Preface

Desensitization is the suppression of a cellular response induced by a
sustained, or repeated, or strong stimulus that causes the response. Desensitization of various responses in the body is negative feedback and the basis for the adaptation of living animals which is one of the most subtle and proficient mechanisms for individual homeostasis and species preservation. There could be no life-scientist who is indifferent to desensitization. This book deals with the receptor-mediated desensitization in various cells and tissues triggered by Ca2+, king of the second messengers. Besides the receptor itself, emphasis is placed on the post-receptor mechanisms because changes in the downstream of the signal transduction strongly affect the final response of the differentiated cell. Changes in the 7 helical transmembrane G protein-linked receptor itself such as photoreceptor rhodopsin, /^-adrenergic, or m2-muscarinic receptor have been explored successfully on a molecular level. The signal transduction, for instance in p2 receptor systems, is rather simple via cyclic AMP, queen of the second messengers, and the changes in the receptor and G protein molecules may well explain the cellular desensitized responses including nuclear regulation. In contrast, the signal transductions in the downstream of the Ca2+-triggering receptor systems such as m3-muscarinic, aradrenergic, or Hiv histamine receptor are very complicated; post-receptor signal transduction from the Gqoc protein spreads manifoldly via phosphoinositides in the cell to various channels and enzymes, but this need not be mentioned further here. The changes in the cell-surface receptors such as coupling with G protein and internalization/down-regulation are of primary importance but they can be diluted by such complex post-receptor mechanisms and often the change in the receptor itself is not enough to explain the cellular desensitization of its own final response. This book provides invaluable information about the various changes in the receptor and post-receptor mechanisms. They are not uniformly desensitized, as you will see. Difference between homologous and heterologous desensitization is also grounded in these facts. The changes are not only so dynamic that they themselves deeply fascinate us but they should also be susceptible of further molecular biological analyses. Such cellular aspects of possible molecular dynamics in desensitization of the Ca2+-signaling receptor system will be an invaluable treasure house filled with various physiological changes underlying desensitization for those who want to clarify the real nature of desensitization on a molecular basis. This book is supported financially by a Grant-in-Aid for scientific publication from the Ministry of Education, Science, Sports and Culture of
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