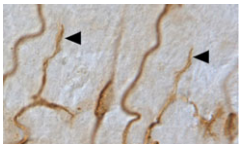
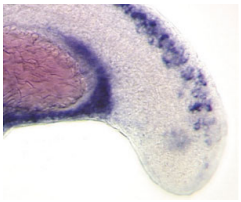


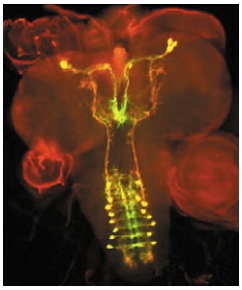
Axon guidance gets per-Plexin

During development, neurons are guided by multiple guidance molecules and their receptors, but how developing neurons integrate these different guidance cues to form neural circuits is unclear. Alex Kolodkin's team has been examining the roles of plexins – receptors for the semaphorin guidance cues – in the developing *Drosophila* nervous system. On p. 2125, these researchers report important new insights into how the multiple components of the semaphorin system interact by showing that the two fly plexins (PlexA and PlexB) have both distinct and overlapping functions in central and peripheral axon pathfinding. Their observation that PlexA and PlexB physically associate in vivo and can use common downstream signalling pathways provides an explanation for their overlapping functions. The researchers' discovery that PlexB is a receptor for the secreted semaphorin Sema-2a – PlexA is a receptor for the transmembrane semaphorin Sema-1a – suggests that the distinct roles of the two plexins in axon pathfinding could be mediated by interactions with different semaphorins. Together, these results reveal how complex neuronal guidance is determined at different molecular levels.



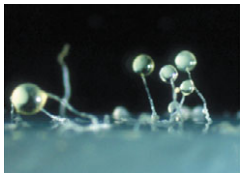
Bmp signals for cloacal development

Bone morphogenetic protein (Bmp) signalling is required for the induction of ventral mesoderm derivatives (e.g. blood, kidney and vascular cells) during early vertebrate development. However, its later effects on ventral mesoderm differentiation are unknown. Now, David Kimelman and colleagues report that sustained Bmp signalling is essential in zebrafish for development of the cloaca, the common gut and urogenital opening (see p. 2275). Using transgenic zebrafish that express an inducible dominant-negative Bmp receptor, the researchers show that inhibiting Bmp signalling at mid-gastrulation causes blood and vascular precursors to expand into the extreme ventral embryonic region where the cloaca normally forms. Cloacal patterning and function, they report, depends on sustained Bmp signalling; this is partly mediated by the Bmp-regulated T-box transcription factor HrT. Overall, the researchers conclude that the function of Bmp signalling changes dramatically over time with respect to its effects on ventral mesoderm development. They also suggest that subtle alterations in Bmp signalling might cause some human cloacal malformations.



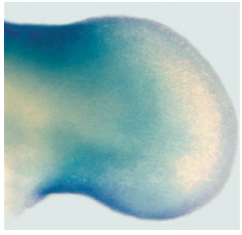
Metamorphosis through death

The life of an adult fly is much more complicated than that of its larva – simple feeding and crawling are replaced after metamorphosis by flying, mating and other complex behaviours. This lifestyle change requires the reorganisation of the larval nervous system through neuronal remodelling and programmed cell death (PCD). Now, on p. 2223, Choi and colleagues describe the molecular mechanisms that drive PCD in vCrz neurons, a group of neurons in the ventral nerve cord of *Drosophila* larvae. They report that vCrz neurons die early in metamorphosis and that signalling through the ecdysone receptor-B is required for their demise. The PCD activator Reaper is also required; *reaper* activates caspases but, the authors report, not through the *Drosophila* inhibitor of apoptotic protein 1, a central regulator of PCD in *Drosophila* embryos. Instead, Reaper might mediate apoptosome assembly, an oligomeric structure that activates caspases. The researchers conclude that activated ecdysone signalling might determine the precise timing of neuronal degeneration during early metamorphosis in *Drosophila*.



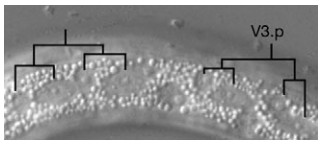
Dicty talk by GABAling

GABA (gamma amino butyric acid) is an important neurotransmitter in *C. elegans*, *Drosophila* and all vertebrates. Now, Anjard and Loomis report that GABA has another role in intercellular communication – inducing sporulation in *Dictyostelium* (see p. 2253). This finding excitingly shows that GABA is not only an important neurotransmitter but also an ancient intercellular signal. Towards the end of *Dictyostelium* development, prespore cells migrate to the top of the fruiting body where they encapsulate in response to a secreted peptide SDF-2, which is generated from a precursor, AcbA, by a prestalk-specific protease. The researchers show that GABA triggers the release and processing of AcbA. By examining the *Dictyostelium* genome, they identified a putative receptor for GABA – GrlE. *Dictyostelium* cells that lack this G-protein-coupled receptor did not produce SDF-2 in response to GABA. Finally, the authors used pharmacological inhibitors and specific mutations to reveal that the effects of GABA on sporulation are mediated by PI3 kinase and a protein kinase B-related kinase, proteins that often act downstream of G-protein-coupled receptors.



Pbx genes extend a limb

For years, developmental biologists have been trying to understand how positional information controls the development of vertebrate limbs. New insights into this three-dimensional puzzle are provided by Capellini and co-workers on p. 2263, who reveal that the homeoproteins Pbx1/Pbx2 regulate distal limb patterning in mice. *Pbx1* is essential for proximal limb development but *Pbx2*-deficient embryos have normal limbs. The researchers now show that compound *Pbx1*$^{-/-}$, *Pbx2*$^{+/-}$ mutant embryos have severe distal limb abnormalities – the fibula and most of the digits are lost in the hindlimb – in addition to exacerbated proximal abnormalities. This distal phenotype resembles that seen in embryos that lack sonic hedgehog (Shh), and indeed, the loss of skeletal elements in mutant hindlimbs is mediated by the absence of *Shh*. This deficit is preceded by a severe perturbation of Hox gene expression. The researchers conclude, therefore, that *Pbx1/Pbx2* regulate vertebrate distal limb patterning partly by controlling the spatial expression of Hox genes and Shh expression.



Keeping *C. elegans* development on time

Postembryonic metazoan development is genetically programmed but its timing can be modified by environmental factors. Because sensory neurons detect these cues, Ruaud and Bessereau are studying the role of the nervous system in the temporal regulation of postembryonic *C. elegans* development. They now report that nicotinic receptor activation caused by exposure to DMPP, a nicotinic-receptor agonist, delays development in the second larval stage (L2) of *C. elegans* but does not affect the timing of moulting (see p. 2211). As a result, the larvae cannot make a proper L3 cuticle in time and they die at the L2/L3 moult. The researchers report that development and moulting can be resynchronised and that DMPP-induced lethality can be avoided by forcing the worms into a previously unrecognised L2 diapause (arrest in development). Further results indicate that UNC-63, a nicotinic acetylcholine-receptor subunit, and DAF-12, a nuclear hormone receptor that regulates larval entry into L3 diapause, are both components of a neuroendocrine pathway that controls developmental timing in L2 in *C. elegans*.

Jane Bradbury