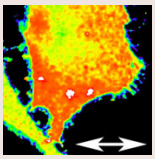
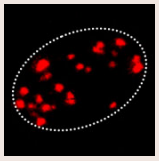
In this issue



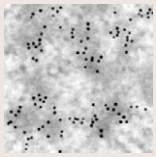
Stretch: one force, many responses

When cells sense a mechanical force, they respond by regulating signalling pathways that affect migration, polarisation and other functions – a process known as mechanotransduction. Many questions remain about how force is transduced, and Christoph Ballestrem, Ralf Kemkemer and colleagues (p. 3644) now identify key mechanistic differences between force-induced cell polarisation and migration. The authors first show that, in response to stretching forces, NIH3T3 cells realign actin filaments, focal adhesions (FAs) and microtubules (MTs) perpendicularly to the direction of stretch; notably, cellular reorientation requires an intact actin cytoskeleton but does not depend on MT function. By contrast, stretch-induced cell migration does require dynamic MTs. The authors next show that the activity of the GTPase RhoA (which regulates the actin cytoskeleton) increases dramatically in response to stretch; again, this effect is independent of intact MTs. Finally, FA reorganisation during force-induced polarisation occurs through an MT-independent sliding mechanism; by contrast, MTs are known to regulate FA dynamics during cell migration. The authors conclude that – despite the important role of MTs in cell migration – force-induced polarisation is largely MT-independent. Their results highlight the complexity of cellular signalling in response to force.



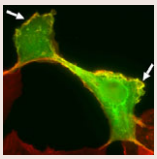
Keeping a lid on organelle fission

Both mitochondria and peroxisomes fuse and divide dynamically, and key proteins of the fission apparatus localise to both organelles – but how are mitochondrial and peroxisomal fission regulated, and is regulation coordinated between the organelles? On page 3673, Agnès Delahodde and colleagues uncover a role for the proteasomal lid protein Rpn11 in peroxisomal fission in *S. cerevisiae*. The authors recently showed that mitochondria have a fragmented morphology in a strain of *rpn11* mutant yeast (interestingly, this effect is independent of the proteasome's proteolytic activity). Now, they show that, under conditions that promote peroxisomal proliferation, peroxisomes are more abundant in *rpn11* mutant yeast than in the wild type, and this is not a consequence of proteasome deficiency. Accordingly, an intact C-terminal domain of Rpn11, rather than the catalytic deubiquitinase domain, is necessary for regulating peroxisomal abundance and mitochondrial fragmentation. The authors identify Fis1 – which localises to both peroxisomes and mitochondria – as the fission-machinery component that is regulated by Rpn11. Finally, they show that Rpn11 co-purifies with both mitochondria and peroxisomes. These data help to clarify how organelle fission is regulated, and how the cell coordinates mitochondrial and peroxisomal morphology.



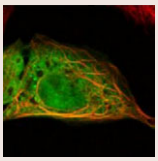
A closer look at stress granules

In response to several types of stress, eukaryotic cells repress translation and instead store mRNA (along with translation initiation factors and other proteins) in cytoplasmic stress granules (SGs). SGs often form in close proximity to pre-existing P-bodies (other mRNA-containing cytoplasmic structures that are thought to mediate mRNA degradation). The functional interplay between SGs and P-bodies has been unclear, in part because ultrastructural images of SGs have been elusive. Now, however, Dominique Weil and colleagues (p. 3619) report a detailed ultrastructural analysis of both species in eukaryotic cells. The authors induce SG formation in HeLa and HEK293 cells by subjecting them to oxidative stress, heat shock or other stressors, and identify SGs and P-bodies by using immunogold EM. They show that SGs are loosely organised fibrillogranular structures with a moderate electron density; by contrast, P-bodies are fibrillar and more dense. Proteins of the small (but not the large) ribosomal subunit are known to be SG components, and the authors show that 18S rRNA (from the small subunit) is also enriched in SGs, whereas 28S rRNA is depleted. Notably – and despite their close physical proximity – SGs and P-bodies appear to remain as distinct compartments. These findings enhance our understanding of mRNA dynamics in eukaryotic cells.



