TNF:TNFR1 binds TRADD, TRAF2 and RIPK1

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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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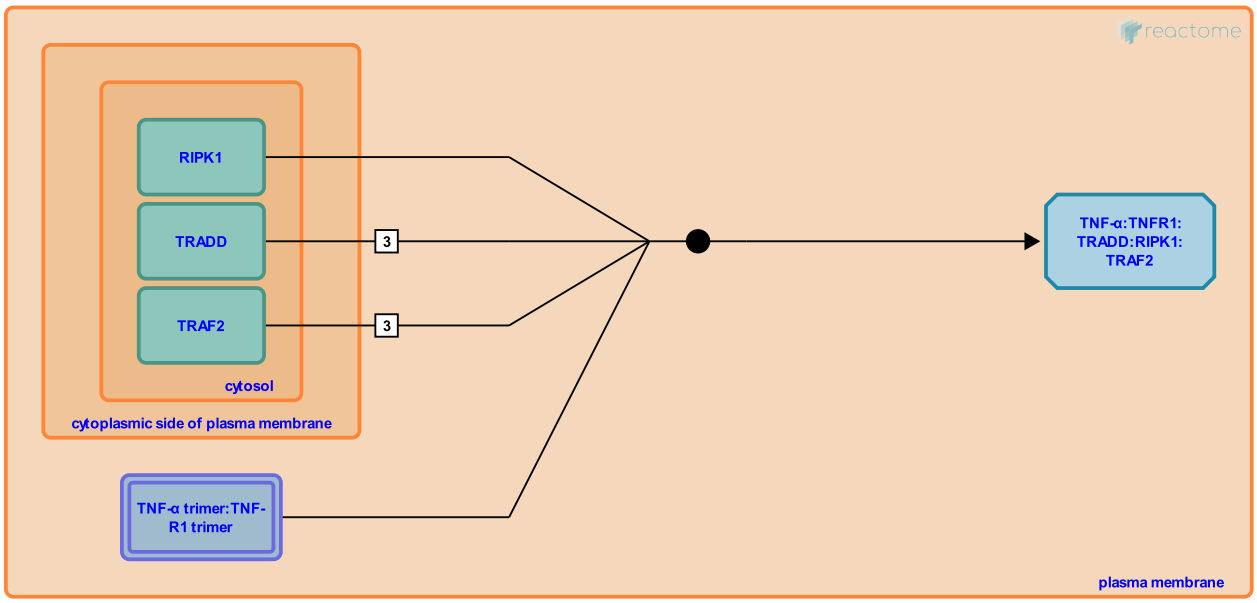
Stable identifier: R-HSA-83656

Type: binding

Compartments: plasma membrane, cytosol



Once the TNF-α:TNFR1:TRADD:RIPK1 complex has been formed there is concomitant recruitment of TRAF2, BIRC2/3 (cIAP1/2) and then of the TAB2:TAK1 and the IKK complex. TRAF2 and BIRC (cIAP1) were found to form a complex in solution (Zheng C et al. 2010), suggesting that TNFR1:TRADD:RIPK1 receptor complex recruits the TRAF2:BIRC complex as a whole. However, the expression levels of BIRCs are typically lower compared to TRAF2 suggesting that TNF-stimulated TNFR1 complex may also recruit TRAF2 alone. RIPK1 and the TRAF2:cIAP1/2 can be released from TNFR1 receptor complex in a poorly understood process associated with internalization and after that there is the formation of a so called complex II containing the adapter protein FADD, caspase-8 and RIPK1. Complex II has the potential to activate caspase-8 (Micheau O & Tschopp J 2003). The steps leading to the JUN, NF kappaB or apoptotic pathways are rife with opportunities for modulation.

Literature references

Hsu, H., Xiong, J., Goeddel, DV. (1995). The TNF receptor 1-associated protein TRADD signals cell death and NF-kappa B activation. *Cell, 81*, 495-504. ↗

Editions

2004-08-25	Authored	Gillespie, ME.
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