Multiple IRAK1 autophosphorylation steps

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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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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. ↗

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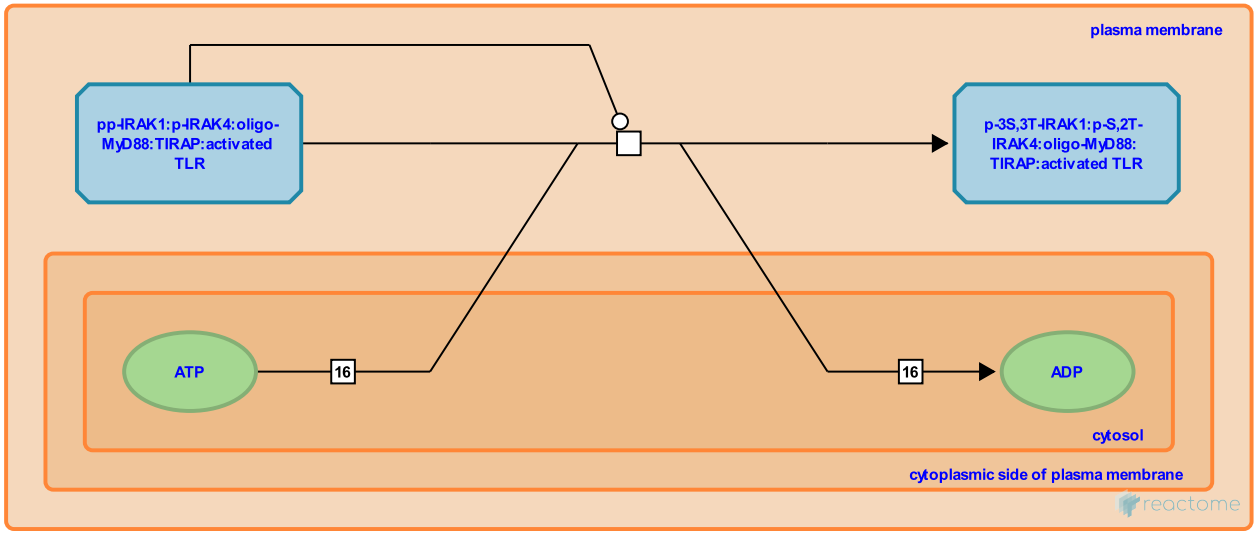
Stable identifier: R-HSA-166286

Type: transition

Compartments: plasma membrane, cytosol



Phosphorylation of IRAK-1 is due to three sequential phosphorylation steps, which leads to full or hyper-phopshorylation of IRAK1. Under in vitro conditions these are all autophosphorylation events. First, Thr-209 is phosphorylated resulting in a conformational change of the kinase domain. Next, Thr-387 in the activation loop is phosphorylated, leading to full enzymatic activity. Several additional residues are phosphorylated in the proline-, serine-, and threonine-rich (ProST) region between the N-terminal death domain and kinase domain. Hyperphosphorylation of this region leads to dissociation of IRAK1 from the activated receptor complex. The kinase activity of IRAK1 is dispensable for IL1-induced NFkB and MAP kinase activation (Knop & Martin, 1999), unlike that of IRAK4 (Suzuki et al. 2002; Kozicak-Holbro et al. 2007), It has been suggested that IRAK1 primarily acts as an adaptor for TRAF6 (Conze et al. 2008).

Literature references

Wesche, H., Li, S., Martin, MU., Knop, J., Neumann, D., Cao, P. et al. (2004). Sequential autophosphorylation steps in the interleukin-1 Receptor-associated Kinase-1 Regulate its Availability as an Adapter in Interleukin-1 Signaling. *J Biol Chem, 279*, 5227-36. ↗

Editions

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