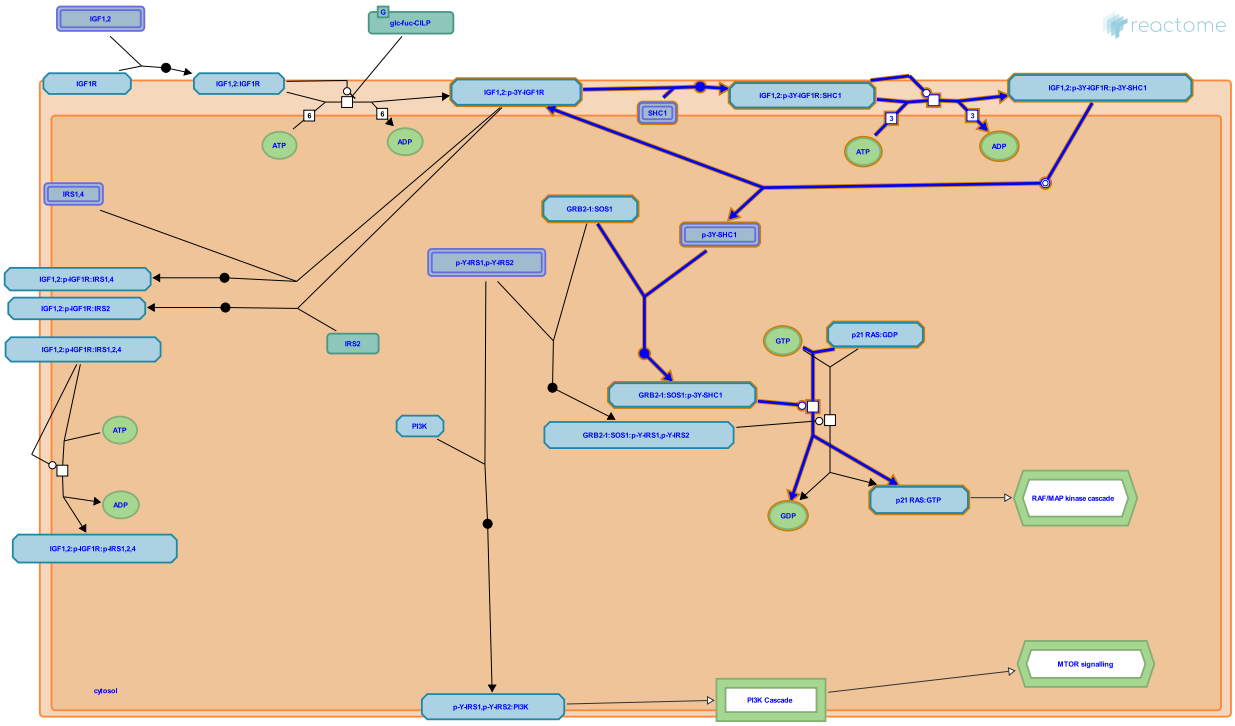
SHC-related events triggered by IGF1R



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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.
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. ↗

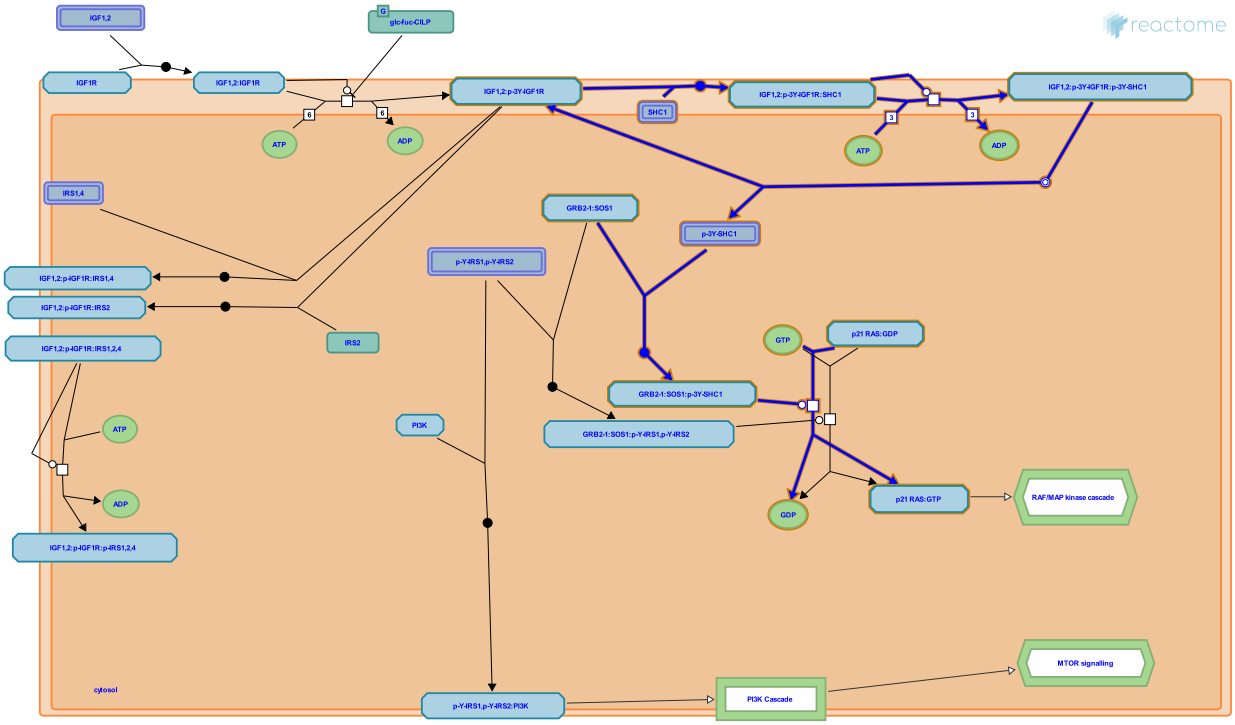
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

