

# GRB2-1:SOS1 binds p-IRS1,p-IRS2

Charalambous, M., Schmidt, EE.

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of <u>Creative Commons Attribution 4.0 International (CC BY 4.0)</u>
<u>License</u>. For more information see our <u>license</u>.

01/05/2024

https://reactome.org

### 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 data-base: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968.

Reactome database release: 88

This document contains 1 reaction (see Table of Contents)

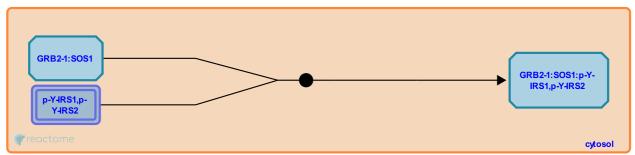
https://reactome.org Page 2

## GRB2-1:SOS1 binds p-IRS1,p-IRS2

**Stable identifier:** R-HSA-74736

**Type:** binding

**Compartments:** cytosol



Inactive p21ras:GDP is anchored to the plasma membrane by a farnesyl residue. Insulin stimulation results in phosphorylation of IRS1/2 on tyrosine residues. GRB2 binds the phosphotyrosines via its SH2 domain. As IRS is phosphorylated by the insulin receptor near to the plasma membrane, the GRB2:SOS1:IRS interaction brings SOS1 and p21 Ras into close proximity.

# Literature references

White, MF., Feldman, EL., Leventhal, PS., Kim, B. (1998). Differential regulation of insulin receptor substrate-2 and mitogen-activated protein kinase tyrosine phosphorylation by phosphatidylinositol 3-kinase inhibitors in SH-SY5Y human neuroblastoma cells. *Endocrinology*, 139, 4881-9.

Yazaki, Y., Kadowaki, T., Takahashi, Y., Tobe, K., Fukushima, Y., Kadowaki, H. et al. (1997). Roles of insulin receptor substrate-1 and Shc on insulin-like growth factor I receptor signaling in early passages of cultured human fibroblasts. *Endocrinology*, 138, 741-50.

Batzer, A., Li, N., Schlessinger, J., Mohammadi, M., Skolnik, EY., Lowenstein, E. et al. (1993). The function of GRB2 in linking the insulin receptor to Ras signaling pathways. *Science*, 260, 1953-5.

Pessin, JE., Okada, S. (1996). Interactions between Src homology SH2/SH3 adapter proteins and the guanylnucleotide exchange factor SOS are differentially regulated by insulin and epidermal growth factor. *J Biol Chem*, 271, 25533-8

Ward, CW., Wang, J., Wan, SS., Gough, KH., Tribbick, G., Rashke, M. (1996). Systematic mapping of potential binding sites for Shc and Grb2 SH2 domains on insulin receptor substrate-1 and the receptors for insulin, epidermal growth factor, platelet-derived growth factor, and fibroblast growth factor. *J. Biol. Chem.*, 271, 5603-9.

### **Editions**

2005-01-07	Authored	Charalambous, M.
2024-03-06	Edited	Schmidt, EE.