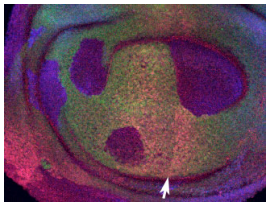
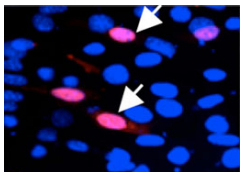


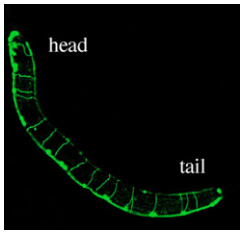
Opposing Sax functions set gradient

Patterning of the *Drosophila* wing imaginal disc involves a Bmp activity gradient that is created by two Bmp ligands (Gbb and Dpp) and two type 1 receptors (Tkv and Sax). On p. 3295, Bangi and Wharton report that Sax shapes this gradient by both antagonizing and promoting Bmp signalling. Previous data have suggested that Sax mediates Gbb signalling while Tkv mediates Dpp signalling; but, puzzlingly, loss of *sax* function does not have the same effect as loss of *gbb* function. The researchers now show that in the absence of *sax* function, the distribution of the downstream effector of Bmp signalling (pMad) is consistent with an increase in Bmp activity, not a decrease, as expected if Sax just transduces Gbb signals. The researchers propose that Sax has two functions: when complexed with itself, Sax antagonizes Bmp signalling by sequestering Gbb; when complexed with Tkv, it facilitates signalling. The balance between these functions, they suggest, will shape and stabilize the Bmp activity gradient across the developing wing.



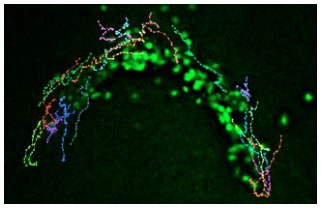
Oligodendrocyte differentiation: it's a wrap

The axons of mature neurons in the mammalian CNS are encased in an insulating myelin sheath, which is made by oligodendrocytes. Although the regulation of earlier stages of oligodendrocyte development is relatively well understood, it is unclear how myelination is controlled. The identification by Wang and colleagues of a new transcription regulator (Zfp488) that controls this process is, therefore, an important advance (see p. 3389). Zfp488 is an oligodendrocyte-specific zinc-finger transcriptional repressor that cooperates with the bHLH transcription factor Olig2 to promote oligodendrocyte differentiation. The researchers identified Zfp488 by screening for genes that were downregulated in the optic nerves of *Olig1*-null mice, in which myelin formation is severely compromised. They show that Zfp488 cooperates with Olig2 to induce ectopic and precocious oligodendrocyte differentiation in the developing chick neural tube, and report that RNAi knockdown of *Zfp488* downregulates myelin gene expression in an oligodendroglial cell line. Thus, they conclude, Zfp488 acts as a transcriptional co-regulator during oligodendrocyte maturation and myelination.



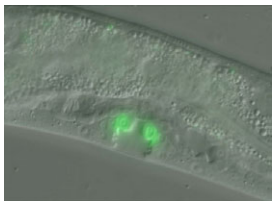
Guiding axon guidance receptors

Growing axons form their correct connections in the developing nervous system by responding to specific guidance molecules. But how are these molecules and their receptors regulated? On p. 3441, Ogura and Goshima report that, in *C. elegans*, the subcellular localisation of UNC-5, the receptor for the axon guidance molecule Netrin (UNC-6), is regulated by the autophagy-related kinase UNC-51 and its binding partner UNC-14 (which may also be involved in vesicle trafficking). UNC-5 normally localizes to small vesicles in the axons and cell bodies of the dorsally extending DD/VD motoneurons. In *unc-51* and *unc-14* mutants, which contain many neurons with guidance defects, UNC-5 (but not other molecules needed for axon guidance) is abnormally localised in the cell bodies of these motoneurons. Furthermore, *unc-5* and *unc-6* interact genetically with *unc-51* and *unc-14* to affect DD/VD axon guidance, and UNC-5, UNC-51 and UNC-14 colocalise in neurons. Ogura and Goshima conclude that UNC-5 uses a unique unknown mechanism for its localisation, which, in turn, probably regulates its activity.



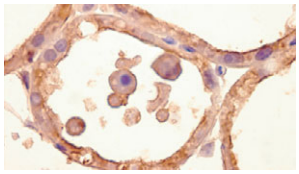
PGCs mind the gap

Gap junctions – channels between cells that are made of connexins – play important roles in development. Connexin 43 (*Cx43α1*) knockout mice, for example, die soon after birth because of a heart defect. They also lack germ cells, and on p. 3451, Francis and Lo report that this second defect is caused by increased apoptosis of primordial germ cells (PGCs). Using an *Oct4-GFP* transgene to track PGCs in mouse embryos, the researchers found no difference in PGC distribution or abundance between wild-type and *Cx43α* hetero- or homozygous knockout embryos during early development. Thus, PGCs are specified and migrate normally in the absence of connexin 43. However, at embryonic day 11.5, *Cx43α* knockout mice had fewer PGCs because of their increased apoptosis. This was associated with abnormal p53 activation and reduced β1-integrin function in the PGCs; inhibition of p53 activation rescued PGC cell death. Francis and Lo conclude that anoikis – apoptosis triggered by the disruption of extracellular matrix binding – is partly responsible for the germ-cell deficiency of *Cx43α* knockout mice.



Repressive PUFs on developmental signalling

The spatial and temporal regulation of gene expression during development occurs at the level of both gene transcription and gene translation. Now, Walser and colleagues reveal that three members of the PUF family of translational repressors that regulate certain aspects of germline development in *C. elegans* also negatively regulate vulval development in this organism (see p. 3461). PUF proteins – so-called because the first to be identified were the *Drosophila* Pumilio and the *C. elegans* FBF proteins – bind to their target mRNAs through PUF repeat motifs. Using detailed genetic analyses, the researchers show that *fbf-1* and *fbf-2* act redundantly to inhibit the specification of the primary vulval cell fate, which is induced by MAPK signalling. *puf-8*, they report, plays a distinct role in vulval development by temporally restricting the response of vulval precursor cells to this and other patterning signals. Because PUF proteins are highly conserved, the researchers suggest that these translational repressors may fine-tune other signalling pathways during animal development.



TWEAKing mammary gland apoptosis

Unlike most organs, mammary glands undergo massive changes during adult life. Epithelial cells proliferate extensively during pregnancy to generate milk for the offspring. When lactation stops, these cells apoptose and the gland is remodelled to its resting state (involution). Baxter and co-workers have been investigating the regulation of involution and, on p. 3485, they report that this process can be halted by the conditional deletion of the gene encoding IKK2 (inhibitor of κB kinase). This is one of the kinases that regulate the nuclear factor-κB (NF-κB) pathway, which controls many cellular responses, including apoptosis. The researchers report that the delayed mammary gland apoptosis and remodelling they see in the conditional mutant is associated with decreased expression of the death receptor ligand TWEAK, which contains binding sites for both NF-κB and FOXO (forkhead transcription factors) in its promoter region. These new insights into the control of apoptosis in a physiological situation may provide new therapeutic approaches to the treatment of breast cancer, suggest the researchers.

Jane Bradbury