

NF-kappa-B inhibitor binds NF-kappa-B complex

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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: 83

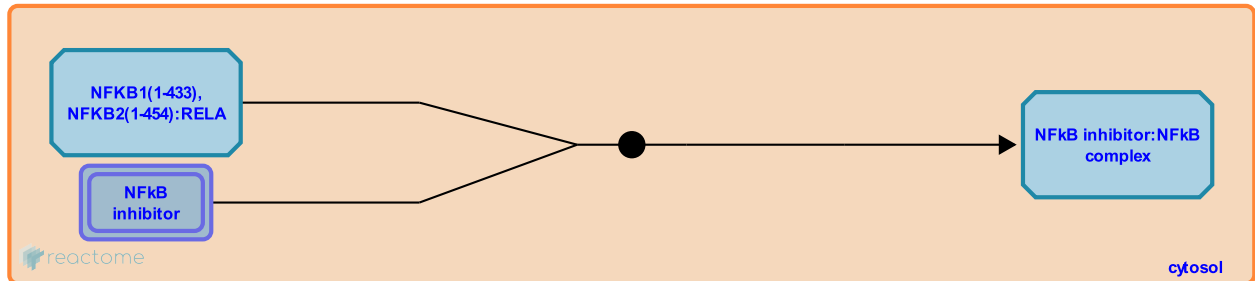
This document contains 1 reaction ([see Table of Contents](#))

NF-kappa-B inhibitor binds NF-kappa-B complex [↗](#)

Stable identifier: R-HSA-9630923

Type: binding

Compartments: cytosol



NF-kappa-B is sequestered in the cytosol of unstimulated cells through the interactions with a class of inhibitor proteins, called NF-kappa-B inhibitors (IkBs, NFKBIA or NFKBIB). IkBs proteins such as NFKBIA, NFKBIB or NFKBIE are characterized by the presence of six to seven ankyrin repeat motifs, which mediate interaction with the Rel homology domain (RHD). RHD mediates DNA binding, dimerization and nuclear localization (Jacobs MD & Harrison SC 1998; Manavalan B et al. 2010). NF-kappa-B inhibitors (IkBs) mask the nuclear localization signal (NLS) of the NF-kappa-B p65 subunit (RelA, p65) preventing the nuclear translocation of NF-kappa-B (Jacobs MD & Harrison SC 1998; Cervantes CF et al. 2011). A key event in NF-kappa-B activation involves phosphorylation of IkB (at sites equivalent to Ser32 and Ser36 of NFKBIA (IkB-alpha) or Ser19 and Ser22 of NFKBIB (IkB-beta) by the IκB kinase (IKK) complex. The phosphorylated NFKBIA is recognized by the E3 ligase complex leading to K48-linked ubiquitination, and targeted for ubiquitin-mediated proteasomal degradation, releasing the NF-kappa-B dimer p50/p65 (RelA:NFKB1) into the nucleus to turn on target genes (Karin M & Ben-Neriah Y 2000, Kanarek N & Ben-Neriah Y 2012; Hoffmann A et al. 2006). Crystal structures of NF-kappa-B inhibitors:NFKB complexes revealed that an NF-kappa-B dimer binds to one IkB molecule (Jacobs MD & Harrison SC 1998; Ghosh G et al 2012).

Literature references

Jacobs, MD., Harrison, SC. (1998). Structure of an IkappaBalpha/NF-kappaB complex. *Cell*, 95, 749-58. [↗](#)

Editions

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