MEKK1
Mouse, Recombinant
Expressed in E. coli

Product Number M 6939
Storage Temperature −70 °C

Synonyms: MAP/ERK Kinase Kinase 1, MAP Kinase Kinase Kinase 1, MKKK1

Product Description
MEKK1 is produced from a DNA sequence corresponding to a 100 kDa protein that is truncated on the amino-terminus and has a histidine-tag at the carboxyl terminus. It is expressed in E. coli and is purified by affinity chromatography on Ni-NTA resin. The resulting recombinant protein contains the 70 kDa catalytic subunit of MEKK1. The accession number for the sequence is P53349. The protein will phosphorylate MEK and JNKK isozymes.

The mitogen-activated protein kinase kinase kinases (MEKKs) are a family of Ser/Thr protein kinases, upstream of the MAP kinase kinases, that, in turn, are upstream of the MAP kinases that play a central role in mitogenic signaling, transducing extracellular signals to intracellular targets, including transcription factors controlling the expression of genes essential to many cellular processes.1,2,5 These upstream kinases are activated by a number of signaling molecules, such as growth factors, or by cellular stress, such as temperature, pH, or osmotic shock. Once activated, MAP kinases phosphorylate a number of cytoplasmic and nuclear regulatory proteins. The cellular response to the initial extracellular signal or event may be differentiation, proliferation, or apoptosis.3 At least three families of MAPKs have been identified in mammals: ERK (extracellular signal-regulated kinases), JNK (c-Jun N-terminal kinases), and p38 MAPK (also called stress-activated protein kinase).4

MEKK1 is regulated by low molecular weight GTP binding proteins in vivo. The serine/threonine kinases NIK (Nck interacting kinase), GLK (GCK-like kinase) and HPK1 (hematopoietic progenitor kinase 1) bind to and phosphorylate MEKK1. MEKK1 is important in mediating survival vs. apoptosis, possibly via its ability to regulate transcription factors, the expression of death receptors and their ligands.5

MEKK1 is a major regulator of the JNK protein kinase cascade by phosphorylating JNKK and M KK7. It also activates the ERK1/2 protein kinase cascade by phosphorylating MEK1/2. It does not activate the p38 MAP kinase cascade. JNK and ERK phosphorylate and regulate many nuclear transcription factors. MEKK1 induces apoptosis in a JNK-dependent manner. Apoptosis is potentiated by caspase-mediated cleavage of MEKK1 to form a 91 kDa fragment containing the kinase domain and a 105 kDa amino-terminal fragment. Recent studies indicate that only the fragment containing the kinase domain is proapoptotic.5

Reagents
Recombinant mouse MEKK1 is supplied as a solution in 50 mM Tris-Cl, pH 7.5, containing 0.1 mM EDTA, 50 mM NaCl, 0.1% 2-mercaptoethanol, and 5% glycerol.

Precautions and Disclaimer
For laboratory use only. Not for drug, household or other uses.

Storage/Stability
The protein is stable for six months at −70 °C. Centrifuge the original vial after thawing and prior to removing the cap for maximum recovery of product. After initial thawing, store the remaining solution in single-use aliquots at −70 °C. Avoid repeated freeze-thaw cycles. Do not store in a frost-free freezer.

Product Profile
By SDS-PAGE with Coomassie blue staining approximately 50% of the mouse recombinant MEKK1 is the 70 kDa catalytic subunit and approximately 20% is the 100 kDa holoenzyme.

Activity is determined using a coupled assay system in which MEKK1 phosphorylates MEK1 that, in turn, phosphorylates MAPK2. One unit of MAPK2 activity equals one nmole of phosphate incorporated into myelin basic protein per minute at pH 7.5 and 30 °C. One unit of MEKK1 activity equals one unit of MAPK2 activity.

References

