MAVS binds TOMM70

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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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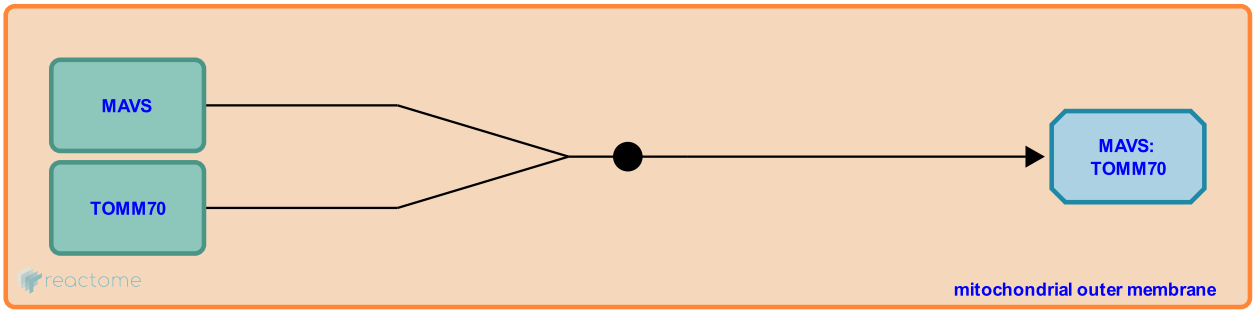
MAVS binds TOMM70 ↗

Stable identifier: R-HSA-9709842

Type: binding

Compartments: mitochondrial outer membrane



Mitochondrial import receptor subunit TOM70 (TOMM70) recognizes mitochondrial protein precursors in the cytosol and mediates their transition to the mitochondrial compartments (reviewed in Fan ACY & Young JC et al. 2011; Sokol AM et al. 2014; Kreimendahl S & Rassow J 2020). The molecular chaperone complexes of heat shock protein 90 kDa (HSP90) and HSP70 deliver precursor proteins to TOMM70 for subsequent import (Young JC et al. 2003; Zanphorlin LM et al. 2016).

During viral infection, cytosolic viral RNA triggers activation of mitochondrial antiviral-signaling protein (MAVS) and the formation of MAVS signalosome (Kawai T et al. 2005; Seth RB et al. 2005; Xu LG et al. 2005). MAVS localizes on the outer membrane of mitochondria through its C-terminal transmembrane (TM) domain. Activated MAVS recruits TANK-binding kinase 1 (TBK1) and interferon regulatory factor 3 (IRF3) to mitochondria leading to the activation of IRF3 and subsequent production of type I interferons.

Immunoprecipitation assays coupled to mass spectrometry analysis revealed that TOMM70 interacted with exogenously expressed MAVS in Sendai virus (SeV)-stimulated human embryonic kidney (HEK293) cells (Liu XY et al. 2010). The TM domains of both MAVS and TOMM70 were required for their interaction. In addition, TOMM70 interacted strongly with the C-terminal motif (EEVD) of HSP90 (Liu XY et al. 2010; Gava LM et al. 2011). TOMM70 also co-immunoprecipitated with TBK1 and IRF3 in HEK293 cells (Liu XY et al. 2010). Further, both TBK1 and IRF3 were found to associate with HSP90, which facilitated signal transduction from TBK1 to IRF3 in SeV-infected HEK293 cells (Yang K et l. 2006). Moreover, SeV infection enhanced the interaction between IRF3 and apoptosis regulator BAX (BAX) in HEK293T cells (Wei B et al. 2015). In SeV-stimulated HEK293 cells, cytosolic BAX translocated to the mitochondrial outer membrane and induced apoptosis in the IRF3-dependent manner via the formation of the TOMM70:HSP90:IRF3:BAX protein complex (Wei B et al. 2015). Knockdown of HSP90 by small interfering RNA (siRNA) decreased the association of TOMM70 with TBK1 and IRF3 (Liu XY et al. 2010). Overexpression of TOMM70 enhanced mRNA levels of IRF3-responsive genes (including IFNB, IFIT1 and RANTES) in HEK293 cells during SeV infection or poly(I:C) stimulation, whereas knockdown of TOMM70 by siRNA showed an inhibitory effect. Similar results were obtained in murine bone marrow-derived macrophages and bone marrow-derived dendritic cells (Liu XY et al. 2010). Thus, the association of MAVS with TOMM70 is thought to potentiate the HSP90-mediated recruitment of TBK1and IRF3 to mitochondria during viral infection thereby inducing IRF3-mediated host antiviral responses. In addition, binding of MAVS to TOMM70 can also trigger BAX-dependent apoptosis (Wei B et al. 2015). TOMM70 also associated with TRADD, TRAF6 and STING in HEK293 cells, further indicating that TOMM70 is a component of MAVS signal complex on mitochondria (Liu XY et al. 2010).

The viral orf9b (9b) proteins derived from SARS-CoV-1 and SARS-CoV-2 inhibit the MAVS-mediated production of type I IFNs by targeting TOMM70 on the mitochondria (Jiang HW et al. 2020).

This Reactome event shows the association of MAVS with TOMM70.

Literature references

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Editions

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