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Science's Next Wave

Editor: John Benditt

EDITORIAL

Protein Kinesis

The molecular architecture of cells provides the basis of life itself. The term "protein kinesis" was developed to describe the various aspects of how cells direct proteins to specific targets and modulate interactions among their intracellular organelles. Protein kinesis has relevance in understanding how various subcellular compartments are generated; how reactions are compartmentalized in order to control metabolic processes; how proteins move from their site of synthesis to their site of action; and how the amounts and locations of particular proteins are controlled during development, during the cell cycle, and in healthy and diseased cells.

This special issue concentrates on several important aspects of protein kinesis rather than providing exhaustive coverage of this diverse field. The article by Dirk Görlich and Iain Mattaj (p. 1513) describes how proteins and RNAs move between the cytosol and the nucleus through the complex molecular assemblages known as nuclear pores. This process involves the recognition of targeting signals on the proteins and RNAs that specify their intracellular itineraries. Gottfried Schatz and Bernhard Dobberstein (p. 1519) compare and contrast how proteins are inserted into and across different cellular membranes—from bacterial to mitochondrial membranes and the endoplasmic reticulum of eukaryotic cells. Many common themes have emerged from multiple studies of how membranes and their constituent proteins are generated and maintained. Randy Schekman and Lelio Orci (p. 1526) discuss how vesicles form during intracellular transport between different membrane-bounded compartments. They examine the role of the exquisite molecular machines—a variety of coat proteins—that mediate this process. The fidelity and efficiency of vesicle budding and targeting must be maintained if the organelles of a cell are to retain their distinctive composition. Pietro De Camilli, Scott Emr, Peter McPherson, and Peter Novick (p. 1533) describe a mechanism by which membrane traffic (communication by vesicular carriers among certain intracellular organelles) is regulated. Finally, Richard Vallee and Michael Sheetz (p. 1539) describe how molecular motors interact with various intracellular cargoes, including chromosomes and vesicles, and with the microtubule tracks along which those cargoes need to be transported. They discuss the protein domains responsible for motor-cargo and motor-microtubule interactions and how these combine to orchestrate directed movement within the cell.

Protein kinesis is one of the fundamental aspects of cell biology. It underlies most of the functions performed by cells, from transcription and translation of genes and proteins, to secretion and endocytosis, to cell motility and organelle biogenesis. Errors in protein kinesis can lead to severe disease and are often incompatible with survival of the cell or organism. The news piece by Gary Taubes (p. 1493) examines the mechanisms of protein folding and how abnormal folding can lead to disease. Another example of the importance of protein kinesis is highlighted by the disease familial hypercholesterolemia. This disease can cause heart attacks in early adulthood and is often due to a defect in the receptor responsible for the endocytosis of low-density lipoprotein particles from the blood. Errors in protein kinesis are also responsible for a class of diseases that are often fatal in infancy, known as lysosomal storage diseases. In patients with these diseases, the degradative enzymes that should be packaged into the cell's garbage disposal system, the lysosome, are secreted in error, which leads to the buildup of toxic molecules in the blood.

Improving the efficiency of some aspects of protein kinesis is also important in biotechnology. Often mammalian proteins, such as hormones, are not efficiently folded, modified, or secreted by microorganisms, and advances in the understanding of protein kinesis can lead to great improvements in the yield of important protein products. Studies of protein kinesis describe the basic principles by which cellular architecture is generated and maintained and will continue to provide information relevant to developmental biology, molecular medicine, and neuroscience, as well as to cell biology.

Stella M. Hurtley

As the printed page can provide only static images, readers might be interested in electronic access to some moving images of cells in action. Links to several sites that are useful for teaching purposes or as an introduction to the power of multiple microscopic techniques are available from our Web site at <http://science-mag.aaas.org/science/scripts/display/full/271/5255/1477.html>.