EGFR downregulation

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.

03/05/2024

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. ↗

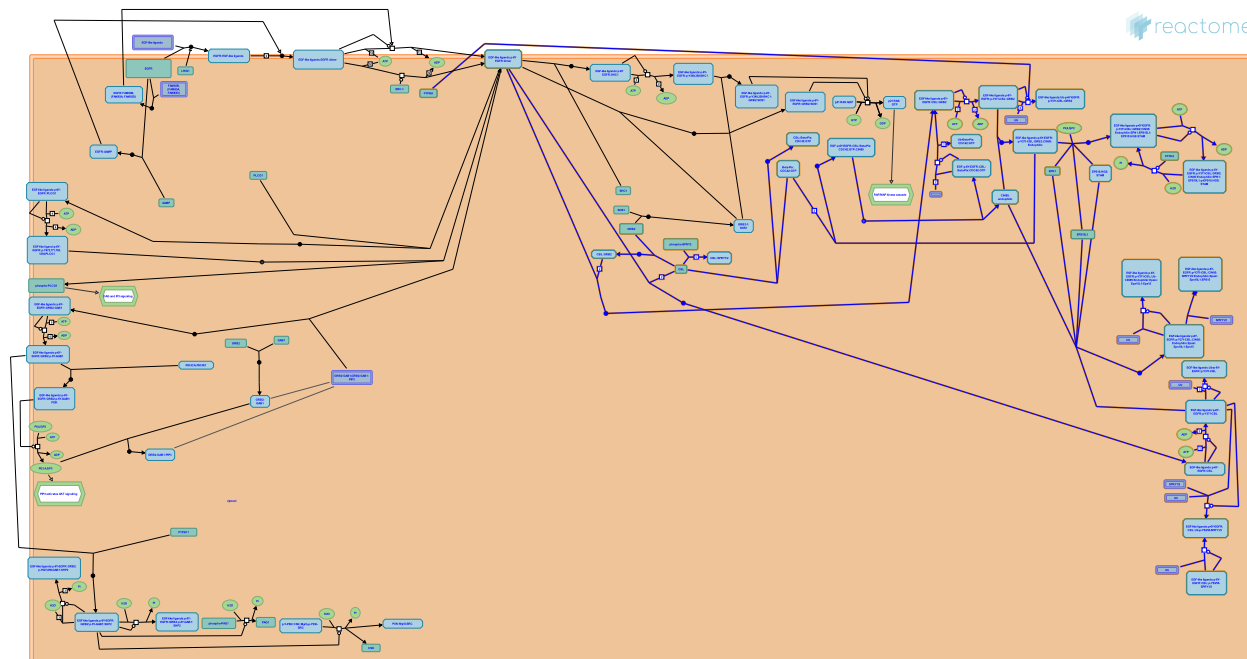Reactome database release: 88

This document contains 1 pathway and 21 reactions (see Table of Contents)

EGFR downregulation ↗

Stable identifier: R-BTA-182971

Inferred from: EGFR downregulation (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp
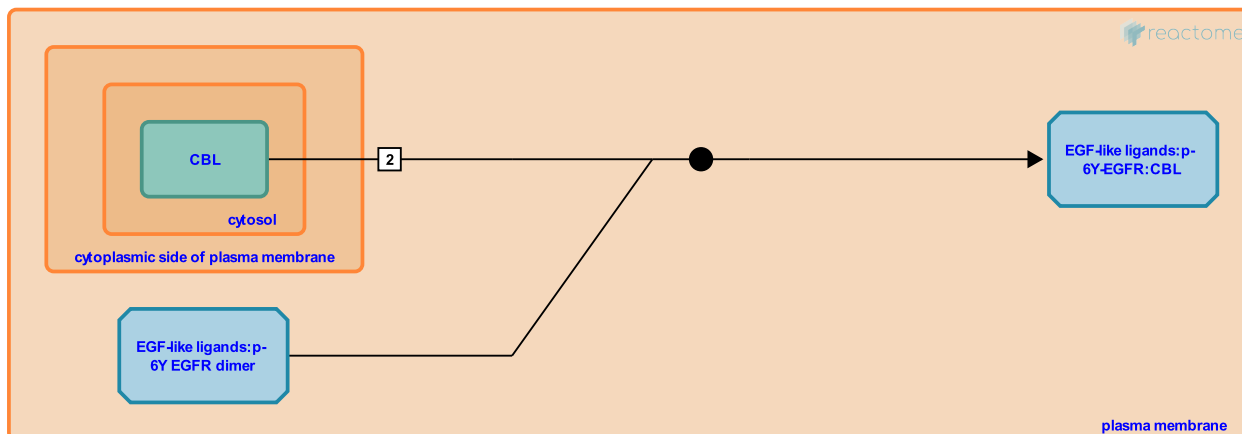
Binding of CBL to EGFR ↗

Location: EGFR downregulation

Stable identifier: R-BTA-183055

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: Binding of CBL to EGFR (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: Phosphorylation of CBL (EGFR:CBL)