SHC-related events triggered by IGF1R ↗

Stable identifier: R-HSA-2428933

Compartments: cytosol, plasma membrane



Phosphorylated IGF1R binds and phosphorylates SHC1 (reviewed in Pavelic et al. 2007, Chitnis et al. 2008, Maki et al. 2010, Parrella et al. 2010, Siddle et al. 2012). Phosphorylated SHC then binds GRB:SOS, which activates RAS-RAF-MAPK signaling.

Literature references

Siddle, K. (2012). Molecular basis of signaling specificity of insulin and IGF receptors: neglected corners and recent advances. *Front Endocrinol (Lausanne), 3*, 34. ↗

Longo, VD., Parrella, E. (2010). Insulin/IGF-I and related signaling pathways regulate aging in nondividing cells: from yeast to the mammalian brain. *ScientificWorldJournal, 10*, 161-77. ↗

Maki, RG. (2010). Small is beautiful: insulin-like growth factors and their role in growth, development, and cancer. *J. Clin. Oncol., 28*, 4985-95. ↗

Knezević, J., Matijević, T., Pavelić, J. (2007). Biological & physiological aspects of action of insulin-like growth factor peptide family. *Indian J. Med. Res., 125*, 511-22. ↗

Chitnis, MM., Macaulay, VM., Protheroe, AS., Pollak, M., Yuen, JS. (2008). The type 1 insulin-like growth factor receptor pathway. *Clin. Cancer Res., 14*, 6364-70. ↗

Editions

2012-08-07	Authored, Edited	May, B.
2012-11-10	Reviewed	Holzenberger, M.

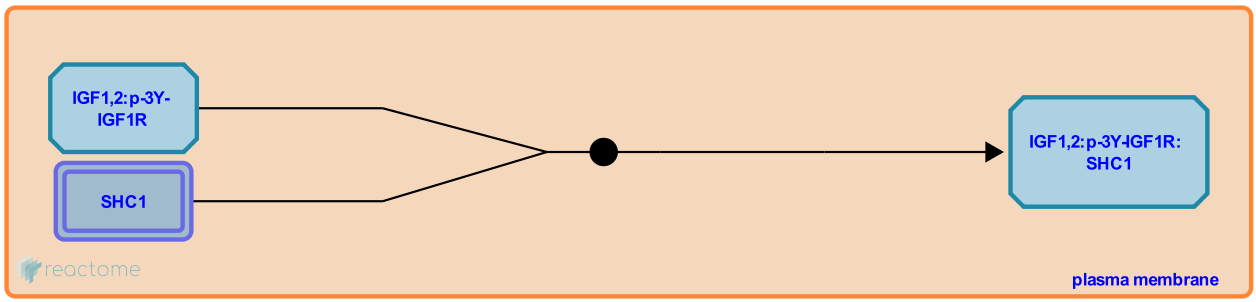
IGF1,2:p-Y1161,1165,1166-IGF1R binds SHC1 ↗

Location: SHC-related events triggered by IGF1R

Stable identifier: R-HSA-2404195

Type: binding

Compartments: plasma membrane



SHC binds the NPEY-juxtamembrane motif of the phosphorylated insulin-like growth factor receptor (IGF1R) (Giorgetti et al. 1994, Tartare-Deckert et al. 1995).

