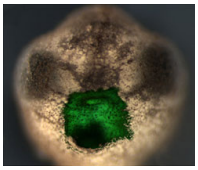
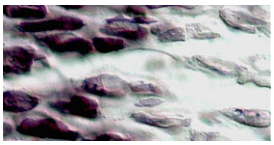


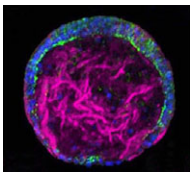
Mouths open with Wnt antagonists

The primary mouth – the initial opening connecting the embryonic foregut to the outside world – forms from a mesoderm-free domain at the front of deuterostome embryos (in which the mouth forms after the anus). Early in the mouth's formation, the basement membrane between the ectoderm and endoderm in this domain disappears. Dickinson and Sive now report that Wnt antagonists locally regulate this process in *Xenopus* embryos (see p. 1071). The researchers show that *frzb-1* and *crescent* – which encode secreted frizzled-related proteins (sFRPs), a class of Wnt antagonists – are transiently and locally expressed in the primary mouth anlage. Other experiments indicate that sFRP function is crucial for primary mouth formation and that Frzb-1 overexpression decreases the expression of the basement membrane genes *fibronectin* and *laminin*, whereas Wnt-8 overexpression increases their expression. These data, which are the first to connect Wnt signalling and basement membrane integrity during primary mouth development, suggest that the modulation of Wnt signalling might regulate basement membrane remodelling during other developmental processes.



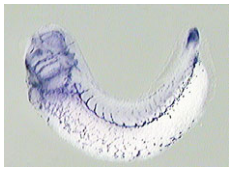
Planar cell polarity signals for bone growth

During long-bone growth, proliferative chondrocytes in the growth plate cartilage form clonal columns of discoid cells, which enlarge to form the hypertrophic chondrocytes that make bone. But what regulates column formation, and is this columnar organisation crucial for bone morphogenesis? On p. 1083, Li and Dudley investigate these questions and, for the first time, implicate a planar cell polarity (PCP)-like pathway in the regulation of bone morphogenesis. They show that the plane of cell division in proliferative chondrocytes in chick long bones is orthogonal to the direction of growth and that the resultant daughter cells, which are initially displaced laterally, intercalate to form a single column of cells. Both the division plane and orientation of the chondrocytes depend on β-catenin-independent, noncanonical Wnt/frizzled signalling, and the disruption of this signalling pathway produces abnormally short and thick long bones. Thus, by regulating the cell polarity of growth plate chondrocytes, noncanonical frizzled signalling (probably via a PCP-like pathway) plays a crucial role in bone morphogenesis.



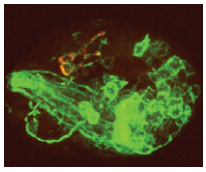
Throw a Six3 for neurogenesis

In sea urchin embryos, Wnt and Nodal signalling centres initiate patterning along the primary and secondary axes, respectively. Now, on p. 1179, Lynne Angerer and colleagues characterise a third, neurogenic patterning centre, the animal pole domain (APD). By investigating the gene regulatory network acting in the sea urchin APD, the researchers discover that the transcription factor Six3 is required for the expression of most of the regulatory genes expressed early in this domain. Six3 is necessary, they report, for the development of the APD and all neurons and is sufficient to suppress Nodal and Wnt signals and to respecify nearly all the cells in the embryo to form an enlarged but appropriately patterned APD. Thus, the APD is a Six3-dependent neurogenic patterning centre in sea urchin embryos and, the researchers suggest, because many Six3-dependent regulatory genes are orthologous to genes expressed in the developing vertebrate forebrain, certain components of the gene regulatory network that regulates neurogenesis may have originated in the common ancestor of echinoderms and vertebrates.



Vascular development by co-operation

The VEGF receptor fetal liver kinase 1 (FLK1) is an early marker of the endothelial lineage and is essential for embryonic vascular development. Now, on p. 1115, Meadows and co-workers report that the transcription factor Krüppel-like factor 2 (KLF2) interacts with ERG (an ETS family transcription factor) to activate *Flk1* expression during vascular development in *Xenopus*. The researchers identify conserved ETS and KLF binding sites within the *Flk1* enhancer and show that the mutation of either site reduces *Flk1* reporter expression in transgenic frogs. Overexpression of either KLF2 or ERG induces ectopic *Flk1* expression in *Xenopus* embryos, whereas inhibition of KLF2 function reduces *Flk1* expression and disrupts vascular development. Furthermore, KLF2 and ERG associate in a physical complex, and the two proteins synergistically activate transcription of *Flk1*. Because several ETS and KLF proteins regulate endothelial gene expression, the researchers suggest that co-operation between these two families of transcription factors could be involved in several aspects of vascular development, function and disease.



CARMIL Racs down neuronal migrations

Many molecules that promote neuronal and axonal growth cone migrations during neuronal development have been identified. Now, however, Vanderzalm and colleagues report that CRML-1 (the *C. elegans* homologue of the mammalian actin-uncapping protein CARMIL) negatively regulates these important migrations in *C. elegans* by inhibiting Rac signalling (see p. 1201). Signalling through Rac GTPases is known to be involved in axonal migration because mutations in Rac GTPases and in their guanine nucleotide exchange factors (GEFs) disrupt axonal migration in *Drosophila* and *C. elegans*. The researchers identify CRML-1 as a negative regulator of neuron and axon migrations in a *C. elegans* genetic screen. They then show that CRML-1 inhibits the Rac GEF activity of UNC-73 (a homologue of the mammalian Rac and Rho GEF Trio) and that CRML-1 lowers the levels of the neuronal guidance receptor SAX-3; UNC-73 increases the levels of this Robo homologue. Together, these results reveal a novel role for a CARMIL homologue – the negative regulation of neuron and axon migrations through the inhibition of Rac signalling.

First testis-specific niche factor identified

Male mammals produce spermatozoa throughout adult life from spermatogonial stem cells (SCCs). Like other adult stem cells, the self-renewal and differentiation of SSCs are supported by a 'niche', but how does this special microenvironment control these essential SSC functions? Partly, suggest Ralph Brinster and colleagues, by producing colony stimulating factor 1 (Csf1), which acts as an extrinsic stimulator of mouse SSC self-renewal (see p. 1191). The researchers made their discovery by searching for genes that are more highly expressed in the SSC-enriched Thy1$^+$ fraction of mouse pup testes than in the Thy1$^-$ fraction. One gene with this pattern of expression encodes the Csf1 receptor. The researchers subsequently found that recombinant Csf1 enhances the self-renewal of mouse SCCs in vitro and that Csf1 expression in mouse testes is localised to Leydig and myoid cells. Together, these results identify Csf1 as a niche factor and suggest that Leydig and myoid cells contribute to SSC niche function in mammals.

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