Phosphorylation of CBL (EGFR:CBL) ↗
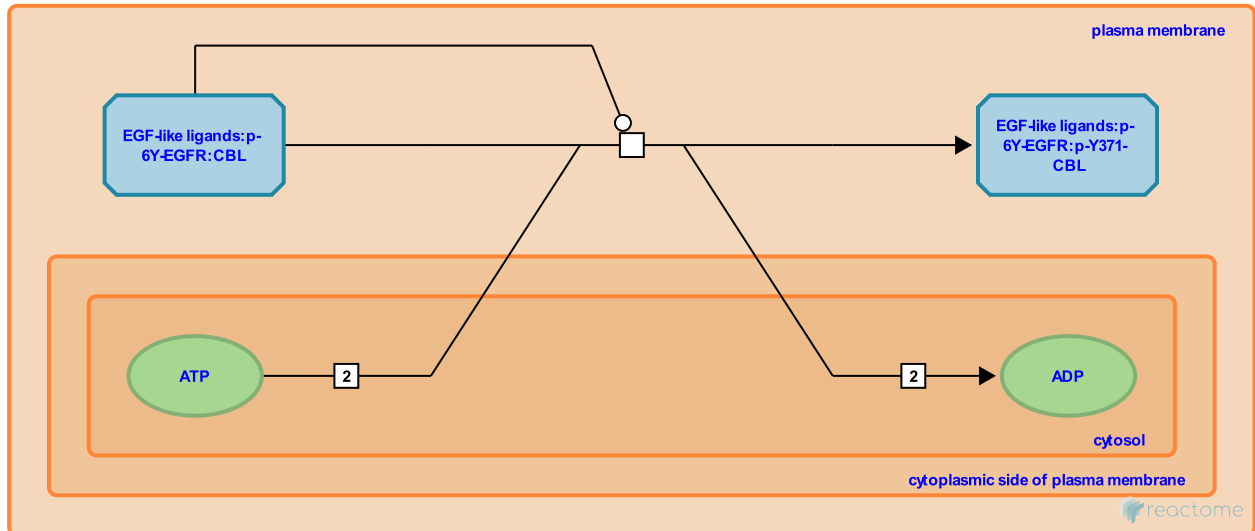
Location: EGFR downregulation

Stable identifier: R-BTA-182969

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Phosphorylation of CBL (EGFR:CBL) (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: Binding of CBL to EGFR

Followed by: Ubiquitination of stimulated EGFR (CBL), CBL binds and ubiquitinates phosphorylated Sprouty
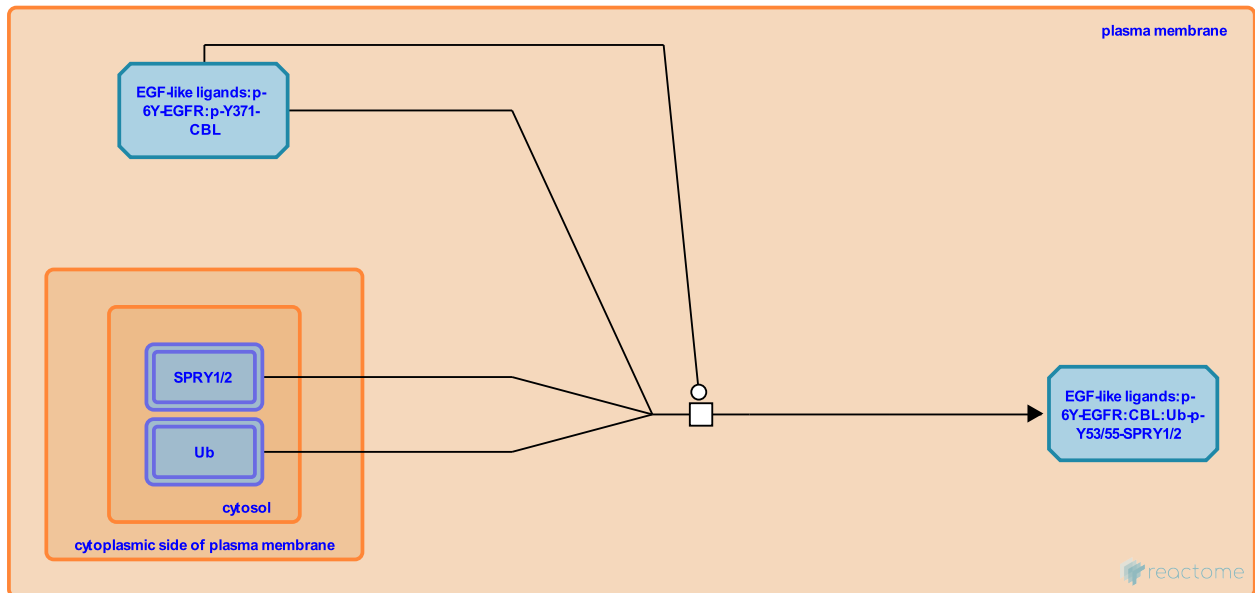
CBL binds and ubiquitinates phosphorylated Sprouty ↗

Location: EGFR downregulation

Stable identifier: R-BTA-183089

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: CBL binds and ubiquitinates phosphorylated Sprouty (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: Phosphorylation of CBL (EGFR:CBL)

