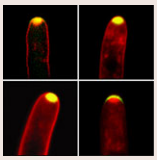
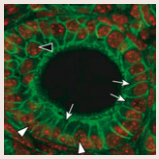
In this issue



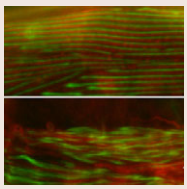
How to grow a faster fungus

In filamentous fungi such as *Ashbya gossypii*, the growth of hyphae can be remarkably rapid, making these organisms a good model system for the study of polarised cell growth. Similar to budding in yeast, hyphal expansion in *A. gossypii* is driven by polarised exocytosis at the hyphal tip, but how is growth rate controlled? On page 3878, Peter Philippsen and colleagues use light and electron microscopy to compare the exocytic machinery in fast- and slow-growing hyphae. The authors show that exocyst components and polarity proteins form a cortical cap at the tips of slow-growing hyphae, and that this defines the zone of vesicle secretion. In fast-growing hyphae, the exocytic zone is only slightly expanded; notably, however, these hyphae contain a Spitzenkörper – a complex multivesicular structure that is found at hyphal tips in several fungi. Moreover, the Spitzenkörper colocalises with several exocyst and polarisome components. The authors next show that actin patches – thought to be sites of endocytosis – are excluded from the exocytic zone, and that the area of exclusion is greater in faster-growing hyphae. On the basis of these data, the authors identify several requirements for fast hyphal extension. Their findings enhance our understanding of polarised exocytosis and cell growth.



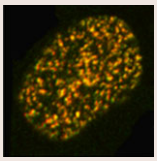
Follicle development feels the force

The early activation of ovarian follicles in the mouse has been closely characterised – the oocyte at the centre of the follicle grows and the granulosa cells (GCs) that enclose it become cuboidal and proliferate within the surrounding basal lamina, eventually forming multiple layers. Despite this knowledge, however, little has been understood about how these events are controlled. Now, Kate Hardy and colleagues (p. 3890) use histomorphometry to address the relationship between GC proliferation and oocyte growth. By labelling cells that express the cell-cycle marker Ki67, the authors first quantify the proliferation rate of GCs, which increases dramatically as they become cuboidal. They next show that GC proliferation can occur independently of oocyte growth. GCs on the basal lamina reach a maximal packing density as the second (inner) layer of GCs starts to appear; moreover, the inner layer forms because the basal GCs change their mitotic-spindle orientation and divide inwards. On the basis of these and other results, the authors propose a model in which the basal lamina (or surrounding cells) mechanically constrains the expansion of GCs, forcing the formation of additional cell layers. This study sheds light on the mechanism of ovarian-follicle activation.



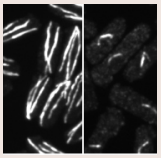
Actin' up with tropomodulin

To maintain the highly ordered structure of striated muscle, the polymerisation and depolymerisation of sarcomeric actin filaments must be precisely regulated. The actin-capping protein tropomodulin and the actin-depolymerising proteins ADF/cofilin and AIP1 are thought to regulate sarcomeric actin assembly – but what is the functional relationship between them? On page 3867, Shoichiro Ono and colleagues use the striated body-wall muscle of the nematode worm *C. elegans* to investigate the in vivo interplay between the worm tropomodulin homologue TMD-1 and other actin regulators. The authors first identify a loss-of-function TMD-1 mutant that has severely disorganised actin filaments in the body-wall muscle. In vitro, they show, TMD-1 antagonises actin depolymerisation by UNC-60B (the worm homologue of ADF/cofilin). Surprisingly, however, knocking down TMD-1 strongly enhances the disorganisation of sarcomeric actin filaments in UNC-60B mutant worms. Moreover, TMD-1 depletion has a similar effect on worms expressing mutant AIP1 or profilin. The authors conclude, therefore, that tropomodulin collaborates with ADF/cofilin, AIP1 and profilin to promote organised actin-filament assembly in sarcomeres. Their data help to decipher how sarcomeric actin is organised in vivo.



