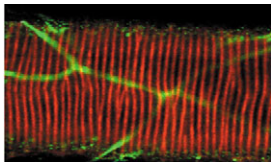
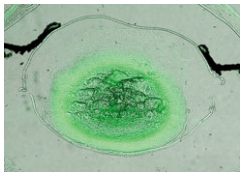
A leg up for tracheal evolution and development

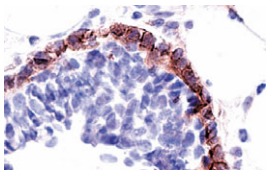
Very small organisms get the oxygen they need for life by diffusion across their body surface, but larger organisms need specialized respiratory organs to do the same job. In insects, the main respiratory organs are the tracheae, an internal tubular network that develops from clusters of ectodermal cells on either side of the thoracic and abdominal embryonic segments. Two papers in this issue of *Development* provide new information about the evolution and development of tracheae. On p. 785, Franch-Marro and colleagues raise the possibility that an evolutionary relationship exists between insect tracheae and the external respiratory gills of crustaceans. These gills are associated with appendages, and Franch-Marro et al. show that *Drosophila* tracheal placodes arise next to leg primordia in the thoracic segments and next to cryptic leg primordia in the abdominal segments; the different fates of the tracheal placode and leg primordia are controlled by Wingless signalling. The researchers also report that homologues of tracheal-inducing genes are expressed in the developing gills of crustaceans. Based on these results, they propose that the ancestors to arthropods had areas on the surface of their body that were specialized for gas exchange, which evolved into crustacean gills and insect tracheae. On p. 957, Matusek and co-workers reveal new details about the development of the *Drosophila* tracheal system by reporting that the formin DAAM (Dishevelled-associated activator of morphogenesis) regulates the tracheal cuticle pattern. The tracheal cuticle resembles a corrugated vacuum-cleaner hose. This structure gives the tracheae rigidity but allows them to bend as the insect moves. The researchers report that in the absence of *DAAM*, an array of actin cables beneath the apical surface of the tracheal cells fails to form properly – formins are key regulators of the cytoskeleton – and consequently the pattern of ridges (taenidial folds) in the tracheal cuticle is disrupted and the tracheal tubes collapse. Other results indicate that *DAAM* activity is regulated by *RhoA* and that *DAAM* works with the non-receptor tyrosine kinases *Src42A* and *Tec29* to organise the actin cytoskeleton and thus determine the cuticle pattern of *Drosophila* tracheae.





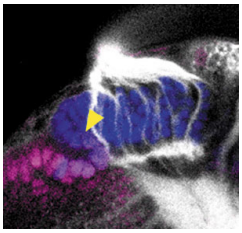
Vision clouded by apoptosis

Vertebrate lenses are transparent because they contain tightly packed primary and secondary lens fibre cells. These cells, which are generated from lens epithelial cells during embryogenesis and throughout adult life, respectively, mature by losing their nuclei and other organelles in a process that uses components of the apoptotic pathway. However, something stops them from completing apoptosis. Morozov and Wawrousek now report that α-crystallin, a major lens protein, suppresses caspase activity in secondary lens fibre cells and prevents their disintegration (see p. 813). α-Crystallin consists of two subunits: αA and αB. αB-crystallin inhibits caspase 3 in vitro but its in vivo effects are unknown. Morozov and Wawrousek report that morphological abnormalities develop in the secondary lens fibre cells of αA/αB-crystallin double knockout mice, which are opaque at birth, and provide data that suggest that these abnormalities result from increased caspase 3 and caspase 6 activity. They also show that there is increased apoptosis in the lenses of the mutant mice and conclude that α-crystallin is an anti-apoptotic agent in the vertebrate lens.



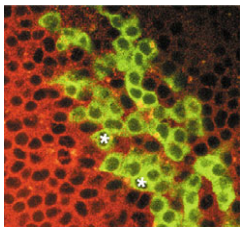
Ductal morphogenesis: new cues

Slits and netrins are well-known neural guidance cues. However, on p. 823, Strickland et al. report that these proteins also act as adhesive cues during mammary gland development, thus providing new insights into ductal morphogenesis. The bilayered branched epithelial tubes of the mammary gland contain an outer cap/myoepithelial cell layer and an inner luminal epithelial layer. The researchers show that both layers express SLIT2 during duct elongation but that only the cap/myoepithelial cells express ROBO1, the SLIT2 receptor. Mice lacking both *Slit2* and *Robo1* have disorganized ductal end buds, which resemble those of mice lacking netrin 1 (*Ntn1*$^{-/-}$ mice). *Slit2*$^{-/-}$; *Ntn1*$^{-/-}$ glands have an even more extreme phenotype that is characterized by the separation of the two ductal cell layers. The researchers confirm this is an adhesive defect by showing that *Slit2*$^{-/-}$; *Ntn1*$^{-/-}$ cells fail to form bilayered organoids in vitro. They conclude that SLIT2 and NTN1 act in parallel as adhesive cues to preserve the bilayer structure of the mammary gland during morphogenetic modelling.



Single-minded connections

Topographic maps – arrangements of synaptic connections that mirror the relationships between neighbouring neurons – ensure the spatially ordered flow of information through the nervous system. Many insights into how these maps are established have come from studying developing visual systems. Now, on p. 791, Umetsu and colleagues report that Hedgehog (Hh) and the transcription factor Single-minded (Sim) regulate the ordered connection of retinal axons with their synaptic partners in the optic lamina of the *Drosophila* visual system. As this system develops, retinal axons extend from the eye into the lamina ganglion layer, where they stimulate proliferation and differentiation of the lamina neurons by secreting Hh. The researchers show that Sim is induced by Hh in the lamina neurons and that this expression is required for the association of retinal axons with lamina neurons – the first step in forming a topographic map. Thus, postsynaptic cells may interact dynamically with presynaptic cells to establish topographic maps rather than waiting passively for axons to arrive, as previously thought.



Straight talking to the pancreas

The transplantation of insulin-producing pancreatic β-cells holds great hope for treating type I diabetes. Supplies of these cells are limited, but a report by Stafford and co-workers that retinoic acid (RA) signalling from the mesoderm directly induces *insulin*-expressing β-cells in zebrafish endoderm advances the prospect of converting stem cells into β-cells for transplantation (see p. 949). The pancreas develops from the endoderm in response to RA synthesized by adjacent mesoderm, but whether RA signals directly or indirectly to the endoderm has been unclear. The researchers used cell transplantation to show that RA synthesis and RA receptor expression in the anterior paraxial mesoderm and endoderm, respectively, but not in other tissues, are required for the development of *insulin*-expressing β-cells. Furthermore, the activation of RA signal transduction in the endoderm alone induces *insulin* expression. Together, these results indicate that mesodermally derived RA is an instructive signal that directly induces pancreatic precursors. Thus, RA could be used to induce stem cells to differentiate into β-cells for therapeutic purposes.

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