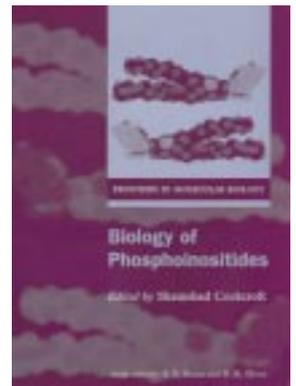


Phosphoinositide biology – messages from lipids

Biology of Phosphoinositides
edited by Shamsad Cockcroft

Oxford University Press · April 2000
Hardback £65/\$115, Paperback £32.50/\$60

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Membrane lipids, once simply regarded as the constituents of a passive barrier, are now increasingly appreciated as playing critical roles in conveying signals to the cell interior. Of particular interest are a small fraction of lipid molecules known as the phosphoinositides, which have been shown to be important in regulating a wide range of cellular activities such as calcium mobilization, cell motility, vesicle transport and cell survival.

The first indication that phosphoinositides are an important source of second messengers came from studies showing that phospholipase C can split phosphatidylinositol-4,5-bisphosphate into diacylglycerol (which activates protein kinase C) and inositol-1,4,5-trisphosphate (which, through binding to its receptors, releases intracellular calcium). The next exciting wave of discoveries revealed that the inositol headgroup of phosphatidylinositol can be phosphorylated at all possible combinations of the 3, 4 and 5 hydroxyl positions. This phosphorylation occurs through a host of highly regulated enzymes, which gives rise to a family of distinct phosphoinositides — most of which are now thought to carry out distinct signalling functions. Subsequent work on protein lipid-binding domains (such as the pleckstrin-homology domain and the FYVE domain) has provided the molecular mechanism by which phosphoinositides talk to downstream signalling molecules. Collectively, these results argue that phosphoinositides play a critical role in the recruitment of proteins to form complexes at localized regions of the membrane — thereby establishing spatial specificity of signal transduction.

This book is a timely and comprehensive update of the rapidly expanding field of phosphoinositide biochemistry and biology. With an emphasis on signal transduction, it covers several important topics regarding the synthesis and biological roles of phosphoinositides. Written by leading researchers in the field, the book strikes a

good overall balance between concepts and details. Those new to the field will find the organization of the chapters clear and easy to follow. Several classes of enzymes, such as phosphoinositide kinases and phosphatases, phospholipases, and phosphatidylinositol transferases are discussed in depth, with particular attention paid to their *in vivo* regulation. In particular, the first three chapters provide the foundation to the field by explaining in detail all the types of phosphoinositide kinases and lipases, how they are regulated and their likely functions in cell signaling. These and subsequent chapters discuss the role of phosphatidylinositol-3,4,5-trisphosphate in cell growth and survival, the function of phosphatidylinositol-3-phosphate in membrane transport and the importance of phosphatidylinositol-4,5-bisphosphate in regulation of the actin cytoskeleton. The discussions are nearly up to date in these rapidly moving fields. Also discussed are the types of protein domains that interact with phosphoinositides and how these interactions are involved in recruitment and activation of downstream responses. Other chapters provide excellent summaries of phosphatidylinositol-transfer proteins, glycosylphosphatidylinositol proteins, and the regulation of phospholipase D by phosphoinositides and of chloride channels by inositol-3,4,5,6-tetrakisphosphate. The book ends with a concise summary of the types of phosphoinositide phosphatases and their roles in signalling.

In summary, this is an authoritative introduction to the biology of phosphoinositides and serves a good purpose in orientating newcomers to the field. Even those who are familiar with the topic may find this book a worthwhile addition to their bookshelves. However, although many aspects of the molecular details of phosphoinositide signalling are pointed out to be unknown, and the possibilities enthusiastically discussed by the authors, many new advances have been made in this fast-moving field since the chapters in question

were written, and readers are urged to keep their eyes open for more excitement to come. □

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