

# 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

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Reactome database release: 90

This document contains 1 reaction ([see Table of Contents](#))

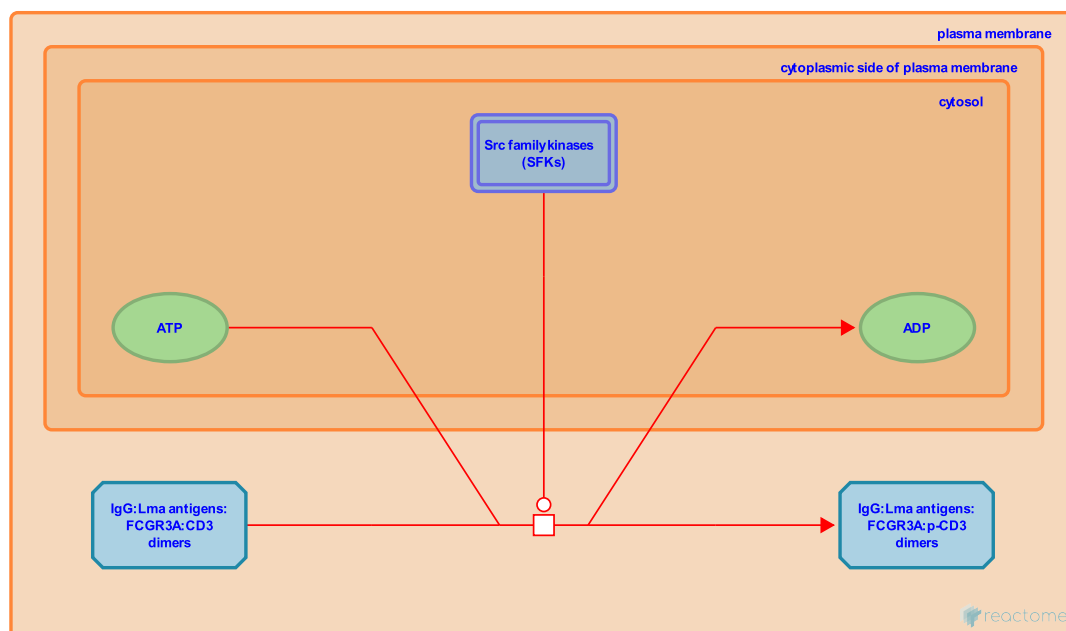
## Src phosphorylates CD3 dimers in IgG:Lma antigens:FCGR3A:CD3 dimers ↗

**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 FCGR1 (Durden et al. 1995), whereas only HCK with FCGR2A (Ghazizadeh et al. 1994) while FGR in neutrophils (Hamada et al. 1993) and LCK in NK cells with FCGR3A (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 completely 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 FCGR2A are the key target sites that are phosphorylated by Src family kinases (Mitchell et al, 1994). In case of FCGR1A and FCGR3A the specific tyrosine residues within ITAMs of the associated gamma/zeta chains are phosphorylated by activated Src family kinases (SFKs) (Park et al. 1993).

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**Editions**

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