Recruitment of ZAP-70 to phosphorylated ITAMs

Garapati, P V., Rudd, C.E.., Trowsdale, J., de Bono, B.

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

04/05/2024

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. ↗

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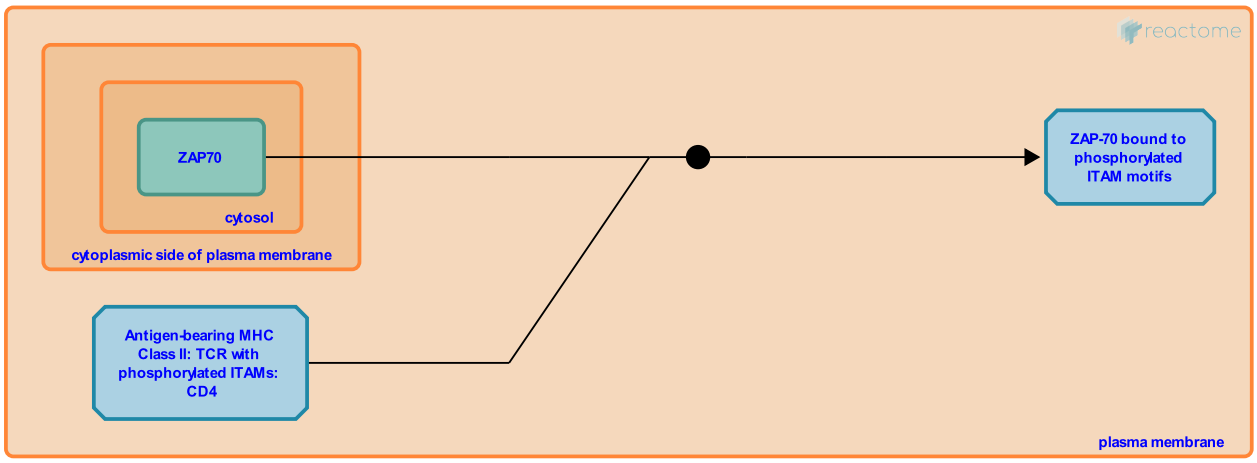
Stable identifier: R-HSA-202344

Type: binding

Compartments: cytosol, plasma membrane



Phosphorylation of the ITAMs by Lck is followed by the recruitment of the ZAP-70 a member of Syk family PTK, to the receptor complex. ZAP-70 is exclusively expressed in T cells and NK cells. The dually phosphorylated ITAMs provide a high-affinity docking site for the tandem SH2-domains of the ZAP-70. Once recruited, ZAP-70 is activated by phosphorylation and will be responsible for the phosphorylation of further downstream molecules. Due to the presence of 10 ITAMs in the TCR complex, up to 10 ZAP-70 molecules may cluster on the fully phosphorylated receptors.

Literature references

Chu, DH., Morita, CT., Weiss, A. (1998). The Syk family of protein tyrosine kinases in T-cell activation and development. *Immunol Rev, 165*, 167-80.

van Oers, NS., Weiss, A. (1995). The Syk/ZAP-70 protein tyrosine kinase connection to antigen receptor signalling processes. *Semin Immunol, 7*, 227-36.

Tasken, K., Mustelin, T. (2003). Positive and negative regulation of T-cell activation through kinases and phosphatases. *Biochem J, 371*, 15-27.

Editions

2008-01-24	Authored	de Bono, B., Garapati, P V., Rudd, C.E..
2008-02-26	Reviewed	Trowsdale, J.