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Sommario/riassunto

Members of the protein kinase C (PKC) family of Ser/Thr kinases are encoded by nine distinct but closely related genes, which give rise to more than 12 different protein isoforms via a mechanism of alternative RNA splicing. Most PKC proteins are ubiquitously expressed and participate in a plethora of functions in most cell types. A majority of PKC isoforms is also expressed in cells of the immune system in which they are involved in signal transduction downstream of a range of surface receptors, including the antigen receptors on T and B lymphocytes. PKC proteins are central to signal initiation and propagation, and to the regulation of processes leading to immune cell proliferation, differentiation, homing and survival. As a result, PKC proteins directly impact on the quality and quantity of immune responses and indirectly on the host resistance to pathogens and tendency to develop immune deficiencies and autoimmune diseases. A significant progress was made in recent years in understanding the regulation of PKC enzymes, their mechanism of action and their role in determining immunocyte behavior This volume reviews the most significant contributions made in the field of immune cell regulation by PKC enzymes. Several manuscripts are devoted to the role of distinct PKC isoforms in the regulation of selected immunocyte responses. Additional manuscripts review more general mechanisms of regulation of PKC enzymes, either by post-translational modifications, such as phosphorylation or controlled proteolysis, or by interaction with

different binding proteins that may alter the conformation, activity and subcellular location of PKC. Both types of mechanisms can introduce conformational changes in the molecule, which may affect its ability to interact with cofactors, ATP, or substrates. This topic will be followed by a discussion on the positive and negative impact of individual PKC isoforms on cell cycle regulation. A second section of this volume concentrates on selected topics relevant to role of the novel PKC isoform, PKC-theta, in T lymphocyte function. PKC-theta plays important and some non-redundant roles in T cell activation and is a key isoform that recruits to the immunological synapse - the surface membrane area in T cells that comes in direct contact with antigen presenting cells. The immunological synapse is formed in T cells within seconds following the engagement of the TCR by a peptide-bound MHC molecule on the surface of antigen-presenting cells. It serves as a platform for receptors, adaptor proteins, and effector molecules, which assemble into multimolecular activation complexes required for signal transduction. The unique ability of PKC-theta to activate the NF-kB, AP-1 and NF-AT transcription factors is well established, and recent studies contributed essential information on the mechanisms involved in the recruitment of PKC-theta to the center of the immunological synapse and the nature of its substrates and the role of their phosphorylated forms in signal transduction. Additional review manuscripts will describe the unique behavior of PKC-theta in regulatory T cells and its role in the regulation of other cell populations, including those of the innate immune response. This volume brings together leading experts from different disciplines that review the most recent discoveries and offer new perspectives on the contributions of PKC isoforms to biochemical processes and signaling events in different immune cell populations and their impact on the overall host immune response.