reactome

IRAK4 binds to the activated TLR7/8 or 9 receptor:MyD88 complex

Gillespie, ME., Shamovsky, V.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

30/06/2022

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

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. ↗

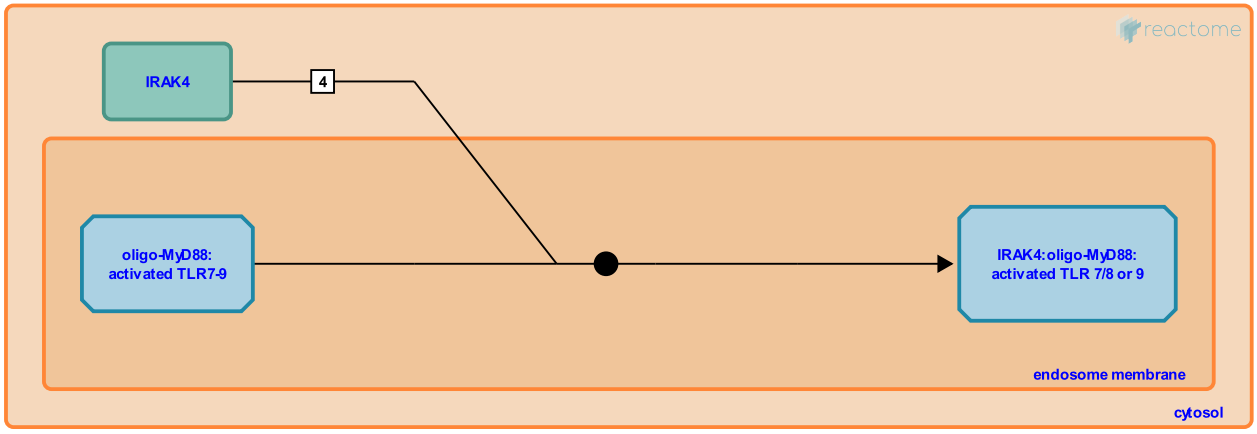
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

IRAK4 binds to the activated TLR7/8 or 9 receptor:MyD88 complex ↗

Stable identifier: R-HSA-975156

Type: binding

Compartments: endosome membrane, cytosol



IRAK4 is the mammalian homolog of Drosophila melanogaster Tube [Towb P et al 2009; Moncrieffe MC et al 2008]. Like Tube, IRAK4 possesses a conserved N-terminal death domain (DD), which mediates interactions with MyD88 at one binding site and a downstream IRAK kinase at the other, thereby bridging MyD88 and IRAK1/2 association [Towb P et al 2009; Lin SC e al 2010]. IRAK-4 plays a critical role in Toll receptor signaling - any interference with IRAK-4's kinase activity virtually abolishes downstream events. This is not the case with other members of the IRAK family [Suzuki N et al 2002; Li S et al 2002].

Literature references

Suzuki, S., Yeh, WC., Suzuki, N. (2002). IRAK-4 as the central TIR signaling mediator in innate immunity. *Trends Immunol, 23*, 503-6. ↗

Ozinsky, A., Casrouge, A., Li, X., von Bernuth, H., Lebon, P., Davidson, D. et al. (2005). Human TLR-7-, -8-, and -9-mediated induction of IFN-alpha/beta and -lambda Is IRAK-4 dependent and redundant for protective immunity to viruses. *Immunity, 23*, 465-78. ↗

Kim, TW., Li, X., Wen, Q., Li, Y., Xiao, H., Yao, J. et al. (2008). The kinase activity of IL-1 receptor-associated kinase 4 is required for interleukin-1 receptor/toll-like receptor-induced TAK1-dependent NFkappaB activation. *J. Biol. Chem., 283*, 31697-705. ↗

Wesche, H., Li, S., Fontana, EJ., Strelow, A. (2002). IRAK-4: a novel member of the IRAK family with the properties of an. *Proc Natl Acad Sci U S A, 99*, 5567-72. ↗

Editions

2010-08-25	Authored	Shamovsky, V.
2010-10-29	Reviewed	Gillespie, ME.
2010-11-15	Edited	Shamovsky, V.