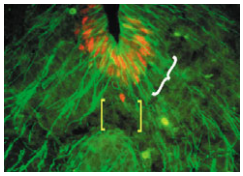
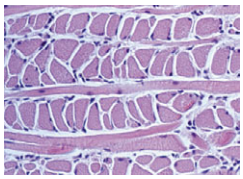


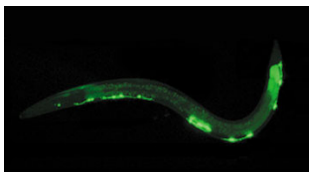
Neural cell lineages: time for change?

The spinal cord is a valuable model system for understanding how neural cells diversify. But the lineage relationships between the neural stem cells (NSCs) and their descendents – the motoneurons, oligodendrocytes and astrocytes – are still unclear. On p. 581, Capecchi and colleagues use conditional cell ablation to help shed light on this. A long-held model proposes that both motoneurons and oligodendrocytes arise from a common precursor that expresses oligodendrocyte transcription factor (Olig) proteins. The authors tested this by deleting Olig1-expressing NSCs, by using Cre to express diphtheria toxin under the control of Olig1 regulation. As expected, they saw an absence of both motoneurons and oligodentrocytes in this system, but they also saw the continuous generation (and death) of their precursor cells, and observed that oligodendrocyte precursors were generated for much longer than were motoneuron precursors. This refutes the idea that motoneurons and oligodendrocytes come from a single precursor type, and instead the authors propose a new 'sequential model' to explain their findings.



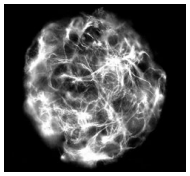
Muscling in on adult muscle development

Although the most dramatic increase in the mass of skeletal muscle occurs after birth, research into skeletal muscle development has tended to focus on the embryo. On p. 601, Klein and colleagues readdress this balance by examining whether adult muscle stem cells recapitulate the mechanisms of embryonic skeletal muscle growth. They focused on the basic helix-group-helix transcription factor myogenin, which is crucial for the development of embryonic skeletal muscle. Surprisingly, they found that conditionally mutant mice that produce no myogenin after late embryogenesis have no consistent muscular abnormalities. At first the authors thought that myogenin might be compensated by other myogenic factors, such as myogenic factor 6, myogenic differentiation 1 and myogenic factor 5. But these proteins were not sufficiently upregulated in the conditional mutants for this to be a plausible explanation. Instead, the authors conclude that adult skeletal muscle development is independent of myogenin, and they speculate on possible roles of the Mef2 proteins, which invertebrates rely on for the development of embryonic muscle.



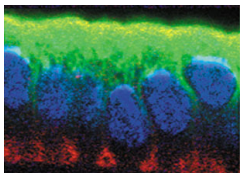
Hox gets surprisingly direct

Almost all animal species use Hox genes to determine developmental cell fate and morphology, and on p. 641, Cameron and co-workers investigate how Hox genes regulate programmed cell death. The *C. elegans* Hox gene *mab-5* is required for the programmed death of two related cells in the posterior ventral nerve cord: P11.aaap and P12.aaap. Programmed cell death in *C. elegans* requires the BH3-domain gene *egl-1*, and the researchers found that, in the P11.aaap cell, MAB-5 (together with its cofactor CEH-20) activates *egl-1* transcription by directly interacting with a consensus binding site in the *egl-1* regulatory sequence (although, remarkably, the death of P12.aaap is determined in a different fashion). This is the first time that a cell biological effector gene – rather than a transcription factor – has been found to be directly regulated by Hox proteins in *C. elegans*. Together with similar findings from *Drosophila*, this indicates that non-homeotic targets of Hox proteins, including targets that control programmed cell death, might be more common than previously thought.



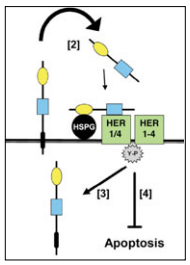
Nucleotide signalling grows up

What extracellular signalling mechanisms control adult neurogenesis? In the adult mouse, neurons are formed in two brain regions, the subventricular zone (SVZ) and the dentate gyrus of the hippocampus. In previous studies, Zimmermann and colleagues have shown that stem cells in these regions express NTPDase2, an extracellular nucleotide hydrolyzing enzyme (also called ecto-nucleotidase) that modulates cell communication by nucleotide receptors. They have now taken this further by investigating whether adult neural stem cells (NSCs) respond to extracellular nucleotide signalling itself (see p. 675). The researchers used NTPDase2-expressing neurospheres (clonal aggregates of NSCs) derived from the SVZ. Using Ca^{2+}-imaging, they show that these neurospheres express the nucleotide receptors $P2Y_1$ and $P2Y_2$. The activation of these receptors increased cell proliferation synergistically with epidermal growth factor and fibroblast growth factor 2, and the researchers confirmed this in $P2Y_1$-knockout mice. Although synergism between extracellular nucleotides and growth factors has long been considered important in the brain, this is the first study to demonstrate an effect in adult NSCs.



Charleston partners needed for shaping cells

The first morphogenetic process of *Drosophila* development is the formation of the primary epithelium by cellularisation, during which invagination of the plasma membrane packages the nuclei into around 6000 distinct cells. Using microarrays, RNAi and time-lapse phenotyping, Lecuit and colleagues have identified several novel genes that profoundly affect cellular architecture during cellularisation. Their paper on p. 711 focuses on one of these genes – *charleston* (*char*). They show that epithelial nuclei lacking Char (owing to mutation or RNAi) fail to elongate during cellularisation and instead remain spherical, which distorts cell shape and the normal columnar morphology of the epithelium. Unexpectedly, the binding of microtubules to the nuclear envelope is unaffected in *char* RNAi embryos. Instead, Char's localisation to the inner nuclear membrane indicates that it directly controls the structural organisation of the nuclear envelope. The authors suggest that Char is a component of a nucleoskeleton needed by the nuclear membrane to respond to microtubules; whether this is true will become clear as its molecular partners are identified.



A breath of air for pre-eclampsia research

Some cell types can survive and proliferate when there is very little oxygen around. In humans, cells of the trophoblast – the outermost layer of cells of the blastocyst – do just this, proliferating in 2% O_2 during the first trimester of pregnancy. But how do such cells sense and respond to low oxygen levels? Armant et al. (p. 751) turned to the heparin-binding EGF-like growth factor (HBEGF), which is expressed in the placenta during normal pregnancy but is downregulated in pre-eclampsia, a disorder associated with poor trophoblast survival. They found that exposing a human first-trimester trophoblast cell line to 2% O_2 caused the upregulation of HBEGF synthesis and secretion, whereas interfering with HBEGF signalling increased apoptosis. The HBEGF receptors HER1 or HER4 were required for this upregulation, indicating that cytotrophoblast survival is maintained by a positive-feedback loop. The authors conclude that low trophoblast survival in pre-eclampsia could be partly due to reduced HBEGF levels, a finding that brings with it new therapeutic possibilities.

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