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BOOK REVIEW

Introduction to Cellular Signal Transduction

(Ari Sitaramayya, ed., Birkhauser, Boston-Basel-Berlin, 1999, 311 p.)

This is the fifth volume in the series "Hormones in Health and Disease" edited by V. K. Moudgil. (Previous volumes have been devoted to the following problems: "*Estrogens, Progestins and Their Antagonists*", Vols. 1-2; "*Hormones and Cancer*"; "*Steroid Hormone Receptors: Basic and Clinical Aspects*"). Fourteen authors contributed to the reviewed volume which includes five sections: "Receptors and G-Proteins", "Second Messengers", "Novel Messengers", "Regulatory Mechanisms and Ion Transport in Signal Transduction", and "Application of Signal Transduction in Disease and Drug Abuse".

In the first chapter, the interaction of primary messengers with cell membranes and membrane receptors as well as the principles of signal recognition depending on receptor conformation are analyzed. Several modes of suppression of receptor function are described including accumulation of activating ligands or degradation, desensitization, or internalization of the receptors or inhibition of their synthesis in the cell. Interaction of a receptor molecule with heterotrimeric G-proteins is characterized, which results in signal transduction to several targets like ion channels, adenylate cyclase, and phospholipases. Different steps of the GTP cycle and the mechanisms of signal amplification by G-proteins are described. A new type of G-proteins is presented that consist not of three typical sub-units (alpha, beta and gamma) but of only one subunit similar to the alpha chain of heterotrimeric G-proteins. A novel biological function of G-proteins is presented related to their interaction with integrins resulting in cell adhesion. A short report is presented referring to animal lines deficient in G-proteins (G-protein knockout animals).

The second chapter dealing with second messengers presents data related to cyclic nucleotides (their synthesis by adenylyl or guanylyl cyclases, structure and isoforms of different cyclases, mode of regulation of cyclase activity including peptidic regulators of guanylyl cyclases) and second messengers of lipid nature being the products of different phospholipases. The family of cellular phospholipases is characterized with special attention to the strategy of interactive kinetics (including correct methods of *in vitro* testing of their activity) and participation of phospholipases in the normal signal transduction cascade and in inflammatory processes. Several novel regulatory mechanisms are described in which phospholipase A_2 is involved (which is regulated by MAP kinase-dependent phosphorylation). Useful data related to specific inhibitors of different phospholipases are presented. In the article related to esterases of cyclic nucleotides, their structure, multiple isoforms, and specificity are analyzed.

A special chapter related to novel messengers collects data related to biological function(s) of nitric oxide. Its formation, isoforms of NO-synthase and their distribution among tissues, and inhibitors and modulators are considered. Comparative characterization is made of NO-synthase isoforms I and II, the former being present both in soluble and membrane bound form while the latter is preferably in the membrane bound state. Both soluble and membrane bound forms of isoenzyme I are activated by calcium ions but inhibited after phosphorylation by several kinases including a Ca-dependent one. Isoenzyme II is also regulated by calcium and because of higher affinity to this ion is activated by traces of calcium, while is inhibited by higher calcium concentrations. Isoenzyme III, being not as widespread as I and II, is found in endothelial cells, lung, and brain and is present only as a membrane bound form. A primary factor for its activation is mechanical stretching of the cell wall that takes place under increased blood pressure. At the same time, isoenzyme III is also sensitive to a number of hormones and to phosphorylation/dephosphorylation. At the end of the chapter, stimulating and suppressing effects of NO on cellular proteins are listed.

Among the problems of the fourth chapter are the regulatory mechanisms of ion channels. Ca^{2+}-activated Cl^--channels and potential-driven ion channels and their regulation by several protein kinases are described. The problem is discussed why for integration of cellular metabolism cascade phosphorylation/dephosphorylation mechanisms were chosen by living systems. The hypothetical answer to this question includes both easy reversibility of the regulatory signal and multistage character of signal transduction allowing precise modulation of the signal for its attenuation or amplification.

The fifth chapter of the book discusses two important problems—modification of native regulatory mechanisms of signal transduction under pathological conditions and the participation of intracellular messengers in drug abuse mechanisms. Both problems are stated elegantly and illustrated by many examples. On the whole, the book is written on a high professional level and is characterized by very up-to-date scientific materials. All 11 articles of the book are supplied with abundant references.

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