## No REST in ES cell determination

The transcriptional repressor REST has been proposed to target transcription factors crucial for neuronal lineage specification or to maintain pluripotency in embryonic stem (ES) cells, but its specific role in ES cell determination remains unclear. On p. 715, Helle Jørgensen, Amanda Fisher and colleagues report that in ES cells, REST is not required for the repression of transcription factors crucial for neural lineage commitment or for maintaining ES cell potential. By analysing REST-depleted ES cells, the researchers demonstrate that neural determinants, such as MASH1 and neurogenin 1 and 2, remain appropriately repressed, and that the multi-lineage potential and dominant reprogramming capacity of ES cells do not depend on REST. However, a group of genes that is highly enriched for the REST-binding motif RE1, which is implicated in the terminal differentiation and function of neurons, is inappropriately expressed in REST-depleted cells, suggesting that REST might serve to regulate neuronal differentiation programmes rather than the initial stages of neuronal lineage commitment.
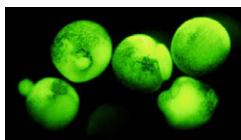
Kaiso role in a DNA bind

The transcriptional repressor Kaiso is reported to bind both methylated DNA and non-methylated CTGCNA motifs and is known to be important for development because morpholino knockdown of Kaiso developmentally delays *Xenopus* embryos during gastrulation. But which DNA binding mode underpins this phenotype? On p. 729, Richard Meehan and colleagues reveal that the main role of Kaiso in *Xenopus* development is associated with its ability to bind methylated DNA. They demonstrate that the CTGCNA-binding function of Kaiso is not evolutionarily conserved, whereas the methyl-CpG-binding function is; this property is also sufficient to rescue the gastrulation phenotype in Kaiso-depleted embryos. Furthermore, these embryos show no change in the expression of key Wnt signalling target genes, which Kaiso's CTGCNA-binding function has been proposed to regulate. In a companion paper (p. 723), the researchers show that Kaiso instead has the potential to perturb Wnt signalling directly by interacting with the Wnt transducer Tcf3, and suggest that this results in the mutual inhibition of the respective DNA-binding functions of Kaiso and Tcf3.
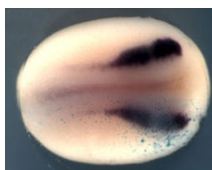
Neural crest does the two-step

Neural crest (NC) cells arise at the dorsal neural tube and give rise to a wide variety of cell types, including parts of the head and the peripheral nervous system. Although NC induction has been proposed to be a multi-step process, and the signals involved in this induction, including Wnt and BMP, have been identified, the spatiotemporal relationships between these factors have remained unclear. Now, on p. 771, Roberto Mayor and colleagues propose a novel two-step model for NC induction. By fate-mapping this tissue in gastrulating *Xenopus* embryos, the authors show that first, signals from a region of the prospective mesoderm, the dorsolateral marginal zone (DLMZ), induce the NC during gastrulation. In a second step, signals from the intermediate mesoderm, which derives from the DLMZ, maintain NC identity during neurulation. The authors further demonstrate that the first step requires Wnt activation and BMP inhibition, whereas the second requires the activation of both pathways, thus resolving long-standing controversies regarding the roles of these two pathways in NC induction.
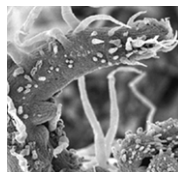
GOBLET sets boundaries in leaf development

All plant leaves originate from an undifferentiated cell cluster, the shoot apical meristem (SAM), and undergo common developmental stages. Subtle differences in these stages generate numerous leaf shapes, from simple leaves with undivided blades (e.g. *Arabidopsis*) to compound leaves, which consist of several subunits called leaflets (e.g. tomato). Now, Naomi Ori and co-workers report that the transcription factor GOBLET, a homologue of the *Arabidopsis* NAM/CUC boundary genes, functions in tomato compound leaf development (p. 823). The authors show that *GOBLET* mRNA localises to the tissue boundaries between the SAM and leaf primordia, and also to the flanks of newly forming leaflets. This localisation is disrupted in loss- and gain-of-function *goblet* mutants, which both give rise to simpler leaf shapes. Leaf-specific expression of the microRNA *miR164*, a negative regulator of *GOBLET*, also results in simpler leaves, an effect conserved in another compound-leaved plant, *Cardamine hirsuta*. From their findings, the authors propose that the precise and context-dependent regulation of GOBLET is used to flexibly pattern leaf shapes.
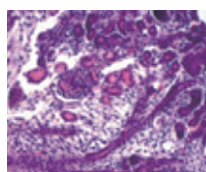
Where integrins, growth factors and Wnts meet

Integrin-growth factor receptor interactions often serve to integrate the local signals from the extracellular matrix (ECM) with those provided by growth factors. Now, on p. 843, Jordan Kreidberg and co-workers show that such an interaction regulates Wnt expression in kidney morphogenesis. The authors report that in mice carrying mutations in either the integrin $\alpha3\beta1$ α subunit or in laminin, its main ECM ligand, the formation of the papilla, a collection of densely packed epithelial tubules in the kidney, is disrupted, and *Wnt7b* and *Wnt4* expression is downregulated. Moreover, they demonstrate that signalling through c-Met – the receptor for Hgf, a growth factor involved in kidney morphogenesis – depends on $\alpha3\beta1$ integrin and that an anti-Hgf antibody also downregulates Wnt7b levels. Finally, they show that Wnt signalling promotes cell survival in the papilla, allowing epithelial tubule elongation and papilla maturation. From their findings, they propose that coordinated integrin–c-Met signalling regulates Wnt expression during kidney development, highlighting the complexity of the input that controls morphogenetic events.
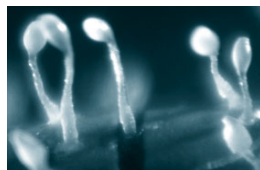
Dicty sporulation on steroids

When individual amoebae of the slime mold *Dictyostelium discoideum* face hard times, up to 100,000 of them form a multicellular aggregate. Because spores, which ultimately form from this aggregate, are unable to move, the timing of sporulation is critical for the successful completion of *Dictyostelium*'s life cycle. On p. 803, Anjard, Su and Loomis identify novel players in the regulation of this event. Previously, these authors had identified the peptide SDF-2 as a sporulation regulator, and had proposed that GABA triggers SDF-2 production by binding to the G-protein-coupled receptor (GPCR) GrlE. Now, they establish that GrlE is probably linked to the $G\alpha7$ subunit. Intriguingly, they also find that cells mutant for the GPCR GrlA and the $G\alpha4$ subunit fail to accumulate SDF-2 in response to GABA. Finally, the authors identify the steroid SDF-3 as a sporulation factor and suggest that it signals through GrlA and $G\alpha4$ to elicit the rapid release of GABA, placing it at the top of the sporulation-inducing cascade.