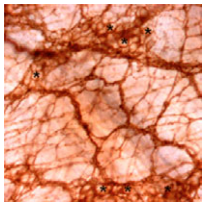
## Heart cell migration outFOXed

Heart development requires precise coordination of morphogenetic movements with cell fate specification and differentiation. Beh and colleagues have been investigating how this is achieved in ascidian embryos and now report that the forkhead transcription factor FoxF is essential for FGF-induced migration of heart precursor cells in *Ciona intestinalis* (see p. 3297). In ascidian embryos, FGF signalling, transduced via the MAPK pathway, activates the transcription factor Ets1/2, which is needed for heart tissue specification and cell migration. Beh et al. show that FoxF is rapidly activated in heart precursors in response to FGF signalling, identify the FoxF minimal heart enhancer, and show that Ets1/2 interacts with this in vivo. Expression of a dominant-negative form of FoxF in heart precursor cells, they report, inhibits their migration but not differentiation and results in the formation of an ectopic beating heart in the tail of juveniles. Overall, these results indicate that FoxF is a direct target of FGF signalling and that it mainly regulates heart cell migration.



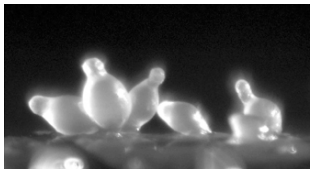
## Vascular remodelling: feel the force

In mouse embryos, the heart begins beating and a network of blood vessels forms in the yolk sac early in development. These initially simple structures are then extensively remodelled. Vascular remodelling needs a normal blood flow, but does this flow deliver oxygen, signalling molecules or mechanical cues? On p. 3317, Lucitti and co-workers report that haemodynamic force drives vascular remodelling in mouse embryos. First, they use time-lapse confocal microscopy and fluorescence recovery after photobleaching (FRAP) to examine blood flow in normal embryos and in embryos lacking myosin light chain 2a (in which impaired cardiac contractility prevents vessel remodelling). These experiments indicate that erythroblast entry into the circulation triggers vessel remodelling. Next, the researchers show that using acrylamide to retain erythroblasts in embryonic blood islands in vivo reduces shear stress and prevents vessel remodelling, which is restored by the addition of a colloid that expands plasma volume. Thus, haemodynamic force is necessary and sufficient to induce vascular remodelling in the mammalian yolk sac.



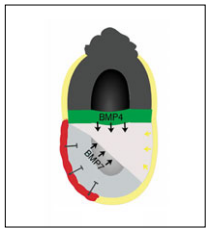
## Sulfs set heparan sulfate code

Heparan sulfate (HS) regulates several extracellular signalling pathways during development, such as the FGF and Wnt pathways. The binding of HS to these ligands and their receptors is regulated by its precise 6-O-sulfated structure, but what controls this 'HS code' and thus the signalling functions of HS? On p. 3327, Ai and colleagues provide the first evidence that the extracellular HS 6-O-endosulfatases SULF1 and SULF2 are essential in vivo regulators of HS-mediated developmental signalling. The researchers identify an oesophageal primary neuronal innervation defect in *Sulf1*$^{-/-}$ *Sulf2*$^{-/-}$ double-null mice and show that aberrant glial cell line-derived neurotrophic factor (GDNF) signalling causes this defect. Other experiments indicate that SULF1 and SULF2 are expressed in the developing oesophagus, that they function redundantly as the major regulators of HS 6-O-desulfation, and that Sulf activity decreases GDNF binding to HS (GDNF binds to HS through its 6-O-sulfate groups). The researchers conclude, therefore, that Sulf activity enhances GDNF signalling in normal mice, consequently promoting neurite sprouting in the embryonic oesophagus.



## Dicty culmination: a breath of ancient air

The soil amoeba *Dictyostelium* is an excellent model system in which to study how environmental signals regulate development. Starvation induces the amoebae to aggregate into a slug, which migrates to the soil surface. Here it 'culminates', forming a fruiting body of spores and stalk cells. Culmination is $O_2$-dependent and, on p. 3349, West and co-workers reveal that the enzyme prolyl 4-hydroxylase-1 (P4H1) acts as an $O_2$ sensor during this stage of *Dictyostelium* development. Culmination normally requires $O_2$ levels above 10%. But, the researchers show, disruption of the P4H1 gene increases this requirement so that culmination is blocked at ambient $O_2$ levels. By contrast, overexpression of P4H1 reduces the $O_2$ requirement of culmination to below 5%. Because P4H1 is an orthologue of the prolyl hydroxlases that sense $O_2$ levels in animals, the researchers suggest that it functions as part of an ancient mechanism for $O_2$ sensing that predates the evolution of animals and that, in *Dictyostelium*, regulates culmination.




## BMPed away from a neural fate

Two main models have been proposed for neural induction in embryos. In the 'default' model, BMP signalling prevents the default, neural differentiation of ectodermal cells. Thus, when BMP signalling is inhibited, no other signal is needed to send these cells down the neural pathway. However, some experiments, particularly in chick embryos, suggest that neural induction also requires FGF signalling. Now, on p. 3359, Di-Gregorio and colleagues report that in the mouse epiblast, loss of BMP signalling is sufficient for neural induction. By examining mice null for *Bmpr1a*, the only type I BMP receptor expressed in the epiblast, the researchers show that BMP2/4 signalling inhibits neural differentiation in the epiblast before gastrulation, in part by maintaining *Nodal* signalling. During gastrulation, BMP7 also helps to maintain the pluripotency of the epiblast. However, inhibition of FGF signalling in post-implantation mouse embryos does not block neural specification. The researchers conclude, therefore, that inhibition of BMP signalling is the critical event required for neural induction in mammals.

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