Multiple IRAK1 autophosphorylation steps within the complex pIRAK4:MyD88:activated TLR7/8 or 9

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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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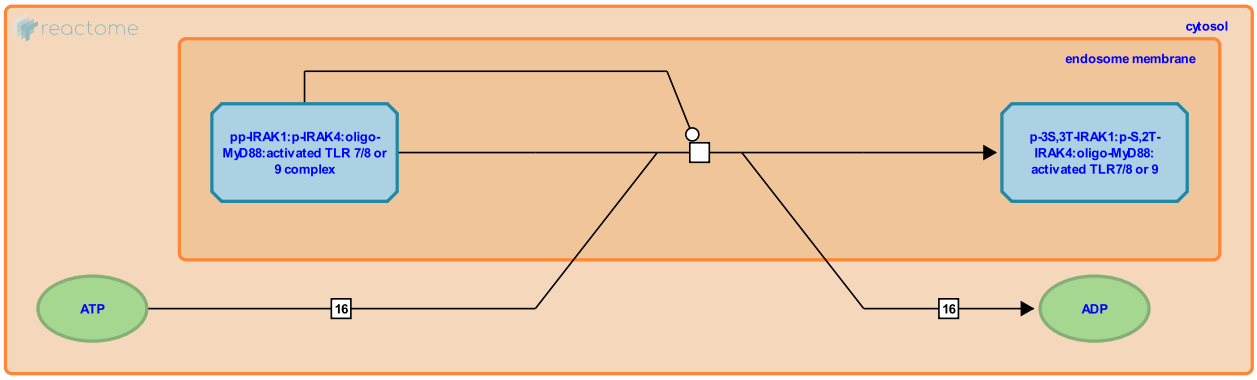
Stable identifier: R-HSA-975125

Type: transition

Compartments: endosome membrane, cytosol



A series of sequential phosphorylation events lead 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 upstream adapters MyD88 and Tollip. The significance of these phosphorylation events is not clear; 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), so IRAK1 is believed to act primarily as an adaptor for TRAF6 (Conze et al. 2008).

Literature references

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Editions

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