TICAM1, RIP1-mediated IKK complex recruitment

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

07/11/2022
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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 82

This document contains 1 pathway and 3 reactions (see Table of Contents)
Receptor-interacting protein 1 (RIP1) mediates the activation of interferon-alpha/beta via intermediate activation of IKK/TBK1 or NFκB pathways.

**Literature references**


**Editions**

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Viral dsRNA:TLR3:TRIF complex recruits RIP1

Location: TICAM1, RIP1-mediated IKK complex recruitment

Stable identifier: R-HSA-168930

Type: binding

Compartments: endosome membrane, cytosol

RIP1 is recruited to the activated TLR receptor by binding to TICAM1(TRIF) via its RHIM motif, followed by its polyubiquitination. Polyubiquitination is possibly mediated by TRAF6 that is also recruited to TICAM1 (Cusson-Hermance N et al. 2005). Other E3-ubiquitin ligases - cIAP1 and cIAP2 - have been reported to promote polyubiquitination of RIP proteins (Bertrand MJM et al. 2011).

RIP3 was shown to inhibit TRIF-induced NFkB activation in dose-dependent manner when overexpressed in HEK293T cells by competing with TRIF to bind RIP1 (Meylan E et al. 2004).

Followed by: K63-linked ubiquitination of RIP1 bound to the activated TLR complex

Literature references


RIP1 polyubiquitination was induced upon TNF- or poly(I-C) treatment of the macrophage cell line RAW264.7 and the U373 astrocytoma line (Cusson-Hermance et al 2005). These workers have suggested that RIP1 may use similar mechanisms to induce NF-kB in the TNFR1- and Trif-dependent TLR pathways.

RIP1 modification with Lys-63 polyubiquitin chains was shown to be essential for TNF-induced activation of NF-kB (Ea et al. 2006). It is thought that TRAF family members mediate this Lys63-linked ubiquitination of RIP1 (Wertz et al. 2004, Tada et al 2001, Vallabhapurapu and Karin 2009), which may facilitate recruitment of the TAK1 complex and thus activation of NF-kB. Binding of NEMO to Lys63-linked polyubiquitinated RIP1 is also required in the signaling cascade from the activated receptor to the IKK-mediated NF-kB activation (Wu et al. 2006).

Preceded by: Viral dsRNA:TLR3:TRIF complex recruits RIP1

Literature references


### Editions

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IKBKG subunit of IKK complex binds K63pUb- RIP1 within the TLR3 complex

**Location:** TICAM1, RIP1-mediated IKK complex recruitment

**Stable identifier:** R-HSA-9014343

**Type:** binding

**Compartments:** endosome membrane, cytosol

Structural studies showed that NEMO binds both Lys-63- and linear polyubiquitin chains, both critical for NF-kB activation.

**Literature references**


**Editions**

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