Mechanisms of Vesicular Transport in Neurite Outgrowth

Beginning on page 889, Martinez-Arca et al. describe the role of the tetanus neurotoxin insensitive vesicle-associated membrane protein (TIVAMP) in neurite outgrowth. Through a combination of biochemical and functional analyses, the authors show that TIVAMP is required for vesicular transport in neurite outgrowth, and identify the NH2-terminal domain of the protein as a major regulator of this process. In addition to providing significant new insight into vesicular trafficking, the findings suggest that TIVAMP could be a valuable pharmacological target in efforts to treat nerve damage.

Structural Transitions at Microtubule Ends

In the first detailed study of microtubule end structure and dynamics performed under physiological conditions, Arenal et al. (page 767) have found that microtubule assembly involves the extension of a two-dimensional sheet of protofilaments which then closes into a tube. In addition to demonstrating the feasibility of studying microtubule end structure in a physiologically relevant system, the results support a model that helps to explain dynamic instability.

Germ Plasm Segregation and Specification

By studying the segregation of vasa gene products, which encode an RNA helicase that marks the germline in a variety of organisms, Knaut et al. (page 875) have obtained strong supporting data for a new model of germ cell specification in zebrafish. The authors propose that vasa RNA, but not its protein, is a component of the zebrafish germ plasm, and that maternal signals trigger the pattern of germ plasm segregation leading to germ-line fate commitment. The new model, combined with the well-defined genetics and transparency of the zebrafish system, should facilitate future studies on this crucial developmental process.
sociated with germ plasm. The RNA segregates asymmetrically during cell division until the late blastula stage, when vasa RNA segregation becomes symmetric in the founder population of primordial germ cells. In embryos carrying a mutation in the maternal effect gene nebel, asymmetric segregation of vasa RNA is impaired. Based on these results, the authors propose that unequal germ plasm segregation establishes a separate population of four cells with the potential to form the germline. A maternal program induces these cells to become the founder population of the germline, and germ plasm is segregated symmetrically in subsequent cell divisions.

Functions of Spectrin in C. elegans

Using different approaches, Moorthy et al. (page 915) and Hammarlund et al. (page 931) have analyzed the roles of spectrin in the biology of C. elegans. The mutually reinforcing results overturn some earlier hypotheses about the functions of the β-G spectrin subunit, and define a variety of specific roles for spectrin subunits in both developing and adult worms.

A major component of the membrane skeleton in most metazoans, β-spectrin has been proposed as a factor in membrane stabilization, the localization of specific membrane proteins, and the generation of cell polarity. Hammarlund et al. found that the unc-70 gene encodes the C. elegans homologue of β-G spectrin, and determined growth conditions that allow the survival of unc-70 null mutants, but axon outgrowth and muscle organization are affected.

Moorthy et al. performed a global analysis of the three spectrins encoded by the C. elegans genome: the β-G spectrin studied by the Hammarlund team, β-H spectrin, and α-spectrin. Using RNAi to inhibit expression, the authors found that the phenotype caused by a loss of α-spectrin is reproduced by inhibiting both β-G spectrin and β-H spectrin. This result, combined with global expression profiles of the three spectrin subunits, support a model in which α-spectrin combines with β-G and β-H subunits in different tissues to carry out the diverse functions of spectrin. In addition, the RNAi experiments confirm that β-G spectrin is not required for establishing cell polarity.

Nuclear Import of RCC1

Nemergut and Macara (page 835) studied the nuclear import of RCC1, the guanine-nucleotide exchange factor for the Ran GTPase, and found that RCC1 import into the nucleus can proceed by at least two distinct mechanisms. The results help explain a puzzling problem: since enrichment of RCC1 in the nucleus is believed to be a requirement for the nuclear import activity of Ran, it was unclear how Ran-dependent mechanisms could account for the initial establishment of a nuclear pool of RCC1.

By time-lapse photography, the authors found that RCC1 import into the nucleus is one of the most rapid nuclear import processes yet described. When the NH$_2$-terminal domain of RCC1, containing a NLS, is deleted, the protein is still imported into the nucleus. In addition to the classical nuclear import pathway, RCC1 can use a pathway that is independent of the NLS, importin-α binding, and Ran. The second pathway is saturable, but does not require energy. Based on their results, and the central role of RCC1 in nuclear import, the authors propose that the second import pathway evolved to scavenge free RCC1 from the cytoplasm and ensure that the protein is enriched in the nucleus.