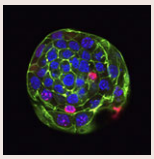
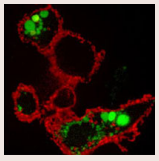
In this issue

By Jane Bradbury



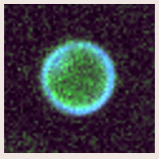
NuSAP: essential for mitosis in vivo

During mitosis, the newly replicated chromosomes must be partitioned equally between the daughter cells. Assembly of the mitotic spindle, which plays a key role in ensuring accurate sister-chromatid separation, is mediated by two processes: a centrosomal and a chromosomal pathway. RanGTP regulates the second of these pathways by stimulating the nucleation and stabilisation of microtubules near chromatin. The RanGTP target NuSAP [nucle(ol)ar spindle-associated protein] is involved in chromatin-induced spindle formation in vitro, but what about in vivo? On page 3244, Geert Carmeliet and colleagues show that the expression pattern of NuSAP, a microtubule- and DNA-binding protein, correlates with cell proliferation in developing and adult mice, and that NuSAP deficiency in mice leads to early embryonic lethality. Spindle assembly in NuSAP-deficient cells is inefficient, note the authors, so the chromosomes remain dispersed in the mitotic cytoplasm, and spindle checkpoint activation prevents completion of mitosis, which eventually leads to apoptotic cell death. Together, these results identify NuSAP as a reliable marker of cell proliferation and reveal that NuSAP is an essential protein in vivo, thereby emphasising the importance of chromatin-induced spindle assembly for proliferation in vivo.



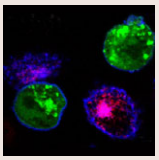
Sweetening apoptotic-cell engulfment

Apoptosis is a form of cell death that removes old, unnecessary and unhealthy cells from multicellular organisms without releasing harmful substances. Apoptotic cells are recognised and engulfed by phagocytes, but the mechanisms underlying apoptotic-cell recognition have been only partly deciphered. Martin Schiller and colleagues (p. 3347) have been investigating whether the composition of the glycocalyx – a sugar-rich coat that surrounds all human cells – constitutes an 'eat-me' signal on apoptotic cells. By using lectins to analyse surface sugar residues on activated human lymphocytes, the authors discover that the amount of sialic-acid residues decreases after the induction of apoptosis. Similar changes occur on the surface of apoptotic membrane blebs released early in apoptosis, but the exposure of sialic-acid residues and fucose residues is increased on blebs released late in apoptosis. Neuraminidase treatment enhances the engulfment of apoptotic cells, apoptotic blebs and non-apoptotic activated lymphocytes, the authors report, but not the engulfment of viable resting lymphocytes. They propose, therefore, that changes in surface glycosylation either directly mediate cellular engulfment or enhance phagocytosis by cooperation with additional engulfment signals.



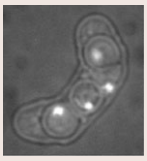
How Nhx1p regulates vacuole fusion

Membrane fusion of endosomal vesicles is crucial for maintaining cellular homeostasis in all eukaryotes. Because the machinery that controls membrane fusion is conserved from yeast to mammals, Quan-Sheng Qiu and Rutilio Fratti have turned to *Saccharomyces cerevisiae* vacuoles (yeast lysosomes), which are large and easily isolated, to study the regulation of homotypic membrane fusion. They now report (p. 3266) that Nhx1p, a Na^+/H^+ antiporter that is homologous to the Na^+/H^+ exchanger family of transporters in mammalian cells, regulates the initiation of vacuole fusion. Nhx1p, which is localized to the vacuolar membrane, regulates the acidification of cytosol and vacuole lumen, and is involved in membrane traffic from late endosomes to the vacuole. The authors show that fusion is attenuated in vacuoles isolated from *nhx1Δ* yeast. Other experiments with *nhx1Δ* vacuoles indicate that Nhx1p regulates an early step in the membrane-fusion pathway, and complementation studies show that ion-transport function is needed for Nhx1p-mediated support of fusion. Finally, the weak base chloroquine restores *nhx1Δ* fusion to wild-type levels. Qiu and Fratti propose, therefore, that Nhx1p indirectly regulates membrane fusion by controlling the pH of the vacuole.



