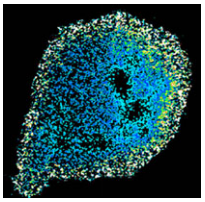
Patterning needs a little sweetener

N-linked glycosylation is a protein modification needed for protein folding in the endoplasmic reticulum (ER). If unfolded proteins accumulate in the ER, then the 'unfolded protein response' (UPR) is triggered, increasing folding rates and reducing translation rates. On p. 1745, Mattias Mannervik and colleagues describe the first embryonic patterning defects known to be caused by an inappropriate UPR. In their screen for maternal factors involved in embryonic patterning, they discovered a mutant – *wollknäuel* (*wol*) – that has reduced Dpp signalling, posterior segmentation defects due to a lack of the transcription factor Caudal, and defects in germband elongation and retraction. *wol* encodes ALG5, a UDP-glucose:dolichyl-phosphate glucosyltransferase involved in N-linked glycosylation, and its mutation causes the accumulation of unglycosylated proteins and triggers the UPR. One component of the UPR is the phosphorylation of the translation initiation factor eIF2α, which attenuates protein translation. These findings suggest that some mRNAs, such as *caudal*, are particularly sensitive to eIF2α phosphorylation, resulting in the *wol* patterning defects.

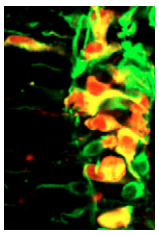
Reaction-diffusion mechanism for ancestral FGF signalling

The sea anenome *Nematostella vectensis* belongs to the Cnidaria phylum, which split from the Bilateria 600 million years ago. Similar to several basal bilaterian species, its larvae have an apical ciliary organ, which is believed to detect conditions suitable for metamorphosis. In their study of FGF signalling in *N. vectensis* development (see p. 1761), Fabian Rentzsch and colleagues used morpholino-mediated knockdown to analyse the function of two FGF ligands, NvFGFa1 and NvFGFa2, and of the NvFGFRa receptor. Their findings show that NvFGFa1 signalling via NvFGFRa is required for apical organ formation and that NvFGFa1 knockdown blocks metamorphosis. They also show that NvFGFa1 not only activates its own expression but also that of the antagonistic NvFGFa2, which possibly binds to NvFGFRa, without activating it, to restrict NvFGFa1's initially broad expression and to prevent ectopic organ formation. These findings provide the first known example of two FGF ligands that have activating and inhibiting effects consistent with a reaction-diffusion mechanism, and highlight an ancestral FGF signalling function.



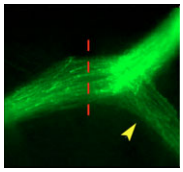
Syn4 and PCP give protrusive cell directions

Directed cell migration is crucially important for development, and is a feature of neural crest (NC) cells, which have remarkable migratory abilities. On p. 1771, Roberto Mayor and colleagues investigate how NC cells keep to the right path in zebrafish and *Xenopus* embryos, by studying the effects of a proteoglycan, Syndecan-4 (Syn4), on NC migration. Syn4, they report, is essential for directional NC migration, and directs NC cell movement by regulating the polarised formation of membrane protrusions, in a manner similar to that of non-canonical Wnt/planar cell polarity (PCP) signalling. To investigate how Syn4 orientates cell protrusions, the authors used in vivo FRET analysis to measure the localised activity of several small GTPases involved in cell migration. Syn4, they discovered, inhibits Rac activity, a small GTPase that controls cytoskeletal dynamics and cell adhesion, while PCP signalling activates RhoA, which also inhibits Rac in NC cells. Thus Syn4 and PCP signalling seemingly control directional NC migration by regulating membrane protrusions by inhibiting Rac at the back of the cell.



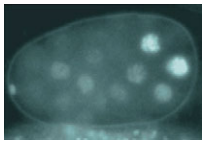
Notch and Sox: different routes to progenitor maintenance

During development of the chick nervous system, a combination of Notch signalling and SoxB1 transcription factors (Sox1, Sox2 and Sox3) maintains a pool of self-renewing stem and progenitor cells. On p. 1843, Jonas Muhr and colleagues investigate whether Notch and SoxB1 proteins suppress neuronal differentiation through the same, or different, pathways. By expressing dominant-negative components of these pathways in chick embryos, they show that, although Notch requires SoxB1 to maintain progenitor characteristics, SoxB1 activity blocks neurogenesis independently of Notch. Notch represses the activity of bHLH proneural proteins via the bHLH transcription factors Hes1 and Hes5, but, the researchers found, also represses E-proteins – the heterodimerizing partners of proneural proteins – through a Hes-independent mechanism. SoxB1 proteins, by contrast, seem to maintain progenitors by creating a molecular environment in which E-proteins and proneural proteins cannot promote neuronal differentiation. As Notch, Sox and bHLH proteins are also expressed in muscle and neural crest progenitor populations, the authors suggest their results could be of broader relevance.



Crossing a line in axon guidance

In bilaterally symmetric animals, the central nervous system is divided into two halves, and, during development, the proper formation of neuronal circuitry sometimes requires that axons choose whether they should project to the same side (ipsilateral) or to the opposite side (contralateral) of the embryonic midline. Many axon guidance molecules contribute to this decision, but little is known of their transcriptional regulation. Now in their study of the optic chiasm – the neuronal structure required for binocular vision – Eloísa Herrera and colleagues (p. 1833) report, for the first time, a link between a transcription factor (Zic2) and an axon guidance molecule (EphB1) in controlling axonal laterality. By manipulating *Zic2* expression in *EphB1*-expressing and *EphB1*-null mice, they show that Zic2 is sufficient to switch the contralateral trajectory of retinal axons to an ipsilateral one. Zic2 can do this via both EphB1-dependent and -independent mechanisms. From their findings, the authors propose that transcription factors can directly and sequentially activate different guidance receptors throughout an axon's journey.



How *nanos* is kept on hold

Many maternally provided transcripts play crucial roles in early development and often require tight translational regulation. During *C. elegans* embryogenesis, the maternal transcript *nanos-2* (*nos-2*) is translationally repressed until the germline founder cell, called P_4, is born. In their dissection of this process (see p. 1803), Kuppuswamy Subramaniam and co-workers have discovered that four additional proteins (OMA-1, OMA-2, MEX-3 and SPN-4) are involved in this repression of *nos-2*. These proteins bind to the 3′ UTR of *nos-2* and repress it at different developmental stages: OMA-1 and OMA-2 in oocytes, and MEX-3 and SPN-4 in the embryo. What eventually releases *nos-2* repression in P_4, the authors propose, is the competition between SPN-4 and POS-1 (a protein required for *nos-2* translation) to bind to *nos-2*. Thus, POS-1 works, not by activating translation, but by de-repressing it; as such, the authors believe that the relative concentrations of POS-1 and SPN-4 have a crucial role in initiating germ cell-specific developmental programmes.

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