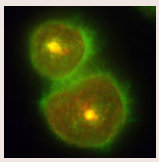
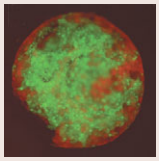
In this issue



Rafts on the go with Myo1c

The plasma membrane of eukaryotic cells is constantly remodelled to adapt to specific cellular functions. The endocytic removal of the plasma membrane is carefully balanced with the reinsertion of intracellular membranes. The small GTPase Arf6 is known to be involved in recycling membranes containing lipid rafts back to the plasma membrane, but, so far, no motor protein involved in this process has been identified. On page 1991, Folma Buss and colleagues now discover that myosin 1c (Myo1c) transports lipid-raft-containing membranes from the perinuclear recycling compartment to the plasma membrane. Depleting cells of Myo1c by using siRNA results in the redistribution of lipid raft markers from the cell surface to intracellular membranes. In addition, Myo1c specifically localises to and stabilises the formation of lipid-raft-enriched membrane tubules that extend from the juxtanuclear recycling compartment towards the plasma membrane. Furthermore, Myo1c is required for cellular functions that depend on lipid raft recycling: cells lacking Myo1c have defects in cell spreading, migration, macropinocytosis and pathogen uptake. This motor protein is, therefore, not only important for regulating dynamic membrane remodelling, but – through its role in lipid raft trafficking – is also crucial for numerous cellular processes.

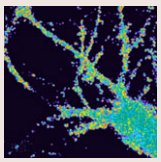


Sorting out the role for adhesion

Cell–cell adhesion is crucial for establishing multicellular structures and maintaining tissue integrity. Changes in cadherin-mediated adhesion are thought to be responsible for cell sorting and tissue boundary formation. Whereas in vitro studies support the notion that quantitative differences in adhesion lead to cell sorting, in vivo evidence for such a link has been missing so far. On page 1877, Rudolf Winklbauer and colleagues now provide evidence that the cell sorting events that occur in response to alterations in cell adhesion in vitro do not necessarily reflect the complex range of factors that influence this process in vivo. By using a C-cadherin morpholino antisense oligonucleotide and a C-cadherin mutant construct that lacks the cytoplasmic domain, and thus cannot recruit β-catenin, they modulate C-cadherin expression and signalling during *Xenopus laevis* gastrulation. Morphogenesis is surprisingly tolerant of changes in cell–cell adhesion: a moderate reduction in adhesion does not affect larvae formation, and only the dissociation of tissues under conditions of very low adhesion affects development. In addition, differences in cadherin expression and adhesion that induce cell sorting in vitro are not sufficient to drive sorting in the intact embryo. Thus, tissue boundary formation and maintenance in vivo seems to require a broader range of factors.

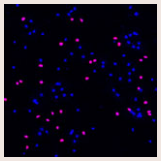
Septate junctions lose anonymity

Epithelia not only separate an organism from the external environment but also provide a diffusion barrier between internal fluid compartments. Occluding junctions between epithelial cells – namely tight junctions in vertebrates and septate junctions (SJs) in invertebrates – are key to establishing epithelial barrier function. In *Drosophila*, two types of SJs exist: pleated SJs (pSJs) are located in ectodermal epithelia, whereas smooth SJs (sSJs) are primarily found in epithelia of endodermal origin, such as the midgut. A number of pSJ proteins have been identified, but the components of sSJs have remained largely unknown. Here, Mikio Furuse and co-workers (p. 1980) identify Snakeskin (Ssk) as a protein that specifically associates with sSJs. Ssk localises to sSJs in the *Drosophila* midgut and Malpighian tubules and is required for sSJ formation. A lack of Ssk in *Drosophila* larvae results in defects in sSJ formation, alters epithelial cell morphology and impairs the barrier function of the midgut epithelium. The authors conclude that further experiments are required to fully elucidate the role of Ssk in sSJ formation and epithelial cell morphogenesis. Nevertheless, these observations provide an important starting point to further elucidate the components and function of sSJs in invertebrates.