Shaping neurons: a new route?

The complex morphology of neurons is key to their function, yet many of the mechanisms that control neuronal shape are not well understood. Isoforms of the actin-associated motor myosin V (MyoV) are known to be important for dendritic-spine formation; now, Marie-France Lisé and colleagues (p. 3810) report that a novel MyoVa-interacting protein, RILP-like protein 2 (RILPL2), regulates spine formation and other aspects of neuronal shape. The authors identify RILPL2 in a yeast two-hybrid screen for MyoVa binding partners in the brain, and show that its overexpression in hippocampal neurons leads to an increase in the number of spine-like protrusions (long-term expression of RILPL2 also alters axonal shape, and its expression in young neurons can block axonal outgrowth). Moreover, knocking down RILPL2 or MyoVa results in reduced protrusions. The authors next show that transient RILPL2 expression in COS-7 cells activates the small GTPase Rac1, and immunoprecipitation experiments using rat brain extracts indicate that the two proteins form a complex. Importantly, knocking down MyoVa in COS-7 cells (or expressing a dominant-negative form) blocks RILPL2-mediated morphological changes. On the basis of their data, the authors propose a novel mechanism of neuronal shape regulation that involves RILPL2, MyoVa and Rac1.



Nuclear import: MTs get subversive

The nuclear import of most proteins is independent of the cytoskeleton but, for some proteins, microtubules (MTs) can promote or inhibit import. The P-protein of rabies virus, for instance, undergoes MT-facilitated nuclear import. Now, Gregory Moseley and colleagues (p. 3652) report the intriguing discovery that MTs can also inhibit nuclear import of P3 (a truncated version of the P-protein that is produced in virus-infected cells). The authors show that the import-inhibiting association of P3 with MTs requires P3 dimerisation, and propose that P3 might switch between oligomerisation states to regulate how it is trafficked to the nucleus. Notably, the MT-P3 interaction also promotes the association of MTs with STAT1 [a key transcription factor in the interferon (IFN) response of host cells to viral infection], and inhibits nuclear import of STAT1 in response to IFN. Accordingly, P3 expression or rabies-virus infection inhibit IFN-dependent signalling in a luciferase assay, and inhibition is relieved by the MT-depolymerising agent nocodazole. Thus, P3 might subvert the IFN response of host cells by switching nuclear import of STAT1 from a conventional to an MT-inhibited mechanism. A role for MTs in viral subversion of the host-cell innate immune response has not previously been reported, and suggests new approaches to the development of antiviral therapies.

Development in press

Spindle alignment in neuroblasts: no rotation necessary?

During development of the CNS in *Drosophila*, neuroblasts undergo asymmetric division (to produce a differentiating ganglion mother cell and a self-renewing neuroblast), which requires mitotic spindles to align along the apicobasal polarity axis of the neuroblast. Evidence suggests that, in embryonic neuroblasts, spindles assemble orthogonally to the polarity axis and rotate later to align with it; in larval neuroblasts, however, the spindles assemble in alignment with the axis. So, when does the switch from rotational to predetermined spindle alignment occur? In a paper published in *Development*, Elena Rebollo and co-workers report that predetermined spindle alignment occurs in all but the first cell cycle of embryonic neuroblasts. The researchers use two-photon confocal microscopy to examine cell divisions in embryonic neuroblasts that express centrosome and microtubule markers. The switch between the two spindle orientation modes occurs in the second cell cycle of the neuroblasts, they report, which is the first division after neuroblasts delaminate from the epithelium. This unexpected result suggests that neuroblasts remain polarised during interphase, but how polarity is maintained is unclear at present.

Rebollo, E., Roldan, M. and Gonzalez, C. (2009). Spindle alignment is achieved without rotation after the first cell cycle in *Drosophila* embryonic neuroblasts. *Development* **136**, 3393-3397.