TANK binds K63-poly-Ub-TRAF3:TICAM1:activated TLR3

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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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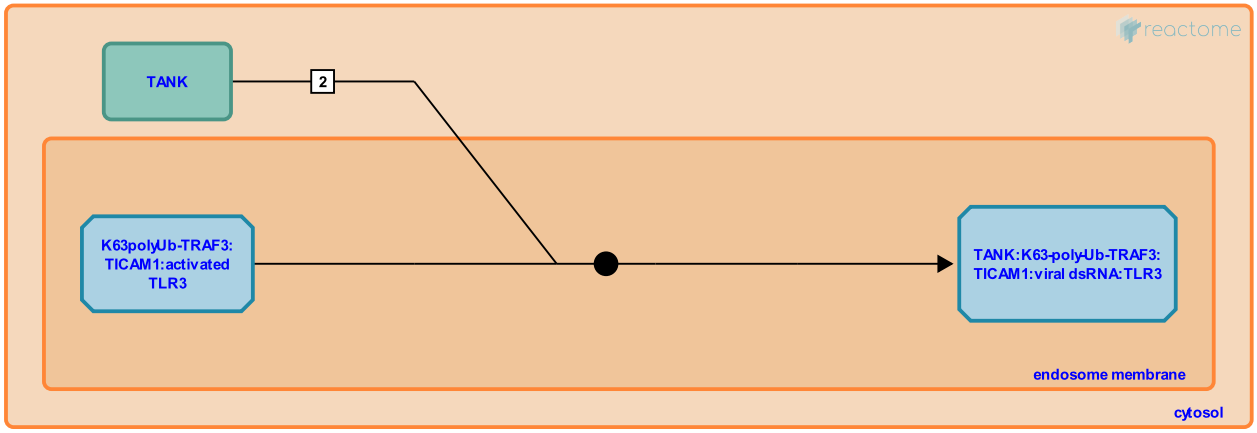
Stable identifier: R-HSA-9013985

Type: binding

Compartments: endosome membrane, cytosol



TRAF family member-associated NFkB activator (TANK or ITRAF) is a TRAF-binding protein that has been implicated in RLR, TNFR and IL-1R/TLR signaling pathways in mammals (Rothe M et a.l 1996; Pomerantz JL and Baltimore D 1999; Li C et al. 2002; Guo B and Cheng G 2007; Konno H 2009). TANK was shown to interact with TBK1, IKK epsilon, IPS-1, TRIF (TICAM1), IRF3 and is thought to be a part of the TRAF3-containing complex (Pomerantz JL and Baltimore D 1999; Guo B and Cheng G 2007; Gatot JC et al. 2007). Upon microbe stimulation TANK is believed to induce IRF-dependent type I IFN production in mammalian cells by linking kinase TBK1 or IKK epsilon with upstream mediators TRAF3/6 (Guo B and Cheng G 2007; Gatot JC et al. 2007). In addition, TANK is thought to act synergistically with IKK epsilon or TBK1 to link them to IKK complex via interaction with NEMO (IKK gamma), where TBK1/IKK epsilon may modulate NFkB activation (Chariot A et al. 2002). TANK influence on NFkB activation was found to occur via either positive or negative regulation (Guo B and Cheng G 2007, Konno H et al. 2009; Pomerantz JL and Baltimore D 1999; Kawagoe T et al. 2009).

Two other adaptor proteins NAK-associated protein 1 (NAP1) and SINTBAD (not shown here) have been implicated in TBK1/IKKepsilon-mediated activation of IRF3 (Sasai M et al. 2005; Ryzhakov G and Randow F 2007). Structural and functional studies showed that TANK, NAP1 and SINTBAD share a common region which mediates association with the coiled-coil 2 in TBK1 (Ryzhakov G and Randow F 2007; Goncalves A et al. 2011; Larabi A et al. 2013; Tu D et al. 2013). TANK, NAP1 and SINTBAD were found to compete for TBK1 binding (Ryzhakov G and Randow F 2007; Goncalves A et al. 2011), TBK1 is thought to form alternative complexes with each adaptor TANK, NAP1 or SINTBAD, rather than a single large multiprotein complex containing all three adaptors (Goncalves A et al. 2011; Larabi A et al. 2013).

Literature references

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Editions

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