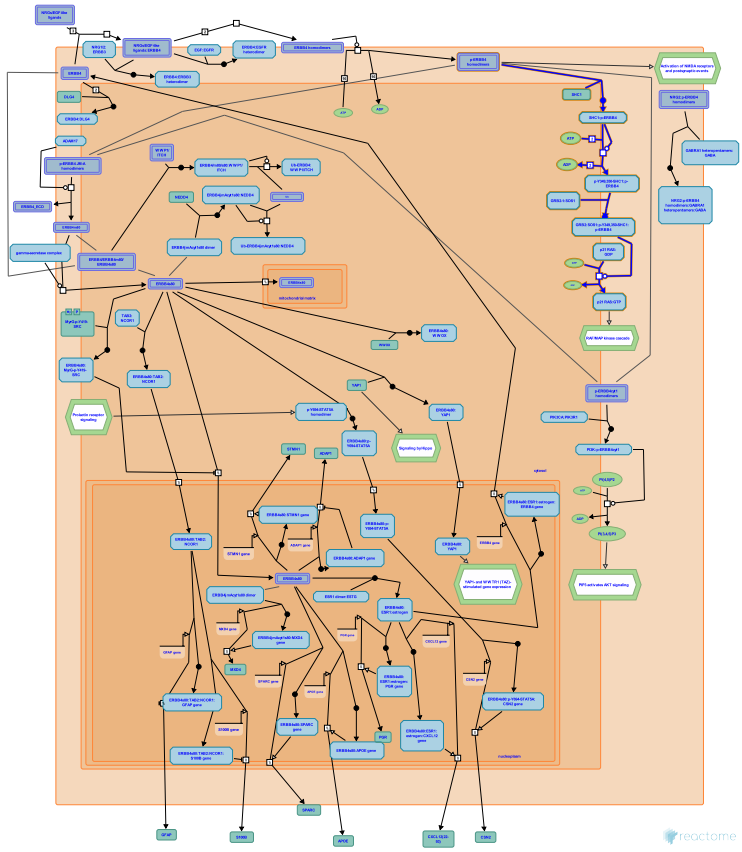
SHC1 events in ERBB4 signaling



Earp HS, 3rd., Harris, RC., Matthews, L., Misior, AM., Orlic-Milacic, M., Stern, DF., Zeng, F.

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

01/05/2024

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. ↗

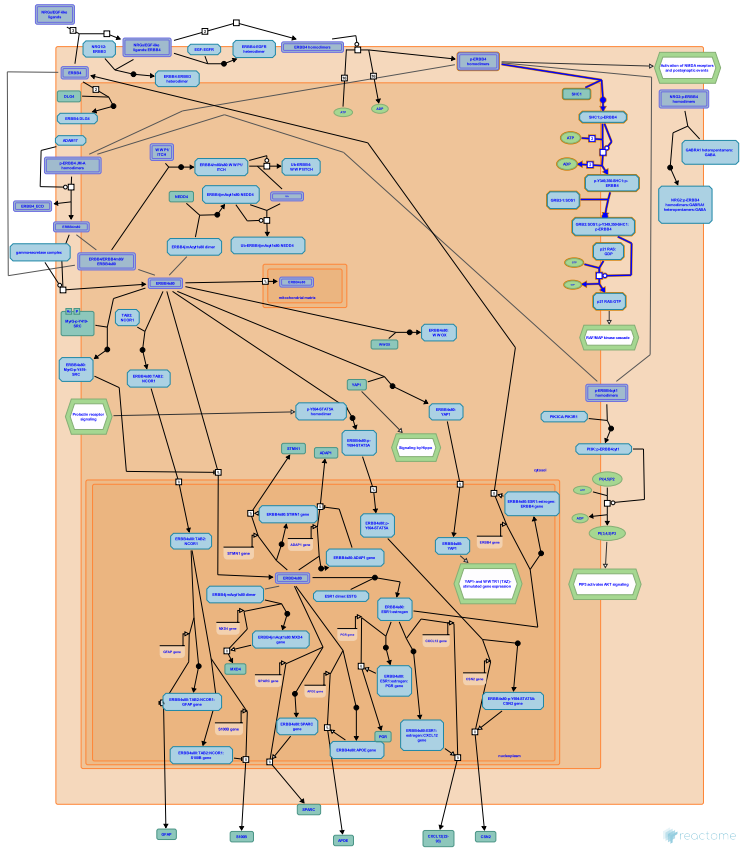
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

SHC1 events in ERBB4 signaling ↗

Stable identifier: R-HSA-1250347



All splicing isoforms of ERBB4 possess two tyrosine residues in the C-tail that serve as docking sites for SHC1 (Kaushansky et al. 2008, Pinkas-Kramarski et al. 1996, Cohen et al. 1996). Once bound to ERBB4, SHC1 becomes phosphorylated on tyrosine residues by the tyrosine kinase activity of ERBB4, which enables it to recruit the complex of GRB2 and SOS1, resulting in the guanyl-nucleotide exchange on RAS and activation of RAF and MAP kinase cascade (Kainulainen et al. 2000).

