Recruitment of SYK to phosphorylated IT-AMs

Garapati, P V., Rosales, C.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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).

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. ↗

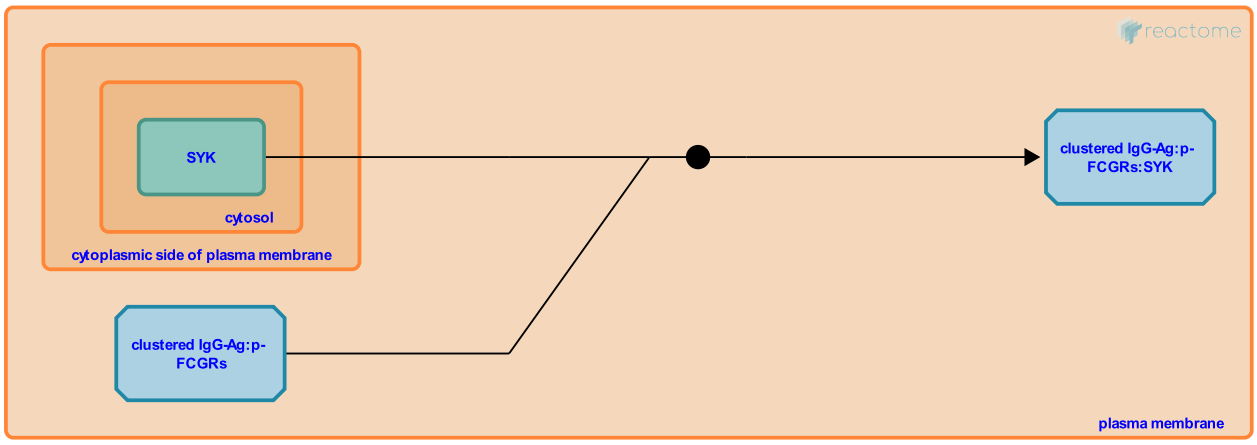
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Recruitment of SYK to phosphorylated ITAMs ↗

Stable identifier: R-HSA-2029452

Type: binding

Compartments: plasma membrane, extracellular region, cytosol



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).

Literature references

Matsuda, M., Hunter, S., Wang, DC., Chien, P., Schreiber, AD., Park, JG. (1996). Abrogation of the Fc gamma receptor IIA-mediated phagocytic signal by stem-loop Syk antisense oligonucleotides. *Mol Biol Cell, 7*, 1095-106. ↗

Fleit, HB., Bolen, JB., Ghazizadeh, S. (1995). Tyrosine phosphorylation and association of Syk with Fc gamma RII in monocytic THP-1 cells. *Biochem J, 305*, 669-74. ↗

Robbins, KC., Salem, P., Agarwal, A. (1993). Involvement of p72syk, a protein-tyrosine kinase, in Fc gamma receptor signaling. *J Biol Chem, 268*, 15900-5. ↗

Rankin, BM., Gilliland, LK., Schieven, GL., Bolen, JB., Kiener, PA., Burkhardt, AL. et al. (1993). Cross-linking of Fc gamma receptor I (Fc gamma RI) and receptor II (Fc gamma RII) on monocytic cells activates a signal transduction pathway common to both Fc receptors that involves the stimulation of p72 Syk protein tyrosine kinase. *J Biol Chem, 268*, 24442-8. ↗

Lowell, C., Costello, PS., Turner, M., Tybulewicz, VL., DeFranco, AL., Meng, F. et al. (1997). A critical role for Syk in signal transduction and phagocytosis mediated by Fcgamma receptors on macrophages. *J Exp Med, 186*, 1027-39. ↗

Editions

2012-01-04	Authored, Edited	Garapati, P V.
2012-05-15	Reviewed	Rosales, C.