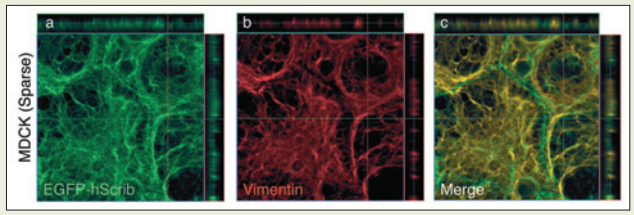
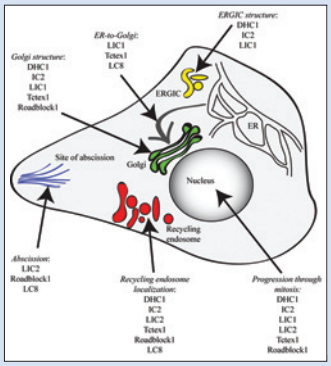
Vimentin Regulates Scribble Activity by Protecting It from Proteasomal Degradation

Dominic C. Y. Phua, Patrick O. Humbert, and Walter Hunziker



Cell polarization—the asymmetric distribution of cellular components into functionally separate regions—is fundamental to processes such as proliferation and movement. Its deregulation plays a central role in human diseases, in particular cancer. The multidomain protein Scribble (Scrib) is a key polarity regulator and neoplastic tumor suppressor in *Drosophila*. Mammalian Scrib is implicated in epithelial cell–cell adhesion and polarization during directed cell migration. The authors characterize a novel interaction between Scrib and the intermediate filament protein vimentin, which has a stabilizing effect on Scrib levels. Vimentin depletion results in the proteasome-dependent degradation of Scrib, which consequently leads to defective epithelial cell–cell adhesion and deregulated cell migration, closely phenocopying Scrib depletion. Double knockdown of Scrib and vimentin causes a phenotype similar to single silencing and suggests that the two proteins function in a single linear pathway. This stabilization of Scrib expression and function by vimentin is consistent with previously reported observations that vimentin is upregulated during epithelial wound healing. The findings imply a possible regulatory function for vimentin in Scrib homeostasis during epithelial migration.



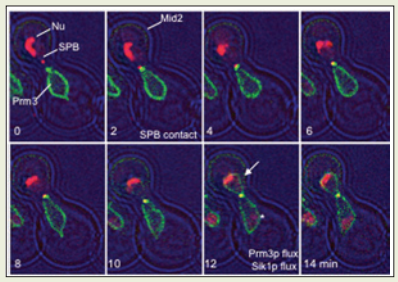
Specificity of Cytoplasmic Dynein Subunits in Discrete Membrane Trafficking Steps

Krysten J. Palmer, Helen Hughes, and David J. Stephens

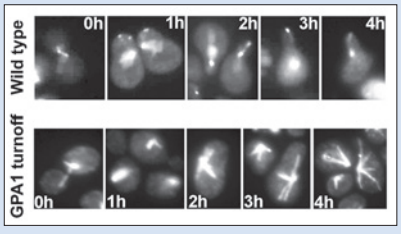
The minus-end–directed microtubule motor protein complex cytoplasmic dynein can exist in multiple forms specified by assembly of distinct polypeptide subunits (heavy, intermediate, light intermediate, and light chains). By means of siRNA depletion and quantitative cell imaging, the authors reveal the specific role of individual subunits in different membrane trafficking events. Loss of heavy chain or intermediate chain subunits has global effects on dynein structure, but suppression of individual light intermediate chain (LIC) or light chain subunits leaves dynein intact. Futhermore, individual subunits are shown to be involved in ER-to-Golgi transport, endosome positioning, mitotic progression, and the completion of cytokinesis. Notably, LICs occur in separate dynein populations and, from cell imaging experiments, LIC1 is implicated in Golgi function, with LIC2 being involved in recycling endosome positioning. Dynein-2, which contains LIC3, was not involved in any of the trafficking events examined. These data show that specific forms of dynein differing in their subunit composition are involved in discrete membrane trafficking steps.

Nuclear Fusion and Genome Encounter During Yeast Zygote Formation

Alan Michael Tartakoff and Purnima Jaiswal



When haploid cells of *Saccharomyces cerevisiae* are mated, parental nuclei congress and fuse in a process called karyogamy. By following cells that express differentially tagged proteins, the authors show that karyogamy involves a preliminary "parting" of the nuclear envelope at the apex of the nucleus, followed by slow flux first of outer and—minutes later—of inner membrane proteins. Using novel assays to investigate the impact of mutations and drugs on karyogamy, the authors document a requirement for two corresponding factors of distinct topology: 1) a protein that participates in membrane fusion in the cytoplasm (Sec18p/NSF), and 2) luminal factors that are sequestered when unfolded proteins accumulate in the ER. After karyogamy, the waist of the nucleus dilates and nuclear pores access the *trans* portion of the nuclear envelope, all before the spindle pole bodies coalesce. The authors also show that tagged loci of parental genomes remain in their respective nucleoplasmic domains after karyogamy, although they are mobile. This restriction reflects their tethering to spindle pole bodies, judging from a requirement for a centromere and intact kinetochores.



The Mating-Specific Gα Interacts with a Kinesin-14 and Regulates Pheromone-Induced Nuclear Migration in Budding Yeast

Sofia V. Zaichick, Metodi V. Metodiev, Scott A. Nelson, Oleksii Durbrovskyi, Edward Draper, John A. Cooper, and David E. Stone

The regulation of the cytoskeleton by external stimuli is essential to many fundamental processes in eukaryotic cells. One well-studied phenomenon that depends on signal-induced changes in cytoskeletal polarity is the fusion of haploid yeast to produce zygotes. In mating mixtures, yeast cells interpret pheromone gradients to locate and grow toward the closest potential mating partner. Preparatory to karyogamy, the nucleus is moved toward the eventual fusion site by the shortening of microtubules that tether it to the cell cortex. The Kar3 microtubule-associated motor protein both stimulates the depolymerization of these microtubules and maintains their cortical interaction as they shorten. It is not known, however, how Kar3 is anchored to the cortex, nor how pheromone regulates its function. Here the authors show that pheromone stimulates interaction between Kar3 and the mating-specific Gα protein Gpa1 and that Gpa1 affects both Kar3 localization and microtubule–cortex contact. These data provide the first example of a Gα protein–kinesin interaction and suggest that Gpa1 is an anchor and an externally regulated positional determinant for Kar3, a previously unappreciated role for Gα proteins. ■