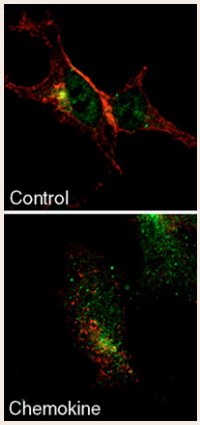
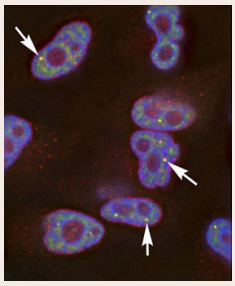
In this issue

by Jane Bradbury



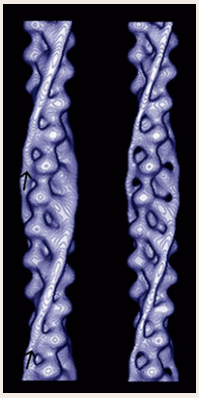
Rho-bust chemokine receptor sorting

Chemokines stimulate immune responses by attracting and activating white blood cells. They bind to receptors such as CXCR2, inducing signalling and clathrin-mediated endocytosis of the receptor. After short-term stimulation, CXCR2 recycles to the plasma membrane via recycling compartments; after long-term stimulation, it instead moves into lysosomes for degradation. But what controls this sorting decision? Part of the answer, report Ann Richmond and co-workers on p. 1559, is the small GTPase RhoB. The authors show that expression of a dominant-negative RhoB (T19N) mutant or knocking down RhoB by RNAi impairs CXCR2-mediated chemotaxis and sorting of CXCR2 to lysosomes after long-term stimulation. By contrast, expression of an activated RhoB (Q63L) mutant (which also inhibits chemotaxis and CXCR2 degradation) impairs receptor recycling through the normal (Rab11a-positive) recycling compartment after short-term stimulation, they report, and makes CXCR2 cycle through alternative pathways. The authors propose, therefore, that the RhoB GTPase activity plays an essential role in determining the differential sorting decisions that optimise CXCR2 trafficking and, consequently, chemotaxis.



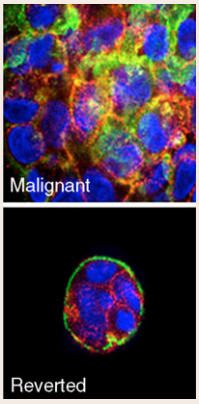
One-way traffic for snRNPs

The mammalian nucleus contains many structures through which proteins and ribonucleoproteins (RNPs) constantly and rapidly move. On p. 1540, Judith Sleeman uses dynamic live-cell microscopy to investigate the unidirectional movement of small nuclear (sn) RNPs through the nucleus. snRNPs (essential splicing factors that contain a uridine-rich snRNA and seven Sm proteins) are assembled in the cytoplasm and then imported into the nucleus, where they pass through Cajal bodies (CBs; spherical nuclear structures where snRNPs mature) to speckles (where mature splicing factors localise). Using fluorescently tagged Sm proteins, Sleeman shows that at steady state, snRNPs exchange freely in both directions between CBs and speckles. By contrast, newly imported snRNPs interact with CBs but not speckles and also exchange with the cytoplasm. Treatment of cells with an inhibitor of CRM1, a protein required for export of snRNA out of the nucleus, she reports, reduces the time spent by snRNPs in CBs. This result identifies CRM1 as a key regulator of the trafficking of snRNPs within as well as out of the mammalian nucleus.