Remodelling the synapse

The postsynaptic density (PSD) is an amorphous structure that is attached to the postsynaptic membrane of glutamatergic synapses. It contains a protein network that targets and anchors postsynaptic components, including glutamate receptors, to the membrane and regulates receptor function. One of the main scaffold proteins, guanylate kinase-associated protein (GKAP, also known as DAP1 and SAPAP), has been shown to bind to the dynein light chain 2 (DLC2), but the importance of this interaction with regards to glutamate receptor trafficking and organisation had not been elucidated. Here, Julie Perroy and co-workers (p. 2030) describe a function for the GKAP–DLC2 complex in remodelling the postsynaptic complex and modulating the activity of excitatory glutamatergic synapses. Using bioluminescence resonance energy transfer (BRET), they show that neuronal activity enhances the association between GKAP and DLC2. This results in the recruitment of GKAP and an additional scaffold protein, PSD95 (also known as SAP90), to dendritic spines. Electrophysiological measurements reveal that the synaptic clustering of GKAP and PSD95 correlates with enhanced electrical currents, and that this effect is dependent on DLC2. Thus, GKAP, together with DLC2, modulates glutamate receptor activity by altering the postsynaptic protein complex in response to initial neuronal activity.



Wnt5a keeps NPCs going

Neurogenesis in the neocortex is a highly coordinated process that occurs during specific developmental stages. Balancing neural progenitor cell (NPC) self-renewal and their differentiation into mature neurons is a crucial aspect in this process that needs to be carefully controlled. The canonical Wnt–β-catenin signalling pathway is known to be important for regulating cell fate during neurogenesis. However, less is known about the role of non-canonical (β-catenin-independent) Wnt signalling pathways, which are activated by Wnt5a and receptor-tyrosine-kinase-like orphan receptors (ROR) 1 and 2. On page 2017, Mitsuharu Endo, Yasuhiro Minami and colleagues now describe a function for ROR1 and ROR2 in maintenance of the NPC population during neocortical neurogenesis. Specifically, Wnt5a signalling through ROR1 and ROR2 is involved in generating neurons by preserving the pool of proliferative neurogenic NPCs. Binding of Wnt5a to either ROR receptor leads to the phosphorylation of disheveled 2 (DVL2) but does not activate signalling pathways that involve β-catenin. Furthermore, the authors illustrate that ROR1 and ROR2, as well as DVL2, are required for the maintenance of NPCs in the developing mouse neocortex. Overall, these results highlight an important role for the non-canonical Wnt signalling pathway in regulating NPC proliferation during brain development.

From *Development*

Joining forces in the neural tube

In developing vertebrates, neural tube closure (NTC) – the formation of the neural tube from a sheet of neural ectoderm – requires both neural ectoderm and non-neural ectoderm. But, whereas cell shape changes, cell rearrangement and cell division in the neural ectoderm are essential for NTC, the cellular changes in the non-neural ectoderm that contribute to NTC are unclear. In *Development*, Naoto Ueno and co-workers now use digital scanned laser light-sheet fluorescence microscopy to examine the movements of non-neural ectoderm cells in *Xenopus* embryos during NTC. The researchers show that the collective movement of deep-layer non-neural ectoderm cells towards the dorsal midline helps to drag along the superficial non-neural ectoderm during NTC. Inhibition of this movement by deletion of integrin β1 function, they report, blocks NTC completion. By contrast, oriented cell division, cell shape changes and cell rearrangement in the non-neural ectoderm have little or no role in NTC. Together, these results suggest that a global reorganisation of embryonic tissues is involved in NTC.

Zarin, A. A., Daly, A. C., Hülsmeier, J., Asadzadeh, J. and Labrador, J. P. (2012). A GATA/homeodomain transcriptional code regulates axon guidance through the Unc-5 receptor. *Development* **139**, 1798-1805.