TAK1
Human, Recombinant
Expressed in E. coli

Product Number T3070
Storage Temperature −20 °C

Synonym: Transforming growth factor-β-activated kinase 1, TGF-β Activated Kinase

Product Description
TAK1 is produced from a DNA sequence corresponding to full-length human TAK1 having a histidine tag at the amino terminus. It is expressed in E. coli and purified by affinity chromatography on nickel-NTA agarose. The molecular weight of the fusion protein is approximately 90 kDa.

The mitogen-activated protein kinase kinase kinases (MKKKs, MEKKs) comprise a family of Ser/Thr protein kinases that are located upstream in the MAP kinase cascades that play central roles in mitogenic signaling, transducing extracellular signals to intracellular targets, including transcription factors controlling the expression of genes essential to many cellular processes. These upstream kinases are activated by a number of signalling 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 ultimate cellular response to the initial extracellular signal or event may be differentiation, proliferation, or apoptosis. 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).

MAPKs are activated by phosphorylation by Thr/Tyr dual-specificity MAPK kinases that phosphorylate specific Thr and Tyr residues on the MAPK. The MAPK kinases are in turn activated by MKKKs that phosphorylate specific Thr/Ser residues. MKKKs are activated by receptor-associated components (receptor tyrosine kinases, receptor-coupled G-proteins, protein kinase C, etc.) that, in turn, are activated by extracellular stimuli.

TAK1 is a member of the MKKK family, and its kinase activity is stimulated in response to various cytokines, including transforming growth factor-β (TGF-β), interleukin-1 (IL-1), bone morphogenetic protein (BMP) and ceramide. A companion protein, TAB1, binds to TAK1 and promotes autophosphorylation. In vivo expression of a constitutively active form of TAK1 activates MKK4/SEK1, and expression of a kinase-negative mutant of TAK1 interferes with the activation of JNK, which is phosphorylated by MKK4/SEK1. In vitro experiments have shown that MKK6/SEK3 and MKK3/SEK2 are also substrates for TAK1.

Reagents
TAK1 is supplied as a solution in 50 mM HEPES buffer, pH 7.5, containing 200 mM NaCl, and 50% 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 −20 °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 −20 °C. Avoid repeated freeze-thaw cycles. Do not store in a frost-free freezer.

Product Profile
Purity is approx. 80% by SDS-PAGE with Coomassie blue staining.

One unit of kinase activity is equal to 1 nmol/min of phosphate transferred to the synthetic substrate KKKVSRSGLYRSPSMPENLNRPR at pH 7.5 and 30 °C.
References

7. Ono, K. et al., An evolutionarily conserved motif in the TAB1 C-terminal region is necessary for interaction with and activation of TAK1 MAPKKK. J. Biol. Chem., 276, 24396-24400 (2001).

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