Editions

2011-11-04	Authored	Orlic-Milacic, M.
2011-11-07	Edited	Matthews, L.
2011-11-11	Reviewed	Harris, RC., Zeng, F.
2012-02-20	Reviewed	Earp HS, 3rd., Misior, AM.
2019-02-21	Authored	Stern, DF.
2019-03-06	Edited	Orlic-Milacic, M.

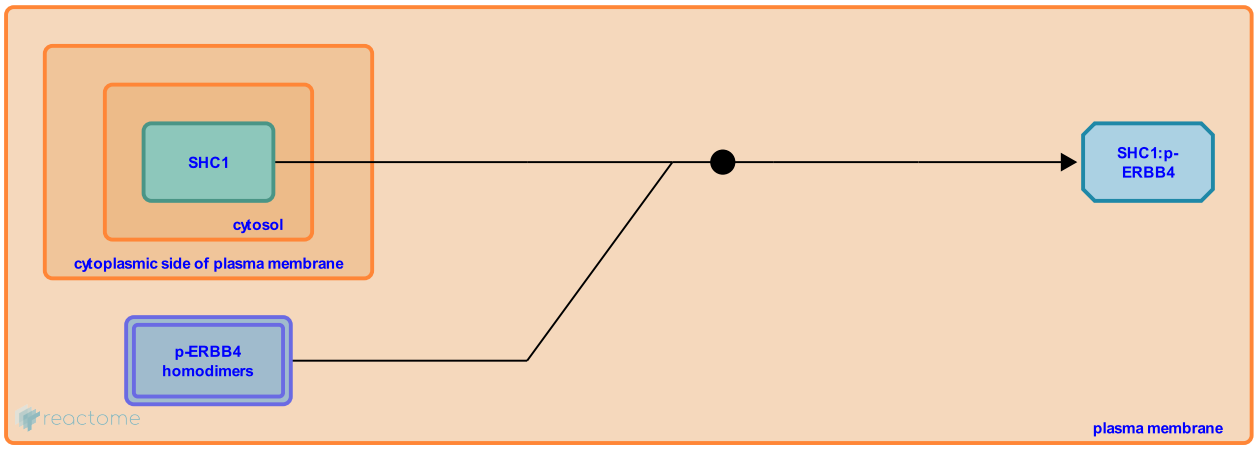
SHC1 binds P-ERBB4 isoform dimers ↗

Location: SHC1 events in ERBB4 signaling

Stable identifier: R-HSA-1250357

Type: binding

Compartments: plasma membrane, extracellular region, cytosol



Phosphorylated tyrosine residues in the C-tail of phosphorylated ERBB4 isoform dimers P-ERBB4jmAcyt1, P-ERBB4jmAcyt2 and P-ERBB4jmBcyt1 recruit SHC1 (Cohen et al. 1996, Pinkas-Kramarski et al. 1996, Kaushansky et al. 2008).

Followed by: Phosphorylation of SHC1 by ERBB4 homodimers

Literature references

Ratzkin, BJ., Klapper, L., Levkowitz, G., Seger, R., Alroy, I., Waterman, H. et al. (1996). Diversification of Neu differentiation factor and epidermal growth factor signaling by combinatorial receptor interactions. *EMBO J, 15*, 2452-67. ↗

Lane, WS., MacBeath, G., Budnik, BA., Rush, J., Kaushansky, A., Gordus, A. (2008). System-wide investigation of ErbB4 reveals 19 sites of Tyr phosphorylation that are unusually selective in their recruitment properties. *Chem Biol, 15*, 808-17. ↗

Fell, HP., Foy, L., Green, JM., Cohen, BD. (1996). HER4-mediated biological and biochemical properties in NIH 3T3 cells. Evidence for HER1-HER4 heterodimers. *J Biol Chem, 271*, 4813-8. ↗

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2019-02-21	Authored	Stern, DF.
2019-03-06	Edited	Orlic-Milacic, M.

