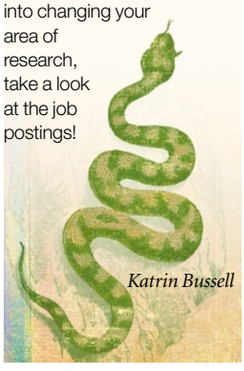
WEB WATCH

Snakes alive!
GPCRDB, a website for G-protein-coupled-receptors (GPCRs) — also known as seven-transmembrane-spanning receptors or serpentine receptors — has existed for a while, but it's recently undergone an extensive update and is well worth a re-visit.

The information on the home page is categorized into three clear titles. Under the 'primary and secondary data' heading, you can access information on various aspects of GPCR data, from chromosomal location, through phylogenetic trees for several of the families, to ligand-dissociation constants.

An exciting feature is the 'snake-like plots for mutant data'. Select this and you can visualize two-dimensional snake-like plots, and also see the consensus sequences for your selected GPCR family. Even better, it also highlights residues that are mutated, and hyperlinks them to GRAP (a database of GPCR mutants), which allows you to find out more about GPCR mutations. Also available are three-dimensional GPCR models, although if you are not a modeller by trade, visualizing these might not be that straightforward.

If you have a specific query about a GPCR, you might find the answer under the 'useful tools' heading. Meanwhile, 'other information' provides links to relevant conferences and a list of companies that work on GPCRs. And if all the information within the GPCRDB has tempted you into changing your area of research, take a look at the job postings!



Katrin Bussell

CELL CYCLE

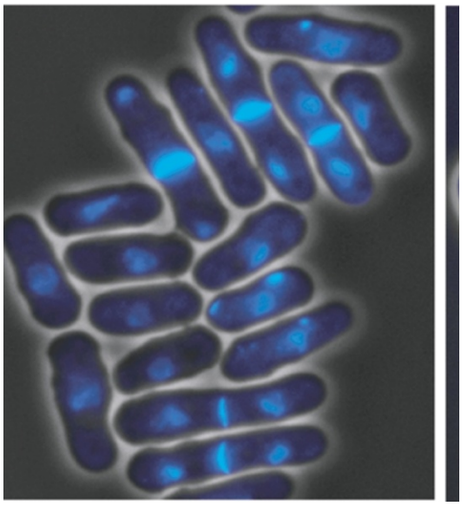
Caught in the actin

Despite its static-sounding name, the actin cytoskeleton is a dynamic structure. As eukaryotic cells progress through the cell cycle, for example, the cytoskeleton is remodelled, culminating in the formation of an actin ring that constricts during cytokinesis. The connection between these changes and the cell cycle has not been clear, but a report in *Nature* now describes a hitherto unknown mitotic checkpoint that specifically monitors the actin cytoskeleton.

This startling finding emerged when Gachet, Tournier and colleagues treated synchronized *Schizosaccharomyces pombe* cells with a drug that inhibits actin polymerization — latrunculin B — and found that these cells stopped during mitosis for upwards of an hour. Not only that but the orientation of the bipolar spindle, which is responsible for segregating the duplicated chromosomes, was disrupted in the treated cells. Given the spindle defect, the authors then asked whether latrunculin B has any effect on sister-chromatid separation. They observed a single signal from a fluorescently labelled marker for centromeres, indicating that the sister chromatids had not separated.

In fission yeast, sister chromatids are glued together by a protein called Rad21, and separate only when this protein is cleaved by a specialized protease known as Cut1 or separase. Cut1 is, in turn, activated by destruction of an inhibitory subunit called Cut 2 (securin), which is ubiquitylated — and targeted for destruction — by the anaphase-promoting complex (APC). Gachet *et al.* showed that, in the presence of latrunculin B, cleavage of Rad21 is delayed. However, destruction of Cut2 was unaffected by this treatment, indicating that disruption of the actin cytoskeleton delays sister-chromatid separation without affecting the APC. The authors also showed this checkpoint to be independent of the spindle-assembly checkpoint, which delays mitosis in response to a defective spindle or when chromosomes fail to attach to the spindle.

So what are the components of this new checkpoint? Gachet *et al.* screened for mutant cells that were more sensitive than wild-type cells to latrunculin B, and pulled out Atf1 (the yeast homologue of the human transcription factor ATF2) and Sty1/Spc1 (a mitogen-activated protein kinase). Both proteins belong to the stress-activated protein kinase pathway (SAPK), with Sty1/Spc1 phosphorylating — and hence activating — Atf1. The figure shows wild-type cells (left) and Δ*atf1* cells (right) in the presence of latrunculin B.



CYTOSKELETON

Switch off your engine!

Like cars, organelles obey traffic rules, moving and stopping when bid to do so by traffic control. In many cases, instead of simply switching off their motor, organelles choose to dump it altogether and pick it up again the next time they need to move. This is the case for melanosomes, which use the molecular motor myosin-V to move along actin tracks during interphase, but release it during mitosis when most membrane transport is put on hold.

The Gelfand group showed two years ago that myosin-V associates with melanosomes in *Xenopus laevis* melanophores and that it is phosphorylated during mitosis, which leads to its release and a marked reduction in the actin-based motility of the organelles. The same group now reports in *Science* that they have found the kinase responsible for this molecular switch.

Karcher and colleagues show that, as expected, myosin-V binds to melanosomes through its globular tail domain, which also contains the mitotic phosphorylation site. Combining multidimensional mass spectrometry with mutagenesis, they mapped the phosphorylation site to a single serine at position 1650.