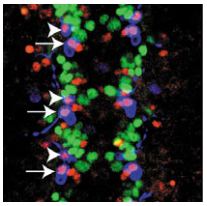
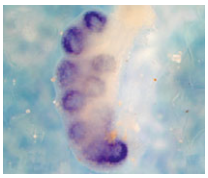


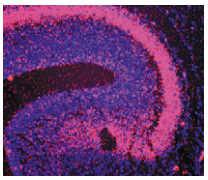
Pioneering work on cracking neuron codes

During nervous system development, combinatorial codes of transcription factors specify different neuronal subclasses. But how is each neuron's identity within a subclass specified? Garces and Thor provide new insights into this question by reporting that a unique genetic cascade specifies the fate of the aCC motoneuron in *Drosophila*, one of seven unique motoneurons in the intersegmental motor nerve (ISN; see p. 1445). Neurons of the ISN neuronal subclass express the regulatory factors *even-skipped* and *zfh1* (which specify this subclass), and *grain*, a GATA transcription factor. Although these regulators are expressed by all seven ISN motoneurons, the researchers show that they only act together in a genetic cascade (in which *even-skipped* regulates *grain*, which regulates *zfh1*) to specify the aCC motoneuron – the first, pioneer, neuron to innervate this nerve's target muscle. Why this cascade is only active in the aCC motoneuron is unclear but might depend on the history of each ISN motoneuron.



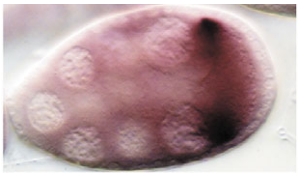
Distinct mesenchymal domains in the lung?

During embryonic lung development, interacting signalling molecules made by the developing lung's outer mesothelium, mesenchyme and bronchial epithelium regulate lung growth and morphogenesis. Fibroblast growth factor 9 (FGF9), which is expressed in the mesothelium and epithelium during early lung development, and sonic hedgehog (SHH), which is expressed only in the epithelium, are required for both processes. On p. 1507, David Ornitz and colleagues use *Fgf9* loss-of-function and inducible gain-of-function mouse models to show that FGF9 and SHH signalling coordinate lung growth and development by regulating two distinct mesenchymal domains. They report that mesothelium-derived FGF9 signals stimulate proliferation in sub-mesothelial mesenchyme and that epithelium-derived FGF9 signals regulate SHH signalling in a distinct sub-epithelial mesenchyme domain; SHH signalling subsequently regulates cell proliferation and survival, and the expression of mesenchyme-to-epithelial signals. The researchers' report of distinct mesenchymal domains in the developing lung, which respond to different combinations of signalling molecules, is a novel finding that is of relevance to the study of other developing organs.



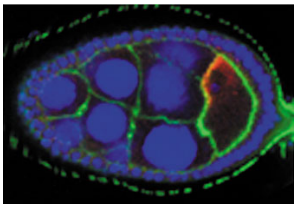
Skin-deep ADAMTS similarities

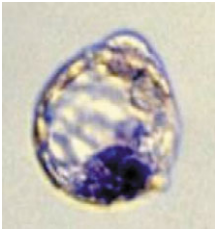
The major structural elements of most tissues are formed from type I, II and III collagens, which are made as procollagens. An aminopropeptidase called ADAMTS2 can remove the N-propeptide of all three procollagens, but, surprisingly, ADAMTS2 defects in animals cause only dermatosparaxis (severe skin fragility caused by a lack of collagen), suggesting that its homologues, ADAMTS3 and ADAMTS14, compensate for its loss in tissues other than skin. Now, by studying the temporal and spatial expression of these proteases and their procollagen substrates during mouse embryogenesis, Le Goff and co-workers show that these closely related proteins have distinct biological roles because of different tissue-specific expression patterns (see p. 1587). For example, the expression pattern of *Adamts3* identifies it as the major procollagen I and II aminopropeptidase during development, and studies of *Adamts2*-null mice reveal that ADAMTS2 is the predominant procollagen III-processing enzyme in mice. Other results confirm that dermatosparaxis occurs in *Adamts2*-null mice because neither ADAMTS3 nor ADAMTS14 is significantly expressed in adult mouse skin.



Making tracks to axis determination

An early event in the development of multicellular organisms is the establishment of the anteroposterior (AP) and dorsoventral (DV) axes. In *Drosophila* embryos, the asymmetric localisation of maternal mRNAs, such as *gurken* (*grk*) and *oskar* (*osk*) mRNAs, is essential for the formation of these axes. mRNA localisation requires an organised microtubule network, and in this issue of *Development* two papers investigate how microtubules are organised in *Drosophila* oocytes. On p. 1477, Trudi Schüpbach and colleagues identify a new protein – Spn-F – that affects microtubule organisation and axis determination during *Drosophila* oogenesis. *spn-F* was originally identified as a mutation that affects the DV polarity of the eggshell. The researchers now report that, in *spn-F* mutants, changes in the pattern of the eggshell are due to defects in the localisation of *grk* mRNA during mid-oogenesis. These arise because of defects in the organisation of the microtubules that move *grk* mRNA around the oocyte. *spn-F*, the authors report, encodes a coiled-coil protein that localises to the minus end of oocyte microtubules, where it might, for example, be required for the transport of *grk* RNA along microtubules. On p. 1467, Shapiro and Anderson report that *Drosophila* Ik2 is also required for mRNA localisation during oogenesis, and that it helps to link microtubule minus ends to the oocyte cortex. Ik2 is an IκB kinase, which the researchers expected to regulate the localisation of the early patterning determinant Dorsal, an NF-κB transcription factor. Instead, *ik2* is essential for the correct localisation of *osk* and *grk* mRNAs in oocytes; its absence produces bicaudal and ventralised embryos that closely resemble *spn-F* mutant embryos. In these mutant embryos, abnormal mRNA localisation is accompanied by defects in the organisation of microtubule minus ends and the oocyte actin cytoskeleton. Interestingly, given the similarities between *ik2* and *spn-F* mutants, both as embryos and as adults, Schüpbach and colleagues show that Spn-F and Ik2 interact directly in a global two-hybrid screen. Both research teams suggest, therefore, that these proteins might cooperate to organise microtubules during *Drosophila* oogenesis to ensure that axis determination goes smoothly.





Cloning: trophoblast fails to get with the program

Nearly ten years after the first cloned mammal was born, nuclear transfer into enucleated oocytes still rarely yields viable mammalian embryos – most cloned embryos implant normally but die after the blastocyst stage. Jouneau and co-workers now report that mouse embryos produced by the transplantation of embryonic stem cell nuclei into enucleated mouse oocytes (ES NT embryos) fail to develop primarily because of trophoblast defects – defects that are characterised by trophoblast overgrowth and subsequent placental abnormalities (see p. 1597). The researchers use embryological studies, gene expression analyses and experiments with chimeric embryos to investigate why ES NT embryogenesis fails. They show, for example, that the peri-implantation death of ES NT embryos can be partly rescued through the injection of normal ES cells or inner cell mass cells. Based on their results, the researchers propose that ES NT embryos fail because of defective epigenetic reprogramming in the trophoblast lineage. Future work should determine whether the same is true for cloned embryos produced by somatic cell nuclear transfer.

Jane Bradbury