MAP Kinase Signaling Protocols
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Edited by

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Mitogen-activated protein kinase (MAPK) signaling cascades are a group of protein kinases that play a central role in the intracellular transmission of extracellular signals. These cascades operate as major lines of communication within a complicated signaling network that regulates many cellular processes, including proliferation, differentiation, development, stress response, and apoptosis. More than 15,000 papers on MAPKs have been published over the past few years, with the number of publications increasing each year. More and more laboratories embark on the study of MAPK cascades in many distinct cellular systems and in particular their role in disease.

Future challenges in the study of MAPK cascades remain in understanding the role of the various components and isoforms of the cascades in the multiple critical functions that they regulate in the whole organism, as well as the diseases caused by their malfunction. Data from gene-disrupted mice suggest that inhibition of the MAPK cascades may have serious consequences on the development and growth of the animals. For example, targeted deletion of MEK1 is lethal, owing to developmental problems of placental vasculature and abnormal fibroblast migration. This lethality occurs in spite of the normal expression of MEK2, indicating that although the two MEK isoforms are apparently similar, they do have distinct functions, at least during embryogenesis. The ERK cascade was also shown to play a central role in brain function and in learning and memory. Thus, inhibition of this cascade by MEK inhibitors may prevent ischemic damages whereas naturally occurring mutations in the downstream target of ERKs (the RSK2) causes mental retardation syndromes. In addition, the ERK cascade also plays a role in the positive and negative selection of T cells in the thymus, angiogenesis, malignancies, and in many other syndromes and diseases. The ERK5, p38MAPK, and JNK cascades may also have a role in stress, inflammation, learning and memory, malignancies, and so on.

One of the most intriguing issues in the study of the MAPK cascades is their involvement in cancer. As mentioned above, the ERK cascade is a major regulator of proliferation, and its involvement in the induction of tumor formation is well established. Moreover, this pathway regulates cell survival and, sometimes, apoptosis in many different cell types. It can counteract the pro-apoptotic signaling of other members of the MAPK cascades (e.g., JNK). Since
cellular transformation is often a result of an imbalance favoring cell survival and proliferative pathways over those of apoptosis, malfunctioning of all MAPK cascades may lead to the induction of cancers under distinct conditions. Finally, many tumors show elevated levels of MAPKs activity, and in particular that of ERK1 and 2, which probably owes to the expression of oncogene products that are upstream regulators of the MAPKs (e.g., Ras, Raf). Therefore, the study of the MAPK cascade is essential for understanding a large number of diseases in general and of cancer in particular.

MAP Kinase Signaling Protocols aims to provide updated information on the various techniques used in the study of MAPK signaling cascades in various cellular contexts, namely the detection and measurement of activity of the MAPKs and other components of their cascades. MAP Kinase Signaling Protocols discusses the following: (1) determination of the subcellular localization of these components, (2) structural and biophysical analysis of the components, (3) identification of novel components of known and unknown signaling cascades, (4) upstream mechanisms of activation of MAPK cascades by various receptors, (5) mechanisms involved in the downregulation of the MAPK cascades, and (6) identification of targets of the MAPK cascades.

Biochemists and cell biologists from various fields of interest, who intend to study MAPK signaling in their experimental systems would find MAP Kinase Signaling Protocols most useful. The book will also interest physicians who would like to study the involvement of MAPKs in health and disease, as well as biotechnologists interested in the use of MAPK signaling as a readout for the influence of drugs. One of the main problems in the field of MAPK today is the large number of different methods that are used to study each of the parameters outlined above. The chapters herein, contributed by the leaders in the field, should provide the appropriate methods to be used in future studies.

Rony Seger
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