Excluded! Membrane-protein endocytosis

Membrane proteins are constantly transported along the secretory and endocytic pathways in eukaryotic cells. Maintenance of the specific composition of each intracellular compartment requires active sorting of these proteins at each step of the transport process. During endocytosis, membrane proteins are concentrated in endocytic vesicles by interactions between their cytoplasmic domains and cytosolic coat proteins. But is exclusion of membrane proteins from transport vesicles also involved in sorting? Pierre Cosson and colleagues investigate this question on page 3329 by examining the endocytosis of chimeric proteins comprising the extracellular domain of CD1b and transmembrane domains (TMDs) of different lengths. In the absence of cytosolic sorting signals, the authors report, TMDs act as sorting signals during endocytosis. Using immunogold labelling, they show that CD1b with an 18-residue TMD is localised in clathrin-coated pits, whereas CD1b with a 21-residue TMD is excluded. Furthermore, when cytosolic signals are present, the combination of TMD and cytosolic sorting determinants controls the efficiency of endocytosis of a given transmembrane protein. The authors suggest, therefore, that TMDs are essential sorting determinants that control the exclusion of membrane proteins from clathrin-coated pits.



SINful spore formation

In the fission yeast *Schizosaccharomyces pombe*, meiosis (a specialised form of the cell cycle) produces four haploid spores that are encapsulated in an ascus. Each spore is surrounded by a wall that is formed from a structure called the forespore membrane (FSM). The septation initiation network (SIN) coordinates mitosis during vegetative growth and spore formation in the meiotic cycle. Now, on page 3284, Viesturs Simanis and colleagues report that the SIN inhibitor dma1p (which is related to the mammalian CHFR family of ubiquitin ligases) plays a role in spore formation in *S. pombe*. When *S. pombe* cells undergo meiosis in the absence of dma1p, the authors report, more than 60% of the resultant asci contain fewer than four spores, which are larger than the spores formed by wild-type meiosis. Notably, nearly all the asci contain four nuclei, which indicates that meiotic division has been successful. FSM formation is defective in the absence of dma1p, however, and the meiosis-specific SIN component mug27p persists for longer than usual. These and other data suggest that dma1p plays multiple roles during fission-yeast meiosis, including regulation of FSM formation.

Development in press

EGFR–Notch signalling makes (proneural) waves

During neurogenesis in the *Drosophila* optic lobe, a wave of differentiation that converts neuroepithelial cells into neuroblasts sweeps across the neuroepithelial sheet in a medial to lateral direction. This wave of differentiation is preceded by the 'proneural wave': the transient expression of the proneural gene *lethal of scute* [*l(1)sc*]. Now, Tetsuya Tabata and colleagues report in *Development* that the epidermal growth factor receptor (EGFR) and Notch signalling play pivotal and coordinated roles in proneural wave progression in the *Drosophila* optic lobe. They show that EGFR signalling is activated in neuroepithelial cells and induces *l(1)sc* expression. Transient, spatially restricted expression of Rhomboid regulates EGFR, they report, and Rhomboid expression is regulated by the EGFR signal, a feedback loop that moves the proneural wave laterally. The researchers also report that Notch signalling, which prolongs the proneural state, is regulated both by itself and by EGFR signalling. Based on these results, the researchers propose that coordinated sequential EGFR and Notch signalling regulates proneural wave progression, which, in turn, induces neuroblast formation in a precisely ordered manner.

Yasugi, T., Sugie, A., Umetsu, D. and Tabata, T. (2010). Coordinated sequential action of EGFR and Notch signaling pathways regulates proneural wave progression in the *Drosophila* optic lobe. *Development* **137**, 3193-3203.