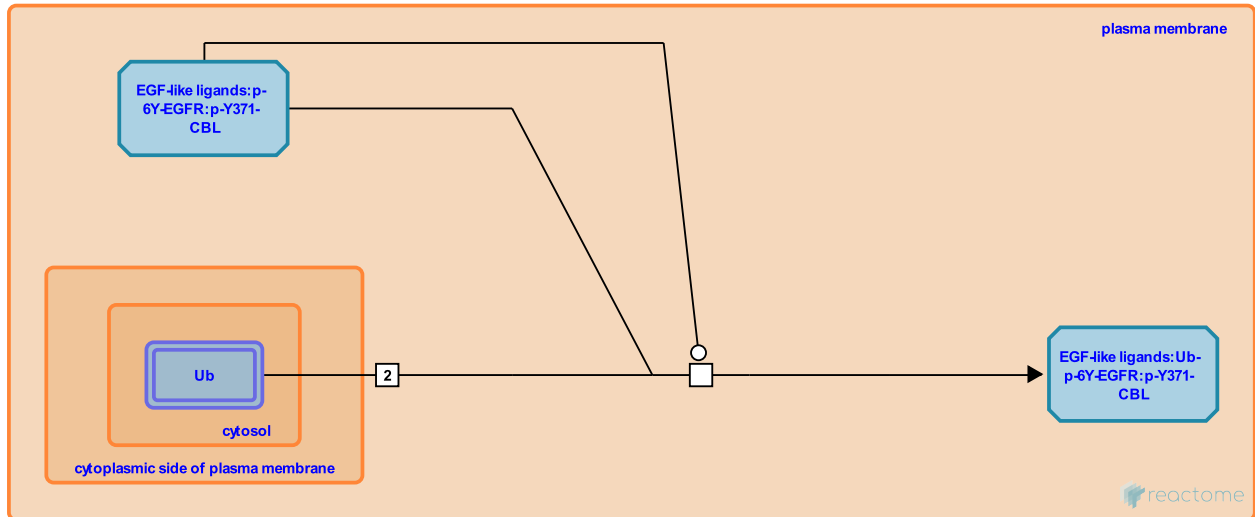# Ubiquitination of stimulated EGFR (CBL) ↗

Location: EGFR downregulation

Stable identifier: R-BTA-182993

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Ubiquitination of stimulated EGFR (CBL) (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: Phosphorylation of CBL (EGFR:CBL)
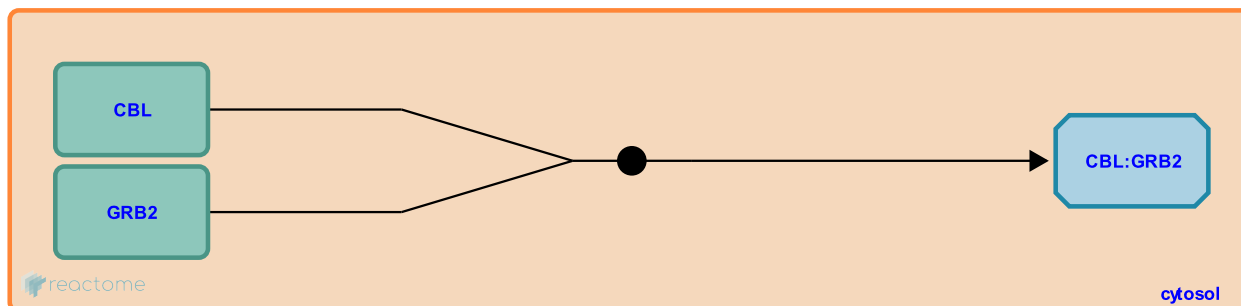
CBL binds to GRB2 ↗

Location: EGFR downregulation

Stable identifier: R-BTA-183052

Type: binding

Compartments: cytosol

Inferred from: CBL binds to GRB2 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: Localization of CBL:GRB2 to the membrane
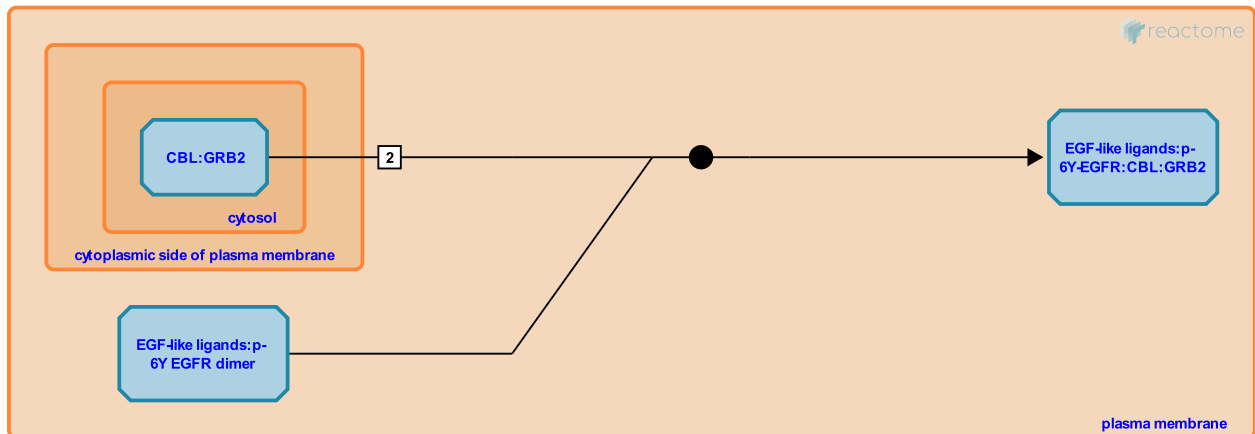
Localization of CBL:GRB2 to the membrane ↗