Followed by: IGF1R phosphorylates SHC1

Literature references

Murdaca, J., Sawka-Verhelle, D., Tartare-Deckert, S., Van Obberghen, E. (1995). Evidence for a differential interaction of SHC and the insulin receptor substrate-1 (IRS-1) with the insulin-like growth factor-I (IGF-I) receptor in the yeast two-hybrid system. *J. Biol. Chem., 270*, 23456-60. ↗

Pelicci, G., Pelicci, PG., Van Obberghen, E., Giorgetti, S. (1994). Involvement of Src-homology/collagen (SHC) proteins in signaling through the insulin receptor and the insulin-like-growth-factor-I-receptor. *Eur. J. Biochem., 223*, 195-202. ↗

Editions

2012-07-08	Authored, Edited	May, B.
2012-11-10	Reviewed	Holzenberger, M.

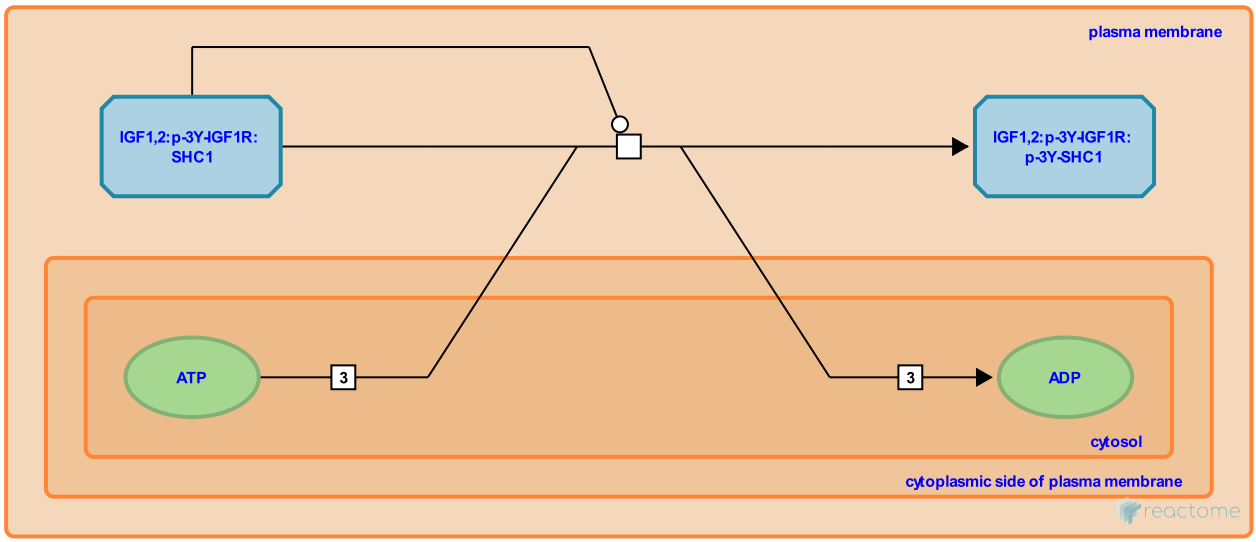
IGF1R phosphorylates SHC1 ↗

Location: SHC-related events triggered by IGF1R

Stable identifier: R-HSA-2404193

Type: transition

Compartments: plasma membrane, cytosol



The phosphorylated IGF1R phosphorylates SHC1 (Giorgetti et al. 1994, Hernandez-Sanchez et al. 1995, Kim et al. 1998). Phosphorylation of SHC1 is sustained whereas phosphorylation of IRS2 by IGF1R is transient (Kim et al. 1998).

Preceded by: IGF1,2:p-Y1161,1165,1166-IGF1R binds SHC1

Followed by: p-3Y-SHC1 dissociates from IGF1R

Literature references

Pelicci, G., Pelicci, PG., Van Obberghen, E., Giorgetti, S. (1994). Involvement of Src-homology/collagen (SHC) proteins in signaling through the insulin receptor and the insulin-like-growth-factor-I-receptor. *Eur. J. Biochem., 223*, 195-202. ↗

Feldman, EL., Cheng, HL., Margolis, B., Kim, B. (1998). Insulin receptor substrate 2 and Shc play different roles in insulin-like growth factor I signaling. *J. Biol. Chem., 273*, 34543-50. ↗

Kalebic, T., Blakesley, V., LeRoith, D., Hernández-Sánchez, C., Helman, L. (1995). The role of the tyrosine kinase domain of the insulin-like growth factor-I receptor in intracellular signaling, cellular proliferation, and tumorigenesis. *J. Biol. Chem., 270*, 29176-81. ↗

Editions

2012-07-08	Authored, Edited	May, B.
2012-11-10	Reviewed	Holzenberger, M.

