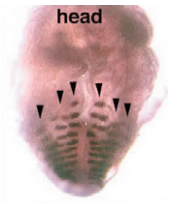
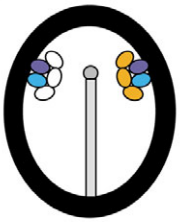


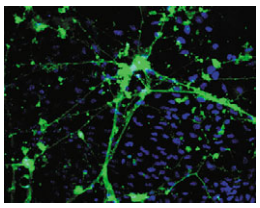
Antagonistic approach to mesoderm development

BMP signalling regulates the development of many cell types throughout embryogenesis. Now, Miura and colleagues report that it is required during gastrulation for the development of the paraxial mesoderm, which forms the connective tissues of the back (see p. 3767). To investigate BMP signalling during gastrulation, the researchers deleted *Bmpr1a* (which encodes a receptor for BMP2 and BMP4) in some epiblast cells of mouse embryos. Whereas *Bmpr1a*-null embryos fail to initiate gastrulation, in these mosaic embryos gastrulation begins normally but then recruitment of prospective paraxial mesoderm to the primitive streak becomes delayed. As a result, cells with paraxial mesoderm character form both in the middle of the streak and at the anterior end where they normally form; strikingly, multiple columns of somites develop as a result. Inhibition of FGF signalling, however, restores the timing of prospective paraxial mesoderm recruitment and partly rescues somite development. The researchers conclude, therefore, that BMP and FGF signalling function antagonistically during the development of paraxial mesoderm.



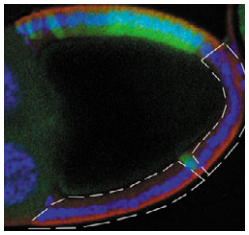
Tsukushi double action in primitive streak induction

The induction of the primitive streak, which defines the axes of the embryo, occurs during gastrulation. In chick embryos, its induction and that of Hensen's node (a thickening of the anterior primitive streak that acts as an organizer) requires VG1 (a TGFβ superfamily member) signals, WNT signals and BMP antagonists. On p. 3777, Ohta and co-workers report that Tsukushi (TSK) – originally identified as a BMP antagonist – cooperates with VG1 to promote the formation of the primitive streak and Hensen's node. They show that alternative splicing of *TSK* mRNA produces TSKA and TSKB; both proteins interact with VG1, but TSKA is the stronger BMP antagonist. *TSKA* expression is highest in Hensen's node (a source of anti-BMP signals), they report, whereas *TSKB* accumulates in the middle of the primitive streak (where *VG1* is expressed) and is required for the induction of Hensen's node. The researchers conclude that the TSK isoforms are crucial modulators of the VG1 and BMP branches of TGFβ signalling during gastrulation.



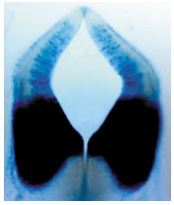
In vitro insights to Wnt roles in vivo

Primitive streak formation and mesoderm development during gastrulation require canonical Wnt signalling. However, determining how it regulates these complex early developmental stages in vivo is a considerable challenge. So Lindsley and colleagues turned to mouse embryonic stem (ES) cells, where they studied the role of canonical Wnt signalling in their differentiation and discovered that it is required for mesoderm induction (see p. 3787). ES cells in which canonical Wnt signalling is inhibited by Dikkopf1, these authors report, fail to generate mesodermal precursor cells. Without Wnt signalling, the differentiating ES cells fail to express genes that are associated in vivo with the development of the primitive streak or with the nascent mesoderm and endoderm lineages. They also report that Wnt signalling alone is insufficient to induce mesodermal gene expression but that it is required during this process and acts cooperatively with Bmp signalling. Overall, these results suggest that Wnt signalling regulates the responsiveness of early embryos to other effector pathways during germ layer induction.



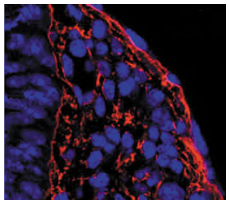
Bottom line for epithelial polarization

The interaction between epithelial cells and the extracellular matrix (ECM) is crucial for epithelial morphogenesis. One component of this interaction is Dystroglycan (Dg), a cellular receptor that links the ECM to the cytoskeleton. On p. 3805, Schneider and colleagues report that Dg interacts with the ECM ligand – Perlecan (Pcan) – to promote and maintain epithelial polarity in the *Drosophila* follicle cell epithelium. The researchers report that follicle cells that lack Pcan (*trol* mutant cells) develop polarity defects similar to those seen in *Dg* mutant cells, and show that Dg and Pcan interact in vitro. They also show that Dg depends on Pcan but not on laminin (another ECM ligand of Dg) for its localization in the basal membrane domain of follicle cells. Dg promotes the differentiation of this cellular domain, the authors report, by recruiting/anchoring the cytoplasmic protein Dystrophin and excluding Neurexin, a basolateral protein. Given these results, the researchers propose that Pcan and Dg interact to promote and maintain polarity in this epithelium.



Megane: a basic requirement for GABAergic identity

Conserved bHLH transcription factors regulate cell-fate decisions and neuronal differentiation in the developing CNS of invertebrates and vertebrates. In *Drosophila*, Hairy and Enhancer of split [H/E(spl)] bHLH proteins maintain neural progenitors in a proliferative state by antagonizing the activity of proneural bHLH proteins. But, as Guimera and co-workers now report, the H/E(spl)-related mouse protein Megane (Mgn) is required for the differentiation of GABAergic neurons in the superior colliculus, part of the dorsal midbrain (see p. 3847). To discover the physiological role of Mgn, the researchers generated *Mgn*-null mice, which made normal numbers of GABAergic progenitor cells during development but failed to express *Gad65* or *Gad67* in the superior colliculus; these genes encode the enzymes that synthesize the inhibitory neurotransmitter GABA. As is consistent with a deficit in GABAergic neurons, the mice also developed epilepsy-like symptoms soon after birth. Thus, the researchers propose that vertebrate *h/E(spl)*-related genes, unlike those in the fly, can be involved in the acquisition of specific neuronal identities.



MAN1y interactions shape vascular development

Although the function of some inner nuclear membrane proteins is known, the function of others – including Man1 – remains unclear. Man1 negatively regulates Tgfβ signalling by interacting with receptor-associated Smads in cultured cells. But what is its role in vivo? On p. 3919, Ishimura and colleagues propose that Man1 regulates angiogenesis during mouse embryogenesis by interacting with Smads. Their findings show that embryos in which the Smad-interaction domain of *Man1* is deleted die at midgestation, owing to defects in their embryonic vasculature. They report that increased Smad2/3 signalling and Tgfβ1 expression in these *Man1*-deficient embryos cause increased extracellular matrix (ECM) deposition, as is also seen in people with *MAN1* mutations. This increased ECM deposition probably inhibits endothelial cell proliferation and migration; the recruitment of smooth muscle cells to the vascular wall is also disturbed. Together, these results suggest that Man1 regulates embryonic vascular remodelling by interacting with receptor-associated Smads at the inner nuclear membrane to ultimately modulate Tgfβ signalling.

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