ATR – putting Rad9 in its place

In response to DNA damage, the kinase ATR is recruited to single-stranded DNA, where it activates the cell-cycle-checkpoint kinase Chk1 – in turn, Chk1 regulates cell-cycle arrest and other aspects of the DNA damage response. Along with ATR, the protein complexes Rad17-RFC and 9-1-1 are both known to be important for Chk1 phosphorylation – Rad17-RFC recruits 9-1-1 to single-stranded DNA and is phosphorylated by ATR, whereas 9-1-1 recruits TopBP1, a protein that phosphorylates ATR. Less is known, however, about how the DNA damage response is propagated and maintained, and this issue is now addressed by Nick Lakin, Veronique Smits and colleagues (p. 3933). In cultured cells, the authors report, genotoxic stress results in the immobilisation of Rad9 (a 9-1-1 component) in nuclear foci; this localisation is Rad17-dependent. Cells expressing a mutated Rad17 ($Rad17^{AA}$) that lacks both ATR phosphorylation sites form fewer Rad9 foci in response to stress, as do cells in which ATR is knocked down. By using FLIP and FRAP to test the retention time of Rad9 at nuclear foci, the authors show that Rad9 is more dynamic when ATR is depleted or $Rad17^{AA}$ is expressed. Thus, ATR and Rad17 might act together to stabilise the DNA damage response, modulating the retention – rather than the recruitment – of Rad9 at sites of DNA damage.



Mto1/2 gets microtubules going

During nucleation – an essential early step in de novo formation of microtubules – the γ-tubulin complex (γ-TuC) is recruited to prospective microtubule-organising centres. Relatively little is known about how this occurs, although it is thought that – in fission yeast – the interacting proteins Mto1 and Mto2 recruit γ-TuC. Ken Sawin and colleagues previously explored how knocking out *mto1* or *mto2* affected nucleation; now, on page 3971, they use site-directed mutagenesis of *mto1* to further investigate the association of Mto1 and Mto2 with γ-TuC. The authors first show that, similar to *Δmto1* mutants, cytoplasmic microtubule nucleation is abolished in fission yeast carrying a mutant *mto1* with a disrupted centrosomin 1 motif (CM1) region; moreover, the mutant Mto1 does not interact with γ-TuC, although it localises normally and interacts with Mto2. By contrast, mutations outside the CM1 region of Mto1 phenocopy *Δmto2* yeast – limited microtubule nucleation does occur, but binding of Mto1 to Mto2 or γ-TuC is inhibited. The authors next show that Mto1 and Mto2 form a γ-TuC-independent complex, and that each protein binds only weakly to γ-TuC in the absence of the other. They conclude that Mto1 and Mto2 act cooperatively to promote the association of the Mto1/2 complex with γ-TuC.

Development in press

Polarity bowled over by Skittles

To establish cell polarity in early development, mRNAs and proteins are localised to restricted cellular domains through asymmetric transport along a polarised microtubule cytoskeleton. Interactions between this cytoskeleton and the plasma membrane establish polarised transport – but what regulates these interactions? In a paper published in *Development*, Antoine Guichet and colleagues identify Skittles (a phosphatidylinositol 4-phosphate 5-kinase) as a regulator of these interactions in *Drosophila* oocytes. The authors show that Skittles helps to establish cell polarity by sustaining the organisation of the microtubule cytoskeleton that asymmetrically localises several axis-determining mRNAs. They report that Skittles activity controls the level of phosphatidylinositol (4,5)-bisphosphate [PtdIns(4,5)P_2] in the oocyte plasma membrane and that PtdIns(4,5)P_2 synthesis is required to activate Moesin, an adaptor protein that links the plasma membrane to the actin-based cytoskeleton. Moreover, Skittles activity is needed for the cortical recruitment of several PAR polarity proteins. Thus, by controlling PtdIns(4,5)P_2 synthesis, Skittles might regulate the interactions between the plasma membrane, PAR proteins and the cytoskeleton that are essential for cell polarisation.

Gervais, L., Claret, S., Januschke, J., Roth, S. and Guichet, A. (2008). PIP5K-dependent production of PIP2 sustains microtubule organization to establish polarized transport in the *Drosophila* oocyte. *Development* **135**, 3829-3838.