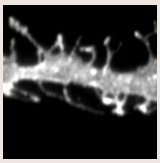
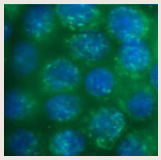
In this issue



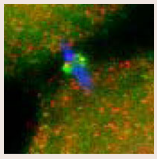
AMPAR activity shows some spine…

Dendritic spines, which are bulbous, mushroom-shaped protrusions that extend from dendrites, form the signal-receiving component of most glutamatergic synapses. During development, spines are formed through the morphological alteration of filopodia-like neuronal protrusions – but how is this process controlled? Previously, Tomoaki Shirao and colleagues showed that the clustering of the actin-binding drebrin, which occurs on dendritic filopodia at nascent synapses, is important for spine formation; now (p. 1211), they demonstrate that drebrin clustering is promoted by synaptic activity. The authors show that, when the activity of AMPA receptors (but not of other glutamate receptors) is blocked pharmacologically, postsynaptic drebrin clustering is prevented in the dendritic spines of developing hippocampal neurons in culture. Conversely, the activation of AMPA receptors promotes clustering. They next show, using FRAP, that AMPA-receptor activity promotes drebrin stabilisation, and that this is a prerequisite for drebrin clustering. Notably, AMPA-receptor blockade suppresses the normal morphological maturation of spines. On the basis of these data, the authors propose that the AMPA-receptor-dependent stabilisation of drebrin in spines is a novel activity-dependent mechanism for spine morphogenesis.



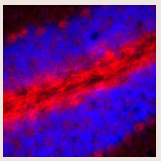
…and the Golgi gets a skeleton

The membrane skeleton (which contains ankyrin, spectrin, protein 4.1R and other proteins) forms a scaffold on the cytoplasmic side of the plasma membrane in many cell types, and helps to maintain cell shape and plasma-membrane integrity. Interestingly, spectrin and ankyrin have been shown to associate with the Golgi complex – however, it has not been clear whether additional skeleton components are present at the Golgi, or what the role of a putative Golgi-associated membrane skeleton might be. Now, Xiuli An and colleagues (p. 1091) show that a 200 kDa protein 4.1B isoform ($4.1B_{200}$; a hitherto-unknown variant of protein 4.1) associates dynamically with the Golgi complex in MDCK cells and human bronchial epithelial cells (HBEs). The authors report that, when the expression of $4.1B_{200}$ is knocked down, the structure of the Golgi complex is perturbed. Moreover, in $4.1B_{200}$-depleted cells, Na^+/K^+-ATPase and the tight-junction proteins ZO-1 and ZO-2 all fail to migrate to the plasma membrane. In subconfluent HBEs (which lack tight junctions), ZO-1 and ZO-2 associate with $4.1B_{200}$ in the perinuclear region. The authors conclude that $4.1B_{200}$ is a likely component of a Golgi-associated cytoskeleton, and is required for structural integrity of the Golgi and targeting of a subset of membrane proteins.



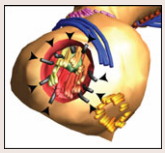
Cytokinesis: p0071 finds its way

During mammalian cytokinesis, the GTPase RhoA directs the formation and contraction of a cortical actomyosin ring at the midzone of the mitotic spindle. Activation of RhoA at the midzone requires the interaction of the plakophilin p0071 and the RhoGEF Ect2 – but how is transport of the two proteins coordinated? On page 1174, Mechthild Hatzfeld and colleagues show that p0071 and Ect2 are transported to the spindle midbody by distinct mechanisms. The authors first demonstrate that the transport of Ect2 to the midbody (which is known to be mediated by the kinesin MKLP1, a component of the centralspindlin complex) occurs before the accumulation of p0071. They next show that p0071 interacts directly with the kinesin-2 family member KIF3b. Notably, a p0071 mutant that does not bind to KIF3b fails to localise at the midbody, and depletion of either KIF3b or p0071 inhibits the accumulation of actin and myosin at the midbody and decreases levels of active RhoA during cytokinesis. Finally, the authors show that a fusion protein of p0071 and the MKLP1 motor domain can rescue RhoA activation at the midbody. Thus, the authors conclude, Ect2 and p0071 are targeted to the midbody by distinct motor proteins. Their data also identify a novel pathway of KIF3b-dependent actin reorganisation in cytokinesis.



