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ProductInformation

Anti-ASK1 (MAPKKK5), C-Terminal
Developed in Rabbit, Affinity Isolated Antibody

Product Number **A 5851**

Product Description

Anti-ASK1 (Apoptosis Signal-regulating Kinase 1, MAPKKK5) C-Terminal is developed in rabbit using as immunogen a synthetic peptide corresponding to amino acids 1356-1375 of the human C-terminal region of ASK1.[1] This sequence differs from that of mouse by the last two amino acids.[2] The antiserum is affinity purified using epitope-specific affinity chromatography. Anti-ASK1 specifically recognizes human ASK1 (155 kDa) in immunoblotting applications.

Mitogen-activated protein kinase (MAPK) cascades consist of a three-kinase module: MAPK, MAPK kinase (MAP2K, MAPKK, or MKK), and MKK kinase (MAP3K, MAPKKK, or MEKK). These kinase cascades relay signals from the cell surface to the nucleus, resulting in gene transcription. Growth factors and mitogens activate the extracellular-regulated kinase (ERK) pathway, while stress stimuli and proinflammatory cytokines activate two closely related but distinct parallel pathways, the c-Jun N-terminal kinase (JNK) or stress-activated kinase (SAPK), pathway and the p38 kinase pathway.

ASK1 (Apoptosis Signal-regulating Kinase 1) also known as MAPKKK5 (Mitogen activated protein kinase kinase kinase 5) was cloned in 1997.[1] The predicted protein contains 1,375 amino acids and is most closely related to yeast SSK2 and SSK22, which are upstream regulators of yeast HOG1 MAPK. ASK1 expression complements a yeast mutant lacking functional SSK2 and SSK22. ASK1 also activates MKK3, MKK4 (SEK1), and MKK6. Overexpression of ASK1 induces apoptotic cell death and ASK1 is activated in cells treated with tumor necrosis factor-alpha (TNF-α). ASK1 interacts with members of the TRAF family and is activated by TRAF2 in the TNF-signaling pathway. After activation by TRAF2, ASK1 activates MKK4, which in turn activates JNK. Thus, ASK1 is a mediator of TRAF2-induced JNK activation.[3]

The HIV-1 Nef protein induces the expression of FAS ligand (TNFSF6) on infected cells and promotes apoptosis in neighboring cells, including HIV-1 specific cytotoxic T lymphocytes. Immunoprecipitation analysis shows that Nef interacts with ASK1 and prevents its activation, thereby enhancing the resistance of infected cells to FAS- and TNF-induced apoptosis, allowing host cells to survive and produce new infectious virions.[4]

In *C. elegans* the viable worms lacking esp2 and esp8, (homologs of the mammalian MAP kinases SEK1 and ASK1) were highly susceptible to and died more rapidly from both a Gram-negative bacterium and a Gram-positive organism than wild-type worms. This is proof that MAP kinase signaling is a conserved element in innate metazoan immunity to diverse pathogens.[5]

Reagent

Anti-ASK1, at approximately 0.5 mg/ml, is supplied as a solution in phosphate buffered saline, containing 0.02% sodium azide. The amount of the reagent is sufficient for 10 blots.

Precautions and Disclaimer

Due to the sodium azide content, a material safety data sheet (MSDS) for this product has been sent to the attention of the safety officer of your institution. Consult the MSDS for information regarding hazardous and safe handling practices.

Storage/Stability

Store at –20 °C. For extended storage, upon initial thawing, freeze in working aliquots. Do not store in frost-free freezers. Avoid repeated freezing and thawing to prevent denaturing the antibody. Working dilution samples should be discarded if not used within 12 hours. The antibody is stable for at least 6 months when stored appropriately.

Product Profile

A recommended working concentration of 0.5 to 1.0 µg/ml is determined by immunoblotting using SW1353 human chondrosarcoma whole cell lysate.

Note: In order to obtain best results in different techniques and preparations we recommend determining optimal working concentration by titration test.

References

1. Ichijo, H., et al., Induction of apoptosis by ASK1, a mammalian MAPKKK that activates SAPK/JNK and p38 signaling pathways. Science, **275**, 90-94 (1997).
2. Wang, X.S., et al., Molecular cloning and characterization of a novel protein kinase with a catalytic domain homologous to mitogen-activated protein kinase kinase kinase. J. Biol. Chem., **271**, 31607-31611 (1996).
3. Nishitoh, H., et al., ASK1 is essential for JNK/SAPK activation by TRAF2. Mol. Cell, **2**, 389-395 (1998).
4. Gelezunias, R., et al., HIV-1 Nef inhibits ASK1-dependent death signalling providing a potential mechanism for protecting the infected host cell. Nature, **410**, 834-838 (2001).
5. Kim, D. H., et al., A conserved p38 MAP kinase pathway in *Caenorhabditis elegans* innate immunity. Science, **297**, 623-626 (2002).

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