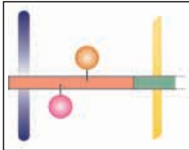


T-cell lipid rafts (p. 3957) *Signal Transduction and Cellular Organization*

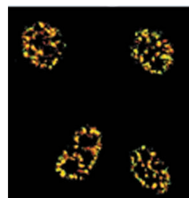
This issue of JCS sees the final instalment of a series of Commentaries entitled *Signal Transduction and Cellular Organization* that has run throughout 2001. This series has reflected our increasing understanding of the organization of signalling networks, in which multiprotein complexes, subcellular localization and signal integration are now known to play key roles. Lipid rafts represent one possible mechanism for organization of signalling machinery, and on p. 3957 Miguel Alonso and Jaime Millán discuss the roles of these membrane microdomains in T cell signalling and trafficking. Recent work has revealed that T cell activation causes recruitment of signalling molecules such as phospholipase C, ZAP70 and Vav to lipid rafts and that costimulatory signals redistribute lipid rafts to T cell receptors. The new data indicate that, as in epithelial cells, rafts play an important role in sorting in T cells. Indeed, MAL - an integral, raft-associated, membrane protein that has an essential role in apical sorting in MDCK epithelial cells - might participate in translocation of raft lipids and proteins to the immunological synapse.

New model for Ste5p action (p. 3967) *Signal Transduction and Cellular Organization*

Given the important roles of scaffolds in organizing signalling pathways, it is fitting that the final Commentary in our *Signal Transduction and Cellular Organization* series features perhaps the archetypal scaffold molecule, yeast Ste5p. Ste5p acts as a scaffold for the MAPK (Fus3p), MAPKK (Ste7p) and MAPKKK (Ste11p) in the yeast mating pathway. It is essential for mating and is thought to provide MAPK signalling specificity. Elaine Elion reviews recent studies that have shed further light on Ste5p function. Genetic and biochemical experiments indicate that Ste5p is not merely a passive scaffold and that its oligomerization is important for activation of the MAPK cascade. Additional work has revealed that membrane localization and nuclear shuttling are important regulatory mechanisms for pathway activation by Ste5p. Elion presents a model for Ste5p action in which pathway activation converts it from a closed inactive conformation to an open active dimer, which can bind to G protein βγ subunits and, consequently, undergo higher-order oligomerization to form a multimeric scaffold lattice.

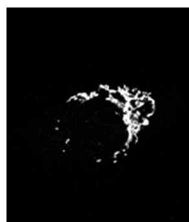
Ca^{2+} puffs - generic Ins(1,4,5)P_3 signals (p. 3979)

Ca^{2+} puffs are local increases in intracellular Ca^{2+} concentration triggered by binding of the second messenger Ins(1,4,5)P_3 to receptors (InsP_3Rs) on intracellular Ca^{2+} stores. The puffs appear to play a key role in the generation and propagation of global Ca^{2+} waves following hormonal stimulation of HeLa cells. But how widespread is the phenomenon, and to what degree is it influenced by the type of InsP_3R expressed? Peter Lipp and co-workers have characterized Ca^{2+} puffs in no less than six different cell types, which express different levels of the three mammalian InsP_3Rs. They find that the Ca^{2+} puffs produced in these cells are almost indistinguishable and exhibit markedly similar amplitudes, spatial spreads and kinetics. In addition, the authors demonstrate that InsP_3R downregulation induced by prolonged hormonal stimulation drastically reduces the number, amplitude and duration of Ca^{2+}puffs and, consequently, the ability of cells to trigger Ca^{2+} waves. The authors' findings indicate that Ca^{2+} puffs are generic and fundamental features of Ca^{2+} signalling that underpin responses to stimuli that generate Ins(1,4,5)P_3.