Location: EGFR downregulation

Stable identifier: R-BTA-183067

Type: binding

Compartments: plasma membrane, extracellular region, cytosol

Inferred from: Localization of CBL:GRB2 to the membrane (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: CBL binds to GRB2

Followed by: Phosphorylation of CBL (EGFR:GRB2:CBL)

Phosphorylation of CBL (EGFR:GRB2:CBL) ↗
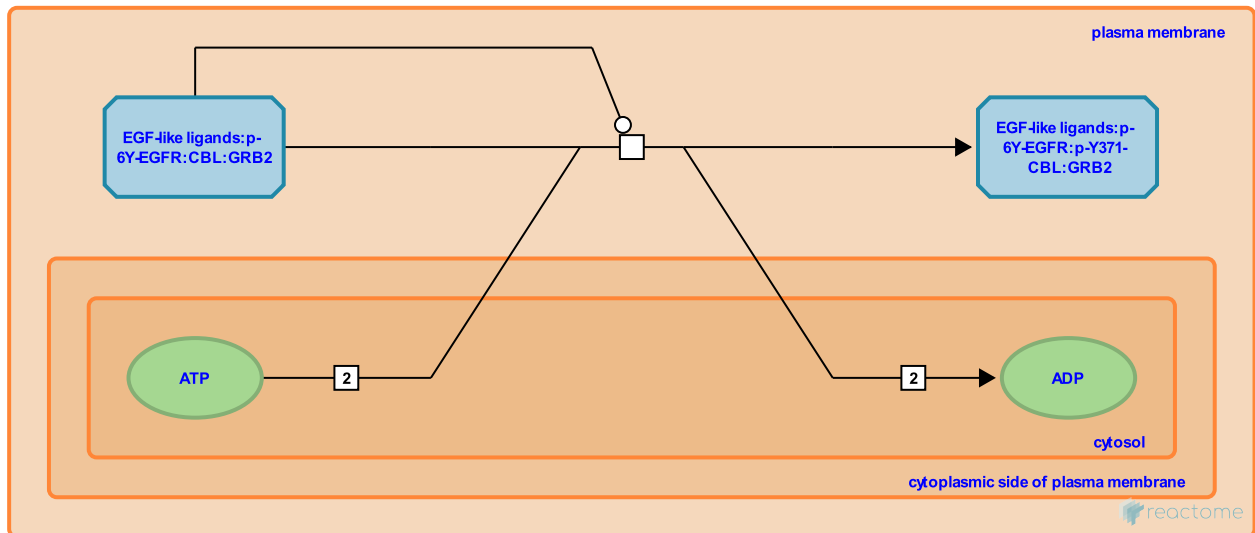
Location: EGFR downregulation

Stable identifier: R-BTA-183058

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Phosphorylation of CBL (EGFR:GRB2:CBL) (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: Localization of CBL:GRB2 to the membrane

Followed by: Ubiquitination of stimulated EGFR (CBL:GRB2)

Ubiquitination of stimulated EGFR (CBL:GRB2) ↗

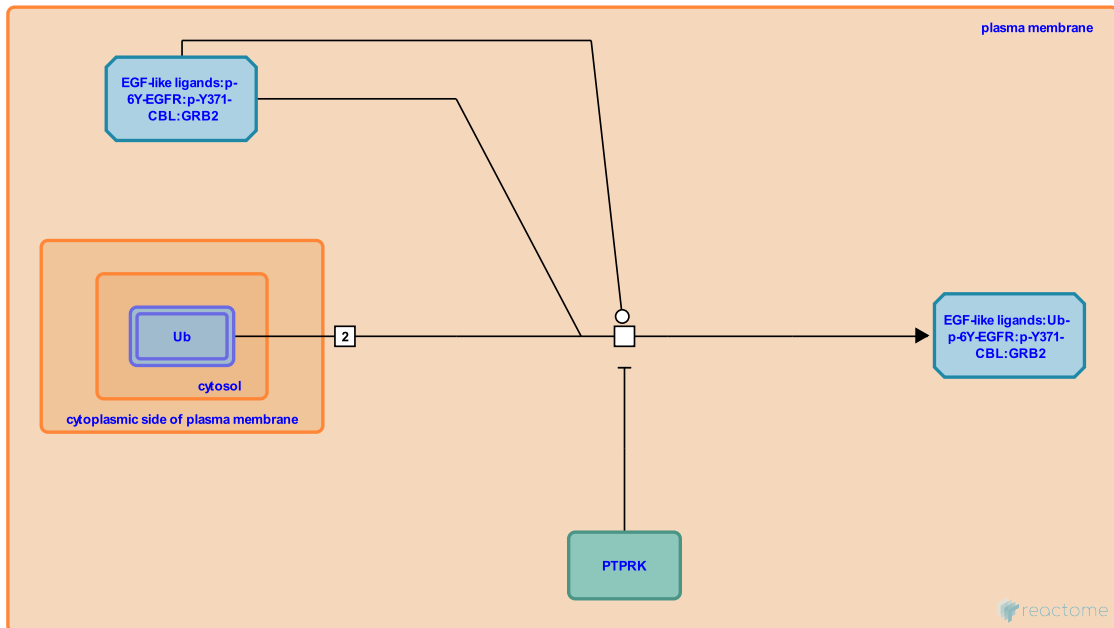**Location:** EGFR downregulation

Stable identifier: R-BTA-183036

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Ubiquitination of stimulated EGFR (CBL:GRB2) (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: Phosphorylation of CBL (EGFR:GRB2:CBL)