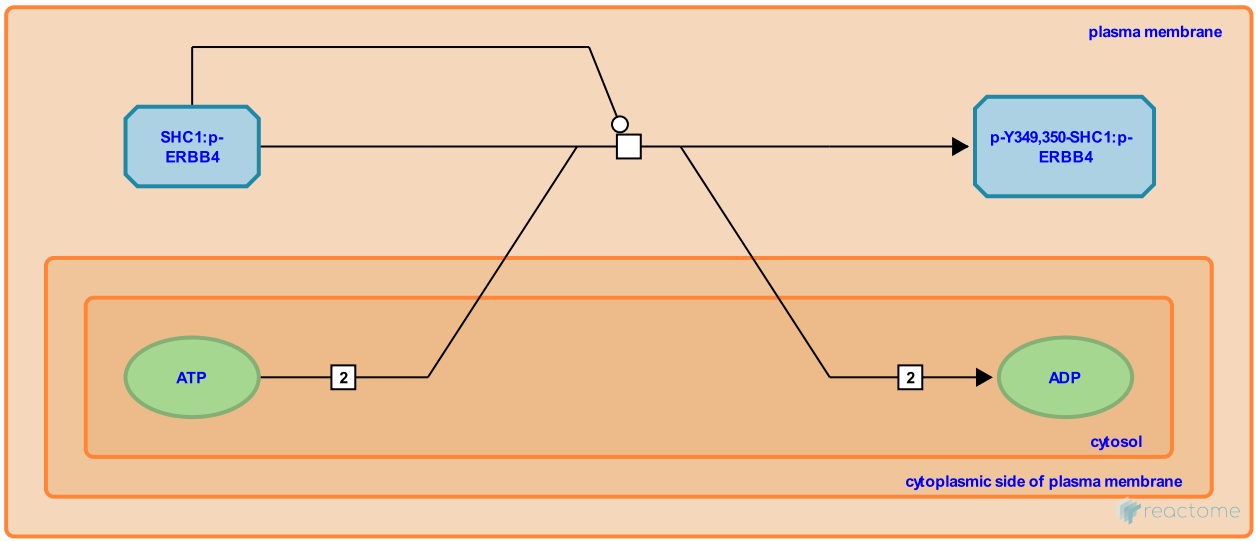
Phosphorylation of SHC1 by ERBB4 homodimers ↗

Location: SHC1 events in ERBB4 signaling

Stable identifier: R-HSA-1250348

Type: transition

Compartments: plasma membrane, extracellular region, cytosol



After binding ERBB4 homodimers, SHC1 gets phosphorylated on tyrosine residues Y349 and Y350 (Kainulainen et al. 2000).

Preceded by: SHC1 binds P-ERBB4 isoform dimers

Followed by: Recruitment of GRB2:SOS1 to phosphorylated SHC1 in complex with phosphorylated ERBB4 homodimers

Literature references

Santiestevan, E., Sundvall, M., Kainulainen, V., Määttä, JA., Elenius, K., Klagsbrun, M. (2000). A natural ErbB4 isoform that does not activate phosphoinositide 3-kinase mediates proliferation but not survival or chemotaxis. *J Biol Chem, 275*, 8641-9. ↗

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2019-02-21	Authored	Stern, DF.
2019-03-06	Edited	Orlic-Milacic, M.

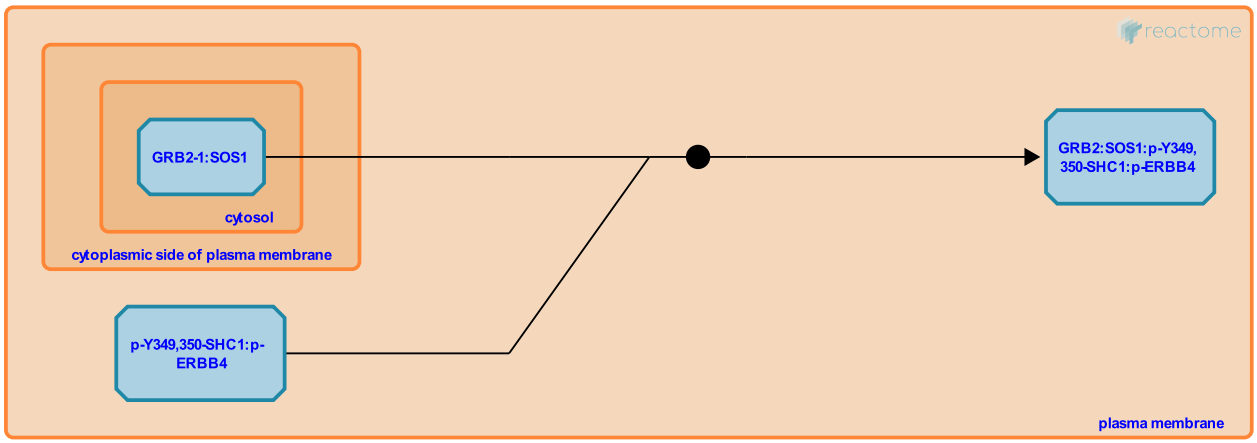
Recruitment of GRB2:SOS1 to phosphorylated SHC1 in complex with phosphorylated ERBB4 homodimers ↗

