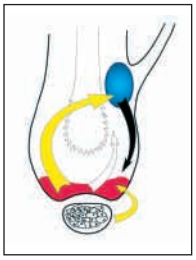
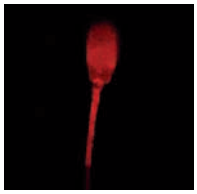
GGA proteins: sorting at the TGN (p. 3413) Commentary

GGA proteins are a recently identified family of proteins that appear to have important roles in membrane trafficking. Members of this family are conserved throughout eukaryotes and share homology in their C-termini with the ear domain of γ-adaptin - a component of heterotetrameric clathrin adaptor complexes. Annette Boman discusses recent work that is beginning to illuminate the roles of this novel protein family. The known members localize to the trans-Golgi network (TGN) and interact with both the small GTPase ARF and clathrin. Their importance in TGN sorting is evident from knockout and overexpression studies in yeast and mammals, which have shown that GGA proteins are required for specific trafficking events between the TGN and endosomes. In vivo work indicates that GGA proteins are ARF effectors that bind to clathrin as well as a defined set of sorting receptors, such as mammalian sortilin and mannose 6-phosphate receptors. They thus appear to function as ARF-dependent monomeric clathrin adaptors that facilitate cargo sorting and vesicle formation at the TGN.



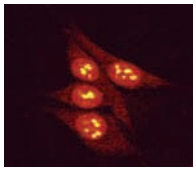
Hair follicle cycling (p. 3419) Hypothesis

In mammals, body hairs do not persist; they are constantly shed and regrown, the hair follicle (HF) undergoing successive cycles of growth, quiescence and regression. The basis for HF cycling is not fully understood. Moreover, many results are contradictory or at odds with the prevailing model of HF cycling - the bulge activation hypothesis - in which the entire HF is proposed to be derived from stem cells present in the HF 'bulge' region. Angela Christiano and co-workers present a novel view of HF cycling that challenges aspects of the bulge activation hypothesis. Backed up by studies of stem cell markers, patterns of cell migration during the hair cycle and the colony-forming ability of different HF cell populations, their hypothesis has two key elements: (1) two populations contribute to HF renewal - bulge cells and the hair 'germ' at the base of the HF; (2) bulge cells are recruited to a 'lateral disc' at the periphery of the hair bulb in one cycle and preprogrammed to form different layers of the inner root sheath and hair shaft in the next.



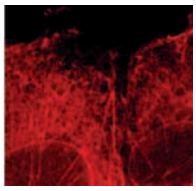
Sperm capacitation (p. 3543)

Capacitation is an essential maturation process that takes place in sperm prior to fertilization. A key event in this process is the activation of sperm by oviduct-resident bicarbonate, which alters membrane lipid architecture and facilitates lipoprotein-mediated cholesterol efflux. Barend Gadella and co-workers have investigated the mechanism of sperm capacitation, using M540 staining (a marker for phospholipid scrambling) as evidence of bicarbonate activation. They find that only a low-cholesterol subpopulation of sperm that has completed epididymal maturation responds to bicarbonate. The authors demonstrate that, in this subpopulation, bicarbonate stimulates lateral redistribution of cholesterol to the apical surface of the sperm, where it then becomes available for albumin-mediated extraction from the plasma membrane. Since proteins typically present in membrane rafts are present at the sperm apical surface, Gadella and co-workers propose that bicarbonate-stimulated phospholipid scrambling allows formation of an apical lipid raft, from which cholesterol can be transported out of the bilayer. This change in cholesterol organization is likely to facilitate interaction with and fertilization of oocytes.



SRP nuclear localization and RanBP8 (p. 3479)

Signal recognition particle (SRP) is a cytoplasmic RNP complex responsible for targeting of nascent polypeptides to the ER. Although resident in the cytoplasm, SRP appears to assemble in the nucleus. However, the mechanisms by which SRP and its subunits are transported between the cytoplasm and nucleus are unclear. Howard Fried and co-workers show that SRP19, the only SRP protein that can bind to SRP RNA independently of other proteins, is imported into the nucleus by two members of the importin β family: RanBP8 and transportin. This observation alone is significant, because it represents the first description of a cargo for RanBP8 and hence confirms its status as a nuclear transport receptor. However, the authors also show that, once in the nucleus, a significant pool of SRP19 is localized to the nucleolus. This finding substantiates an earlier suggestion that at least one step in SRP assembly takes place in the nucleolus; furthermore, it strongly supports the idea that the function of the nucleolus is not limited to synthesis of ribosomes.



Actin disassembly and resealing the plasma membrane (p. 3487)

Rupture of the plasma membrane is common in many cell types. Survival of the cell depends on a rapid resealing response involving Ca^{2+}-dependent application of a membrane 'patch' provided by cytoplasmic vesicles. Actin rearrangements might also play a role, since cortical actin is an obvious physical barrier to vesicle transport. Confusingly, however, inhibition of actin polymerization has been reported both to stimulate and to inhibit resealing. Katsuya Miyake and co-workers have now used a variety of approaches to demonstrate that disruption of cortical actin promotes resealing. They find that F-actin levels are reduced at plasma membrane disruption sites. Furthermore, they show that the actin-depolymerizing agent DNase I enhances resealing whereas actin-stabilizing agents inhibit it. Finally, the authors demonstrate that cells that 'naturally' contain high cortical F-actin levels (owing to pre-wounding) exhibit a compromised resealing response, which can be restored by actin-depolymerizing agents. Miyake and co-workers conclude that, in common with other exocytic processes, resealing requires localized F-actin disassembly, which is consistent with the Ca^{2+} dependence of both resealing and actin depolymerization.

Sticky Wicket - separating science and scientist (p. 3407)

In a recent article, Caveman attacked the way we look up to cult figures in science, stating that we should focus on ideas not names. Now he is forced to defend this view in response to a reader who argues that remembering the names reminds us that people are not perfect and that science is by no means objective.

In the next issue of JCS