SHP1 and SHP2 bind the common beta chain

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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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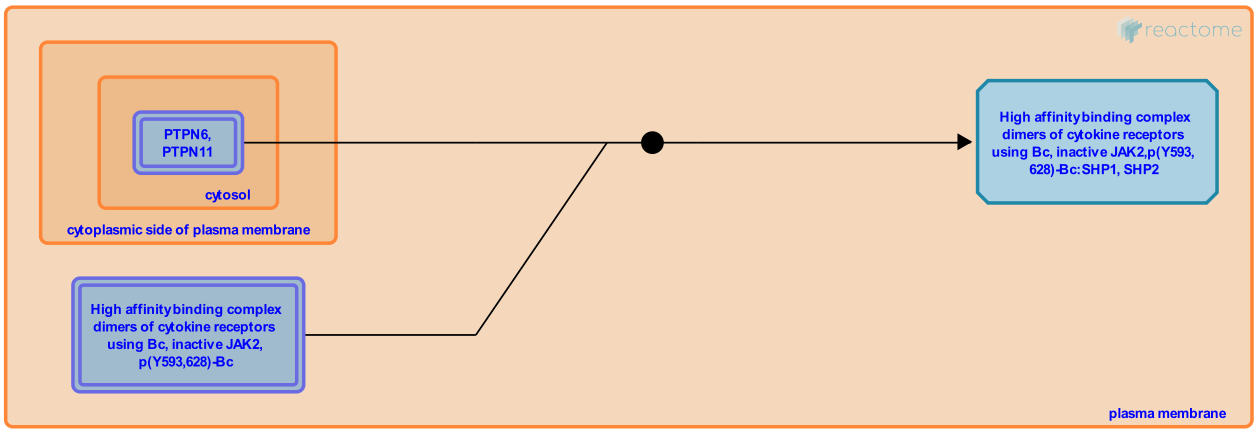
Stable identifier: R-HSA-909738

Type: binding

Compartments: cytosol, plasma membrane



The common beta chain (Bc) has at least at least one direct binding site for SHP-1/SHP-2 (PTPN6/PTPN11). The SH2 domains of SHP1 and SHP2 associate with Y628 of Bc following IL-3 stimulation (Pei et al. 1994, Bone et al. 1997). SHPs act as regulators of signaling. SHP1 is thought to be a negative regulator of growth that terminates signals. Binding of SHP1 to EpoR leads to SHP1 activation and dephosphorylation of JAK2, terminating proliferative signals (Klingmuller et al. 1995). SHP1 has also been shown to interact directly and dephosphorylate JAK2 (Jiao et al. 1996). Although SHP-2 competes for the same binding site, it is thought to be a positive modulator. SHP2 associates with JAK1/2 and is phosphorylated at Y304 by these kinases, creating a GRB2 recognition motif (Yin et al. 1997). IL-3 induces the phosphorylation of SHP2 and its association with Grb2 (Welham et al. 1994). SHP2 could thereby act as an adaptor between Bc and Grb2 leading to activation of the ras/mitogen-activated protein kinase pathway. SHP2 can also associate with the p85 subunit of phosphatidylinositol 3-kinase (Welham et al. 1994) so SHP2 may also regulate this pathway.

Literature references

Dechert, U., Jirik, F., Bone, H., Welham, MJ., Schrader, JW. (1997). SHP1 and SHP2 protein-tyrosine phosphatases associate with betac after interleukin-3-induced receptor tyrosine phosphorylation. Identification of potential binding sites and substrates. *J Biol Chem, 272*, 14470-6. ↗

Editions

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