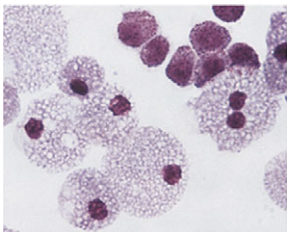
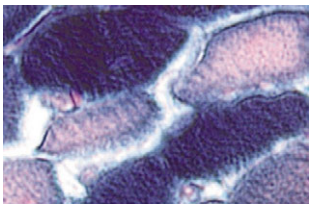


Haematopoiesis and placental potential

During mouse embryonic development, haematopoietic cells develop at several sites in the embryo, such as the yolk sac. The mid-term placenta also contains many haematopoietic cells but, until now, it has been unclear whether it is a source of haematopoietic cells or a stem cell niche. On p. 4183, Zeigler and co-workers help resolve this issue by demonstrating that the placenta has haematopoietic potential. The chorio-allantoic placenta of mammals forms through the fusion of the allantois (the precursor of the umbilical cord) and the chorion, which forms the chorionic disc. By isolating the allantois and chorion from mouse embryos before the establishment of the embryonic circulation, the researchers show that both tissues contain cells that express Runx1, a transcription factor that is required for haematopoietic stem cell formation. Furthermore, both tissues form myeloid and erythroid cells in explant cultures, even before chorio-allantoic fusion. The researchers conclude that both of the tissues that form the mammalian placenta, like the allantois in avian embryos, have intrinsic haematopoietic properties.

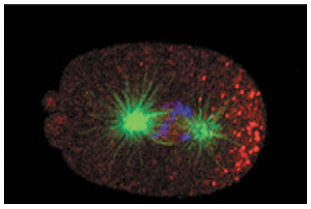
(Non)coding for silence

During early embryogenesis, epigenetic marks (e.g. DNA methylation) are added to clusters of imprinted genes to direct their subsequent expression from one parental allele. Lewis, Green and co-workers have been analysing the epigenetic modifications to, and the allele-specific expression patterns of, the genes in the mouse *Kcnq1* imprinted domain and now describe the epigenetic dynamics of this cluster (see p. 4203). The *Kcnq1* domain contains one paternally expressed gene (the non-coding antisense transcript *Kcnq1ot1*), several nearby genes that are paternally repressed in all lineages by this transcript and other more distant genes that are paternally repressed in only placental lineages. The researchers report that *Kcnq1ot1* silences the ubiquitously imprinted genes by the blastocyst stage – a similar timing to that of imprinted X inactivation. By contrast, the genes that are imprinted only in the placenta, although also regulated by *Kcnq1ot1*, are inactivated later during trophoblast differentiation. The researchers conclude that epigenetic gene silencing by non-coding RNA may depend on the distance from the RNA and on lineage- and differentiation-specific factors.



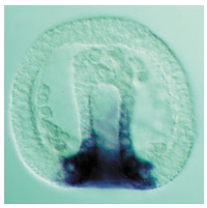
An enhanced view of myocardin transcription

Myocardin, an early cardiac and smooth muscle cell lineage marker, is a transcriptional co-activator of serum response factor (Srf), which regulates the expression of many myogenic genes. But what regulates myocardin expression? On p. 4245, Eric Olson's team reports that a combination of Mef2, Tead and Foxo transcription factors regulates myocardin expression during cardiovascular development. By examining the expression of a *lacZ* reporter gene linked to various non-coding regions of the gene in transgenic mice, the researchers identified a 10 kb fragment that recapitulates the expression pattern of myocardin during cardiogenesis. They then homed in on a 350 bp enhancer region within this fragment, the activity of which requires the combined action of Mef2 and Foxo in cardiomyocytes, plus Tead in smooth muscle cells. Other results indicate that, unlike most myogenic genes, myocardin expression does not depend on Srf. Instead, myocardin activates its own enhancer via Mef2. This suggests that a unique positive-feedback loop regulates smooth- and cardiac-muscle-specific transcription during cardiovascular development.



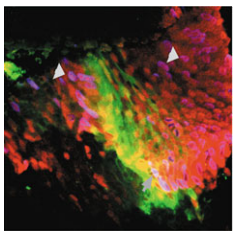
A new player in patterning by proteolysis

The transition from egg to embryo in *C. elegans* involves fertilisation, meiosis, exit from meiosis and the establishment of the anteroposterior (AP) axis. These last two processes may be connected – many mutants with meiotic defects, including several that affect ubiquitin-mediated proteolysis, have polarity defects. Now, Bruce Bowerman and colleagues report that PAM-1, a puromycin-sensitive aminopeptidase that might act in conjunction with the proteasome to degrade ubiquitin-tagged proteins, is required for both meiotic exit and AP polarity in one-cell worm embryos (see p. 4281). The researchers show that meiotic exit is delayed and the AP axis is not specified in *pam-1* mutants. As inactivation of the B-type cyclin CYB-3 rescues the first (but not the second) of these defects, PAM-1 may regulate CYB-3 during meiotic exit but presumably targets other proteins to regulate polarity. The researchers conclude that PAM-1 contributes to the proteolytic machinery that triggers cell-cycle progression and the establishment of AP polarity in the early worm embryo, and possibly in other embryos.



Finding the Notch-TCF connection

During early mesoderm induction in sea urchin embryos, maternal signalling through the Wnt/β-catenin/TCF pathway activates the expression of endomesodermal genes. It also drives the expression of the Notch ligand Delta, which regulates the formation of mesodermal precursors. However, later on, Wnt signalling is downregulated in the mesodermal precursors. Now, on p. 4341, Röttinger and co-workers reveal that the Nemo-like kinase (NLK) acts downstream of Notch/Delta signalling to downregulate TCF activity during mesoderm induction in sea urchin embryos. They show, for example, that the expression of *nlk* in the mesodermal lineage is regulated by Notch/Delta signalling and that Delta-induced expression of *nlk* inhibits TCF function in mesodermal lineages. These results and those from other model systems suggest that, through its ability to inhibit TCF, NLK functions as a conserved negative regulator of Wnt signalling during animal development. They also provide intriguing insights into how the Notch/Delta pathway, although initially activated by Wnt signalling, subsequently acts through NLK to downregulate Wnt signalling.



Fishing for adult neural stem cells

The recent discovery of neural stem cells in the adult rodent forebrain advances attempts to develop treatments for neurodegenerative disorders and brain damage. However, to achieve this goal, the mechanisms that control adult neurogenesis must be understood. To investigate these, Laure Bally-Cuif and colleagues have turned to adult zebrafish, where they have now identified a pool of neural stem cells at the midbrain-hindbrain boundary (MHB; see p. 4293). They show that Her5 – one of the Hairy/Enhancer of Split [H/E(Spl)] transcription factors that regulates embryonic neuronal stem cells – is expressed in a few adult brain cells at the MHB. This cell population proliferates slowly, self renews, expresses neural stem cell markers and is multipotent in situ. The researchers propose that Her5 specifies both the adult and the embryonic neural stem cell state and suggest that a systematic examination of the expression of H/E(Spl) transcription factors in zebrafish adult brain might reveal new details about the regulation of adult neural stem cells.

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