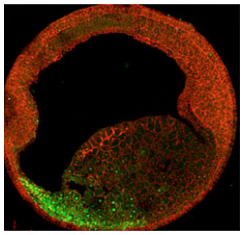
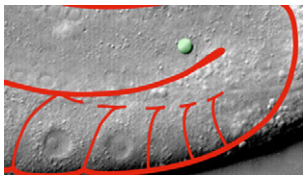


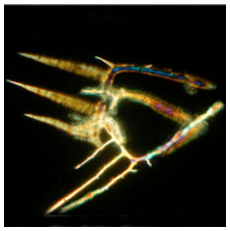
Wnt off: liver on

The liver and the pancreas are specified from the foregut endoderm, but how early foregut precursors form remains unknown. Aaron Zorn's group now report that in *Xenopus*, the Wnt pathway links early gastrula-stage endoderm patterning to organ specification. Their results, on p. 2207, show that while in anterior endoderm, Wnt/β-catenin activity is repressed, inducing liver and pancreas specification, it's upregulated in the posterior endoderm, where foregut fate is inhibited and intestinal development occurs. Their experimental repression of β-catenin activity in the embryonic posterior endoderm induced ectopic organ buds to form that express early hepatic and pancreatic markers; increased β-catenin activity in the foregut endoderm repressed liver and pancreas formation. The early foregut marker, *hhex*, is a target of this β-catenin activity and is repressed indirectly via the transcriptional repressor Vent2. Wnt signalling later enhances liver development. Thus, turning Wnt signalling on/off at the right moment is essential for these organs' proper formation, a finding that should advance the differentiation of liver and pancreatic tissue from stem cells.



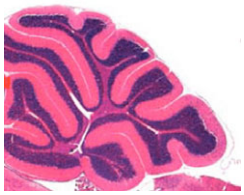
Streamlining oocyte growth

Cytoplasmic streaming – in which RNA and protein is transported from polyploid nurse cells to the growing oocyte – in *Drosophila* is well documented; however, little is known about how cytoplasmic materials accumulate in growing *C. elegans* oocytes, which lack nurse cells. James Priess's lab now reveals that mitochondria and germline-specific proteins – in addition to injected foreign material, such as oil droplets or polystyrene beads – travel from the gonad region, where pachytene nuclei are situated, to the oocyte, supporting the view that pachytene-stage nuclei function as transient nurse cells before differentiating into oocytes (see p. 2227). Interestingly, and in contrast to *Drosophila* where cytoplasmic materials are pushed into the oocyte from nurse cells, in the worm cytoplasmic material is pulled into the enlarging oocyte by acto- and myosin-dependent forces generated adjacent to, or even within, the enlarging oocyte. RNAi-knockdown studies reveal that microtubules are not essential in this streaming event. Future studies are likely to focus on the molecular mechanisms that regulate this key process.



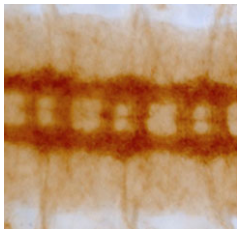
VEGF to the bones

Spicules – mineralised rods that constitute the sea urchin skeleton – form from a small number of primary mesenchymal cells (PMCs). During gastrulation, these PMCs locate along the ectodermal wall in a stereotypical pattern that determines skeletal morphology. As yet unknown guidance cues from the ectoderm are thought to control PMC positioning. VEGF/VEGFR signalling between the ectoderm and PMCs is now shown by Christian Gache's lab on p. 2293 to be the missing link that directs PMC migration and, thus, skeletal morphology. While VEGFR is expressed in PMCs, its ligand, VEGF, is expressed in the overlying ventrolateral ectoderm. Impaired VEGFR signalling perturbs PMC positioning (and spicules subsequently don't form), whereas VEGF overexpression results in skeletal abnormalities. Ectopically expressing VEGF in embryos in which endogenous VEGF expression is blocked restores spicule formation. These and other findings reveal that localized VEGF acts as both a guidance cue and differentiation signal, providing a crucial link between the positioning and differentiation of PMCs and embryonic skeletal morphogenesis.



Brain subdivisions; the engrailed way

The developing nervous system's morphology is crucial for establishing functional circuits. The Joyner lab previously showed that engrailed 1 (*En1*) mouse mutants lack most of the tectum and cerebellum (Cb) and die at birth, whereas *En2* mutants survive but have smaller cerebellums; the earlier expression of *En1*, rather than differences in protein function, account for these differences. This group now report that En proteins mediate a dosage-dependent genetic subdivision of the tectum into its two functional systems and the cerebellum into six distinct regions (see p. 2325). The posterior tectum is reduced when *En1* is conditionally deleted before E9; however, two copies of *En2* can sustain Cb development in these mice. A functional comparison of *Drosophila engrailed, En1* and *En2* indicates that *En2,* but not *engrailed* can rescue *En1* mouse mutant brain defects in the absence of endogenous *En2*. Interestingly, *En1/2* double mutants have neural phenotypes similar to those of Fgf mutants, indicating that En1/2 either maintains Fgf expression or acts downstream of it.



Integrins on the Cas(e)

Cas family Src homology-3 (SH3)-domain-containing signalling proteins regulate, in non-neuronal cells, actin cytoskeletal dynamics. In neurons, guidance cues and receptors modify cytoskeletal components in growth cones; however, a detailed understanding of the downstream signalling events that influence axon and dendritic pathfinding has remained elusive. On p. 2337, Jonathan Terman's and Alex Kolodkin's groups now identify a *Drosophila* Cas (DCas) protein; it is highly expressed in neurons and functions in axon guidance with integrins by regulating the degree of axonal fasciculation. A series of loss-of-function and overexpression experiments in flies shows that DCas interacts in a dose-dependent manner with the α1, α2 and β1 integrin receptor subunits to regulate motor axon defasciculation and guidance. The loss of DCas or integrin receptors from *Drosophila* motor neurons causes axons to grow past, or to stall at, their normal defasciculation point. Integrin-dependent hyperfasciculation defects occur in neurons where DCas is overexpressed. Integrin/DCas-mediated signalling is necessary but not sufficient for axonal defasciculation, thus other components involved in this process await identification.

The web of death

Programmed cell death (PCD) in the interdigit region of developing vertebrate limbs generates separated rather than webbed digits. Previous models have proposed that bone morphogenetic proteins (BMPs) directly trigger such PCD; however, they might also act indirectly by regulating fibroblast growth factors (FGFs), which act as cell survival factors. To investigate this question, Mark Lewandoski's group inactivated the BMP receptor gene *Bmpr1a* specifically in the limb bud's apical ectodermal ridge (AER) – a source of FGF activity. They report on p. 2359 that in mice, BMP signalling mediates AER induction. However, it subsequently inhibits the expression of the AER survival factors *Fgf4* and *Fgf8*, leading to interdigit PCD. By generating conditional mutant mice, the authors show that *Bmpr1a* inactivation induces *Fgf4* and *Fgf8* upregulation in the AER. Webbing persists in mice where *Bmpr1a* and *Fgf8* are inactivated, but disappears when one copy of *Fgf4* is also inactivated. Evolutionary alterations in AER FGF activity might account for changes in limb morphology in different species.