TRAF3:NIK binds TRAF2:cIAP1/2

Garapati, P V., Rajput, A., Virgen-Slane, R., Ware, CF.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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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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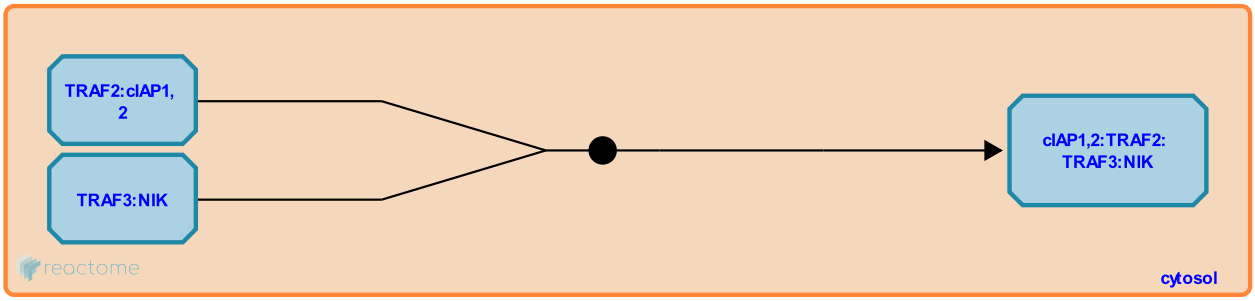
Stable identifier: R-HSA-5668543

Type: binding

Compartments: cytosol



Mitogen-activated protein kinase kinase kinase 14 (MAP3K14 also named as NIK) is a central signalling component of the non-canonical pathway which integrates signals from TNFR2 and activates IkB kinase-alpha (IkBA) for triggering p100 phosphorylation and processing (Sun 2011). A tight control of NIK stability is essential to achieve controlled activation of the noncanonical NF-kB signalling upon TNFR2 activation. In unstimulated cells the level of NIK protein is extremely low, which is due to constant degradation by a ubiquitination-dependent mechanism (Liao et al. 2004). Proteasomal degradation of NIK occurs on assembly of a regulatory complex through TRAF3 complexed with NIK and TRAF2 which exists in a preassembled complex with cellular Inhibitor of apoptosis 1 (cIAP1) and cIAP2 (cIAP1,2:TRAF2::TRAF3:NIK). The c-IAPs do not directly contact TNFR2, but rather associate with TRAF2 through their N-terminal BIR motif-comprising domain (Rothe et al. 1995, Shu et al. 1996). TRAF3 functions as a bridging factor between cIAP1/2-TRAF2 E3 complex and NIK enabling cIAP to mediate K48 linked ubiquitination of NIK (Zarnegar et al. 2008, Vallabhapurapu et al. 2008, Li et al. 2004).

Literature references

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Editions

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