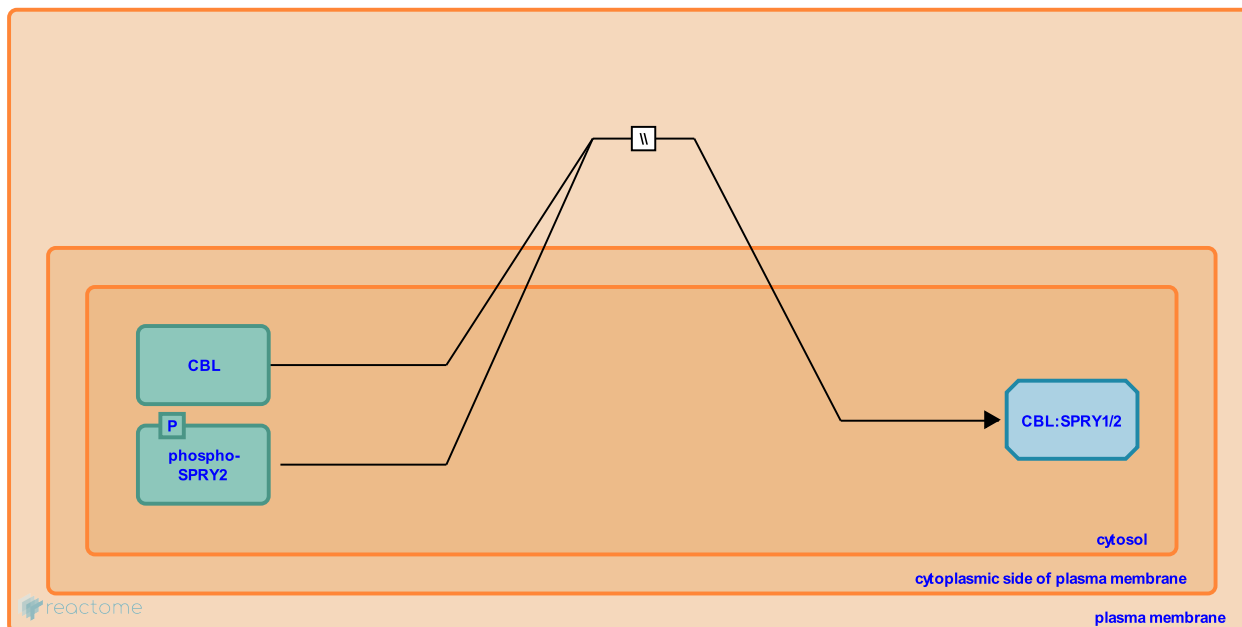# Sprouty lures CBL away from EGFR ↗

Location: EGFR downregulation

Stable identifier: R-BTA-182988

Type: omitted

Compartments: plasma membrane

Inferred from: Sprouty lures CBL away from EGFR (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

CDC42:GTP binds CBL:Beta-Pix ↗
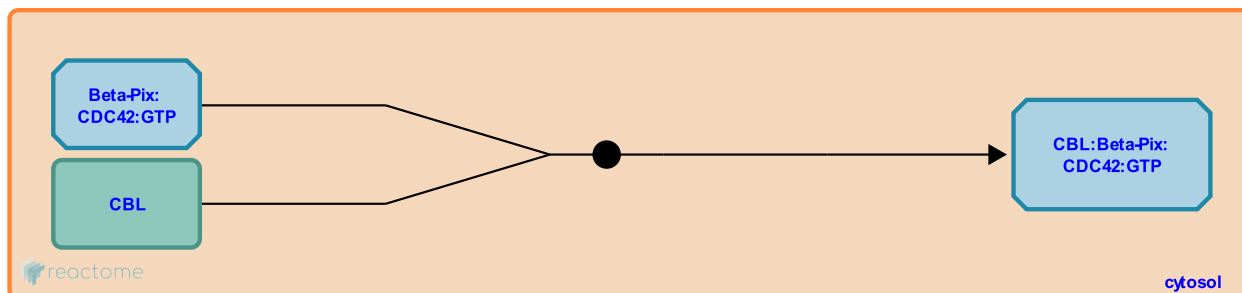
Location: EGFR downregulation

