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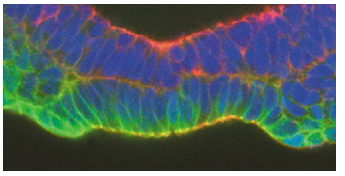
By Jane Bradbury

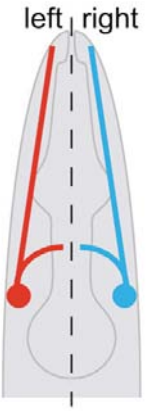
Wnt3a: telling left from right

Building the 3D vertebrate body is a feat of cellular engineering during which each axis is laid down at the correct orientation to the other two axes. The left-right (LR) axis is determined last under the control of the node, an embryonic structure that also controls trunk elongation. On p. 5425, Nakaya and co-workers reveal that *Wnt3a*, which is expressed in the node, is required for LR asymmetry determination in the mouse embryo. They show that the heart and other anterior internal organs in *Wnt3a*$^{-/-}$ embryos have defects that arise from the incorrect specification of the LR axis. They also report that Wnt3a regulates the expression of the left determinant gene *Nodal*, as well as of several other genes involved in trunk elongation through the Notch signalling pathway. Thus Wnt3a functions in the trunk organizer to coordinate patterning and morphogenesis along multiple body axes.



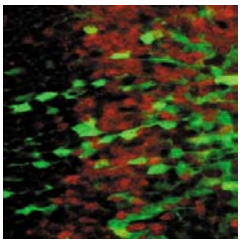
Fate determination by microRNA control

The patterns of gene expression that define differentiated cells are controlled by complex regulatory networks of transcription factors and microRNAs. Johnston and Hobert now identify a new component of the network that controls left/right asymmetry in the gustatory neurons of *Caenorhabditis elegans* – the zinc finger transcription factor *lsy-2* (see p. 5451). The nematode's gustatory neurons ASE left (ASEL) and ASE right (ASER) are morphological mirror images but have left/right asymmetric functions. The researchers show that, although *lsy-2* is expressed in both ASEL and ASER, it is a permissive factor for the expression of the microRNA *lsy-6* in ASEL – *lsy-6* is a component of the regulatory network that controls ASEL fate. By identifying a factor that is involved in the spatial expression of a microRNA gene, the researchers provide an important new insight into how terminal cell fates are specified.



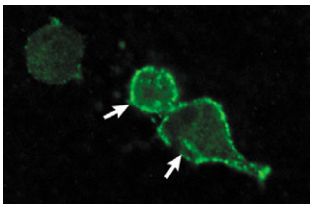
A painful determinant: neuronal specification by Ptf1a

Pain responses are modulated by GABAergic (inhibitory) and glutamatergic (excitatory) neurons in the spinal cord dorsal horn – too many glutamatergic neurons and even minor injuries are very painful. GABAergic and glutamatergic neurons are alternative fate choices in the developing neural dorsal tube, and now, Glasgow and colleagues report that the basic helix-loop-helix transcription factor Ptf1a directs developing neurons in the mouse dorsal horn towards a GABAergic fate (see p. 5461). The researchers show that *Ptf1a* is expressed in the precursors of GABAergic dorsal horn neurons, and report that, in mouse embryos that lack Ptf1a activity, the GABAergic neurons are mis-specified, resulting in an increase in glutamatergic neurons. The researchers conclude that Ptf1a contributes to the transcription factor code that specifies spinal cord neurons by having a selector function opposite to that of the homeodomain genes *Tlx1* and *Tlx3*, which specify glutamatergic neurons.



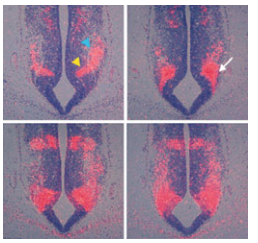
Arrow targets Wingless for degradation

An important way of controlling certain signalling pathways, such as the Wingless (Wg) pathway, is through the endocytic degradation of extracellular ligands. Now, Piddini et al. report that, in *Drosophila* wing imaginal discs, the degradation of Wg (which is required to form a gradient of this morphogen) is cooperatively controlled by Arrow and Frizzled2, two receptors involved in Wg signal transduction (see p. 5479). The researchers show that although Frizzled2, a seven-transmembrane receptor, stimulates the internalisation of Wg in wing imaginal discs and cultured cells, it does not take Wg to a degradative compartment. This requires the LDL receptor-related protein Arrow, which stimulates the targeting of the Frizzled2-Wg complex to lysosomes for degradation. The separation of ligand capture and degradation between two receptors, the researchers suggest, could help to generate a reliable concentration gradient of Wg and other morphogens during development.



Axon guidance made SIMple

During brain development, attractive and repulsive signals establish functional connections within the brain by guiding the growth of axons. The genetic and transcriptional regulation of axonal guidance is poorly understood but, on p. 5527, Marion et al. report that, in the developing mouse brain, the transcription factors SIM1 and SIM2 are required for the correct targeting of mammillary body axons, part of the neuronal circuitry involved in spatial learning. The authors show, for example, that, in mouse embryos that lack both copies of *Sim1* and one or two copies of *Sim2*, mammillary body neurons form but fail to lay down normal axonal projections. Overall, the researchers conclude that *Sim1* and *Sim2* play similar roles in vivo, and suggest that they should be added to the growing list of transcription factors that regulate the expression of molecules that control axonal morphology and connectivity.



Insulating niches for stem cells

Adult regenerative tissues, including the hair, are maintained throughout life by stem cell (SC) self-renewal and differentiation. These rare and hard to identify cells are thought to be maintained by a poorly understood microenvironment – the SC niche. On p. 5589, Osawa and colleagues, by molecularly characterizing the melanocyte SCs present at the base of hair follicles, provide new insights into how SC niches work. The researchers describe a new method for isolating melanocyte SCs, and other melanocyte subsets, from mouse hair follicles to obtain single-cell-based gene expression patterns from the different cell types. Noting that the transcription of key molecules needed for melanocyte proliferation and differentiation – such as Sox10, Kit and Lef1 – is downregulated in melanocyte SCs, the researchers propose that SC niches insulate SCs from activating stimuli, thus maintaining them in a quiescent state.