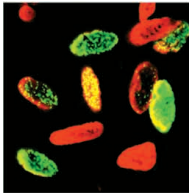


Myosin V: walking along actin without falling off (p. 1981) **Commentary**

Single motor proteins that transport cargo over long distances alone must remain attached to their cytoskeletal tracks while undergoing many productive catalytic cycles - i.e. they must be processive. This is certainly true of the microtubule-based motor conventional kinesin, but what about the actin-based myosin motors? Can the deciphered kinetic schemes of the non-processive myosins I and II be adapted to accommodate the prolonged actin binding that a processive myosin would require? And, if so, how could such a myosin negotiate the helical actin track without becoming entangled in the cytoskeleton. Amit Mehta discusses recent single-molecule analyses, solution-kinetic experiments and structural studies of myosin V that have answered these questions. The new data indicate that myosin V is indeed a highly processive motor and has a kinetic scheme in which the rate constants of the myosin I/II scheme are tuned to favour strong actin binding. Furthermore, they reveal that myosin V takes massive (36-nm) steps along actin, which, given the 36-nm pseudorepeat of the actin helix, allow it to follow a linear rather than a helical path. Molecular models for kinetic processivity that are based on these data depart significantly from schemes proposed for other processive enzymes.



Replication licence revoked (p. 2027)

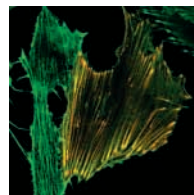
Licensing of chromatin in G1 phase is a key step in control of cell proliferation and allows DNA

replication to initiate at replication origins. The process involves sequential assembly of pre-replication complexes (pre-RCs) containing CDC6 and MCM proteins, which subsequently dissociate during S phase. Gareth Williams and co-workers have analysed pre-RC regulation in cycling, quiescent, differentiated and replicative senescent cells, using a cell-free replication system and extracts from cultured human cells. They show that downregulation of CDC6 and MCM proteins is a common mechanism for loss of proliferative capacity: both are absent in quiescent (G0 phase) cells and, perhaps more unexpectedly, replicative senescent cells - previously thought to arrest in G1 phase (and thus contain pre-RC components) rather than G0 phase. Intriguingly, the authors also show that in breast luminal epithelia a high proportion of cells contain MCM proteins despite lacking conventional proliferation markers. Such cells might therefore be arrested not in G0 but in G1 phase and thus more susceptible to inappropriate proliferation and tumorigenesis.

Trio: a GEF for axon guidance (p. 1973) **Signal Transduction and Cellular Organization**

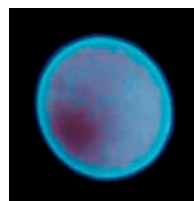
During neuronal development, a variety of extracellular cues guide growing axons towards

their destinations. These cues activate intracellular signalling networks that coordinate cytoskeletal rearrangements necessary for motility and steering of the growth cone. Rho family GTPases are known to be key components of such networks, but their upstream regulators have proven elusive. Jack Bateman and David Van Vactor discuss recent work implicating members of the Trio family of Dbl-related proteins in control of axon guidance and neuronal migration. These guanine-nucleotide-exchange factors (GEFs) interact with LAR proteins - receptors for extracellular guidance cues - and activate Rho GTPases such as RhoG. Genetic studies indicate that Trio mediates fine-scale mapping of neuronal cell positions in the mammalian brain and pathfinding of retinal axons in *Drosophila* - possibly by activating the Rac/Cdc42 effector PAK. Given the widespread defects in *Trio* mutants from different organisms, Bateman and Van Vactor propose that Trio molecules are part of a common signalling network used by multiple guidance cues during neuronal development.



Plectin-mediated actin bundling (p. 2065)

Plectin, a member of the plakin family, is an important cytoskeletal component that associates with desmosomes, intermediate filaments, microtubules and actin stress fibres. It acts as a multifunctional linker that connects the three cellular filament systems and might also be involved in reorganization of the actin cytoskeleton. Arnoud Sonnenberg and co-workers have now used a variety of approaches to investigate the role of plectin in actin dynamics. They demonstrate that a putative actin-binding domain (ABD) in plectin indeed binds to actin, and interacts preferentially with polymerized actin. The sequences responsible are located at the C-terminal end of the first of two calponin-homology domains (CH1) that make up the ABD. The authors also find that the plectin ABD can stimulate actin polymerization and bundle actin filaments - probably by mediating dimerization of filament-bound plectin molecules. Since plectin forms heterodimers with another plakin, dystonin, Sonnenberg and co-workers propose that dimerization of plectin and related molecules is a novel mechanism that regulates reorganization of the F actin network.



Building a new plasma membrane (p. 2009)

The coenocytic green alga *Bryopsis plumosa* exhibits an interesting wound response, regenerating new cells from cytoplasm extruded after disruption of the cell membrane. The regeneration process is poorly understood - how a structure as complex as a new plasma membrane forms has been particularly hard to

fathom. Gwang Hoon Kim and co-workers have analysed *B. plumosa* regeneration in detail and reveal that it occurs in four stages: (1) aggregation of organelles; (2) an increase in mass and adoption of a spherical shape; (3) primary envelope formation; and (4) secondary membrane development. Perhaps the most interesting finding is that the cells initially become surrounded by a polysaccharide envelope. This exhibits some characteristics of a cell membrane (e.g. semipermeability and selective transport) and gradually transforms into a polysaccharide-lipid complex, before being replaced by a lipid-based plasma membrane. Since staining reveals lipid material at the centre of the protoplasmic masses, the authors propose that remnants of the original membrane are initially compressed in the centre but then are gradually incorporated into the primary envelope.



Sticky Wicket - editors (p. 1969)

On what basis do journal editors accept/reject manuscripts, and do they really read them or simply base decisions on the comments of referees?

Responding to a letter from an alpine troglodyte, Caveman suggests that editors should pick reviewers carefully and take on fewer manuscripts, so that they have time to read them thoroughly enough to make informed decisions.

In the next issue of JCS

STICKY WICKET

Life in the Stone Age. Caveman

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COMMENTARIES

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The organisation and functions of local Ca²⁺ signals. M. D. Bootman et al.

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Yeast Gea1p and Gea2p act at the Golgi. A. Peyroche et al.

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Involvement of pp60^{c-src} in matrix adhesion. T. Volberg et al.

Assembly of *C. elegans* apical junctions. L. McMahon et al.

Melanogenesis inhibition by oxidative stress. C. Jiménez-Cervantes et al.

Nuclear translocation of corneal ferritin. C. X. Cai and T. F. Linsenmayer

Operation of EGFR autocrine system. A. E. DeWitt et al.

NG2 expression induces cell polarization. W. B. Stallcup and K. Dahlin-Huppe

Bub2/Bfa1 control of metaphase. S. E. Lee et al.

FasL targeting via a proline-rich domain. E. J. Blott et al.

GalT interaction with SSeCKS. M. J. Wassler et al.