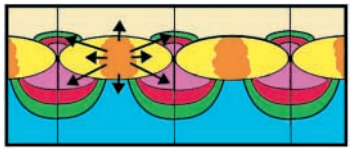
In this issue

Try a little tendon-ness

The vertebrate axial musculoskeletal system arises from distinct somitic compartments: the axial skeleton develops from the sclerotome, the skeletal muscle from the myotome and the axial tendons from a region of the sclerotome close to the myotome, called the syndetome, which is defined by expression of the gene scleraxis (*Scx*). On p. 3885, Brent and Tabin determine the molecular mechanisms responsible for positioning the syndetome. The group has shown before that FGF signalling from the myotome is necessary and sufficient for *Scx* expression. Here, the researchers report that two transcriptional targets and effectors of FGF signalling – *Pea3* and *Erm* – are required for FGF-mediated induction of *Scx*. They propose a model for tendon development in which FGFs from the myotome activate *Pea3* and *Erm* expression in the sclerotome. Further FGF signalling then activates *Pea3* and *Erm*, which directly or indirectly trigger the transcription of *Scx*.



Ribosomal insights from *Minute* mice

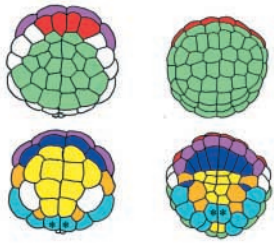
Minute mutations – first described in *Drosophila* as a class of mutants with remarkably similar phenotypes – are mutations in ribosomal proteins that have provided insights into cell autonomy, compartmental development and cell competition. While numerous in fruit flies, *Minutes* are apparently rare in mammals, and, on p. 3907, Oliver et al. provide the first detailed characterisation of a mammalian *Minute*. The semi-dominant mutation belly spot and tail (*Bst*) affects pigmentation, somitogenesis and retinal cell fate determination, and as the researchers report, is caused by an intronic deletion in the *Rpl24* riboprotein gene, affecting *Rpl24* mRNA splicing and disrupting ribosome biogenesis, protein synthesis and cell proliferation. Furthermore, in chimeras, *Bst/+* cells grow more slowly than wild-type cells, reminiscent of the cell competition effect observed in *Minute Drosophila* cells. These findings highlight the possible roles of riboprotein mutations in human growth, skeletal and ocular diseases.

News Dispatch: Hedgehog trafficking update

Hedgehog (Hh) proteins – membrane-associated signals involved in many developmental processes – can elicit signalling responses at considerable distances away from the cells that secrete them, and the transmembrane protein Dispatched (Disp) plays a key role in this journey. Tian and colleagues (p. 4021) now investigate the function of mammalian Disp1 during embryogenesis, and shed light on the mode of Disp action. Using mice with a hypomorphic *Disp1* allele, the researchers found that Disp1 has a dose-dependent effect on the severity of Hh-dependent phenotypes, such as those affecting facial morphology, and ventral forebrain, telencephalon and neural tube patterning. Furthermore, as Disp1 levels are reduced, ventral cell identities in the neural tube are progressively lost, while increasing Hh levels restores ventral cell types. The researchers conclude that Disp1 regulates the levels of Hh protein available in the target tissue, and they discuss several possible mechanisms of Disp action during Hh signaling.

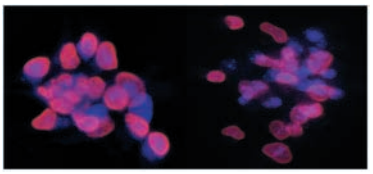
Ascidian networking

The ascidian tadpole possesses a basic chordate body plan with a simple mode of development; almost all cells are restricted to a single tissue type by the 110-cell stage. On p. 4047, Imai and colleagues report, in a transcriptional survey of *Ciona intestinalis* embryonic development, that only 65 transcription factors are zygotically expressed at or before this 110-cell stage, implying that the ascidian requires only 65 transcription factors for larval tissue specification. To see how these transcriptional factors might operate in transcriptional networks, the authors next suppressed three genes essential for endomesoderm specification – *β-catenin*, *FoxD* and *Fgf9/16/20* – then assayed for changes in the regulation of the transcription factors normally expressed in the early embryo. From this, the researchers were able to deduce possible regulatory relationships between transcription factors. They predict that this approach will lead to the construction of gene networks, revealing fundamental insights into chordate development.



Telomere erosion in neural stem cells

It has been known for some time that telomeres get shorter with each round of DNA replication. To prevent this, highly proliferative cell types elongate their telomeres using the reverse transcriptase telomerase. On p. 4059, Ferrón et al. investigate the effect of telomere erosion on the proliferation of neural stem cells (NSCs). Using mice that lack functional telomerase, they show that progressive telomere shortening impairs the proliferation of adult NSCs in vitro. Surprisingly, however, telomere erosion does not affect the proliferation of embryonic NSCs, despite their accumulation of chromosomal abnormalities. The researchers conclude that adult and embryonic NSCs have very different responses to telomere shortening, and that some types of stem cell can bypass DNA damage checkpoints. They point out that by understanding the intracellular mechanisms that regulate NSC cycling, techniques for activating neurogenesis might emerge for use in treating brain disease.



Tbx5 gets the heart beating

Holt-Oram syndrome (HOS), which results from mutations in the gene *TBX5*, causes cardiac rhythm abnormalities. Moskowitz et al. (p. 4107) now report several distinct roles for Tbx5 in the patterning and maturation of the mouse heart conduction system – the myocardial cells that coordinate the contraction of the multi-chambered heart. They show that *Tbx5* is expressed throughout the central conduction system from early heart development. Mice with *Tbx5* haploinsufficiency have postnatal morphological and functional defects in the proximal atrioventricular conduction system and earlier patterning abnormalities in the distal atrioventricular conduction system. In particular, the complete absence of a part of the conduction system – the right bundle branch – results in a conduction delay. *Tbx5* is the first gene implicated in both the patterning and maturation of the central conduction system, and Moskowitz et al. consider how this may shed light on the pathology of HOS.