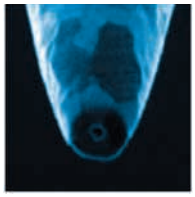
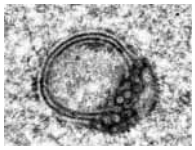
Integrin-tetraspanin complexes (p. 4143) Commentary

The tetraspanins are a family of plasma membrane proteins that contain four transmembrane domains and a trademark Cys-Cys-Gly motif in a large extracellular loop between transmembrane domains 3 and 4. They are implicated in various processes, including cell migration, proliferation and differentiation, but no physiological receptor/ligand has been identified, and there are few clues to their cell biological role(s). Fedor Berditchevski reviews accumulating evidence that one role of tetraspanins is to regulate integrin function. Several integrins have been shown to associate with tetraspanins as part of a 'tetraspanin web', and recent work indicates that tetraspanins can modulate integrin-dependent cell migration. Given that tetraspanins associate with signalling molecules such as phosphatidylinositol 4-kinase and protein kinase C, they might also facilitate adhesion-dependent integrin signalling by tethering such enzymes to integrins. This compartmentalization could extend to formation of tetraspanin-rich membrane microdomains, since integrins and tetraspanins co-localize with the lipid raft component GM1. Furthermore, it could include integrin sorting and turnover, in which tetraspanins are also implicated.



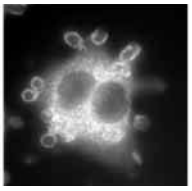
Beyond the diffraction limit (p. 4153) Commentary

Conventional fluorescence microscopy is an immensely useful, highly sensitive and non-invasive cell-biological tool. The diffraction limit imposed by the wavelength of the light, however, restricts its attainable resolution to ~250 nm. Carl Figdor and co-workers discuss a novel technique, near-field scanning optical microscopy (NSOM), that has allowed fluorescence imaging to achieve resolutions of only a few tens of nanometres. In common with atomic force microscopy (AFM), NSOM uses a fine probe to scan the sample surface. However, in NSOM, the probe is also a light source, funnelling incident light to dimensions substantially below the diffraction limit. Indeed, the technique brings single-molecule detection sensitivity within reach. Figdor and co-workers have demonstrated the potential of NSOM by using it to investigate the distribution and orientations of single integrins on the surface of fixed murine fibroblasts. They speculate that, in the near future, developments in NSOM will allow it to produce results comparable to those obtained by transmission electron microscopy - but in living cells under physiological conditions.



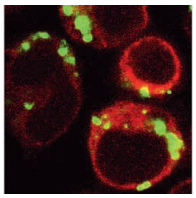
Intranuclear endoplasmic reticulum (p. 4253)

Prior to implantation of the fertilized egg, human endometrial cells develop a unique network of intranuclear membrane stacks termed the nucleolar channel system (NCS). The NCS appears to be essential for fertility, but its precise function has remained enigmatic for forty years. Thomas Meier and co-workers now demonstrate for the first time that NCS-like structures can be generated in cultured cells. They show that overexpression of the nucleolar chaperone Nopp140 induces the formation of stacks of membrane cisternae whose ultrastructure and composition are remarkably similar to those of the NCS. Using light and electron microscopy and an array of nuclear envelope and ER markers, the authors demonstrate that the channels comprise bona fide ER that is produced by invagination of the inner nuclear membrane (INM). These findings thus not only implicate Nopp140 in human reproduction but, since they indicate that ER and outer nuclear membrane proteins can diffuse through the pore membrane domain into the INM, have profound implications for our understanding of both membrane generation and nuclear envelope topology.



A complex controlling actin rearrangements during phagocytosis (p. 4307)

During phagocytosis of foreign material by macrophages and neutrophils, recognition of antibody-coated particles by Fc receptors (FcRs) generates intracellular signals that stimulate local reorganization of the actin cytoskeleton and consequently formation of the pseudopodia that engulf the particles. Several molecules are implicated in FcR signalling, including Syk, PI 3-kinase and phospholipase C; however, the components of the pathway that regulates actin reorganization have remained unclear. Antonio Sechi and co-workers have now identified several key molecules. They show that recruitment of Ena/VASP proteins - a family of profilin-binding actin regulators - to the phagocytic cup is required for FcR-dependent actin rearrangements and particle internalization. Moreover, the authors demonstrate that these proteins are part of a multimolecular complex containing SLP-76, Fyb/SLAP, Nck and WASP that forms during phagocytosis. Sechi and co-workers suggest that the adaptor SLP-76 is the central component in this complex and links two signalling events - (1) Fyb/SLAP-dependent recruitment of Ena/VASP proteins and profilin, and (2) Nck-dependent recruitment of WASP and the Arp2/3 complex - which converge to control the localized actin rearrangements required.



ER-mitochondrion crosstalk in apoptosis (p. 4161)

Bcl-2 and other anti-apoptotic Bcl-2-family proteins protect cells from apoptosis induced by a variety of stimuli. They appear to sequester pro-apoptotic proteins such as Bax, and prevent breakdown of the mitochondrial membrane potential, cytochrome C release and consequent activation of caspase-9 - key stages in the mitochondrial apoptosis pathway. Our understanding of Bcl-2 function is complicated by the fact that it localizes not only to mitochondria but also to the ER and nuclear membranes. Claus Belka and co-workers have therefore used Bcl-2 mutants targeted to different subcellular compartments to analyse the importance of its localization. Their key finding is that an ER-targeted Bcl-2 mutant (Bcl-2/ER) protects cells against radiation-induced apoptosis as effectively as wild-type or mitochondrion-targeted Bcl-2. They also demonstrate that Bcl-2/ER efficiently inhibits the breakdown of the mitochondrial membrane potential and activation of caspase-9. The authors conclude that there is crosstalk between the ER and mitochondria in the mitochondrial apoptosis pathway, speculating that this could occur at the level of calcium homeostasis.

Sticky Wicket - fear of fifty (p. 4137)

Caveman is fifty! Well, not exactly. This issue sees the appearance of his fiftieth article for JCS. To mark the occasion, the troglodyte pauses to reflect on what inspires his columns and why the misguided Editors of JCS asked him to write in the first place.

In the next issue of JCS

STICKY WICKET

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Lamin defects in human disease. W. H. Raharjo et al.
Nuclear envelope disorganization in fibroblasts from FPLD patients. C. Vigouroux et al.
Yeast cyclin function and localization. N. P. Edgington and B. Futcher
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Fibulin-1 suppression of adhesion and motility. W. O. Twal et al.
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Interaction of Mns1p and Sec12p with Rer1p. M. J. Massaad and A. Herscovics
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Rab5a and trafficking to lysosomes. J. L. Rosenfeld et al.
snRNP protein expression enhances Cajal bodies. J. E. Sleeman et al.
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Emerin-BAF interaction in mitosis. T. Haraguchi et al.