

2x p-5Y-RET:GDNF:GFRA complexes bind GRB2-1:SOS1

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09/10/2024

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

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Reactome database release: 90

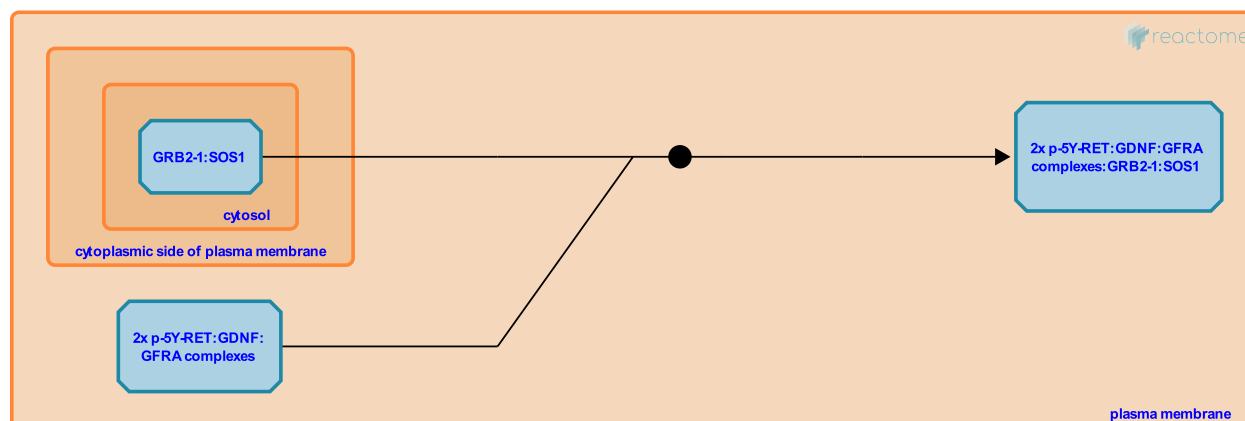
This document contains 1 reaction ([see Table of Contents](#))

2x p-5Y-RET:GDNF:GFRA complexes bind GRB2-1:SOS1 [↗](#)

Stable identifier: R-HSA-8854899

Type: binding

Compartments: cytosol, extracellular region, plasma membrane



RET has been shown to bind GRB2 directly, via Tyrosine-1096 (Y1096) (Alberti et al. 1998, Besset et al. 2000). GRB2 is found in a complex with SOS1 in unstimulated cells (Hayashi et al. 2000).

GDNF stimulation of neuronal cells induces the assembly of a large protein complex containing RET, GRB2 and tyrosine-phosphorylated SHC1, p85 subunit of (PI3K), GAB2 (GAB1 in Hayashi et al. 2000) and Tyrosine-protein phosphatase non-receptor type 11 (PTPN11, SHP-2) (Besset et al. 2000). This suggests that at least two distinct RET-SHC1 protein complexes can assemble via phosphorylated Y1062, one involving GRB2 and SOS1 leads to activation of the RAS-RAF-ERK pathway, another involving GRB2, GAB2 and p85 leads to the PI3K-AKT pathway. This latter complex can also assemble directly onto phosphorylated Y1096 (Besset et al. 2000).

RET can activate the RAS-RAF-ERK signaling pathway (van Weering et al. 1995, Ohiwa et al. 1997, van Weering & Bos 1997, Trupp et al. 1999, Hayashi et al. 2000). RAS signaling is markedly impaired by mutations of RET Y1062 (Hayashi et al. 2000). RET RAS signaling and the effect of the Y1062 mutation are believed to be mediated by RET complexes involving GRB2:SOS1, well known as mediators of signaling to RAS in other receptor systems (Ravichandran 2001).

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Editions

2016-01-25	Authored	Jupe, S.
2016-04-28	Edited	Jupe, S.
2016-05-06	Reviewed	Morales, D.
2016-05-17	Reviewed	Luo, W.