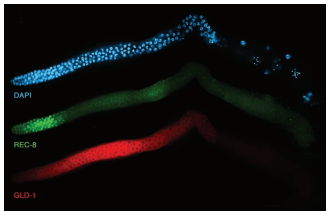
In this issue

By Jane Bradbury

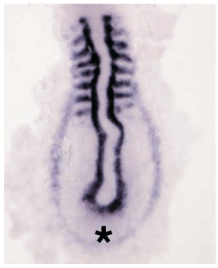
How *C. elegans* maintains its germline

In stem cell populations, proliferation and differentiation are finely balanced to ensure that the stem cells are maintained but do not overgrow and that non-renewable tissues are generated as required. On p. 93, Hansen et al. report that in the *C. elegans* germline, the accumulation pattern of GLD-1, an RNA-binding protein, controls the spatially determined balance between proliferation and meiosis. They show that at the distal end of the gonad, a low GLD-1 concentration allows stem cell proliferation; whereas, at more proximal regions, a high GLD-1 concentration promotes the entry of stem cells into meiosis and, ultimately, differentiation into gametes. To explain the accumulation pattern of GLD-1, the researchers propose that GLP-1/Notch signalling and FBF (a homologue of the *Drosophila* RNA-binding protein Pumilio) inhibit GLD-1 accumulation distally, while NOS-3 (a homologue of the *Drosophila* translational regulator Nanos) and the poly(A)polymerase GLD-2 act redundantly to promote GLD-1 accumulation proximally.



The tail-end of development

Formation of the posterior of the vertebrate body involves cell movements like those that shape the anterior body during gastrulation, as well as cell movements that are posterior specific. Some of the genes needed for tail formation have previously been identified. Now, on p. 203, Marlow et al. propose that the transcription factor encoded by *no tail* (*ntl*; the zebrafish homologue of mouse *brachyury*) and components of the non-canonical Wnt pathway – encoded by *pipetail* (*ppt*) and *knypek* (*kny*) – function in parallel, partly redundant pathways to regulate the cell movements underlying posterior body formation in zebrafish. The double mutants *kny*;*ntl* and *ppt*;*ntl* both exhibit synergistic posterior trunk and tail shortening that the researchers show is not due to impaired posterior mesoderm specification and patterning, decreased proliferation, or apoptosis. Instead, convergence and extension cell movements, which also operate in gastrulation, and tailbud-specific subduction movements are all impaired in the double mutants.

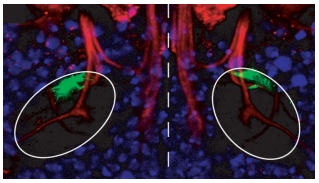


New BMP inhibitor hits the joint

Bone morphogenetic proteins (BMPs) are important in many developmental processes but were originally identified as factors inducing the ectopic formation of bone and cartilage. On p. 229, Nakayama and colleagues bring the BMP story full circle by identifying a new chordin-like secreted BMP inhibitor, CHL2, that is expressed almost exclusively in the chondrocytes of developing joint cartilage. The researchers show that recombinant mouse CHL2 (mCHL2) interacts directly with several BMPs and inhibits many BMP-dependent processes in vitro. In particular, the addition of exogenous mCHL2 to a chondrogenic culture system reduces cartilage matrix deposition and mineralisation. The findings indicate that CHL2 may regulate the formation and maintenance of articular cartilage. Finally, *CHL2* expression is upregulated in middle zone chondrocytes of osteoarthritic joint cartilage; thus, this novel BMP inhibitor could also be involved in the pathogenesis of degenerative joint disease.

Mapping the sense of smell

In the *Drosophila* olfactory system, axons of the olfactory receptor neurons (ORNs), each of which typically expresses a single specific olfactory receptor, converge onto specific glomeruli in the antennal lobe to create a spatial odour map. Olfactory information is relayed from glomeruli to higher brain centres by projection neurons (PNs), each of which forms synaptic connections with a single class of ORNs. To investigate how this wiring is established, Jefferis et al. have used 'mosaic analysis with a repressible cell marker', MARCM, to study PN development at single-cell resolution (see p. 117). Surprisingly, given that previous work suggested that ORNs are central to olfactory map formation, PN dendrites established a prototypic neural map in the antennal lobe before ORN arrival. The researchers propose that this coarse PN dendritic map interacts with a coarse map formed by developing ORNs to generate the mature glomerular organisation.



Head start on homeobox gene expression

Otx2, a paired-type homeobox gene, plays a vital role during embryonic rostral head development in vertebrates but regulation of its expression is poorly understood. On p. 57, Kimura-Yoshida et al. describe the embryonic expression pattern of *Fotx2*, the pufferfish *Otx2* gene. Then, taking advantage of the small size of the *Fotx2* gene compared with *Otx2*, the researchers surveyed the entire *Fotx2* genomic region for cis-acting regulators by examining expression of a *lacZ* reporter linked to different *Fotx2* fragments in transgenic mice. They identified seven independent cis-regulators that mediated *lacZ* expression in spatiotemporally non-overlapping subdomains of the developing rostral head. Two of these regulators were also tested and found to work in zebrafish embryos. The researchers conclude that multiple cis-regulators in the *Otx2* promoter are required to control the highly coordinated processes that occur during vertebrate head development.

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Sperm capacity decreased

Prior to fertilization, spermatozoa must undergo capacitation, whereby they react to signals in the female reproductive tract and acquire the ability to undergo tyrosine phosphorylation in response to cyclic AMP. Ca^{2+} is a potential regulator of the process, but its effects on capacitation and tyrosine phosphorylation are disputed. Aitken et al. now demonstrate that Ca^{2+} negatively regulates this signalling pathway, showing that extracellular Ca^{2+} reduces the extent of tyrosine phosphorylation in human and mouse spermatozoa. Interestingly, they find that this is associated with reduced ATP levels. Suspecting that Ca^{2+}-dependent ATPases such as the SERCA Ca^{2+} pump may be involved, the authors then demonstrate that spermatozoa have many such ATPases. Their findings indicate that Ca^{2+} inhibits tyrosine phosphorylation during capacitation and reveal the potential importance of ATP-dependent Ca^{2+} pumps – which could be significant in the context of male infertility.

Baker, M. A. et al. (2004). Analysis of the mechanism by which calcium negatively regulates the tyrosine phosphorylation cascade associated with sperm capacitation. *J. Cell Sci.* **117**, 211-222.