

Preface

Phospholipids were originally considered as plasma membrane components that primarily provided cellular structural and functional integrity. However, these are now also recognized as the source of molecules that act as biological mediators of cell function. Some of these mediators serve as extracellular lipid-signaling molecules while others act as intracellular second messengers that regulate effector enzymes. The activation of phospholipases is a primary step in the generation of lipid mediators and the initiation of intracellular signal transduction pathways in a variety of cell types. Neurotransmitters, hormones, and growth factors evoke intracellular responses by activating phospholipases. Most of these mediators are produced upon activation of many different forms of phospholipase A, phospholipase C, and phospholipase D.

The contribution of different phospholipases and their related signaling mechanisms to altered function during different pathophysiological conditions is not completely understood. Resolution of this issue is essential for both the understanding of different disease conditions and for determining if components of the phospholipid-signaling pathways could serve as appropriate therapeutic targets. Furthermore, the interaction between the different lipid molecules and the different phospholipases adds to the complexity of phospholipid-signaling mechanisms. While phospholipases also reside in the cytosolic compartment of the cell, these must migrate to a membrane compartment where their physiological substrates reside. Indeed, phospholipases were considered to localize primarily to the plasma membrane; however, they are also located in intracellular compartments including the cytoskeleton, endo(sarco)-plasmic reticulum, the Golgi apparatus, and the nucleus.

This book has been compiled to present a comprehensive and up-to-date view of the phospholipase research field. A wide range of topics covered here are of interest to basic research scientists, clinicians, and graduate students, who are devoted to the study of human health and disease. Furthermore, these chapters are directed towards increasing our understanding of novel strategies for the prevention/treatment of different diseases. Twenty three chapters in this book are organized into four parts.

The first part consisting of four chapters discusses general aspect of phospholipases. The subsequent three parts are designed to specifically highlight the most characterized forms of the phospholipases. The second part consists of seven chapters and covers the role and function of phospholipase A in different pathophysiological conditions. Phospholipase A continues to be the subject of considerable interest in the field, since it hydrolyzes membrane phospholipids to produce substrates for the biosynthesis of prostaglandins, thromboxanes, leukotrienes, and other oxygenated metabolites of arachidonic acid as well as platelet-activating factor. Some of the products of phospholipase A activity also serve as molecules for the activation of intracellular signal transduction pathways.

The third part comprises nine chapters and is focussed on phospholipase C which is believed to play a central role in transmembrane signaling. The first signal-activated phospholipase that was established as a key player in signal transduction was a phosphoinositide-specific phospholipase C. The phosphoinositide-specific phospholipase C hydrolyzes phosphatidylinositol 4,5-bisphosphate to generate two second messenger molecules, namely, diacylglycerol and inositol 1,4,5-trisphosphate known to regulate a diverse range of cell function through the activation of various forms of protein kinase C enzymes as well as mobilization of Ca^{2+} from intracellular stores.

The fourth part has three chapters concerning phospholipase D, which is present in a variety of different cells. In fact, phospholipase D was originally discovered in plants and the first indication of its presence in mammalian cells was by Kanfer and his colleagues almost three decades ago. This phospholipase hydrolyzes membrane phospholipids to produce phosphatidic acid and releases the free polar head group. Although phosphatidic acid is central to glycerolipid metabolism, it is also considered as an important lipid signaling molecule involved in a wide range of cellular processes, including vesicular trafficking, cytoskeletal organization as well as cell growth, proliferation, and survival. This part is relatively short; however, the subject matter highlighting the unique features of this particular phospholipase is also referred to in the first part.

In summary, this book covers a broad range of topics related to general aspects of the different phospholipases and their role in cell function pertaining to human health and disease. We hope that the reader will understand that membrane phospholipids are a rich source of lipid-signaling molecules that are produced through receptor-mediated activation of phospholipases and serve as second messengers. Furthermore, the underlying message presented in this book is that the activation of phospholipases is of fundamental importance in signal transduction affecting cell function under normal and diseased conditions.

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