Stable identifier: R-BTA-183094

Type: binding

Compartments: cytosol

Inferred from: CDC42:GTP binds CBL:Beta-Pix (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Beta-Pix:CDC42:GTP binds CBL in EGF:p-6Y-EGFR:CBL:CIN85 ↗
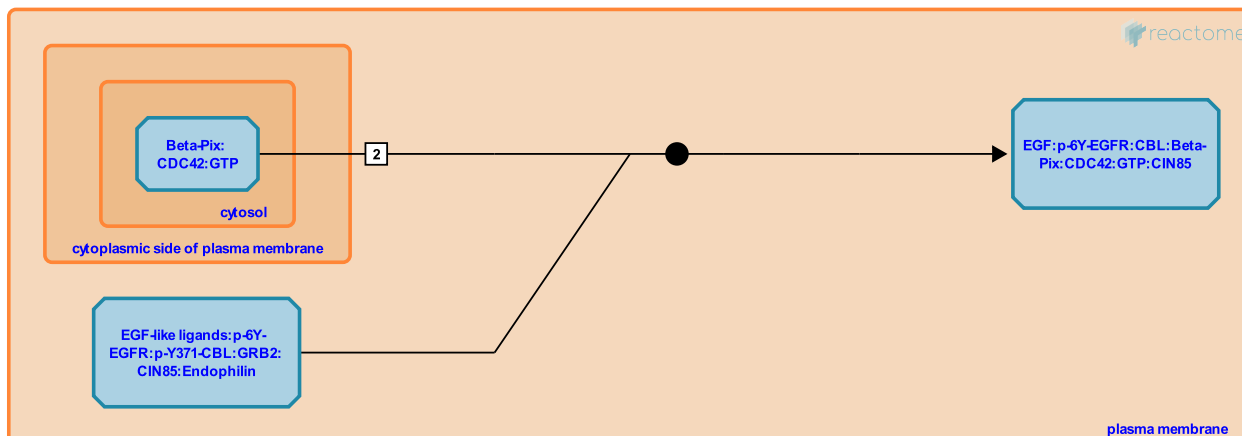
Location: EGFR downregulation

Stable identifier: R-BTA-183002

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: Beta-Pix:CDC42:GTP binds CBL in EGF:p-6Y-EGFR:CBL:CIN85 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: CIN85 dissociates from EGF:p-6Y-EGFR:CBL:Beta-Pix:CDC42:GTP:CIN85

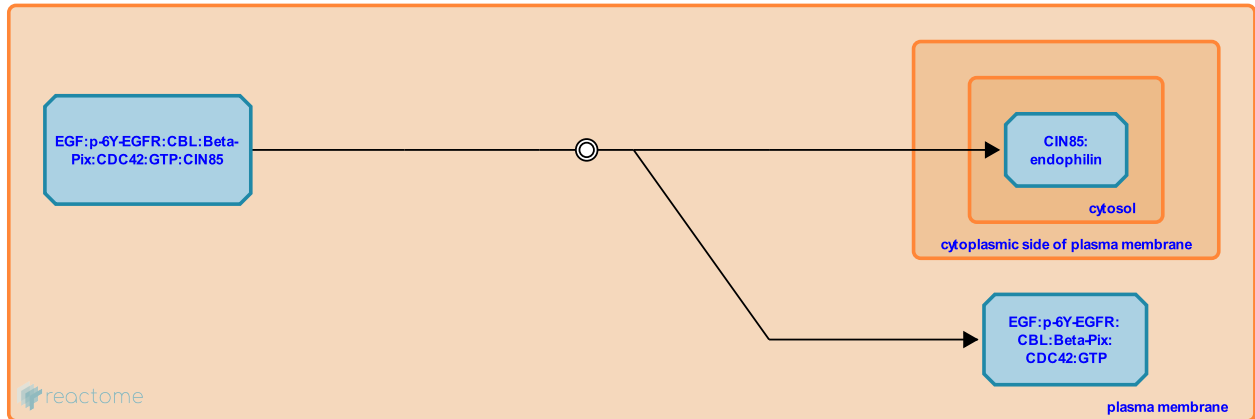## CIN85 dissociates from EGF:p-6Y-EGFR:CBL:Beta-Pix:CDC42:GTP:CIN85 ↗

Location: EGFR downregulation

Stable identifier: R-BTA-8951490

Type: dissociation

Compartments: plasma membrane, cytosol

Inferred from: CIN85 dissociates from EGF:p-6Y-EGFR:CBL:Beta-Pix:CDC42:GTP:CIN85 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: Beta-Pix:CDC42:GTP binds CBL in EGF:p-6Y-EGFR:CBL:CIN85

Followed by: CBL escapes CDC42-mediated inhibition by down-regulating the adaptor molecule Beta-Pix

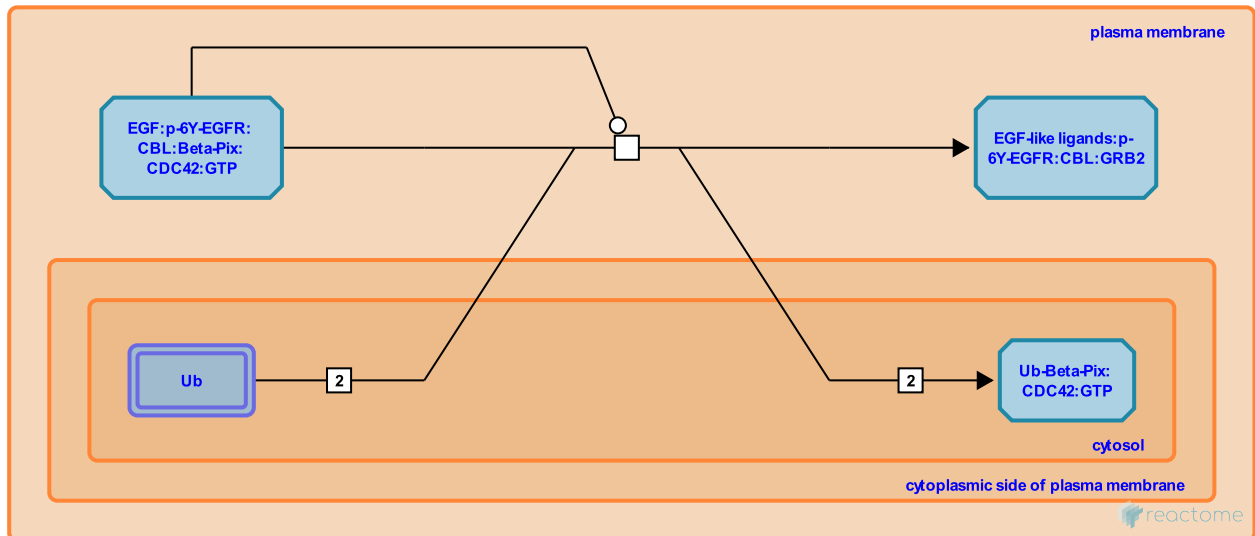## CBL escapes CDC42-mediated inhibition by down-regulating the adaptor molecule Beta-Pix ↗

