Editorial & Letters

EDITORIAL

Cell Biology of the Cytoskeleton

Cells come in a huge variety of shapes and sizes, from the almost spherical lymphocyte, to amoeboid cells such as macrophages, to flattened spindle-shaped fibroblasts or polygonal epithelial cells, to neuronal cells with the complex branching extensions the dendrites and the very long extension the axon. Such cellular architecture is constructed and maintained by the cytoskeleton, a dynamic network of intracellular proteinaceous structural elements. The cytoskeleton is responsible for cell shape, motility, migration, and polarity, and for establishing intercellular contacts to produce tissue architecture. In addition, the cytoskeleton plays many roles inside the cell. For example, in cell division it forms the scaffold on which chromosomes are segregated to daughter cells and separates the daughter cells after mitosis. Like the vertebrate skeleton, certain types of cytoskeletal elements are more or less permanent features of cells, including the actin and myosin filament bundles in muscle cells and the microtubule arrays in cilia and flagellae. Other cytoskeletal structures are very dynamic, continuously assembling and disassembling like the tracks of a child's train set as part of their functional cycle or for use in various cellular processes. One particularly radical example of cytoskeletal dynamics is the complete remodeling of the microtubule array of a cell during mitosis—it changes from a network radiating throughout the cell to the compact, bipolar, mitotic spindle.

In this special issue of *Science*, some of the emerging areas of research on cytoskeletal dynamics are examined. The basic building blocks of the cytoskeleton include actin microfilaments (about 7 nm in diameter), tubulin microtubules (about 24 nm in diameter), and a variety of intermediate filaments (about 10 nm in diameter). Each filament type is composed of linear polymers of globular protein subunits, which are assembled and disassembled by the cell in a carefully regulated fashion, sometimes at astonishing rates. One of the classical images of the cytoskeleton is the molecular machinery of muscle tissue, in which microfilament arrays are linked by myosin motor filaments, forming sliding filaments that expand and contract in generating force. Mermall and colleagues (p. 527) review the current state of knowledge about the roles of nonmuscle myosins, which do not form filamentous structures, in various cellular processes, including membrane traffic, cell movement, and signal transduction. Microtubules play fundamental roles in the formation of complex cellular geometries such as axons, the extremely elongated processes of neurons. Microtubule-based motors use microtubule tracks to move a variety of cargoes around cells—the movement of chromosomes along the mitotic spindle during mitosis is an example. Hirokawa (p. 519) describes the large number of microtubule-based motors, encoded by the kinesin and dynein multigene families, and elaborates on their roles in intracellular transport. A kinesin Web site has details on many of the aspects of the cell biology and biophysics of this important intracellular motor protein (http://www.blocks.fhcrc.org/~kinesin/). The actin cytoskeleton also shapes cellular processes; for example, in the formation of filopodia or cell contact sites. Hall (p. 509) looks at the interplay between actin architecture and the signal transduction machinery of the cell in promoting profound changes in cell shape and motility in response to extracellular signals. Less is known about the role of intermediate filaments in cells, mainly because of a lack of tools with which to study their assembly and disassembly. Fuchs and Cleveland (p. 514) summarize recent advances in our understanding of the roles of multiple types of intermediate filaments, which have become clear through the discovery of several diseases linked to intermediate filament pathology. A Research News story by Elizabeth Pennisi (p. 477) focuses on the kinetochore, the part of the chromosome that interacts with the microtubules of the mitotic spindle. Finally, Echard and co-workers (p. 580) describe a putative new motor that is likely to play a role in intracellular transport through the secretory pathway.

Problems with the cytoskeleton can cause disorders of the skin, the nervous system, and the muscles. Changes in the cytoskeleton are key, and even diagnostic, in the pathology of some diseases, including cancer. Understanding the basic cell biology of the cytoskeleton has contributed to our understanding of the pathology of some of these disorders and will continue to affect approaches to understanding, diagnosis, and therapy for various conditions.

Stella M. Hurtley

LETTERS

On balance

Calculation of the appropriate reference dose of mercury in fish is discussed. How to sort out what is causing deformities in North American frogs is said to be a possible "scientific nightmare." A group of physicists who are collaborating to produce high-energy gamma-ray beams defend their role in the project. And protein-protein and protein-lipid interactions that "should greatly contribute to our understanding of the etiology of Alzheimer's disease" are explored.

Mercury in Fish

The Policy Forum "Balancing fish consumption benefits with mercury exposure" by Grace M. Egeland and John P. Middaugh (12 Dec., p. 1904) questions the wisdom of the Environmental Protection Agency's (EPA's) using our Iraqi data (*1*) to calculate their reference dose (Rfd), arguing that our Seychelles study (*2*) is more appropriate.

We agree. The Seychelles population is a more appropriate sentinel population for fish consumers in the United States: (i) the major source of methylmercury is open ocean fish, where the average concentrations are similar to those on the U.S. market, and (ii) the concentrations in hair are, on average, 10 to 20 times the average in the United States, because the Seychellois consume about 12 fish meals per week (*3*). Thus, any potential adverse effects of methylmercury in fish should be detected in the Seychelles long before such effects are seen in the United States.

The Policy Forum quotes our results for children up to 29 months of age. We now have findings for the same cohort tested at 66 months (*4*). We obtained tests scores of six different measures of child performance; general cognitive abilities, language ability, drawing and copying, pre-arithmetic achievement, letter word reading, and behavioral assessment. In all of these tests, no negative correlation with pre- or postnatal mercury levels was observed. To the contrary, the children performed at a level comparable to that of healthy, well-developed children in the United States.

The same examiner repeated in the Seychelles (*5*) exactly the same tests (neur-