TRAF3/or TRAF6 interacts with IPS-1

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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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

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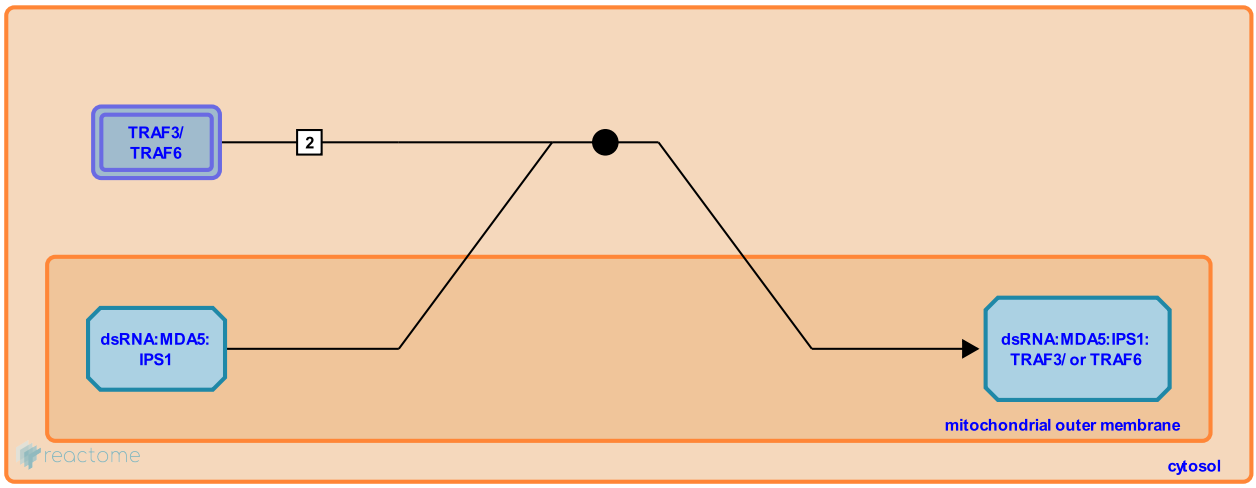
Stable identifier: R-GGA-1227891

Type: binding

Compartments: mitochondrial outer membrane, cytosol

Inferred from: Recruitment of TRAF3 to MAVS (Homo sapiens)



In mammals, the response to viral infection is mediated through direct and specific interaction between a TRAF-interaction motif (TIM) of IPS-1 and TRAFs, which can recruit other molecules into signaling complex [Ye H et al 2002, Xu LG et al 2005, Saha SK et al 2006, Konno H et al 2009]. IPS-1 harbors few distinct TIMs. One of the motifs is located at aa 143-PVQET-147 and binds both TRAF2 and TRAF3, while TRAF6 exclusively binds to aa 153-PGENSE-158 & 455-PEENEY-460 motifs. IPS-1 mediated response to viral infection in mammals requires:

- TRAF6 to activate NFkB, MAPK and IRF7, but not IRF3.[Xu LG et al 2005, Yoshida R et al 2009, Konno H et al 2009].
- TRAF3 to activate IRF3 and IRF7 [Saha SK et al 2006, Oganesyan G et al 2006].
- TRAF2 to activate p38 MAPK and contribute to NFkB induction [Mikkelsen SS et al 2009, Xu LG et al 2005].

Predicted chicken TRAF2, TRAF3 and TRAF6 proteins show 75, 82 and 73% amino acid sequence identity to their human counterparts respectively. In this project we assume that chicken TRAF proteins function similar to mammalian TRAFs upon viral infection.

Literature references

Xu, LG., Shu, HB., Han, KJ., Wang, YY., Zhai, Z., Li, LY. (2005). VISA is an adapter protein required for virus-triggered IFN-beta signaling. *Mol Cell, 19*, 727-40. ↗

Takeuchi, O., Kato, A., Goto, H., Tsunetsugu-Yokota, Y., Su, B., Yamazaki, K. et al. (2009). TRAF6 establishes innate immune responses by activating NF-kappaB and IRF7 upon sensing cytosolic viral RNA and DNA. *PLoS One, 4*, e5674. ↗

Pietras, EM., Saha, SK., Oganesyan, G., He, JQ., Wang, Y., Shahangian, A. et al. (2006). Regulation of antiviral responses by a direct and specific interaction between TRAF3 and Cardif. *EMBO J, 25*, 3257-63. ↗

Editions

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