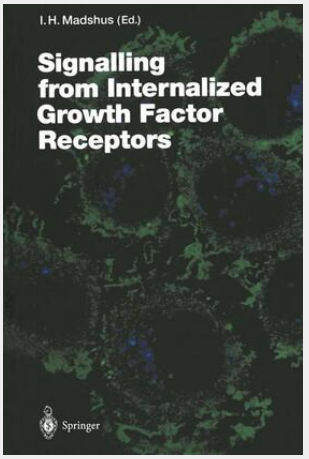
Madshus

Signalling from Internalised Growth Factor Receptors



Mammalian cells are to a large extent controlled by the environment. Dif fusible factors (growth factors, cytokines, and hormones) released by oth er cells in the body bind to and activate receptors localized at the cell sur face. In the case of the fibroblast growth factor receptor, there seems to be receptors both at the plasma membrane and in the nucleus. Cellular recep tors control growth, apoptosis, immune function, differentiation, develop and upon dysregulation, cancer progression and metastasis. Upon li ment, gand binding, most receptors are internalized. However, the mechanisms of endocytosis are diverse, and receptors are taken into cells from different membrane microdomains. Activation of receptors results in two important interconnected processes, namely, signal transduction and endocytosis. In terestingly, signal transduction controls endocytosis and endocytosis con trols signalling. In both processes sequential formation of transient protein machineries is crucial. Currently, characterization of such complex ma chineries is advancing rapidly. It has recently become appreciated that sev eral post-translational modifications directly control the affinity of pro tein-protein interactions. This volume of Current Topics in Microbiology and Immunology focuses on the recent understanding of signalling from in ternalized activated growth factor receptors. This includes information on pathways by which the rate and specificity of endocytosis and intracellular sorting are controlled. It further includes information on how specialized signalling and trafficking platforms are formed at the plasma membrane and on intracellular vesicles.

This book reviews knowledge on the interconnection of signal transduction and endocytosis/intracellular trafficking. The chapters cover knowledge obtained by using different model systems. The first chapter deals with Receptor Tyrosin Kinases (RTKs) with emphasis on the Epidermal Growth Factor Receptor (EGF receptor) and the Platelet Derived Growth Factor Receptor (PDGF receptor). The second chapter deals with the RTK c-Met and with how this RTK becomes carcinogenic. The third chapter reviews recent understanding on the mechanisms of action of the numerous fibroblast growth factors and their receptors. In the fourth chapter we learn about the trafficking of and signalling from the Growth Hormone Receptor and how this receptor is controlled by ubiquitination. The fifth chapter is devoted to the Interleukin Il receptor, essential for activation of T cells. Links between ubiquitination, signalling, endocytosis, and sorting are reviewed. The last chapter discusses current views on how monoubiquitination controls both signalling and trafficking and thereby the final outcome of receptor activation.

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