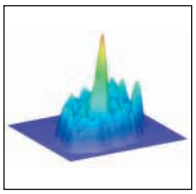
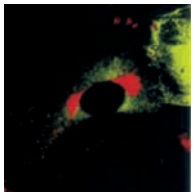


Ca^{2+} signalling (p. 2213 and p. 2223) *Signal Transduction and Cellular Organization*

The mechanisms by which Ca^{2+} is released from intracellular stores and enters across the plasma membrane (PM) are important features of the cell biology of this intracellular messenger. They allow cells to generate a variety of distinct spatiotemporal Ca^{2+} signals and provide a mechanism for maintaining intracellular Ca^{2+} homeostasis. In this issue, Commentaries in our *Signal Transduction and Cellular Organization* series focus on two important aspects of Ca^{2+} release and entry: the generation of 'local' Ca^{2+} signals and capacitative Ca^{2+} entry.

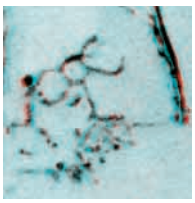
On p. 2213, Martin Bootman and co-workers review our understanding of the roles of local Ca^{2+} signals - spatially restricted rises in cytosolic [Ca^{2+}] such as the Ca^{2+} 'puffs' and 'spikes' of non-excitable cells and the Ca^{2+} 'sparks' of excitable cells. These local signals vary from 10 nm to several micrometres in diameter and can produce specificity in the response by restricting Ca^{2+} to particular targets. Adenylyl cyclase, for example, is more sensitive to Ca^{2+} entering through store-operated Ca^{2+} channels (SOCCs) than to that entering through voltage-operated Ca^{2+} channels (VOCCs) - presumably because SOCCs are localized close to the enzyme. Local Ca^{2+} signals can also trigger much larger signals that spread throughout the cell. For example, coordinated recruitment of Ca^{2+} puffs arising at sites containing multiple inositol 1,4,5-trisphosphate (Ins(1,4,5)P_3) receptors generates the characteristic Ca^{2+} waves observed during hormonal stimulation. Local signals can thus not only have local effects in particular microdomains but also have far-reaching effects with long-term consequences.

On p. 2223, Jim Putney and co-workers continue the discussion of Ca^{2+} signalling, focusing on the mechanism(s) by which depletion of ER Ca^{2+} stores induces influx of Ca^{2+} through PM channels - a phenomenon known as capacitative Ca^{2+} entry. One possibility is that the ER stores regulate PM Ca^{2+} channels by controlling the level of Ca^{2+} (which inhibits the channels) in their immediate vicinity. Alternatively, stores might release a diffusible messenger that opens PM Ca^{2+} channels - indeed, such an activity (calcium-influx factor; CIF) has been isolated. Perhaps the most compelling model, however, is 'conformational coupling', in which ER Ins(1,4,5)P_3 receptors communicate the filling state of the ER by interacting directly with PM Ca^{2+} channels. Recent work, including the observation that in excised PM patches certain channels require Ins(1,4,5)P_3 receptors for activity, provides strong support for conformational coupling. Nevertheless, since capacitative Ca^{2+} entry can operate in cells lacking Ins(1,4,5)P_3 receptors, Putney and co-workers conclude that multiple mechanisms underlying this phenomenon probably exist.



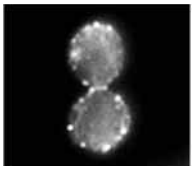
A scaffold for β1,4-galactosyl-transferase (p. 2291)

β1,4-galactosyltransferase I (GalT) is a transmembrane glycoprotein responsible for galactosylation of certain glycoconjugates in the Golgi. Unlike many glycosyltransferases, GalT is also present at the surface: it acts as a lectin-like matrix receptor that facilitates cell spreading by associating with the cytoskeleton and activating cell-specific signalling cascades. Barry Shur and co-workers have used a two-hybrid approach to identify signalling proteins with which GalT interacts. They show that the cytoplasmic domain of GalT binds to SSeCKS - a PKC target that is homologous to gravin and functions as a scaffolding protein and an organizer of the cytoskeleton. Furthermore, they demonstrate that this unprecedented glycosyltransferase-scaffold interaction occurs in vivo, SSeCKS and GalT colocalizing in both the Golgi and filopodia. The authors show that the interaction is functional, since SSeCKS constructs containing the GalT-interaction sites can reverse the spreading defect caused by a dominant negative GalT mutant. They propose that the SSeCKS scaffold orchestrates the signalling/cytoskeletal functions of GalT, suggesting that its binding could be coupled to GalT-dependent FAK activation and/or recruitment of signalling molecules to the GalT microenvironment.



