SYK binds IgG:Lma antigens:FCGR3A:p-CD3 dimers

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19/05/2024

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).

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Reactome database release: 88
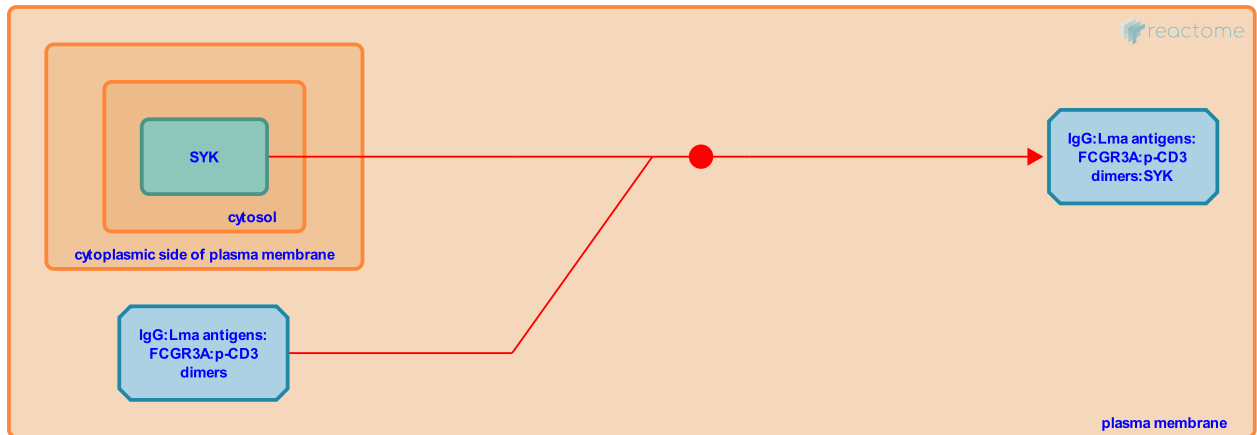
This document contains 1 reaction (see Table of Contents)

SYK binds IgG:Lma antigens:FCGR3A:p-CD3 dimers ↗

Stable identifier: R-HSA-9664273

Type: binding

Compartments: plasma membrane, cytosol, extracellular region

Diseases: cutaneous leishmaniasis

SYK is a tyrosine kinase related to ZAP70 that is expressed in all hematopoietic cells and coimmunoprecipitates with the gamma chain associated with FCGRIIIA in macrophages and with FCERI in mast cells. SYK is very important for FCGR phagocytosis and is recruited to these phosphorylated ITAM residues through its two SRC homology 2 (SH2) domains (Agarwal et al. 1993). When SYK kinase expression is inhibited with antisense oligonucleotides both in vitro and in vivo, phagocytosis and inflammation are abolished (Matsuda et al. 1997). The domain structure of SYK comprises a regulatory region at the N-terminus consisting of a pair of SH2 domains separated by an inter-SH2 linker called interdomain A, an SH2-domain-kinase linker termed interdomain B, and a C-terminal kinase domain (Arias-Palomo et al. 2009). In resting state SYK exists in an auto-inhibited conformation by the interactions between the SH2-SH2 regulatory region and the inter-SH2 linker and the catalytic domain. This interdomain interaction reduces the conformational flexibility required by the kinase domain for catalysis (Arias-Palomo et al. 2007). Changes in the orientation of the SH2 domains could control the disruption of the auto inhibitory interactions and the activation of SYK. These movements could be totally or partially induced by the binding to phosphorylated ITAMs and/or phosphorylation of tyrosine residues in interdomain A or B (Arias-Palomo et al. 2009). Tsang et al. suggested that SYK functions as an OR-gate switch with respect to phosphorylation and ITAM binding, as either one stimulus OR the other is sufficient to cause full activation (Tsang et al. 2008).

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Editions

2019-10-22	Authored	Murillo, JI.
2020-02-04	Reviewed	Gregory, DJ.
2020-02-05	Edited	Murillo, JI.