Location: EGFR downregulation

Stable identifier: R-BTA-183084

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: CBL escapes CDC42-mediated inhibition by down-regulating the adaptor molecule Beta-Pix (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: CIN85 dissociates from EGF:p-6Y-EGFR:CBL:Beta-Pix:CDC42:GTP:CIN85
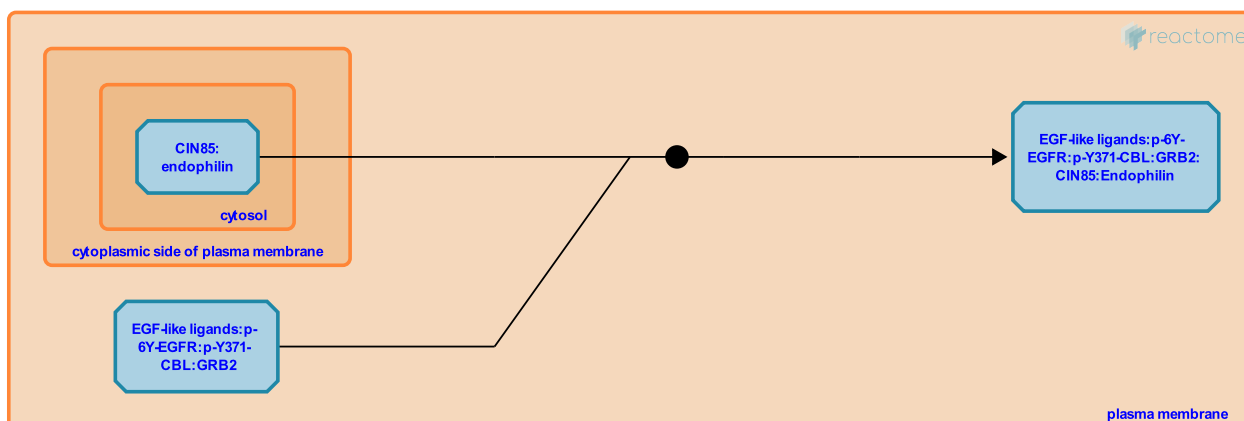
## Assembly of EGFR complex in clathrin-coated vesicles ↗

Location: EGFR downregulation

Stable identifier: R-BTA-182994

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: Assembly of EGFR complex in clathrin-coated vesicles (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: EGFR binds EPS15, EPN1, EPS15L1

EGFR non-clathrin mediated endocytosis ↗

Location: EGFR downregulation

Stable identifier: R-BTA-183072

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: EGFR non-clathrin mediated endocytosis (Homo sapiens)
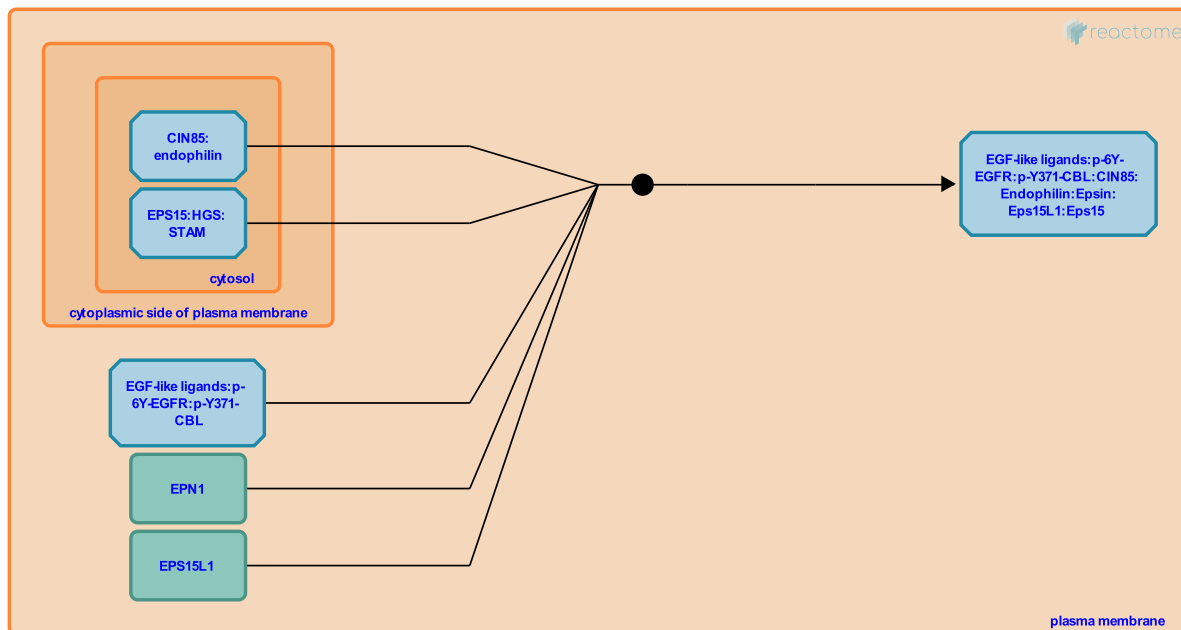
This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: Sprouty sequesters CBL away from active EGFR, CBL-mediated ubiquitination of CIN85

