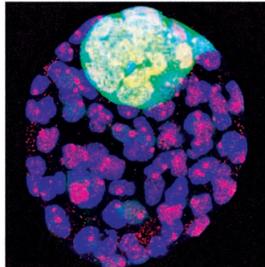


Maternal Ezh2 required for early mouse development

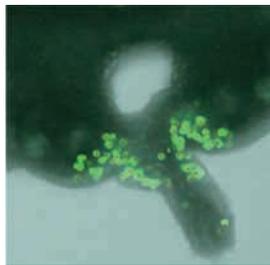
Heritable epigenetic control of gene expression is essential for the early development of most organisms. One protein involved in this process is enhancer of zeste 2 (*Ezh2*), which is maternally inherited, contains a conserved SET domain and is involved in methylating lysine residues on histone tails. To investigate the role of *Ezh2* in early mouse development, Erhardt et al. used a conditional *Ezh2* allele to deplete oocytes of maternal *Ezh2* (see p. 4235). Even though embryonic transcription of *Ezh2* occurred as early as the four-cell stage, loss of maternal *Ezh2* resulted in severely retarded foetal and neonatal growth. The authors attribute this effect to the disruption of the asymmetry in histone methylation that is normally established in the zygote by maternal *Ezh2*. They also report that maternal *Ezh2* is required for crucial epigenetic changes in trophectoderm and epiblast cells.



Germ cell migration: signalling the way

Gonad development usually involves the migration of primordial germ cells (PGCs) to the eventual site of gamete production. In zebrafish, this migration requires a signalling system comprising stromal cell-derived factor 1 (SDF1) and the G-protein coupled receptor CXCR4. On p. 4279, Molyneux and colleagues have investigated whether PGC migration mechanisms are conserved between zebrafish and mice; they report that mice share many of the same requirements.

For example, in cultured mouse embryos, exogenous SDF1 diverted PGCs from their normal route from the gut to the genital ridge. Similarly, in *Cxcr4*^{-/-} embryos, germ cells did not colonise the genital ridge normally. However, *Cxcr4*^{-/-} mouse germ cells still migrated from the primitive streak to the gut, whereas in zebrafish, SDF1-CXCR4 signalling is needed for this stage of migration.



Wise control of Wnt signalling

Neural anteroposterior (AP) patterning requires numerous signalling molecules, including the Wnts. But how are these many signals integrated? On p. 4295, Itasaki et al. tackle this question by performing a functional screen for activities that alter the AP character of *Xenopus* animal caps, which have been neuralised with *noggin* RNA. They report the isolation of Wise (for Wnt modulator in surface ectoderm) from this screen, a novel, secreted cysteine knot factor that can activate or inhibit Wnt signalling in a context-dependent manner. For example, in an animal cap assay, Wise can induce posterior neural markers by activating the Wnt signalling pathway. By contrast, in an assay for secondary axis induction, Wise inhibits Wnt signalling. These results, together with data showing that Wise and Wnt8 compete for binding to LRP6, a Wnt co-receptor, add a new dimension to our understanding of Wnt signalling during development.



Proneural gene evolution

Because the *achaete-scute* (*ac/sc*) genes seem to initiate nervous system development in all arthropods, knowing how their number and function varies between Arthropoda species should provide insights into the evolution of nervous system development in insects. On p. 4373, Wheeler et al. describe the *ac/sc* genes of the red flour beetle (*Tribolium castaneum*), which diverged from *Drosophila* ~300 million years ago. Both species encode a single neural precursor gene – *asense* – which is expressed in all neural precursors. However, whereas *Drosophila* encodes three proneural genes (*achaete*, *scute* and *lethal of scute*), which promote neural precursor formation, *Tribolium* encodes a single proneural gene – *achaete-scute homologue* (*Tc-ASH*). *Tc-ASH* alone can promote neural precursor formation from ectodermal cells, but unlike *achaete* and *scute*, it plays no apparent role in the fate specification of individual neural precursors, hinting at a recent evolutionary specialisation in the *Drosophila* lineage.



Kekkon 1: from development to cancer therapy?

Signalling through the *Drosophila* EGF receptor (DER), which is involved in several developmental processes, is controlled by activating and inhibiting ligands. On p. 4483, Ghigliione et al. examine how one inhibitor, Kekkon 1 (Kek1), achieves the negative feedback control of DER that occurs during *Drosophila* oogenesis and imaginal disc development. Their structure-function analyses show that the extracellular, leucine-rich repeat domains of Kek1 are needed for the in vivo association of Kek1 and DER as a heterodimer. Their findings also show that, in mammalian cell-based assays, the interaction of Kek1 with mammalian ErbB growth factor receptor tyrosine kinases blocks activating ligands from binding these receptors, as well as blocking their autophosphorylation and subsequent signal transduction. Given the overexpression of some of these receptors in human tumours, Ghigliione et al. suggest that Kek1 or its unknown mammalian homologues might have clinical utility as anti-tumour agents.

In Journal of Cell Science

VEGFR-1: receptor, antagonist, integrin ligand

Vascular endothelial growth factor receptor-1 (VEGFR-1), which is involved in vasculature organization, is not just a receptor tyrosine kinase: it is also secreted as a soluble splice variant, sVEGFR-1, that is thought to sequester ligands or form non-signalling heterodimers with VEGFR-2. Orecchia et al. now reveal that sVEGFR-1 has an additional role as an integrin ligand. They show that cultured endothelial cells deposit sVEGFR-1 in the ECM, and that anchored sVEGFR-1 can stimulate endothelial cell adhesion, spreading and migration – antibodies against $\alpha 5 \beta 1$ integrin block these effects. Moreover, sVEGFR-1 binds directly to this integrin in vitro, indicating that sVEGFR-1 has a novel function in angiogenesis that extends beyond that of a simple VEGF receptor – a finding that is significant given the possible role of this integrin in tumour-induced angiogenesis.

Orecchia, A. et al. (2003). Vascular endothelial growth factor receptor-1 is deposited in the extracellular matrix by endothelial cells and is a ligand for the $\alpha 5 \beta 1$ integrin. *J. Cell Sci.* **116**, 3479–3489.