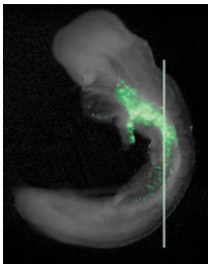
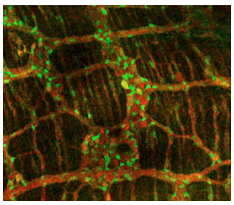


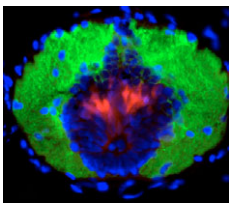
Left-right patterning de-mystified

The generation of left-right (LR) patterning depends on the activity of Cerberus-related proteins in the node region. Charon (zebrafish) and Cerberus-like-2 (Cerl-2; mouse) prevent the spread of the Nodal signal to the right side in developing embryos, but the role of the chick Cerberus-related protein (cCer) in LR patterning has been less clear. However, its role is now clarified by Belo and co-workers, who report that Nodal activates *cCer* transcription in the left-side mesoderm; cCer then negatively regulates Nodal signalling (p. 2051). From the *cCer* promoter, they identify a left-side enhancer that contains FOXH1- and SMAD-binding sites and that is Nodal responsive. This element is sufficient to induce *cCer* transcription in the left side, and cCer overexpression in the left side represses *Nodal* expression. Significantly, ectopic Nodal expression occurs in the right side of *cCer*-knockdown embryos. These results reveal cCer as a negative regulator of Nodal asymmetric signalling and indicate that cCer appears to have a similar role to Charon and Cerl-2 in restricting Nodal activity to the left side.



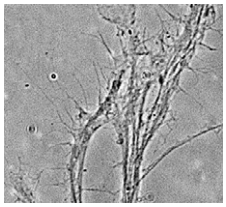
Enteric neurons: different in death

The regulated death of immature neurons, in response to the absence of neurotrophic factors, is crucial to the architecture of the developing nervous system. The enteric nervous system (ENS) regulates motility, secretion and blood flow in the gastrointestinal tract. However, unlike in other areas of the developing nervous system, neuronal apoptosis has not been detected, and survival signals that prevent it have yet to be identified. Jeffrey Milbrandt's and Hideki Enomoto's laboratories (p. 2171) now report that the survival of enteric neurons depends on GFRα1, a receptor for glial cell line-derived neurotrophic factor (GDNF). Using conditional *GFRα1* mutant mice, the authors show that during late ENS development, *GFRα1* inactivation induces the widespread death of enteric neurons in the distal gastrointestinal tract in a caspase-independent manner. Because Hirschsprung's disease in humans is associated with mutations in the RET receptor kinase – the signalling component of the GDNF receptor complex – it will be interesting to determine whether caspase-independent neuronal cell death underlies the etiology of this human condition.



Regeneration: location matters

If the tail of a salamander is amputated then, amazingly, it completely regenerates. But how is a functional central nervous system reconstituted? On p. 2083, Tanaka and colleagues identify the neuronal stem cell population that repopulates the regenerating tail of the urodele amphibian, the axolotl. Using cell fate mapping and transplantation techniques, they show that a 500 μm region of the mature spinal cord that abuts the amputated plane generates the neuronal progenitors required for regeneration. They map the progeny of these precursors as the regenerating spinal cord extends. Most progeny remain close to the dorsoventral (D/V) location of the parent cell, but some migrate to occupy multiple D/V positions, thus acquiring different expression profiles and fates. The most distally localised cells in the regenerating tail are molecularly distinct from those in more proximal regions, perhaps indicating that, in this zone, progenitor identity is destabilised or altered. Surprisingly, ventral cells in this region can migrate dorsally and exit the spinal cord into the blastema. The fate of these cells remains to be determined.



Enabling axonal branching

Growing axonal growth cones form actin-rich protrusions – filopodia – which extend the axon towards its target. Enabled/vasodilator-stimulated phosphoprotein (Ena/VASP) proteins are enriched at the tips of neuronal growth cone filopodia and are required for filopodia formation. Chemically induced elimination of filopodia in the developing vertebrate visual system causes misdirected axon growth. Cecile Lebrand and colleagues now show that, in the *Xenopus* developing visual system, reduced Ena/VASP protein activity in retinal ganglion cells (RGCs) does not affect axonal pathfinding, but does prevent the formation of branches in the optic tectum (p. 2137). Lebrand and colleagues have eliminated Ena/VASP function in *Xenopus* RGCs by using a sequestration strategy that mislocalises these proteins to the mitochondrial membrane. Filopodia formation is drastically reduced in these retinal growth cones. Despite this, guidance errors do not occur, but growth cones advance slowly in the optic tract. Surprisingly, these proteins therefore seem to have a role in establishing terminal arborisations rather than in pathfinding; whether this is the case in other axonal pathways and organisms remains to be tested.

Plant hormones get the GISt

Gibberellins (GA) and cytokinins – plant hormones – induce antagonistic signals during leaf formation and in meristem maintenance. Both hormone signalling pathways are required in *Arabidopsis* for the initiation of their defensive epidermal structures, trichomes. GA act via the transcription factor (TF) GLABROUS INFLORESCENCE STEMS (GIS). The downstream mechanisms by which cytokinin signalling regulates this process are less clear. Now, Pierre Broun's group show that the GIS-related transcription factors GIS2 and ZFP8, but not GIS, mediate this response to cytokinins (p. 2073). A series of overexpression and RNAi-knockdown experiments in both wild-type and mutant plants reveal that GIS, GIS2 and ZFP8 play overlapping roles in GA signalling, but that GIS is dispensable for cytokinin signalling. The molecular interactions between the two hormone signalling pathways are thus uncovered and, interestingly, despite shared mechanisms of action, these TFs have evolved differential responses to GA and cytokinin signalling.

IN *JOURNAL OF CELL SCIENCE*

PI3Ks in the blood

Phosphoinositide 3-kinases (PI3Ks) are crucial for cell proliferation and differentiation during early development. Heather Bone and Melanie Welham describe a study, designed to uncover the role of PI3Ks in the development of the haematopoietic system, using embryonic stem (ES) cells and embryoid bodies (EBs). The researchers manipulated PI3K activity both pharmacologically (using a general PI3K inhibitor) and genetically (using ES cells lacking 3-phosphoinositide-dependent protein kinase 1, a kinase downstream of PI3K) and found that PI3K signalling is required for cell proliferation during early development in EBs. They also found that PI3Ks are needed during developmental haematopoiesis. Specifically, PI3K signalling is required for the expansion of the blast-colony-forming cells (primitive haematopoietic progenitors) and is involved in haematopoietic cell differentiation – both myeloid and erythroid lineages are affected by reduced PI3K activity. The authors conclude that PI3Ks have several different roles at different times during the development of the haematopoietic system.

Bone, H. K. and Welham, M. J. (2007) Phosphoinositide 3-kinase signalling regulates early development and developmental haemopoiesis. *J. Cell Sci.* **120**, 1752-1762.