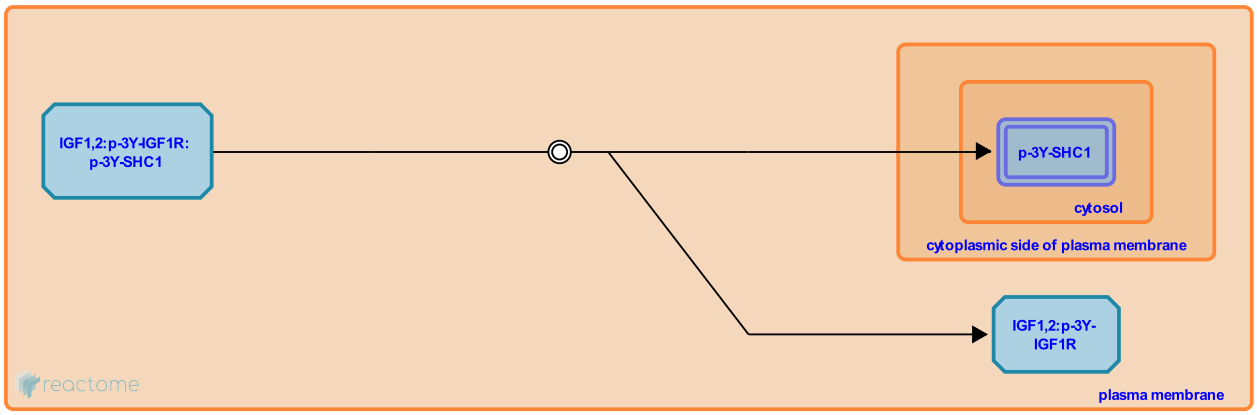
p-3Y-SHC1 dissociates from IGF1R ↗

Location: SHC-related events triggered by IGF1R

Stable identifier: R-HSA-5686072

Type: dissociation

Compartments: plasma membrane, cytosol



Release of tyrosine-phosphorylated SHC from IGF1R triggers a cascade of signalling events via SOS, RAF and the MAP kinases.

Preceded by: IGF1R phosphorylates SHC1

Followed by: GRB2-1:SOS1 binds p-3Y-SHC1

Literature references

Pelicci, G., Pelicci, PG., Van Obberghen, E., Giorgetti, S. (1994). Involvement of Src-homology/collagen (SHC) proteins in signaling through the insulin receptor and the insulin-like-growth-factor-I-receptor. *Eur. J. Biochem., 223*, 195-202. ↗

Feldman, EL., Cheng, HL., Margolis, B., Kim, B. (1998). Insulin receptor substrate 2 and Shc play different roles in insulin-like growth factor I signaling. *J. Biol. Chem., 273*, 34543-50. ↗

Kalebic, T., Blakesley, V., LeRoith, D., Hernández-Sánchez, C., Helman, L. (1995). The role of the tyrosine kinase domain of the insulin-like growth factor-I receptor in intracellular signaling, cellular proliferation, and tumorigenesis. *J. Biol. Chem., 270*, 29176-81. ↗

Editions

2015-03-31	Authored	Jupe, S.
2015-04-08	Edited	Jupe, S.

