Src phosphorylates CD3 dimers in IgG:Lma antigens:FCGR3A:CD3 dimers

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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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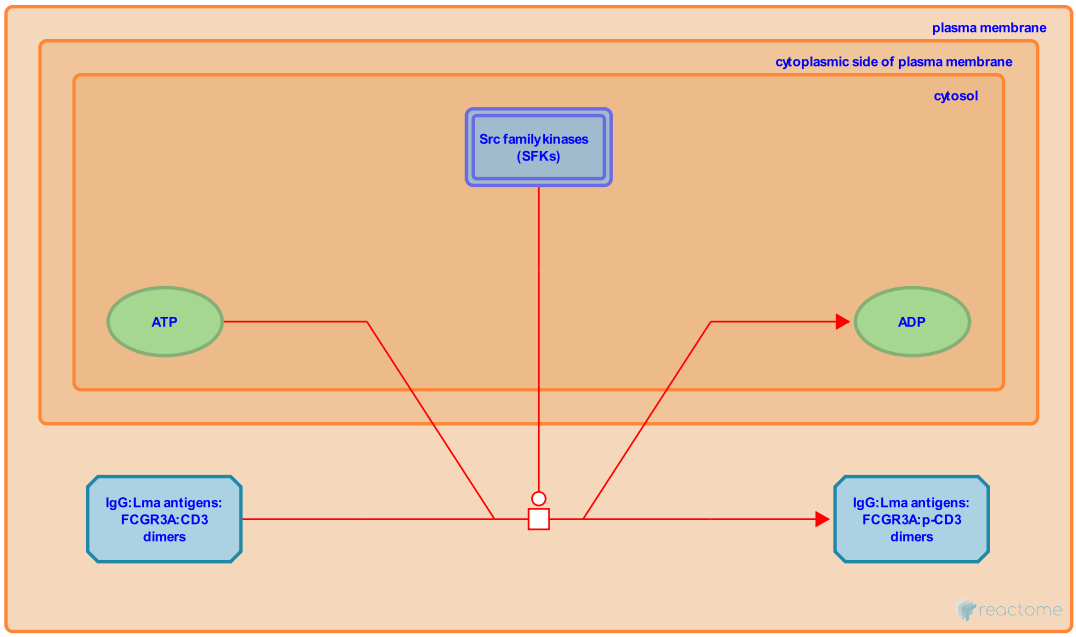
Stable identifier: R-HSA-9664275

Type: transition

Compartments: plasma membrane, cytosol, extracellular region

Diseases: cutaneous leishmaniasis



After cross linking, Fc gamma receptors are sequestered to lipid rafts where they are complexed with some of the tyrosine kinases of Src family and undergo phosphorylation on the tyrosine residues contained in conserved ITAM sequences. At least six out of nine members of the Src family kinases (SRC, FYN, FGR, HCK, YES and LYN) have been identified in the phagocytic cells and are implicated in the initiation of Fc gamma mediated signaling. (Suzuki et al. 2000, Majeed et al. 2001, Kwiatkowska et al. 2003). Some of these kinases have been found associated with specific receptors. In monocytes HCK and LYN have been found associated with FCGRI (Durden et al. 1995), whereas only HCK with FCGRIIA (Ghazizadeh et al. 1994) while FGR in neutrophils (Hamada et al. 1993) and LCK in NK cells with FCGRIIIA (Pignata et al. 1993)
The implication of Src kinases in phosphorylation was first supported by pharmacological findings that herbimycin A, a tyrosine kinase inhibitor relatively specific for Src-family kinases, potently suppressed Fc receptor mediated functions (Greenberg et al. 1993, Suzuki et al. 2000). However, their particular involvement in phagocytosis remains unclear, as targeted disruption of single or multiple Src family genes did not result in significant alterations in phagocytosis (Hunter et al. 1993, Fitzer Attas et al. 2000, Suzuki et al. 2000). HCK, FGR and LYN triple-deficient (-/-) macrophages have shown significant delays in FCGR mediated phagocytosis, but these deficiencies do not completly disrupt the process (Fitzer Attas et al. 2000).
Tyrosine residues Y288 and Y304 (Y282 and Y298 according to the literature reference, it is 6 residues shorter compared to uniprot entry due to an alternate initiation codon usage), within ITAM sequence in the cytoplasmic domain of FCGRIIA are the key target sites that are phosphorylated by Src family kinases (Mitchell et al, 1994). In case of FCGRIA and FCGRIIIA the specific tyrosine residues within ITAMs of the associated gamma/zeta chains are phosphorylated by activated Src family kinases (SFKs) (Park et al. 1993).

Literature references

Okada, M., Honda, Z., Hirose, N., Yamamoto, T., Suzuki, T., Kono, H. et al. (2000). Differential involvement of Src family kinases in Fc gamma receptor-mediated phagocytosis. *J Immunol, 165*, 473-82. ↗

Huang, MM., Brugge, JS., Hoxie, JA., Indik, Z., Brass, LF., Schreiber, AD. (1992). Activation of Fc gamma RII induces tyrosine phosphorylation of multiple proteins including Fc gamma RII. *J Biol Chem, 267*, 5467-73. ↗

Indik, ZK., Worth, RG., Kim, MK., Barreda, DR., Huang, ZY., Chien, P. et al. (2006). Differential kinase requirements in human and mouse Fc-gamma receptor phagocytosis and endocytosis. *J Leukoc Biol, 80*, 1553-62. ↗

Strzelecka, A., Kwiatkowska, K., Sobota, A. (1997). Tyrosine phosphorylation and Fcgamma receptor-mediated phagocytosis. *FEBS Lett, 400*, 11-4. ↗

Editions

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