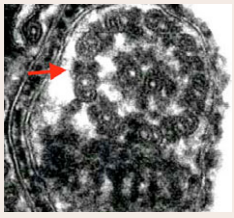
Bigger actin' role for tropomyosin

Tropomyosins promote and maintain actin filaments in many cell types and also regulate the interaction of myosin motors with actin. In fission yeast, a single tropomyosin – Cdc8 – localises to the actinomyosin ring that separates cells at mitosis and is essential for its function. Now, Kalomoira Skoumpla and colleagues report that Cdc8's role is broader – it stabilises actin filaments throughout the cell cycle – and that it is regulated by acetylation (see p. 1635). The authors use several techniques to show that Cdc8 localises to cytoplasmic actin filaments throughout the cell cycle, that it is kept at a constant level, and that 80% of it is always acetylated at the N-terminus. Acetylation, they report, increases the affinity of Cdc8 for actin and enhances its ability to regulate the interaction of actin with myosin. Furthermore, Cdc8 polymers adopt a 'closed' conformation on actin filaments that inhibits the interaction of myosin with actin. Thus, the authors conclude, acetylation of Cdc8 provides a regulatory mechanism for modulating both actin filament stability and myosin motor activity.



Epithelial differentiation goes nuclear

The apical-basal polarity and distinct nuclear organisation that characterise differentiated epithelial cells are lost in cancer. But does the loss of epithelial tissue architecture control the changes in nuclear organisation? On p. 1596, Sophie Lelièvre and colleagues show that it does and that this control mechanism critically determines epithelial cell fate. In three-dimensional cultures, normal human mammary epithelial cells form polar structures and exit the cell cycle; a survival programme is also induced. Malignant cells, by contrast, form nonpolarised nodules. Induction of basal polarity, cell-cycle exit and the survival programme in malignant cells, report the authors, restores several differentiation-specific features of nuclear organisation, including the formation of NuMA (nuclear mitotic apparatus protein) foci. However, whereas differentiated nonmalignant cells apoptose when treated with anti-NuMA antibodies, these partly differentiated malignant cells re-enter the cell cycle, which indicates that tissue architecture controls cell fate. The authors suggest, therefore, that tissue polarity and nuclear organization combine to control epithelial cell behaviour and that the loss of polarity, which happens early during breast cancer development, influences nuclear organisation.



Reverse gear for trypanosomes

Trypanosomes and other protozoa, such as *Chlamydomonas*, move using flagella powered by dynein motors. These contain one or more catalytic heavy chains and several light and intermediate chains, but how these subunits contribute to motor assembly and function is poorly understood. Kent Hill and colleagues now report that the *T. brucei* dynein light chain 1 (TbLC1) stabilises the outer dynein arms and is required for forward flagellar motility (see p. 1513). The authors show that TbLC1 is localised along the length of the flagellum and that knocking it down by RNAi causes complete loss of the normal tip-to-base flagellar beat and the emergence of a reverse beat that moves the cells backwards. They also report that the outer arm dyneins are disrupted in TbLC1 mutants, a surprising result given that *Chlamydomonas* LC1 binds to the catalytic domain of dynein rather than to the domain involved in its oligomerisation. Overall, this first analysis of LC1 function provides important insights into flagellar motility that could aid efforts to exploit the trypanosome flagellum as a drug target in sleeping sickness.

Development in press

Endocytosis regenerated

The regenerative ability of planarians is truly remarkable – they can regenerate their entire body from a tiny tissue fragment. How the brain regenerates is particularly interesting. In a paper published in *Development*, Agata and colleagues now show that a key component of the endocytic machinery – the clathrin heavy chain (DjCHC) – is required for neurite extension and maintenance during planarian regeneration. They used a novel in vitro culture system in which primary cultures of neurons from regenerated heads were sorted according to the markers displayed, after the authors had knocked down various genes expressed in the regenerating CNS by RNAi. This in vitro assay revealed that neurite extension but not neuronal differentiation depends on DjCHC. In uncut planarians, the patterning and differentiation of neural cells is normal when DjCHC is knocked down; however, neurites subsequently regress and neural cells die, which results in atrophy of the CNS. This surprising link between endocytosis and CNS regeneration will be of interest to both neurobiologists and those studying regeneration.

Inoue, T., Hayashi, T., Takechi, K. and Agata, K. (2007). Clathrin-mediated endocytic signals are required for the regeneration of, as well as homeostasis in, the planarian CNS. *Development* **134**, 1679-1690.