

Preface

Membrane Microdomain Signaling not only explores a fascinating aspect of cell biology that is emerging as pivotal for a variety of signaling processes in cells throughout the body, but also focuses on abnormalities in lipid rafts for various pathological conditions. Membranes of most—if not all—cells contain discrete regions that are rich in cholesterol and sphingolipids and function as sites where various receptors, cell adhesion proteins, signal transduction molecules, and cytoskeletal elements are concentrated. These microdomains, called lipid rafts, are now recognized as playing fundamental roles in the regulation of a range of cellular processes from proliferation and differentiation to signal transduction responses to a variety of stimuli.

In *Membrane Microdomain Signaling*, experts in the field of lipid rafts and signal transduction provide detailed reviews on the current state of understanding these membrane microdomains and their physiological and pathophysiological roles. The first chapter by Ephraim Yavin and Annette Brand reviews the lipid structure of membranes and how asymmetries in the membrane are formed, maintained, and modified. The reader is introduced to the various lipids and their organization within membranes.

János Matkó and János Szöllosi next describe recent findings related to dynamic aspects of lipid rafts, how they change in cells over time, and how they respond to various environmental signals. Elizabeth Luna and colleagues review the structural interactions between lipid rafts, the extracellular matrix, and the cell cytoskeleton.

Chris Fielding focuses on cholesterol, a fundamental component of lipid rafts, and describes how this ancient and critical lipid modulates the signaling functions of lipid rafts. Arnold van der Luit and colleagues discuss the role of lipid rafts as portals for endocytic uptake of an anti-cancer and anti-apoptotic alkyl-lysophospholipid. Furthermore, they describe how cellular resistance to this agent is associated with a defect in sphingomyelin synthesis, new raft formation, and raft-mediated endocytosis. Markus Delling and Melitta Schachner describe emerging evidence of critical roles for lipid rafts as well as signaling pathways in lipid rafts in the regulation of synaptic function in the nervous system. It appears that lipid rafts are concentrated in synapses and play major roles in such processes as learning and memory. Wu Ou and Jonathan Silver review the evidence suggesting that lipid rafts are sites at which viruses bind and enter cells, focusing on this aspect of

diseases. My colleagues and I then describe emerging evidence implicating alterations in raft lipid metabolism in the pathogenesis of such neurodegenerative disorders as Alzheimer's disease and amyotrophic lateral sclerosis. Mordechai Liscovitch and colleagues then review information concerning the roles of lipid rafts in cancer. In particular, the raft associated protein caveolin-1 has been linked to various cancers. Finally, the importance of dietary lipids in modifying function and affecting risk for disease in the context of lipid rafts is briefly considered. It is clear that lipid components of rafts can be modulated by diet, with dietary cholesterol and sphingolipids being examples.

A better understanding of the effects of dietary lipids on raft function may lead to novel prevention and treatment methods for various diseases that involve abnormalities in lipid rafts. Collectively, the information in this book will provide a valuable resource for graduate students, postdoctoral fellows, and established investigators interested in membrane signaling and the lipid and protein components of rafts. There is much to be learned in this emerging and critical area of cell biology, and we hope that *Membrane Microdomain Signaling* will provide a foundation for the development of research projects by various investigators in a broad array of fields in the biological and biomedical sciences.

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