LRP1 – quick on the (myelin) uptake

The degradation of the myelin sheath that surrounds neurons is a key feature of multiple sclerosis (MS), and the presence of degraded myelin in the extracellular space is thought to be pathogenic; thus, its internalisation by CNS cells might modify disease progression. Now, Steven Gonias and colleagues (p. 1155) identify low-density liporotein receptor-related protein 1 (LRP1) as an important receptor for the phagocytosis of degraded myelin. Using myelin vesicles (MVs) as a model of degraded myelin, the authors first show that these are internalised by mouse embryonic fibroblasts only when the cells express LRP1; moreover, uptake is blocked by receptor-associated protein (RAP), which prevents the interaction of LRP1 with other ligands. The authors next prepare primary cultures of oligodendrocytes, astrocytes and microglia, and show that all three cell types express LRP1, and internalise MVs when RAP is absent. In vitro, myelin basic protein (MBP; a major myelin component) binds to LRP1, and a MBP-specific antibody inhibits MV internalisation by oligodendrocytes. Finally, the authors report that LRP1 expression is increased in the CNS of mice with experimental autoimmune encephalomyelitis (an established model of MS). On the basis of their results, the authors propose that LRP1 might function as an important regulator of MS progression.



The flagellar pocket in 3D

Kinetoplastid parasites such as trypanosomes contain a specialised plasma-membrane domain known as the flagellar pocket – a bulbous invagination of the membrane at the site where the flagellum exits the cell body. The pocket is the sole site of trypanosome exo- and endocytosis, and has important roles in immune evasion; however, a detailed understanding of its architecture has been lacking. Now, Keith Gull and colleagues (p. 1081) use electron tomography, modelling and iterative testing to develop a detailed three-dimensional (3D) model of the flagellar pocket, and its associated cytoskeleton, in *Trypanosoma brucei* (which causes African sleeping sickness). The authors show that the pocket is asymmetrical, and that this asymmetry correlates with the position of the probasal body and the Golgi complex. They identify several novel pocket-associated structures, and describe the organisation of numerous aspects of the flagellar pocket – these include the collar and collarette (two boundary structures that associate with the entry and exit points of the flagellum), the neck region and the overall cytoskeletal structure. Their tomographic analysis enhances our understanding of the structural organisation of the flagellar pocket, and should inform future studies of its function.

Development in press

Syncytial nuclei go with the flow

Nuclear movements are important for a wide range of cellular and developmental processes. Although the intracellular mechanisms of nuclear movement have been studied in detail, the role of surrounding cells remains poorly understood. Now, in a paper published in *Development*, Carl-Philipp Heisenberg and colleagues reveal that, during zebrafish gastrulation, the nuclear movements seen in the yolk syncytial layer (YSL) are guided by surrounding tissues. Some yolk syncytial nuclei (YSNs) are located below a tissue called the mesendoderm, which contains mesoderm and endoderm progenitors. During gastrulation, the movements of these YSNs and of the mesendoderm are very similar. The authors demonstrate that these movements are coordinated, and that the mesendoderm directs YSN movements by modulating cortical flow (a concerted flow of actin filaments associated with the plasma membrane) within the YSL, which contains the YSNs. They also find that the coordinated movement of YSNs and the mesendoderm requires E-cadherin. Thus, they propose that nuclear movements can be guided by surrounding tissues and are mediated by cortical flow.

Carvalho, L., Stühmer, J., Bois, J. S., Kalaidzidis, Y., Lecaudey, V. and Heisenberg, C.-P. (2009). Control of convergent yolk syncytial layer nuclear movement in zebrafish. *Development* **136**, 1305-1315.