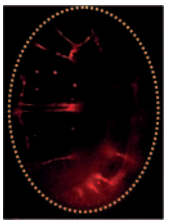
In this issue

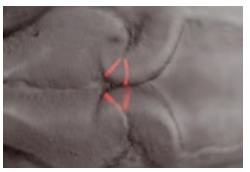
By Jane Bradbury

Enclosed: the conserved non-kinase roles of FRK-1 kinase

Transforming a spheroid nematode embryo into a worm shape begins with the embryo being enclosed by the epidermis through concerted epithelial cell movements. Modulation of cell adhesion is important in this process, as in all morphogenesis. On p. 3185, Putzke and co-workers report that embryonic closure in *C. elegans* requires Fer-related kinase-1 (FRK-1), an orthologue of the mammalian non-receptor tyrosine kinase Fer, which mediates epithelial cell adhesion. Unexpectedly, the kinase activity of FRK-1 is not required for enclosure, suggesting that FRK-1 has a non-enzymatic role during morphogenesis. The researchers also show that β-catenin and β-integrin are required for normal FRK-1 localization to the plasma membrane, and report that truncated mouse Fer rescues the morphogenetic defects of *frk-1* mutant worms, while expression of FRK-1 in mammalian cells reduces cell adhesion. Thus, the researchers suggest, Fer-like proteins may play an evolutionarily conserved role in epithelial morphogenesis.



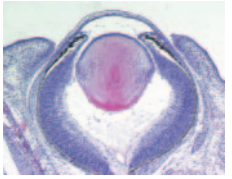
Lineage restriction: from fly wing to vertebrate brain



The developing vertebrate hindbrain is subdivided into functional segments called neuromeres. Cells can mix within but not between neuromeres – so-called lineage restriction – a process discovered in *Drosophila* wing development. Langenberg and Brand now reveal that brain segmentation extends at least as far as the midbrain-hindbrain boundary (mhb) region in zebrafish (see p. 3209). The researchers used continuous single cell analysis in a GFP transgenic zebrafish line to trace the movement of nuclei in the developing mhb region and analyzed the final position of each nucleus with an antibody against Otx, a midbrain marker. Their results identify a lineage restriction boundary in the mhb region that is probably established during late gastrulation. Lineage restriction between these regions may serve to constrain the mhb organizer cell population during brain development, conclude the researchers. Such a link has been well studied in flies but poorly characterized in vertebrate brain development.

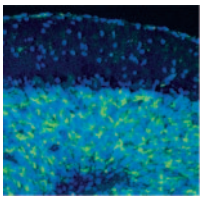
Eyes wide open

During mammalian development, eyelid growth, fusion and subsequent reopening involve cellular proliferation, shape changes, migration and death. On p. 3217, Tao et al. report that fibroblast growth factor 10 (FGF10) controls the proliferation and coordinated migration of epithelial cells during eyelid development. The researchers investigate eyelid development in *Fgf10*-deficient mice, which are born with open instead of shut eyelids. They show, for example, that activin βB and transforming growth factor α, both of which are critical for eyelid development, are downregulated in the leading epithelial edge of the developing mutant eyelid, but are upregulated in explanted cultures of normal eyelid primordia after FGF10 treatment. Overall, their results indicate that FGF10 signalling is required early in eyelid development for cell shape changes and proliferation of the prospective eyelid epithelium, and later for the cellular changes underlying epithelial cell migration during eyelid closure, a process that resembles wound healing.



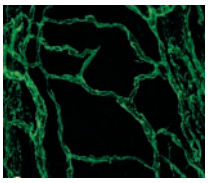
Essential glial cues for cerebellar development

During CNS development, intrinsic and extrinsic signals guide the migration of neurons to form laminae, compartments in which neurons differentiate. Defects in neuronal migration are known to cause brain malformations in humans, but whether defects in glial cells, which provide environmental cues for neuronal migration, cause similar problems is less clear. Yue and colleagues now provide the most compelling evidence to date that Bergmann glia are important for neuronal migration in the mouse cerebellum (see p. 3281). They show first that deleting the tumour suppressor gene *Pten* in both neurons and glia leads to severe lamination defects. Then, by specifically deleting *Pten* in Bergmann glial cells, they reveal that the premature differentiation of Bergmann glial cells caused by PTEN loss produces severe defects in cerebellar neuron migration and laminar formation. Thus, they conclude, Bergmann glia provide crucial, developmental stage-dependent extrinsic cues during cerebellar development.



Enlarging vessels the angiopoietin way

The development of the vascular system begins with the proliferation, coalescence and sprouting of endothelial cells to form a nexus of undifferentiated microvessels. This is remodeled in a poorly understood process to form a network of different-sized vessels. Now, on p. 3317, Thurston and colleagues show that angiopoietin 1, unlike other vascular growth factors, induces circumferential vessel enlargement without inducing angiogenic sprouting. They report that the treatment of neonatal mice and rats with angiopoietin 1 causes blood vessels to enlarge specifically on the venous side of the circulation. This enlargement, which only occurs during a brief postnatal period, is associated with endothelial cell proliferation. The identification of the molecular factors that regulate vessel plasticity, the researchers suggest, could be crucial for developing new pro- and anti-angiogenic therapies.



In *Journal of Cell Science*

Peri-implantation at a PINCH

During metazoan development, integrins act through integrin-associated molecules to regulate essential aspects of cell-cell and cell-matrix adhesion, cell polarity and cell survival. Now Li and co-authors report that the integrin-associated protein PINCH1 regulates all four of these processes during the peri-implantation stage of mouse development. PINCH1 interacts with integrin cytoplasmic tails at focal adhesions via integrin-linked kinase (ILK). The authors show that, like β1-integrin- and *Ilk*-deficient mice, mouse embryos with a disrupted *PINCH1* gene arrest at the peri-implantation stage. When the authors examined *PINCH1*-null embryoid bodies (EBs), they found that many had the same defects as β1-integrin- and *Ilk*-mutant EBs (including abnormal epiblast polarity and cell detachment from the matrix). Mutant EBs also showed abnormal cell-cell adhesion and increased endodermal apoptosis. Thus, the authors conclude, PINCH1 acts in both an ILK-dependent and an ILK-independent manner during mouse peri-implantation.

Li, S. et al. (2005). PINCH1 regulates cell-matrix and cell-cell adhesions, cell polarity and cell survival during the peri-implantation stage. *J. Cell Sci.* **118**, 2913-2921.