GRB2 events in EGFR signaling

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16/03/2020
**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**


Reactome database release: 71

This document contains 1 pathway and 3 reactions (see Table of Contents)  

[https://www.reactome.org](https://www.reactome.org)
Autophosphorylated EGFR tyrosine residues are docking sites for many downstream effectors in EGFR signaling. The adaptor protein GRB2 binds to phosphotyrosine residues in the C-tail of EGFR through its SH2 domain. GRB2 is constitutively associated with SOS, a guanine nucleotide exchange factor of RAS. GRB2 binding to phosphorylated EGFR results in the recruitment of SOS to the plasma membrane where it comes in proximity to RAS. This mechanism has been seen to be the model for RAS activation.

**Literature references**


**Editions**

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GRB2-1 binds SOS1

Location: GRB2 events in EGFR signaling

Stable identifier: R-HSA-109813

Type: binding

Compartments: cytosol

In the cytoplasm of unstimulated cells, SOS1 is found in a complex with GRB2. The interaction occurs between the carboxy terminal domain of SOS1 and the Src homology 3 (SH3) domains of GRB2.

Followed by: GRB2:SOS1 complex binds to EGF:EGFR complex

Literature references


Editions

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GRB2:SOS1 complex binds to EGF:EGFR complex

**Location:** GRB2 events in EGFR signaling

**Stable identifier:** R-HSA-177943

**Type:** binding

**Compartments:** cytosol, plasma membrane, extracellular region

Cytoplasmic target proteins containing the SH2 domain can bind to activated EGFR. One such protein, growth factor receptor-bound protein 2 (GRB2), can bind activated EGFR with its SH2 domain whilst in complex with SOS through its SH3 domain. GRB2 can bind at either Y1068 and/or Y1086 tyrosine autophosphorylation sites on the receptor.

**Preceded by:** GRB2-1 binds SOS1

**Followed by:** SOS1-mediated nucleotide exchange of RAS (EGF:EGFR:GRB2:SOS1)

**Literature references**


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The guanine nucleotide exchange factor SOS1 interacts with EGFR through the adaptor protein, GRB2. Upon formation of this complex, SOS activates RAS by promoting GDP release and GTP binding.

**Preceded by**: GRB2:SOS1 complex binds to EGF:EGFR complex

**Literature references**


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