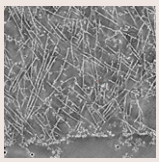
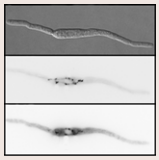
In this issue



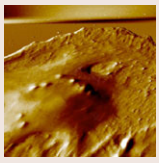
Actin – to branch or not to branch?

Actin polymerisation is crucial for the protrusion of lamellipodia. Initial studies proposed that high levels of actin branching in the lamellipodium generates short stiff filaments that create the necessary force for protrusion. This idea was challenged by electron tomography studies, which revealed long actin filaments with only a few branches at the lamellipodium tip. Victor Small and colleagues (p. 2775) now employ correlated live-cell imaging and electron tomography to shed light on this controversy. Using these approaches, they map entire actin filament trajectories in three dimensions and identify actin branch junctions on the basis of their bifurcation angle and morphology. They find that actin branch density parallels actin filament density across the lamellipodium and that actin filaments within this network have different lengths. This supports the idea that new filaments are continuously nucleated at the membrane and that existing linked filaments exhibit retrograde flow. Thus, actin filaments of all lengths contribute to pushing the lamellipodium outwards. Furthermore, the researchers find that branching from 'mother filaments' that lie parallel to the cell membrane is the first step in lamellipodium formation. These branched 'daughter-filaments' then act as new mother filaments for end branching, which is required for maintaining the lamellipodium.



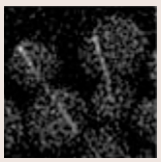
mRNPs rely on endosomes

The specific subcellular distribution of proteins as a result of localised translation is crucial for establishing cell polarity. The relevant mRNA molecules – as part of large ribonucleoprotein complexes (mRNPs) – are transported along cytoskeletal tracks by motor proteins. Kinesins and dynein are known to be involved in long-range transport of mRNPs along microtubules, but it has remained unclear which set of motors is required for mRNP transport and how the interplay between different motors is regulated. On page 2740, Michael Feldbrügge and colleagues now identify the combination of motors that is required for Rrm4-containing mRNP transport in *Ustilago maydis*. In this pathogen, plus-end-directed transport is mediated by Kin3, a kinesin-3 type motor, whereas minus-end-directed transport is carried out by the split dynein Dyn1–Dyn2. The plus-end-directed kinesin Kin1 also has a role in this process: it returns Dyn1–Dyn2 that has moved along the microtubule to the plus-ends. In *U. maydis*, the same motor proteins are used for endosome transport, which raises the question of whether mRNP shuttling is connected to membrane trafficking. Indeed, the authors find that Rrm4-containing mRNPs and shuttling endosomes are co-transported and that functional endosomes are essential for the correct movement of mRNPs along microtubules.



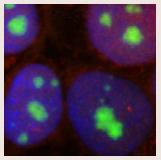
Actin gives vesicles a squeeze

Exocytosis is often viewed as a relatively simple process that involves the fusion of a vesicle with the plasma membrane, the instantaneous release of cargo and the collapse of the vesicle. However, this classical view is increasingly being challenged, and recent studies have shown that post-fusion events are crucial for secretion of certain cargos. On page 2765, Manfred Frick and co-workers now provide evidence that the secretion of pulmonary surfactant – a bulky lipoprotein complex – requires active extrusion mechanisms that involve actin and myosin II. Surfactant does not readily diffuse out of its secretory vesicles (called lamellar bodies) following their fusion with the plasma membrane and fusion pore opening. Instead, lamellar bodies become coated with actin after they have fused with the plasma membrane, and this process is required for surfactant release. Preventing actin coat formation inhibits secretion from these vesicles. Rho activation is required for actin coating, and formins mediate actin nucleation on fused vesicles. Furthermore, the authors show that contraction of the actin coat, which is mediated by myosin II, is required to actively compress the vesicles and expel their cargo. These findings provide evidence that the active 'squeezing' of vesicles through compression of an actin coat is necessary for bulky cargos to be released from vesicles.



