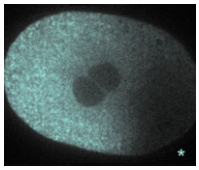
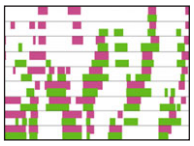


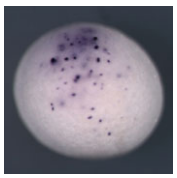
MEX-5 takes its PARtners for asymmetry

Anteroposterior polarity in the *C. elegans* embryo begins with the sperm-induced formation of an anterior cortical actomyosin cap and the asymmetric cortical localisation of the PAR polarity proteins. The subsequent accumulation of the zinc finger protein MEX-5 in the anterior cytoplasm converts this cortical asymmetry into cytoplasmic mRNA and protein asymmetries, but what establishes MEX-5 asymmetry? Tenlen and co-workers now uncover a novel link between the PAR polarity proteins and this asymmetry (see p. 3665). MEX-5 has restricted mobility before fertilisation and in the anterior of one-cell embryos, they report, but in the embryo's posterior its mobility increases as asymmetry develops. They show that a C-terminal domain is required for this increased mobility and identify a crucial residue (Ser458) in the domain that is phosphorylated in vivo. Because the kinase activities of PAR-1 and PAR-4 are required to phosphorylate this residue, the researchers suggest that its phosphorylation might be the elusive link between the PAR proteins and the cytoplasmic asymmetry of MEX-5.



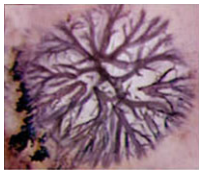
How flies burst into a crawl

The development of proper motor functions is critical to the survival of most animals, but how are stereotypical movement patterns, such as walking and breathing, first generated and then refined? On p. 3707, Sarah Crisp and colleagues report that the first muscle contractions seen in *Drosophila* embryos are generated by spontaneous activity in the muscle cells themselves. However, a drastic change in the pattern of muscle contraction later takes place, with simultaneous bursts of activity occurring in numerous muscles on both sides of the embryo. This transition, the authors find, requires motor, but not sensory, activity, which consists not of the spontaneous firing of individual motoneurons, but rather of the activity of a developing central, pattern-generating motor network. Following the onset of this activity, the muscle contraction pattern that occurs during these bursts begins increasingly to resemble that of crawling larvae. As such, the authors propose that these activity bursts are important for the maturation and development of the central motor network and for coordinated movement.



Boning up on BMP–Wnt interactions

Bone morphogenetic proteins (BMPs) were discovered because they induce ectopic bone formation but now, on p. 3801, Kamiya and colleagues unexpectedly report that BMP signalling negatively regulates bone mass during embryogenesis by upregulating the formation of bone-reabsorbing cells (osteoclasts). To investigate the role of BMP signalling during endogenous bone formation, the researchers disrupted the expression of the BMP receptor BMPR1A in osteoblasts (bone-forming cells) in mouse embryos. They show that levels of bone-resorption markers are reduced in these embryos (which indicates inhibition of osteoclastogenesis) and that bone mass is increased. Wnt signalling (which inhibits the RANKL-OPG pathway, an important mediator of osteoclastogenesis) is upregulated in the *Bmpr1a*-deficient osteoblasts, they report. Other experiments indicate that BMPR1A deficiency upregulates Wnt signalling by downregulating sclerostin, a Wnt inhibitor and bone mass mediator. Thus, the researchers suggest, BMP signalling in osteoblasts restrains endogenous bone mass indirectly by downregulating canonical Wnt signalling through sclerostin and, possibly, by directly upregulating the RANKL-OPG pathway.

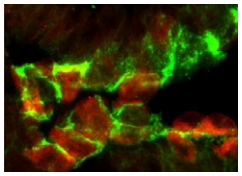


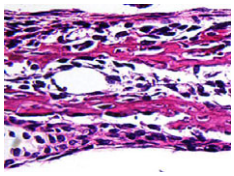
Signals for a good blood supply

The body's organs and tissues depend on a functional vasculature to supply them with nutrients and oxygen. Now, two papers in *Development* shed light on the signalling pathways that control the development of this essential blood vessel network.

In the first study, Christof Niehrs and colleagues identify R-spondin 3 (Rspo3; an activator of Wnt/β-catenin signalling) as a novel, evolutionarily conserved angiogenic factor in embryogenesis (see p. 3655). In vertebrate embryos, blood cells and vascular endothelial cells develop from bi-potent haemangioblasts, but the factors that control haemangioblast fate remain largely unknown. Niehrs' team now shows that Rspo3, which is expressed in blood-forming organs, regulates the balance between endothelial and haematopoietic differentiation in *Xenopus* embryos by promoting the specification of blood-vessel-forming angioblasts and inhibiting haematopoietic (blood-cell) specification. They also report that targeted disruption of *Rspo3* in mouse embryos causes lethal vascular defects, and that R-spondin signalling promotes proliferation and sprouting angiogenesis in human endothelial cells in vitro. Finally, the researchers show that Rspo3 triggers Wnt/β-catenin signalling to induce the expression of VEGF (which promotes endothelial differentiation), indicating for the first time that Wnt and VEGF signalling function in an integrated pathway that enhances angiogenesis.

In the second paper, Rong Wang and colleagues reveal that Notch and ephrin B2/EphB4 signalling play important but different roles in the development of a functional vasculature. Both pathways, they report, coordinate the sizes of arteries and veins formed during angiogenesis and consequently ensure that proper interfaces form between them (see p. 3755). By examining the effects of gain-of-function and loss-of-function *Notch* alleles in mouse embryos, Wang's team shows that Notch signalling promotes arterial specification, which controls the proportion of arterial to venous endothelial cells and thus regulates the relative sizes of the developing dorsal aorta and cardinal vein. Disruption of ephrin B2/EphB4 signalling also alters the relative sizes of these vessels, they report, but by causing endothelial cells with venous identity to mislocalise into the aorta. Overall, these results suggest that the Notch and ephrin B2/EphB4 signalling pathways are both essential for balanced ateriovenous development during blood vessel formation.





A Wnt-Wnt situation

Wnts are a large family of secreted signalling proteins that act via two main pathways, the canonical and non-canonical pathways, to play important roles in development. At least fifteen different Wnts are found in vertebrates, and each one appears to function in just one pathway and independently of other Wnts. Now, on p. 3719, Janet Heasman and colleagues report that two Wnts, Wnt5a and Wnt11, act together to activate both the canonical and non-canonical pathways during dorsoventral (DV) patterning in the *Xenopus* embryo. The authors arrive at this finding through investigating the action of maternal Dkk1, a canonical Wnt inhibitor, in DV patterning. Dkk1 turns out to inhibit both the canonical and non-canonical pathways by targeting maternal Wnt5a and Wnt11, which the authors show interact with each other. Surprisingly, they find that these Wnts are present as homodimers, rather than as monomers, which interact to generate larger signalling complexes. Future work should reveal whether such interactions form a general, hitherto unrecognised feature of Wnt signalling.