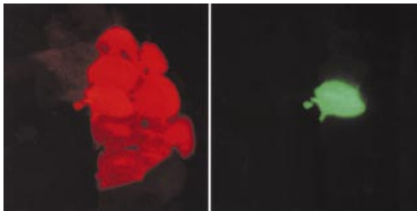
New Insights into Gap Junction Communication

In a surprising finding, Landesman et al. (page 929) obtained results that diverge from previous analyses of junctional communication during *Xenopus laevis* embryogenesis. While a number of studies have reported that asymmetries arise in the patterns of gap junction communication during dorso-ventral patterning, this new work suggests a new model to explain these apparent asymmetries.

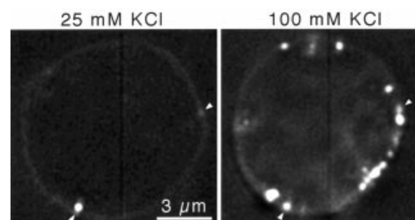


Xenopus embryos have been the principal model for studies on gap junctional intercellular communication in development. Earlier studies tracing the transfer of Lucifer yellow between cells led to models in which better gap junctional coupling between dorsal cells compared with ventral cells plays a role in dorso-ventral patterning. To analyze this process more thoroughly, the authors compared the transfer of Lucifer yellow and neurobiotin in embryos, coinjecting the junction-permeable tracer with a fluorescent dextran which cannot pass through gap junctions. Though their results in whole-mount embryos agreed with previous observations, Lucifer yellow was not transferred through junctions at all in fixed and sectioned embryos. The team found junctional communication using neurobiotin, a more permeable tracer, but it was completely symmetric, a pattern not altered by treatments that ventralized the embryos.

To explain the discrepancies in the results, the authors propose a model in which light scattering through whole embryo mounts, and the differential pigmentation of ventral and dorsal blastomeres, combine to give the appearance of asymmetrical distribution of the marker dye.

Regulating Compound Exocytosis

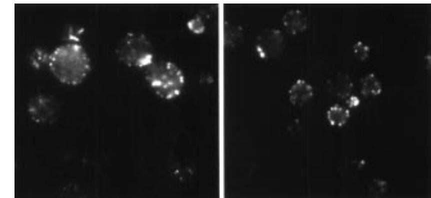
Beginning on page 839, Cochilla et al. demonstrate that granule-to-granule and granule-to-plasma membrane fusion events are differentially regulated during compound exocytosis, a process in which multiple granules fuse together to share a single exocytic opening in the plasma membrane. The observations identify a point at which exocytic secretion can be regulated by different second messenger pathways, and suggest a physiological role for compound exocytosis in neuroendocrine cells.



Though compound exocytosis was known to occur in neuroendocrine cells, the biological significance of this process has remained unclear. In the new work, the authors used a combination of fluorescence imaging of individual exocytic events and electron microscopy to observe granule-to-plasma membrane and granule-to-granule fusion events in rat pituitary lactotrophs. Stimulating secretion with hormones causes the formation of exocytic structures, the majority of which consist of multiple granules fused together to share a single exocytic opening. Elevating cyclic AMP appears to increase the number of granule-to-granule fusion events, while activating protein kinase C increased both granule-to-granule and granule-to-plasma membrane fusion. The results suggest a mechanism in which different second messenger pathways are able to target compound exocytosis in different ways in order to modulate the level of secretion from neuroendocrine cells.

Functional Significance of Nucleotide Exchange by Profilin

By extensively mutagenizing the Saccharomyces cerevisiae profilin gene, Wolven et al. (page 895) found that catalyzing nucleotide exchange is an important in vivo function of profilin. The results help address a controversy over the significance of profilin-mediated nucleotide exchange, and provide new insight into the function of the protein, which plays a critical role in establishing and maintaining cytoskeletal organization.



