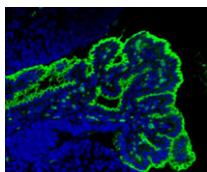


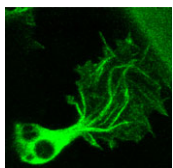
### Lunatic fringe notches up lateral inhibition

During neurogenesis, Notch ligands expressed by differentiating neurons inhibit the differentiation of neighbouring cells. This 'lateral inhibition' maintains a pool of progenitor cells next to differentiating neurons within which neurogenesis can be initiated when the neuron migrates away from the neural epithelium. Now, David Wilkinson and colleagues report that Lunatic fringe (Lfng), a Notch modifier best known for its roles in boundary formation, promotes the lateral inhibition of neurogenesis in the zebrafish hindbrain (see p. 2523). The researchers show that Lfng is expressed by neural progenitors in neurogenic regions of the hindbrain and is downregulated in cells that have initiated differentiation. Loss-of-function studies and analysis of mosaic embryos reveal that Lfng is required cell autonomously to limit the amount of neurogenesis in the hindbrain and to maintain neural progenitors. Based on their results, the researchers suggest that Lfng acts in a feedback loop that, by promoting Notch activation, maintains the competence of progenitor cells to receive lateral inhibition from differentiating neurons.



### Shh, choroid plexus growth in progress

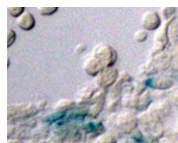
Choroid plexuses – secretory organs in the brain that produce cerebrospinal fluid (CSF) and that function as the blood-CSF barrier – regulate the internal environment of the brain. Little is known, however, about the development and growth of these crucial organs. On p. 2535, Huang and co-workers begin to remedy this situation by reporting that sonic hedgehog (Shh) signalling regulates a novel epithelial progenitor domain in the mouse hindbrain choroid plexus (hChP). Shh is strongly expressed in the epithelium of the differentiated hChP but the researchers now identify a distinct epithelial domain in the developing hChP that does not express Shh. Instead, this domain, which adjoins the lower rhombic lip (a germinal zone or cellular birth place), displays Shh signalling. The researchers show that this Shh target field contributes directly to the development of the hChP epithelium by acting as a progenitor domain. Finally, by analysing conditional *Shh* mouse mutant embryos, they provide evidence that tissue-autonomous Shh production and signalling regulates the growth of the hChP throughout development.



### Fascin-ating fly blood cell migration

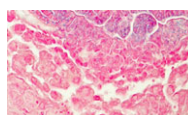
Remodelling of the actin cytoskeleton is required for the dynamic cell shape changes that underlie cell migration, a pivotal developmental process. But what are the key regulators of actin reorganisation during cell migration?

On p. 2557, Zanet and colleagues reveal that the migration of a subpopulation of motile blood cells (macrophage-like plasmatocytes) during *Drosophila* embryogenesis involves the actin-bundling protein Fascin. They show that plasmatocytes express high levels of Fascin and that Fascin is required for their polarisation and migration during development and during an inflammatory response to epithelial wounding. Fascin, they report, localises to, and is essential for the assembly of, actin-rich microspikes that extend beyond the leading edge of the migrating plasmatocytes. Finally, they show that Fascin activity is regulated post-translationally by phosphorylation in a tissue-specific manner. In humans, increased Fascin expression is correlated with the invasiveness of various tumours. Thus, these unique insights into Fascin function and regulation during normal development might help to explain how *fascin* misregulation contributes to cancer progression.



### Hedgehog: haematopoietic stem cell inducer?

The haematopoietic system is not generally regarded as a tissue that undergoes patterning during development. However, on p. 2613, Elaine Dzierzak and co-workers report that instructive signalling from ventral embryonic tissues affects the specification of haematopoietic stem cells (HSCs) in the aorta-gonad-mesonephros (AGM) region of the mouse embryo. The ventral position of haematopoietic clusters in the AGM suggests that signals from embryonic tissues ventral to the AGM (for example, the gut) might influence HSC specification. The authors tested this possibility by measuring the HSC content of AGMs cultured with dorsal or ventral tissues. Ventral tissues, they report, increase the number of HSCs in the AGM, whereas dorsal tissues decrease it. Using chimaeric explant cultures, the authors show that instructive signalling from ventral tissues, rather than the influx of ventrally derived HSCs or their precursors into the AGM, accounts for the effect of ventral tissue on AGM HSC activity. Finally, the researchers suggest that Hedgehog, although not ventrally restricted, is an HSC-inducing signal, a possibility that requires confirmation in future studies.



### Proteolytic chop for tissue morphogenesis

Numerous membrane-associated proteases (for example, matriptase) modulate cell behaviour during development. Consequently, mutations in the inhibitors that control the activity of these proteases can have dire developmental effects. For example, mutations in the human *SPINT2* gene, which encodes the serine protease inhibitor HAI2, cause organogenesis defects. Now, Szabo and colleagues report that HAI2 is essential for placental development, neural tube closure and embryonic survival in mice (see p. 2653). The researchers identify matriptase as a key target for HAI2 during mouse tissue morphogenesis and show that the inactivation of matriptase in HAI2-deficient embryos completely restores placental development and embryonic survival; the incomplete prevention of neural tube defects in these doubly deficient embryos suggests, however, that HAI2 has additional targets during neural development. Finally, the researchers use genetic complementation to reveal that a functional interaction between HAI2 and the related inhibitor HAI1 regulates matriptase activity during development. Thus, they suggest, tissue morphogenesis requires the regulation of membrane-associated serine proteases by a network of partly redundant inhibitors.



### Gata-way to a normal heart beat

The cardiac conduction system (a tract of cardiomyocytes that propagates electrical impulses through the heart) coordinates heart contractions. Abnormalities in this system cause life-threatening arrhythmias but the molecular basis of its development is poorly understood. Now, Eric Olson and colleagues report that the transcription factor Gata4 regulates the system's development (see p. 2665). Atrioventricular (AV) delay (delayed impulse propagation through a structure called the AV node) coordinates atrial and ventricular contraction. In mice, AV delay requires expression of the gap junction protein connexin 30.2 (Cx30.2) in the AV conduction system. The authors identify an enhancer in the *Cx30.2* gene that is necessary and sufficient to direct its expression to the developing AV conduction system, and show that its correct expression requires the Gata4 and Tbx5 transcription factors. Furthermore, *Gata4*<sup>-/-</sup> mice have faster AV conduction than their wild-type littermates. Overall, these results reveal an unexpected role for Gata4 in normal AV conduction and might bring the development of effective anti-arrhythmia drugs closer.

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