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Phosphoinositides in Subcellular Targeting and Enzyme Activation

With 20 Figures and 4 Tables

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Cover Illustration by Gerald Hammond et al. (this volume):

Phosphoinositides and their soluble analogues inositol polyphosphates are widely distributed in the cell and function as essential co-factors for cytoplasmic and nuclear processes. The presence of a nuclear pool of PtdIns(4,5)P_2 (not associated with a membrane bilayer) is here demonstrated using a specific monoclonal antibody against this lipid; the staining reveals a speckled pattern resembling interchromatin granule clusters (IGC, in green) in the nuclei of HeLa cells. IGC represent a functional compartment of the nucleus (central scheme), together with nucleoli, Cajal bodies and their associated gemini of coiled bodies (see Hammond et al., this volume).

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Preface

Cells of the immune system are activated by a variety of stimuli that are derived from other cells, ingested material or from invading micro-organisms. A common denominator of such stimulation is that it causes a transient assembly of intracellular signalling complexes, which orchestrate cellular responses ranging from altered gene transcription to cell migration and phagocytosis. While some signalling complexes assemble in the cytosol or nucleoplasm, the majority of such assemblies occur on cellular membranes. Clearly, cells are equipped with machineries that enable a rapid and reversible recruitment of cytosolic proteins to specific intracellular membranes, such as the plasma membrane, phagosomes or endosomes. Besides protein–protein interactions, lipid–protein interactions are crucial in this context. In particular, phosphoinositides, which are phosphorylated derivatives of phosphatidylinositol, are important for recruiting and activating the right proteins at the right membranes. This volume *Current Topics in Microbiology and Immunology* focuses on the mechanisms of phosphoinositide-mediated protein recruitment to intracellular membranes. Recent advances in cell biology and bioinformatics have revealed the existence of several conserved protein modules, such as PH, FYVE, ENTH and PX domains, which endow proteins with the ability to bind specific phosphoinositides and thereby enables their targeting to specific membranes. It is fascinating to learn how this recruitment regulates receptor signalling, membrane trafficking, cytoskeletal function, chemotaxis and microbial killing—cellular functions that keep the immune system up and going. While the role of membrane-associated phosphoinositides in protein targeting has been well characterized, a new and unexpected role of phosphoinositides is also emerging. Several phosphoinositides have been detected in the nucleus, mainly outside the membrane bilayers. As discussed in the final review of this volume, evidence is accumulating that these nuclear phosphoinositides function as steric regulators of multi-enzymatic functions such as chromatin remodelling and pre-mRNA processing. This opens up a new and exciting area of research that promises to shed light on some of the most fundamental and complex processes in cell biology.

August 2003 Harald Stenmark

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List of Contributors

(Their addresses can be found at the beginning of their respective chapters.)