



The JNK Signaling Pathway

Anning Lin

Ben May Institute for Cancer Research
University of Chicago
Chicago, Illinois, U.S.A.

Signal transduction is one of the most exciting research areas in modern biology as it deals with how information flows from the extracellular environment into a living cell to change its metabolism, genotype and phenotype. With the completion of the genomes of human and several other species, it becomes even more important to elucidate the molecular mechanisms that govern cellular functions. The intracellular signaling network, which is composed of many signaling pathways, regulates most, if not all, fundamental cellular activities, from proliferation to programmed cell death (apoptosis). Over the past decade, many signaling pathways have been “mapped” out. Nowadays, we know in great detail about how a specific signal is transmitted via specific signaling pathways, from the membrane to the nucleus, to change the functions of a cell. In this book, a group of experts present a comprehensive review of one of such signaling pathways, the JNK signaling pathway.

In the first chapter, Ewen Gallagher and Michael Karin discuss the discovery of JNK. In addition, these authors present a comprehensive review of the biological functions of JNK. In the next chapter, Maria Julia Marinissen and J. Silvio Gutkind present an extensive review of the regulation of JNK by small GTP-binding proteins of the Rho family.

The next three chapters focus on the genetic analysis of the biological functions of JNK and its upstream kinase JNKK (MKK4/MKK7). Using knockout mouse models, Kanaga Sabapathy presents an extensive discussion about the physiological roles of different JNKs, and Hiroshi Nishina and Toshiaki Katada present a comprehensive review of the biological functions of JNKs and its upstream kinase JNKKs (MKK4/MKK7). Using *Drosophila* as a model system, Changwan Lu and Steven X. Hou present an extensive review of the versatile roles of JNK in *Drosophila*, from embryonic dorsal closure, larval thorax closure, adult wound healing, planar cell polarity, immune response, synaptic plasticity, neuronal cargo transport, to apoptosis and lifespan.

The role of JNK in cell death is an intensively studied and also highly controversial topic in JNK biology. Anning Lin presents a comprehensive review of the role of JNK in both apoptosis and cell survival. The author discusses the molecular mechanisms underlying the pro- and anti-apoptotic role of JNK and proposes the “breaking the brake on apoptosis” model. Han-Ming Shen and Zheng-gang Liu present an extensive review of the regulation of JNK by reactive oxygen species (ROS) and the role of JNK in ROS-mediated cell death. The authors discuss the signaling mechanisms of ROS-mediated JNK activation and the role of JNK in ROS-mediated cell death (both apoptosis and necrosis).

In the last chapter, Brydon Bennett and Yoshitaka Satoh present an extensive review of the search for the inhibitors of JNK, based on the belief that deregulation of JNK activity may be involved in human diseases. The authors report that the first JNK inhibitors are actually now entering clinical trials to determine safety and efficacy limits in humans. It is possible that small molecules that can specifically inhibit JNK activity could be potential future therapy for certain human diseases.

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