Though profilin has been the subject of extensive biochemical analyses, in vitro experiments have produced some conflicting results. In particular, it remained unclear whether the ability of profilin to enhance nucleotide exchange on actin was functionally important. In the new work, the authors demonstrate that the actin-binding region of profilin is critical in vivo, and that an actin mutant with an increased intrinsic rate of nucleotide exchange can suppress defects in a profilin mutant. Using an in vitro assay containing actin, profilin, and cofilin, the team found that profilin is required for rapid actin dynamics in this system. The results suggest that profilin regenerates ATP actin from the pool of ADP actin-cofilin produced during filament disassembly, allowing rapid actin movement. Alternatively, the ability of profilin to promote ATP exchange on actin may lead to the dissociation of cofilin from ADP actin.

Novel Technique to Probe Cytokinesis

Using a new library complementation strategy in *Dictyostelium discoideum*, Robinson and Spudich (page 823) identified four genes involved in cytokinesis. In addition to providing new information about the mechanism of cytokinesis, the work paves the way for future studies of interaction genetics in the cellular slime

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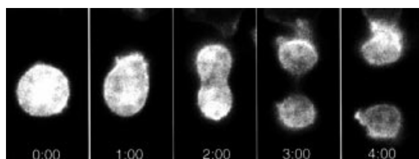
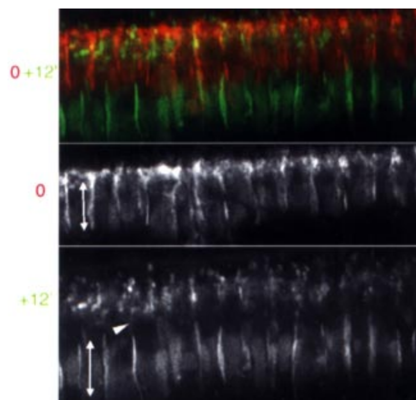
mold. Many of the proteins involved in cytokinesis have been discovered in *D. discoideum*, but the lack of a meiotic phase in laboratory strains has inhibited mutation mapping and the identification of epistatic relationships in this organism.



In the new work, the authors screened chemically mutagenized cells for defects in cytokinesis, then performed library complementation on one of the mutants to find genes involved in the process. The screen recovered the previously characterized protein cortexillin I, coronin, a new member of the ERM family of proteins, and one novel protein, which the team named dynacortin. Dynacortin is found in the cell cortex during cytokinesis, somewhat enriched at the poles and reduced in the cleavage furrow. Characterization of dynacortin and its interactions with other gene products suggests that contraction of the medial ring is mediated by spatially restricted cortexillin I and myosin II, and globally distributed dynacortin, coronin, and RacE.

The availability of the new library complementation technique should also facilitate future studies in *D. discoideum*. In separate work awaiting publication, the same laboratory has already used this approach to identify new genes involved in the transition from vegetative growth to differentiation.

Linking Cellularization and Polarization



Lecuit and Wieschaus (page 849) developed techniques that combine cell surface labeling and particle tracking to study the dynamics of membrane insertion during cellularization in the *Drosophila* embryo, a process that leads to the formation of a polarized epithelium. Their results suggest that membrane growth and polarization occur simultaneously in this system, and that membrane from an intracellular pool is inserted in a defined sequence at specific sites.

The mechanisms of membrane growth in *Drosophila* cellularization are poorly understood, despite efforts to identify the source of new membrane and the sequence of events leading to epithelial polarization. The authors developed techniques that allow the visualization of membrane protein movement in living embryos during cellularization, and compared the resulting dynamic patterns to the distribution of a newly synthesized transmembrane protein in staged fixed embryos. In this system, membrane populations derived from the ER and/or Golgi apparatus insert at precise locations, suggesting a mechanism in which a polarized pattern of membrane growth is linked to subsequent polarization of the cells. In this model, the massive insertion of new membrane overwhelms membrane diffusion in order to establish polarization. The data also suggest that the membrane may play a more active role in polarization than previously thought.

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