Activation of IKK by MEKK1

Akira, S., Garapati, P V., Kawai, T.

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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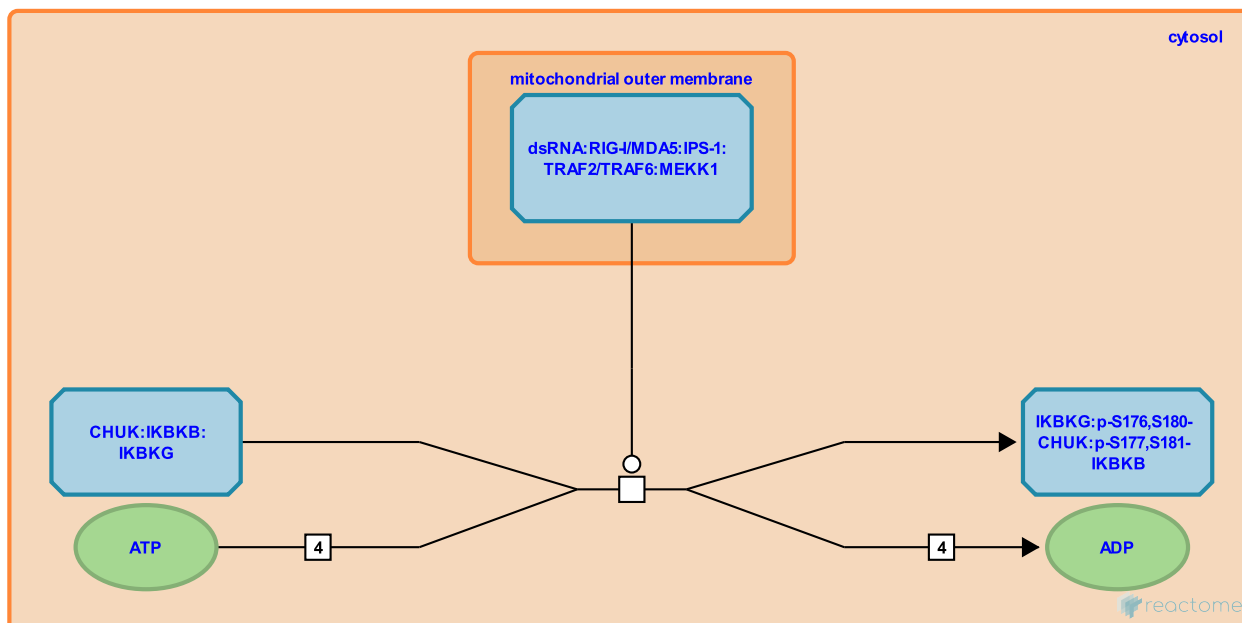
Reactome database release: 88

This document contains 1 reaction (see Table of Contents)

Activation of IKK by MEKK1 ↗

Stable identifier: R-HSA-933530

Type: transition

Compartments: cytosol, mitochondrial outer membrane

In Human, IKKs - IkB kinase (IKK) complex serves as the master regulator for the activation of NF-kB by various stimuli. It contains two catalytic subunits, IKK alpha and IKK beta, and a regulatory subunit, IKKgamma/NEMO. The activation of IKK complex and NFkB mediated antiviral responce are dependent on the phosphorylation of IKK alpha/beta at its activation loop and the ubiquitination of NEMO.[Solt et al 2009]; [Li et al 2002]. NEMO ubiquitination by TRAF6 is required for optimal activation of IKKalpha/beta; it's remained unclear if NEMO subunit undergoes K63-linked or linear ubiquitination.

This basic trimolecular complex is referred to as the IKK complex. Each catalytic IKK subunit has a N-term kinase domain a leucine zipper (LZ) motifs, a helix-loop-helix (HLH) and a C-ter NEMO binding domain (NBD). IKK catalytic subunits are dimerized through their LZ motifs.

IKK beta is the major IKK catalytic subunit for NF-kB activation. MEKK1 can activate both IKK-alpha (IKKA) and IKK-beta (IKKB) in vivo. MEKK1 phosphorylates Ser-176 and Ser-180 in IKKA and Ser-177 and Ser-181 in IKKB activation loop and thus activate the IKK kinase activity, leading to the IkB alpha phosphorylation and NF-kB activation.

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Editions

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