Location: SHC1 events in ERBB4 signaling

Stable identifier: R-HSA-1250380

Type: binding

Compartments: plasma membrane, extracellular region, cytosol



Phosphorylated SHC1 bound to phosphorylated ERBB4 homodimers recruits GRB2:SOS1 complex (Kainulainen et al. 2000).

Preceded by: Phosphorylation of SHC1 by ERBB4 homodimers

Followed by: RAS guanyl-nucleotide exchange mediated by SOS1 in complex with GRB2 and p-Y349,350-SHC1:p-ERBB4

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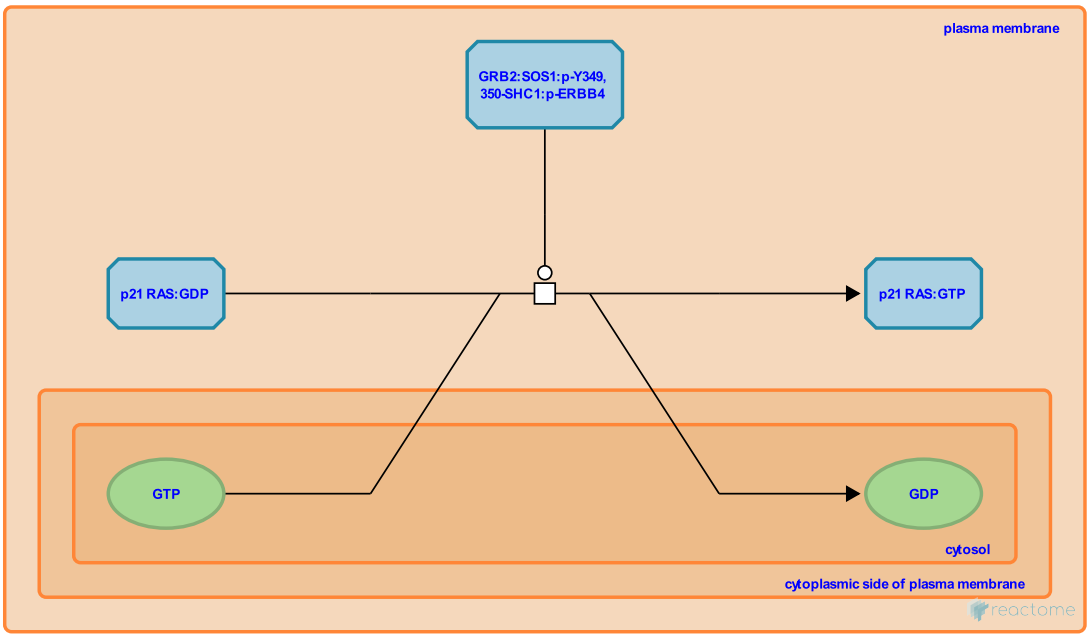
RAS guanyl-nucleotide exchange mediated by SOS1 in complex with GRB2 and p-Y349,350-SHC1:p-ERBB4 ↗

Location: SHC1 events in ERBB4 signaling

Stable identifier: R-HSA-1250383

Type: transition

Compartments: plasma membrane, cytosol



SOS1 in complex with GRB2 and p-Y349,350-SHC1:p-ERBB4 activates RAS by mediating guanyl nucleotide exchange, which results in the activation of RAF/MAP kinase cascade (Kainulainen et al. 2000).

Preceded by: Recruitment of GRB2:SOS1 to phosphorylated SHC1 in complex with phosphorylated ERBB4 homodimers

Literature references

Santiestevan, E., Sundvall, M., Kainulainen, V., Määttä, JA., Elenius, K., Klagsbrun, M. (2000). A natural ErbB4 isoform that does not activate phosphoinositide 3-kinase mediates proliferation but not survival or chemotaxis. *J Biol Chem, 275*, 8641-9. ↗

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