beta-TRCP ubiquitinates IkB-alpha in p-S32,33-IkB-alpha:NF-kB complex

Garapati, P V., Geijtenbeek, TB.
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


Reactome database release: 73

This document contains 1 reaction (see Table of Contents)
beta-TRCP ubiquititates IkB-alpha in p-S32,33-IkB-alpha:NF-kB complex

**Stable identifier:** R-HSA-5607728

**Type:** omitted

**Compartments:** cytosol

Two major signaling steps are required for the removal of IkappaB (IkB) alpha an inhibitor of NF-kB: activation of the IkB kinase (IKK) and degradation of the phosphorylated IkB alpha. IKK activation and IkB degradation involve different ubiquitination modes; the former is mediated by K63-ubiquitination and the later by K48-ubiquitination. Mutational analysis of IkB alpha has indicated that K21 and K22 are the primary sites for addition of multiubiquitination chains while K38 and K47 are the secondary sites. In a transesterification reaction the ubiquitin is transferred from the ubiquitin-activating enzyme (E1) to an E2 ubiquitin-conjugating enzyme, which may, in turn, transfer the ubiquitin to an E3 ubiquitin protein ligase. UBE2D2 (UBC4) or UBE2D1 (UBCH5) or CDC34 (UBC3) acts as the E2 and SCF (SKP1-CUL1-F-box)-beta-TRCP complex acts as the E3 ubiquitin ligase (Strack et al. 2000, Wu et al. 2010). beta-TRCP (beta-transducin repeats-containing protein) is the substrate recognition subunit for the SCF-beta-TRCP E3 ubiquitin ligase. beta-TRCP binds specifically to phosphorylated IkB alpha and recruits it to the SCF complex, allowing the associated E2, such as UBC4 and or UBC5 to ubiquitinate Ikappa B alpha (Baldi et al. 1996, Rodriguez et al. 1996, Scherer et al. 1995, Alkalay et al. 1995).

**Literature references**


**Editions**

<table>
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<th>Action</th>
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