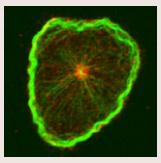
Fine-tuning Rho signals

The activity of Rho GTPases must be carefully regulated to allow them to control a variety of cellular processes. Spatiotemporal control of Rho activation depends, in part, on different guanine-nucleotide-exchange factors (GEFs). Here, Joseph Gray and co-workers (p. 2721) dissect the functional specialisation of two RhoGEFs, Rom2 and Tus1, in budding yeast. Using mutant strains lacking Rom2 and Tus1, respectively, they show that the two GEFs differentially activate Rho1 effector pathways: whereas Rom2 is more important for the activation of glucan synthase and the yeast protein kinase C homologue Pkc1, Tus1 has a more prominent role in activating the Rho1–Yfc1 pathway. In addition, the loss of Rom2, or its closely related homologue Rom1, cannot be rescued by the overexpression of Tus1. The researchers also address whether the functional specialisation of these GEFs is a result of differences in their localisation. They find that Rom2 localises to the bud neck and bud cortex in an Ack1-dependent manner. By contrast, Tus1 localisation specifically depends on the association of this GEF with the previously unidentified protein Ypl066w (Rgl1). Together, these observations highlight that the RhoGEFs not only act in distinct cellular compartments, but that they can achieve functional specialisation through the activation of distinct Rho effector pathways.



Catching a glimpse of miRNA biogenesis

MicroRNA (miRNA) biogenesis involves a number of different steps. The processing of the primary transcripts (pri-miRNAs) into long hairpin-shaped intermediates (pre-miRNAs) in the nucleus is mediated by the microprocessor complex (which contains DROSHA and DGCR8). So far, however, little is known about how miRNA biogenesis is spatially organised within nucleus and how the microprocessor recognises pri-miRNAs. Here, Jérôme Cavaillé and colleagues (p. 2709) visualise the nuclear distribution of pri-miRNAs and the dynamic recruitment and release of the microprocessor complex. Using RNA and DNA fluorescence in situ hybridisation, they show that the pri-miRNAs generated at the chromosome 19 miRNA cluster (C19MC) form a single large nuclear signal in the vicinity of the C19MC gene. The microprocessor complex is recruited to the pri-miRNAs and processes them in the vicinity of their transcription sites. In addition, the authors provide insight into the microprocessor dynamics by showing that DGCR8 can be recruited independently of DROSHA, but that, by contrast, DROSHA recruitment requires DGCR8. Furthermore, although the two proteins are recruited to pri-miRNAs as a pre-assembled complex, they dissociate separately, which provides additional insight into the temporal regulation of this processing machinery.



How TIG3 stops growth

The tumour suppressor TIG3 (also known as retinoic acid receptor responder protein 3) is highly expressed in the suprabasal epidermis and suppresses keratinocyte growth and proliferation. Reduced TIG3 expression results in keratinocyte hyperproliferation, which is associated with psoriatic lesions and skin tumours. But how does this protein cause growth arrest? On page 2604, Richard Eckert and colleagues provide an answer by showing that TIG3 suppresses proliferation by affecting the centrosome and microtubules. They illustrate that TIG3 strongly colocalises with centrosomal markers and that expression of this tumour suppressor results in the redistribution of microtubules into a broad band at the cell periphery, which is linked to the centrosome through thin microtubule projections. TIG3 expression also increases the level of insoluble α-tubulin as well as α-tubulin acetylation and detyrosination, which suggests that TIG3 stabilises microtubules. Furthermore, TIG3 reduces anterograde microtubule growth towards the cell periphery and prevents centrosome separation. Taken together, these effects result in reduced S and M phase progression in cells expressing TIG3. This leads the authors to suggest that TIG3 arrests cell growth and reduces cell survival by affecting microtubule distribution and stability, and by affecting centrosome function.