

G6B binds PTPN6,PTPN11

Akkerman, JW., Jupe, S.

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

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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: 88

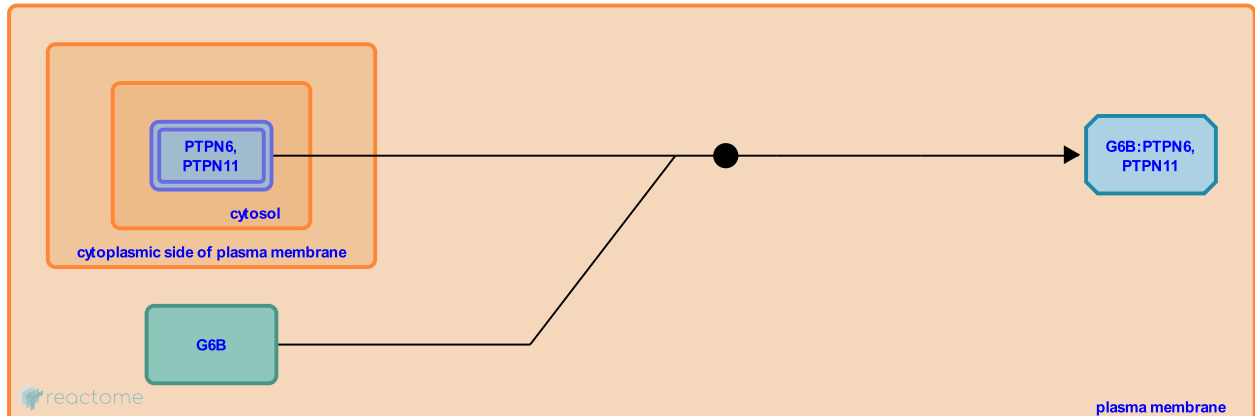
This document contains 1 reaction ([see Table of Contents](#))

G6B binds PTPN6,PTPN11 [↗](#)

Stable identifier: R-HSA-5684169

Type: binding

Compartments: cytosol, plasma membrane



G6B is a member of the immunoglobulin superfamily. The G6B-B variant is the only variant to contain both a transmembrane region and two immunoreceptor tyrosine-based inhibitory motifs (ITIMs) that support binding to the SH2 domain-containing protein tyrosine phosphatases PTPN6 (SHP1) and PTPN11 (SHP2) (de Vet et al. 2001, Senis et al. 2007). ITIMs are defined by the consensus sequence (L/I/V/S)-X-Y-X-X-(L/V) and are commonly present in pairs separated by 15 to 30 amino acid residues. ITIM-containing receptors were originally identified by their ability to inhibit signaling by ITAM receptors (Bijsterbosch & Klaus 1985). Expression of the GPVI-FcR gamma-chain complex or C-type lectin domain family 1 member B (CLEC1B, CLEC2) in DT40 (chicken) B cells leads to the generation of both constitutive and agonist-induced signals that are inhibited by G6B. This effect is dependent on the two ITIMs in the cytosolic tail of G6B, but is reported to be independent of the two SH2 domain-containing tyrosine phosphatases PTPN6 and PTPN11, and the inositol lipid 5''-phosphatase SHIP1 (Mori et al. 2008). A more recent study (Coxon et al. 2011) found that other SH2 domain-containing proteins including SYK and PLCgamma2 also recognize G6B phosphomotifs, which may explain why G6B remains inhibitory in the absence of both PTPN6 and PTPN11.

The tandem SH2 domains of PTPN11 have a 100-fold higher binding affinity for G6B than that of PTPN6. PTPN6 has an absolute binding requirement for phosphorylation at both ITAM motifs, while PTPN11 can associate with G6B when only one motif is phosphorylated. The presence of dual phosphorylated G6B in washed human platelets reduced the EC(50) for both CRP and collagen-induced aggregation (Coxon et al. 2011). G6B is proposed to inhibit sustained constitutive signaling from GPVI-FcRgamma and CLEC1B (Mori et al. 2008).

Literature references

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Editions

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