Lamin rearrangements during muscle differentiation (p. 4001)

Inherited forms of muscular dystrophy such as Emery-Dreifuss muscular dystrophy are caused by mutations in A-type lamins - key components of the nuclear lamina. Lamins are not confined to the nuclear periphery, however: they also form 'speckles' in the interior, associating with splicing factor compartments and DNA replication centres. Using an antibody that specifically recognizes A-type lamins in intranuclear speckles, Veena Parnaik and co-workers now show that lamin A/C speckles (but not lamin B or splicing factor speckles) disappear during myocyte differentiation and quiescence. Significantly, the loss of speckling occurs only in myocytes, and extraction of the cells by detergent and nuclease causes the speckles to reappear, which suggests that the epitope recognized is somehow masked during differentiation and quiescence. The authors conclude that muscle differentiation is accompanied by regulated rearrangements in the organization of A-type lamins. Indeed, if dystrophy-producing lamin A mutations hinder such rearrangements, this could explain why the mutations specifically affect muscle tissue despite almost ubiquitous expression of the lamin.



Bypassing the ER: direct-to-Golgi trafficking (p. 4105)

Every cell biology student knows that proteins destined for the Golgi and beyond must first pass through the ER. But in some cases trafficking via the ER might have drawbacks. For example, passage of Golgi-vesicle-tethering proteins such as GM130 through the ER could cause mistargeting of Golgi-destined vesicles. To investigate the possibility that alternative trafficking routes exist, Nobuhiro Nakamura and co-workers have analysed trafficking of GM130 and its partner GRASP65 - two peripheral membrane proteins implicated in organization of Golgi cisternae. They show that following pulse labelling GM130 and GRASP65 can be detected in Golgi but not ER membrane fractions. The authors also find that GM130 and GRASP65 localize to the Golgi even when ER-to-Golgi transport is blocked. In addition, they demonstrate that GM130 and GRASP65 synthesized in vitro can bind to purified Golgi membranes but not microsomal membranes. Rather than assembling on ER membranes and undergoing vesicular transport to the Golgi, GM130 and GRASP65 thus appear to use a novel trafficking route that targets them directly to the Golgi.

Sticky Wicket - working hours (p. 3955)

Arrive early, leave early; 9 to 5; or the night shift: different people choose different working hours. And is time spent in the lab proportional to productivity? Despite an early start tomorrow, Caveman finds time to investigate the various approaches to lab-time management and show off to those in other time zones.

In the next issue of JCS

STICKY WICKET

Reflections on turning fifty. Caveman

CELL SCIENCE AT A GLANCE

The p53 functional circuit. S. Jin and A. J. Levine

COMMENTARIES

Complexes of tetraspanins with integrins. F. Berditchevski

Cell biology beyond the diffraction dimit. F. de Lange et al.

RESEARCH ARTICLES

BP180 and actinins. A. M. Gonzalez et al.

PIX dimerization induces ruffles and microvilli. C.-G. Koh et al.

Suppression of SAPK/JNK by H_2O_2. D. Kyun Kim et al.

Bcl-2 in cellular compartments. J. Rudner et al.

Asymmetric cell division in fucoid algae. S. R. Bisgrove and D. L. Kropf

Actin cytoskeleton dynamics during phagocytosis. M. G. Coppolino et al.

Control of fibroblast length. E. M. Levina et al.

***Chlamydomonas* profilin.** D. R. Kovar et al.

N-RAP in myofibril assembly. S. L. Carroll et al.

Telomere pairing in *Arabidopsis* meiosis. S. J. Armstrong et al.

GSK3β activity in PC12 cell differentiation. R. G. Goold and P. R. Gordon-Weeks

Proteasome degradation of hDlg. F. Mantovani et al.

Dynamic targeting of nuclear PP1. L. Trinkle-Mulcahy et al.

Spermiogenesis in *Marsilea*. C. W. Tsai and S. M. Wolniak

Intranuclear ER induced by a nucleolar protein. C. Isaac et al.

Microtubules, tension and spindle checkpoint. R. B. Nicklas et al.

EGF mediates Ca^{2+} signaling in response to injury. V. E. Klepeis et al.