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Our present understanding of the complexity of how cells function has come through insights that have been possible by the combined use of techniques spanning disciplines such as structural and molecular biology to cell biology and genetics. The reviews presented in the Annual Review of Cell and Developmental Biology, vol. 21, are an excellent testimony to the importance of using a combination of powerful techniques to understand a specific system. Most of the articles are highly topical and address problems that have been studied in a variety of organisms, though there is a natural bias towards mammalian systems and studies of disease mechanisms.

In a new feature in this series, the first article is an autobiographical account of the contributions of David Sabatini, one of the founders of modern cell biology. His first major contribution was the development of electron microscopic techniques to preserve fine structural details. In 1971, together with Blobel, Sabatini introduced the notion of signal peptides as targeting signals for transport into organelles. The past few decades have seen the field of intracellular sorting of proteins grow by leaps and bounds. The basic steps of protein transport into each cellular organelle have now been deciphered; more recent structural and mechanistic studies highlight the complexities involved in the transport of specific classes of substrates. Osborne and colleagues have outlined the steps by which soluble proteins translocate across the endoplasmic reticulum (ER) while membrane proteins integrate into the lipid bilayer, with new insights being provided by the X-ray structure of the Sec Y complex. A surprisingly high amount (30%) of nascent polypeptides is misfolded and subsequently degraded. Römisch has reviewed recent information on the chaperone-mediated recognition of specific lesions in defective proteins in the secretory pathway, their targeting for export from the ER by the Sec 61 channel in association with multiple accessory proteins, and cytosolic degradation by proteosomes. Kolter and

Sandhoff have discussed the mechanism of selective degradation of complex lipids by the lysosomal compartment, which is able to avoid self-digestion by an underlying thick glycocalix. Inherited deficits of activator proteins or lysosomal enzymes involved in degradation lead to lysosomal storage disorders. The phagosome, a heterogeneous compartment with the capacity to engulf large particles (>1 µm) has evolved from a nutritional requirement in amoeba to an immune function in vertebrates. In their review, Jutras and Desjardins examine the roles of phagosomes in antigen processing and loading onto both MHC class I and II molecules in the adaptive immune response, and in innate immunity by killing microorganisms.

There is currently considerable interest in studying nuclear structure and compartmentalization of nuclear functions, with a view to understanding a range of inherited disorders. Hetzer and colleagues have written a comprehensive review on the nuclear envelope, with special emphasis on the nuclear pore complex, including its dynamics during cell division. Cioce and Lamond present new data on the composition and likely functions of the Cajal bodies in cell proliferation, stress and ageing. These nuclear domains enriched in snRNPs were first described about 100 years ago by Ramon Y. Cajal. Doxsey and colleagues report on the participation of centrosomes that play a central role in the organization of mitotic spindles, in additional regulatory processes such as cell cycle progression and check-point control. New evidence in the past decade has demonstrated the existence of variants of the core histones and their specific roles in nuclear processes. Henikoff and Ahmad describe histone variants such as H3.3 and H2AZ and the assembly processes that allow replacement of the core histones. An additional level of regulation of gene expression that occurs at the stage of mRNA localization and local control of translation, particularly in neurons, is the focus of a review by Kindler and associates. The topic of RNA silencing, which is of tremendous current interest, is dealt with by Meins and coworkers, with emphasis on the mechanics of RNA silencing systems in plants.

Phosphorylated derivatives of phosphatidylinositol termed phosphoinositide phosphates are crucial signalling intermediates. Niggli has reviewed new information on selected targets of pho-

sphoinositide phosphates required for control of actin assembly, as well as other signalling molecules like GTP-binding proteins and proteins involved in membrane traffic. The Rho GTPases are an important class of Ras-related GTPases that control key processes such as morphogenesis, polarity, movement and cell division; these are discussed by Jaffe and Hall. TGF-β signalling pathways control cellular responses during growth and differentiation; Feng and Derynck focus their review on combinatorial interactions between TGF-B receptors and Smads, which provide a high degree of specificity and versatility of signalling. Some of the best understood signalling pathways are those involved in apoptosis or programmed cell death. Yan and Shi have described insights obtained into the molecular mechanisms of apoptosis by studies on protein-protein interactions based on crystal structures of key intermediates. New structural data reviewed by Arnaout and colleagues, have provided a clearer view of the dynamic structure of integrin.

In the reviews in mammalian developmental biology, important methodologies that are highlighted are the use of mouse gene knockout models, with a focus on developmental defects and possible therapies. In a highly topical review, Li and Xie define the microenvironment where adult stem cells reside, termed the stem cell niche, in different tissues of various organisms. Oliver and Alitalo discuss about the genes required for embryonic development of the lymphatic vasculature. Two reviews cover interesting facets of neural development. Lemke and Reber have focused on recent advances in the role of ephrin signalling in neuronal topographic mapping from the retina to the mid-brain. Marszalek and Lodish discuss the importance of polyunsaturated fatty acids in the development of the nervous system and mention the defects in brain function that can result from alteration of levels of polyunsaturated fatty acids. Two reviews focus on a new multiphoton-based tool for in vivo imaging that uses cells labelled with markers such as green fluorescent protein. Halin and associates describe studies on trafficking of lymphocytes in mice through the blood vasculature. Condeelis and coworkers discuss new insights into tumour invasion and metastasis. Cellular polarization is an essential feature of development by which a uniform layer of cells becomes polarized, and newer theories on polarization, including the involvement of specific signalling pathways are reviewed by Klein and Mlodzik.

Unlike processes of cell migration and motility used by animals to build organs, plants shape their organs by expansion of their cell walls. Baskin has discussed the controls of anisotropic expansion of plant cell walls and their dependence on alignment of cellulose microfibrils. Smith and Oppenheimer highlight recent work on the role of cytoskeletal filaments in influencing the pattern in which cell-wall materials like cellulose are deposited. Plant growth

is controlled by a group of polyhydroxylated steroid hormones called brassinosteroids, and their signalling pathways are reviewed by Vert and coworkers. A wellstudied model of plant development is the establishment of the root apical meristem, which is discussed in detail by Jiang and Feldman, with special emphasis on the control of root development by auxin. Bacteria can synchronize certain types of behaviour on a population-wide scale and thus function as multicellular organisms. This process, termed quorum-sensing, operates through chemicals such as certain oligopeptides or other small organic molecules, and is described in detail by Waters and Bassler.

Special emphasis on both cell and developmental biology in this series encourages the reader to take a holistic view of the organism. An essential book for all libraries and research groups in biology.

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