ABSTRACT

Ebashi Setsuro Award Lecture

EAL Exploring mechanisms of cell contraction, movement and polarity toward understanding molecular pathology of various diseases

Kozo Kaibuchi

Dept. Cell Pharmacol., Nagoya Univ. Grad. Sch. Med.

Rho and its effector Rho-associated kinase/ROCK/ROK (Rho-kinase) are implicated in cell contraction, migration and polarity. Rho-kinase not only directly phosphorylates myosin light chain (MLC) but also phosphorylates MLC phosphatase and inactivates it, thereby promoting actomyosin contraction. Rho-kinase also phosphorylates adducin, ezrin/radixin/moesin, and LIM-kinase for actin filament remodeling, and tau, MAP2 and CRMP-2 for microtubule depolymerization. Additionally, Rho-kinase phosphorylates Par3 and p190RhoGAP to regulate cell polarity and Rho family GTPase activities. The Rho/Rho-kinase-mediated pathway is also involved in the pathogenesis of various diseases including atherosclerosis, coronary spasm and glaucoma. However, the above substrates cannot fully account for all Rho-kinase functions. We have recently developed novel approaches to comprehensively identify the substrates of specific protein kinases using Rho-kinase. I here summarize how Rho family GTPases regulate cell contraction, movement and polarity, and discuss the phospho-proteomic approaches to identify the substrates of specific kinases including Rho-kinase, PKA and MAPK to understand their neuronal and non-neuronal functions.