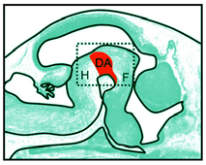
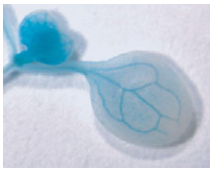


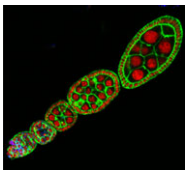
Pitx3 SM(a)RTly derepresses DA neurons

The orphan nuclear receptor Nurr1 and the transcription factor Pitx3 are key regulators of dopaminergic (DA) neuron specification in the mesodiencephalic (md) region, which has been intensively studied owing to the importance of mdDA neurons in Parkinson's disease. Now, Marten Smidt and colleagues demonstrate a functional relationship between these two factors (p. 531). The authors show that both Nurr1 and Pitx3 bind to the co-repressor PSF and that both target the same genomic promoter regions, suggesting that Pitx3 might regulate the activity of the Nurr1 transcriptional complex. Indeed, in *Pitx3*$^{-/-}$ embryos, Nurr1 target gene expression is reduced, in accordance with increased interaction between Nurr1 and the co-repressor SMRT. The researchers also succeeded in partially rescuing Nurr1 target gene expression by interfering with SMRT signalling activity. Based on these findings, the authors propose a novel model in which Pitx3 regulates the capacity of Nurr1 to induce mdDA neuron specification by inducing the release of the SMRT repressor from the Nurr1 transcriptional complex.



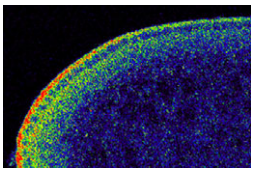
Kinases PIN down auxin transport

The proper distribution of the plant hormone auxin is of crucial importance to plant development. To this end, a complex and strictly regulated system of active auxin transport is in place, but the role of cell-signalling molecules in this system remains largely unexplored. Now, on p. 627, Claus Schwechheimer and colleagues report that a family of plant protein kinases (PKs) regulate polar auxin transport in *Arabidopsis*, probably by phosphorylating PIN auxin efflux carriers. By examining mutations in a subfamily of plant AGC kinases called D6PKs, the authors establish a redundant role for these kinases in auxin transport. They find that, despite lacking any obvious localisation motifs, the D6PKs are localised at the basal membrane of various root cell types, where they colocalise with PIN proteins. Further experiments reveal that PIN proteins are in vitro and in vivo phosphorylation targets of D6PKs, leading the authors to suggest that this might be the functional interaction through which D6PKs regulate directional auxin flow.



Gurken shapes up with lipids

Despite being present in all eukaryotic cell membranes and being implicated in a wide range of biological processes, including human disease, little is known about the in vivo function of glycosphingolipids (GSLs). Now, on p. 551, Sandrine Pizette and co-workers reveal that GSLs are required for the full activation of EGFR signalling during *Drosophila* oogenesis, and that they regulate the formation of an extracellular gradient of the EGFR ligand Gurken. Egghead (Egh) and Brainiac (Brn) are two non-redundant *Drosophila* glycosyltransferases that are crucial for GSL biosynthesis. Using *egh* and *brn* mutant flies, the researchers show that during oogenesis GSLs are required in oocytes, which produce Gurken, but not in follicle cells, which express EGFR. Furthermore, they demonstrate that GSLs do not regulate Gurken trafficking or secretion, as previous data have suggested. Instead, GSLs shape an extracellular Gurken gradient by allowing Gurken to diffuse efficiently. Future work and novel tools will be required, however, to fully understand the mechanism by which GSLs affect Gurken diffusion.



Bicoid gradient: starting with mRNA?

The concentration gradient formed by Bicoid (Bcd), a transcription factor that patterns anterior *Drosophila* development, declines exponentially with distance from the anterior pole of the syncytial embryo, and is a standard paradigm for how a morphogen provides positional information. Now, Markus Noll, Stefan Baumgartner and colleagues challenge a widely accepted model – the SDD model – for the establishment of this gradient (see p. 605). The SDD model proposes that the gradient arises when Bcd is synthesised from a *bcd* mRNA source localised at the anterior pole; Bcd then diffuses away and is uniformly degraded. However, the authors convincingly show that, instead of *bcd* mRNA being localised anteriorly, a *bcd* mRNA gradient is formed and maintained during the syncytial stages, in agreement with publications predating the SDD model. Because Bicoid mRNA and protein patterns are similar to those of Staufen protein, which functions in mRNA localisation in oogenesis, the authors propose a gradient-formation model based on active mRNA transport, which awaits further experimental testing.

Craniofacial development: jaw-dropping insights

Large parts of the craniofacial and pharyngeal skeleton derive from cranial neural crest cells (NCCs) that migrate from the edge of the dorsal neural tube (DNT) to populate the pharyngeal arches (PAs – a series of transient structures that contribute to head and neck formation) and the frontonasal process (which contributes to the forehead and nose). In this issue, two papers provide important new insights into the signalling events involved in this morphogenetic process.

On p. 637, Filippo Rijli, Denis Duboule and colleagues reveal that the first four PAs share a common NCC gene expression ground state. NCCs that contribute to individual PAs express distinct Hox gene combinations that determine PA-specific regional identities; for example, the NCCs that populate the first PA are Hox-negative. Previously, these authors have shown that the first and second PA NCCs in mice share a common Hox-free patterning programme. Now, they demonstrate that deleting the entire HoxA cluster in cranial NCCs leads to the partial homeotic transformation of the third and fourth PA towards a first PA identity. Amongst other effects, this results in the partial quadruplication of Meckel's jaw cartilage, an evolutionarily ancient structure from which the lower jaw and middle ear develop. These findings support the idea that all PAs are part of a single series of segmental structures, and invite the suggestion that the elaboration of regional identity in such structures on top of a shared gene expression ground state constitutes a general evolutionary strategy.

In their study, Hiromi Yanagisawa and colleagues turn to later NCC differentiation events in craniofacial bone development in mice, and report that endothelial signalling through the transcription factor Hand2 negatively regulates the differentiation of NCC-derived osteoblasts in PAs (see p. 615). The authors demonstrate that a decrease in PA-specific *Hand2* expression leads to accelerated osteoblast differentiation associated with the increased and ectopic expression of the transcription factor Runx2, a master regulator of bone differentiation. Based on these and other findings, the authors propose that a vertebrate-specific domain of Hand2 interacts directly with the DNA-binding domain of Runx2 to negatively regulate its activity.