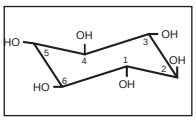
3D organization of the yeast secretory pathway (p. 2231)

The classic textbook diagram of the Golgi apparatus shows a series of independent flattened sacs. This might be an accurate representation of the mammalian Golgi. But what of the more elusive yeast Golgi? Alain Rambourg, Catherine Jackson and Yves Clermont have studied the Golgi apparatus and other membrane structures of the budding yeast secretory pathway under 3D stereo electron microscopy - employing brefeldin A treatment and *sec21* ts mutants to identify the ER and Golgi compartments. They observe that the structures involved are polygonal tubular networks connected to fenestrated ER sheets. Interestingly, the Golgi elements generally appear to exist not as flattened sacs or cisternae but instead as tubular networks - a morphology that segments of the ER can also occasionally adopt. The authors demonstrate that secretory granules are progressively segregated at the intersections of the tubules making up the polygonal networks. The granules are liberated by rupture of these tubular networks rather than, as previously predicted, by budding from the edges of saccular elements. The authors' findings suggest that cargo transport along the yeast secretory pathway involves vectorial membrane flow through a series of membrane transformations rather than transport between fixed structural compartments.



Control of mitotic exit by Bub2p-Bfa1p (p. 2345)

The spindle assembly checkpoint (SAC) ensures that cells possessing damaged spindles or unattached kinetochores arrest in metaphase and do not exit mitosis. In budding yeast, Bub2p and Bfa1p appear to be key components of the arm of the pathway that blocks mitotic exit. The two proteins might function as a GTPase-activating protein (GAP) that regulates Tem1p - a GTPase that is part of the mitotic exit network (MEN) and is activated by the exchange factor Lte1p. Leland Johnston and co-workers show that Bub2p andBfa1p are present as a complex throughout the cell cycle and associate with Tem1p during M phase and early G1 phase. Furthermore, they show that Lte1p and Bfa1p (but not Bub2p) are phosphorylated in a cell-cycle-dependent manner and after SAC activation - phosphorylation of both proteins being in part due to the Polo-related kinase Cdc5p. The authors propose that, following SAC activation, phosphorylation of Bfa1p by Cdc5p stimulates Bub2p GAP activity, which, combined with inhibitory phosphorylation of Lte1p, blocks activation of Tem1p and consequently mitotic exit.



Cell Science at a Glance - inositides (p. 2207)

The attachment of lipid and phosphate groups to the inositol ring generates an astonishing array of molecules - confusing enough even before you try to get to grips with the nomenclature and the multitude of enzymes. In this issue's Cell Science at a Glance, Stephen Shears and co-workers present a user-friendly summary of all the phosphoinositides, inositol phosphates and enzymatic reactions involved, which we hope will make this metabolic pathway a little less confusing.

In the next issue of JCS

STICKY WICKET
A pod of botanists, an affinity of pharmacologists, an aggregate of structural biologists? No, the collective noun is 'department'. **Caveman**

CELL SCIENCE AT A GLANCE
The mitotic roles of Polo-like kinase. M. M. Donaldson et al.

COMMENTARIES
PTEN: a multifunctional tumor suppressor. **K. M. Yamada and M. Araki**
p300/CBP proteins: HATs for transcriptional bridges and scaffolds. **H. M. Chan and N. B. La Thangue**

RESEARCH ARTICLES
Microsphere-based analysis of EGF signaling. **R. Brock and T. M. Jovin**
Serine phosphorylation of β1 integrin. **J. P. Mulrooney et al.**
A conserved CHMP family. **T. L. Howard et al.**
Lateral diffusion of LPS receptors. **K. Triantafilou et al.**
cAMP receptor affinity controls wave dynamics. **D. Dormann et al.**
CHMP1 functions in the nucleus. **D. R. Stauffer et al.**
Coordinated segregation of sister chromatids. **C. A. Hodges et al.**
Apoptosis-like death in *Leishmania donovani*. **M. Das et al.**
de novo Rabl formation. **B. Goto et al.**
Incomplete RNA polymerase II phosphorylation in *Xenopus laevis* early embryos. **B. Palancade et al.**
FasL targeting via a proline-rich domain. **E. J. Blott et al.**
Rab7 and phagosome maturation. **A. Rupper et al.**
Lysosomal membrane chaperone complex. **F. A. Agarraberes and J. F. Dice**
Three calcium wave pacemakers in ascidian eggs. **R. Dumollard and C. Sardet**
PtdIns(4,5)P_2 and pre-mRNA splicing. **S. L. Osborne et al.**