MyD88 oligomerization within the complex of activated TLR 7/8 or 9 : MyD88

Gillespie, ME., Shamovsky, V.

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

04/07/2022

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. ↗

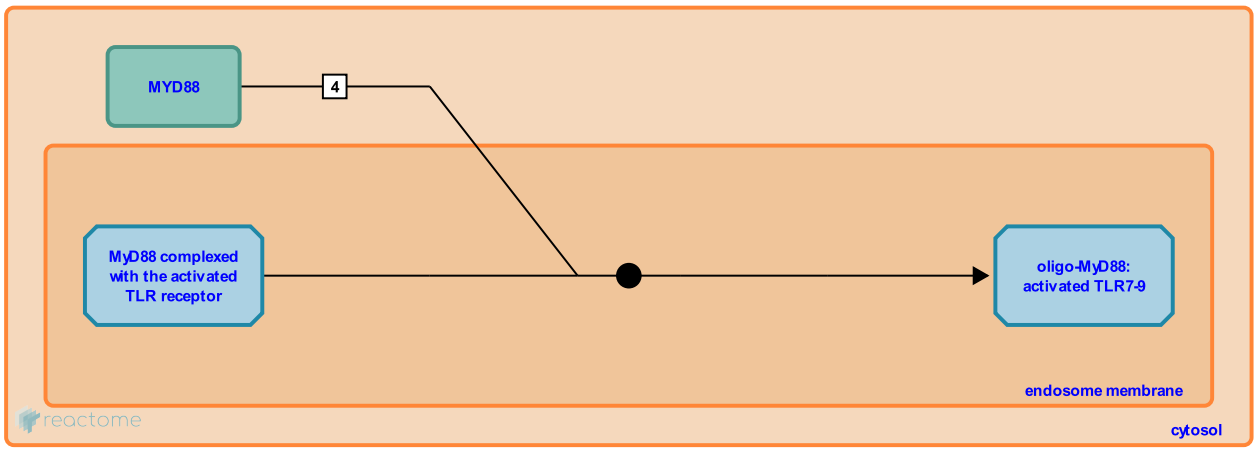
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

MyD88 oligomerization within the complex of activated TLR 7/8 or 9 : MyD88 ↗

Stable identifier: R-HSA-975098

Type: binding

Compartments: endosome membrane, cytosol



Structural analysis of MyD88:IRAK4 and MyD88:IRAK4:IRAK2 suggested that upon MyD88 recruitment to an activated dimerized TLR the MyD88 death domains clustering induces the formation of Mydosome, a large oligomeric signaling platform (Motshwene PG et al 2009, Lin SC et al 2010). Assembly of these Myddosome complexes brings the kinase domains of IRAKs into proximity for phosphorylation and activation. The oligomer complex stoichiometry was reported as 7:4 and 8:4 for MyD88:IRAK4 (Motshwene PG et al 2009), and 6:4:4 in the complex of MyD88:IRAK4:IRAK2(Lin SC et al 2010).

Literature references

Lo, YC., Lin, SC., Wu, H. (2010). Helical assembly in the MyD88-IRAK4-IRAK2 complex in TLR/IL-1R signalling. *Nature, 465*, 885-90. ↗

Wang, H., Hill, AV., Mills, TC., Motshwene, PG., Rautanen, A., Gay, NJ. et al. (2011). Two human MYD88 variants, S34Y and R98C, interfere with MyD88-IRAK4-myddosome assembly. *J. Biol. Chem., 286*, 1341-53. ↗

Motshwene, PG., Sandercock, AM., Moncrieffe, MC., Kao, C., Latz, E., Grossmann, JG. et al. (2009). An oligomeric signaling platform formed by the Toll-like receptor signal transducers MyD88 and IRAK-4. *J Biol Chem, 284*, 25404-11. ↗

Editions

2010-09-22	Authored	Shamovsky, V.
2010-10-29	Reviewed	Gillespie, ME.
2010-11-15	Edited	Shamovsky, V.