Interaction of GRB2:SOS complex with p-SHC1

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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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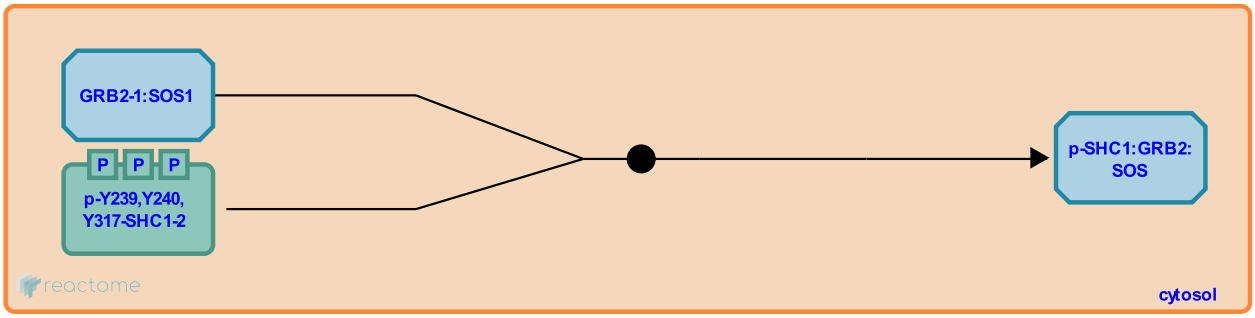
Stable identifier: R-HSA-2730844

Type: binding

Compartments: cytosol



GRB2 is an adapter protein that contains a central SH2 domain flanked by N- and C-terminal SH3 domains. GRB2 acts downstream of receptor protein-tyrosine kinases and is involved in Ras and MAP kinase pathway activation by associating with the guanine exchange factor (GEF) SOS. GRB2 is constitutively bound to SOS through its SH3 domains, which interact with a proline-rich sequence in the C-terminal part of SOS (Chardin et al. 1993). GRB2-SOS complex binds to phosphotyrosine Y239 and Y317 of SHC1. SHC1 associates with the tyrosine-phosphorylated ITAMs of the FCERI beta-chain and can recruit SOS to membrane. SHC1 and SOS have also been described to associate with LAT via GRB2. Shc binding to Phospho-ITAMs (in vitro binding to phospho peptides) has never been linked to any biological function (activation) and is probably not relevant in a physiological setting.

Literature references

Lessmann, E., Rivera, J., Alvarez-Errico, D. (2009). Adapters in the organization of mast cell signaling. *Immunol. Rev., 232*, 195-217. ↗

Harmer, SL., DeFranco, AL. (1997). Shc contains two Grb2 binding sites needed for efficient formation of complexes with SOS in B lymphocytes. *Mol Cell Biol, 17*, 4087-95. ↗

Gale, NW., Camonis, JH., Chardin, P., Schlessinger, J., Wigler, MH., Bar-Sagi, D. et al. (1993). Human Sos1: a guanine nucleotide exchange factor for Ras that binds to GRB2. *Science, 260*, 1338-43. ↗

Editions

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