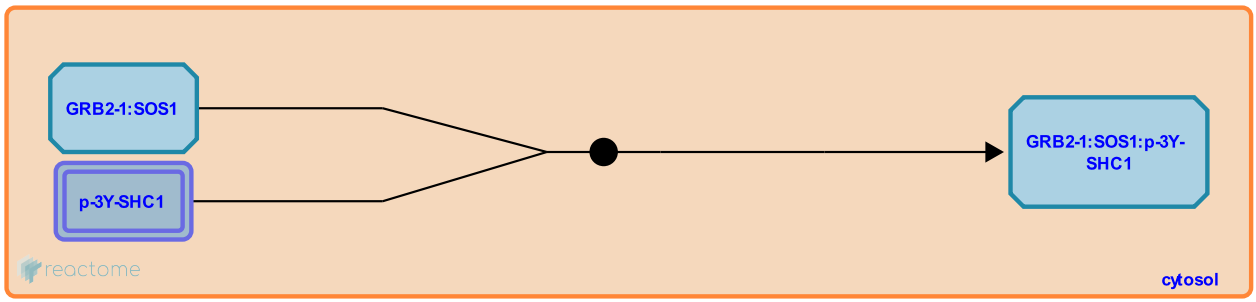
GRB2-1:SOS1 binds p-3Y-SHC1 ↗

Location: SHC-related events triggered by IGF1R

Stable identifier: R-HSA-5686073

Type: binding

Compartments: cytosol



Phosphorylated SHC1 recruits the SH2 domain of the adaptor protein GRB2, which is in a complex with SOS, an exchange factor for p21ras and RAC. Besides SOS, the GRB2 SH3 domain can associate with other intracellular targets, including GAB1. Erk and Rsk mediated phosphorylation results in dissociation of the SOS-GRB2 complex. This may explain why Erk activation through Shc and SOS-GRB2 is transient. Inactive p21ras-GDP is found anchored to the plasma membrane by a farnesyl residue. As Shc is phosphorylated by the the stimulated receptor near to the plasma membrane, the SOS-GRB2:Shc interaction brings the SOS enzyme into close proximity to p21ras.

Preceded by: p-3Y-SHC1 dissociates from IGF1R

Followed by: GRB2-1:SOS1:p-3Y-SHC1 mediated nucleotide exchange of RAS

Literature references

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 . ↗

Editions

2015-04-08	Edited	Jupe, S.

GRB2-1:SOS1:p-3Y-SHC1 mediated nucleotide exchange of RAS ↗

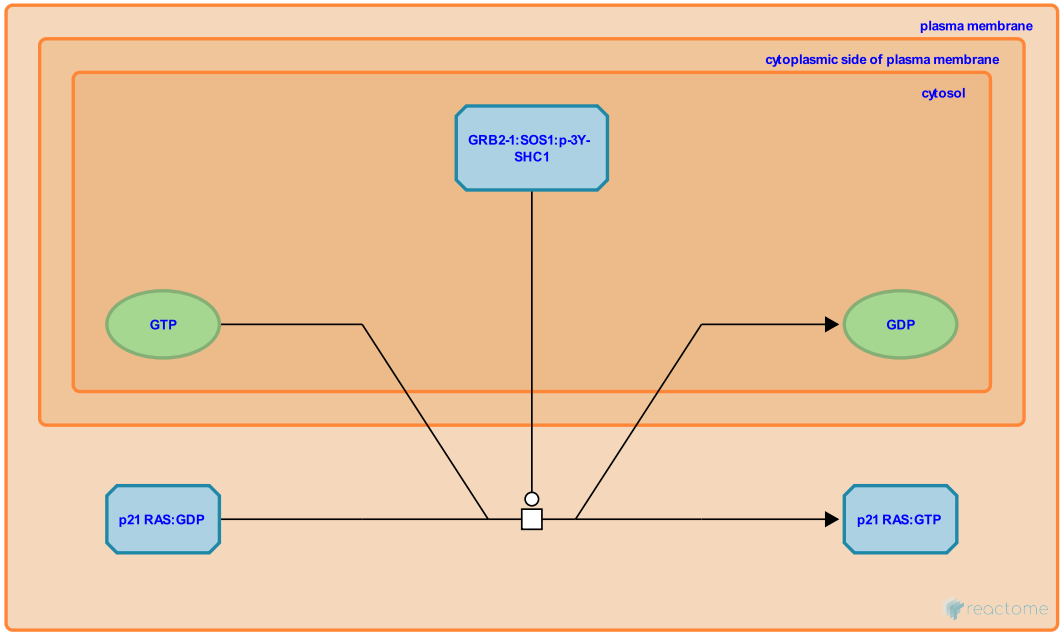
Location: SHC-related events triggered by IGF1R

Stable identifier: R-HSA-5686318

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: SOS mediated nucleotide exchange of RAS (SHC) (Rattus norvegicus)



SOS promotes the formation of GTP-bound RAS, thus activating this protein. RAS activation results in activation of the protein kinases RAF1, B-Raf, and MAP-ERK kinase kinase (MEKK), and the catalytic subunit of PI3K, as well as of a series of RALGEFs. The activation cycle of RAS GTPases is regulated by their interaction with specific guanine nucleotide exchange factors (GEFs) and GTPase-activating proteins (GAPs). GEFs promote activation by inducing the release of GDP, whereas GAPs inactivate RAS-like proteins by stimulating their intrinsic GTPase activity.

Preceded by: GRB2-1:SOS1 binds p-3Y-SHC1

Literature references

Boriack-Sjodin, PA., Margarit, SM., Kuriyan, J., Bar-Sagi, D. (1998). The structural basis of the activation of Ras by Sos . *Nature, 394*, 337-43. ↗

Editions

2015-04-08	Edited	Jupe, S.

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