CBL ubiquitinates Sprouty ↗

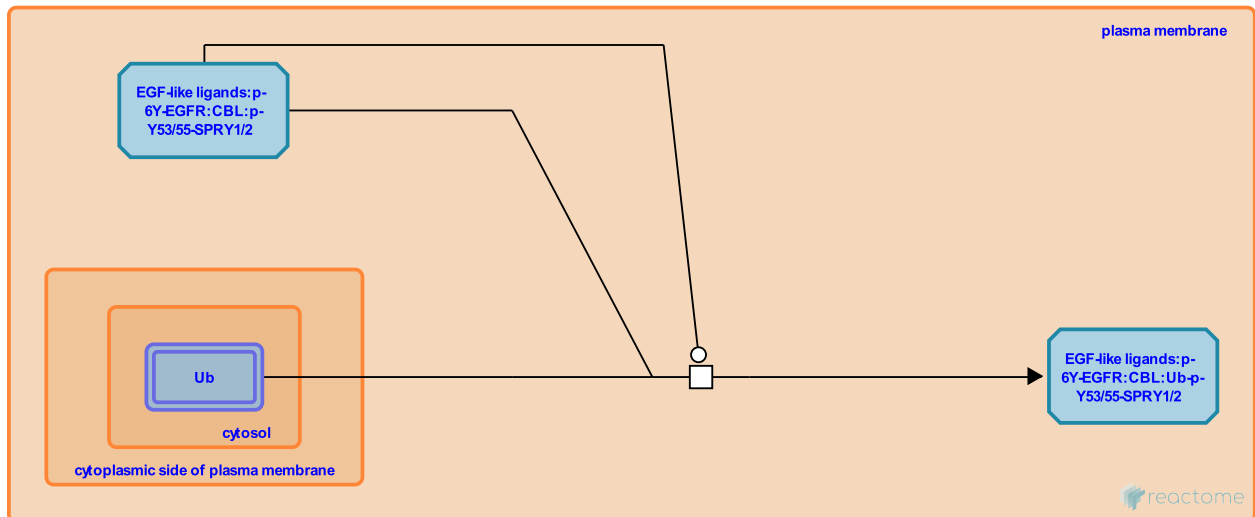**Location:** EGFR downregulation

Stable identifier: R-BTA-183051

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: CBL ubiquitinates Sprouty (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

CBL-mediated ubiquitination of CIN85 ↗

Location: EGFR downregulation

Stable identifier: R-BTA-182986

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: CBL-mediated ubiquitination of CIN85 (Homo sapiens)
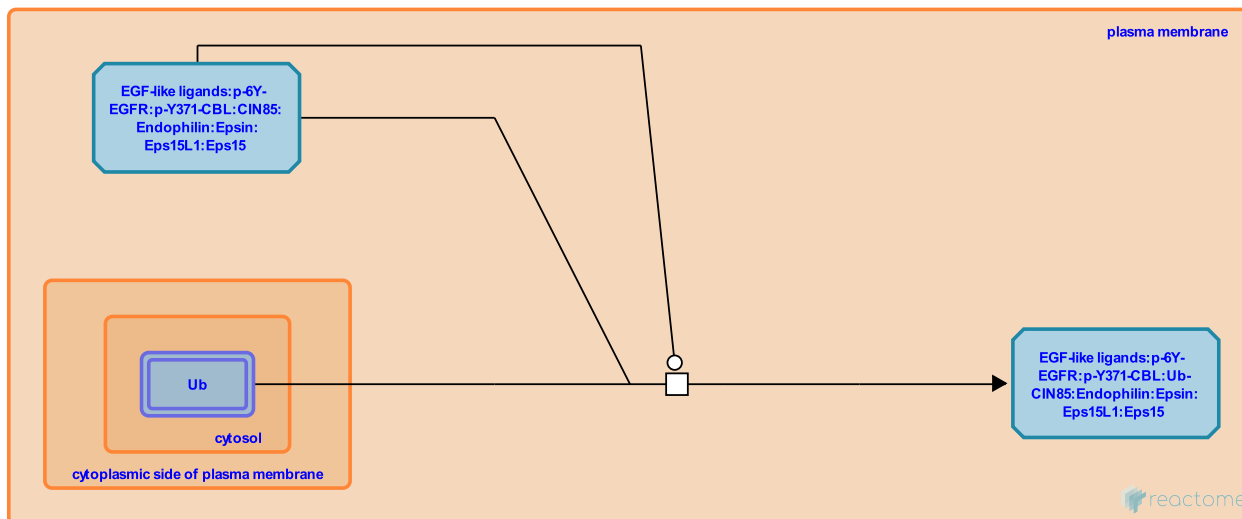
This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: EGFR non-clathrin mediated endocytosis

Sprouty sequesters CBL away from active EGFR ↗
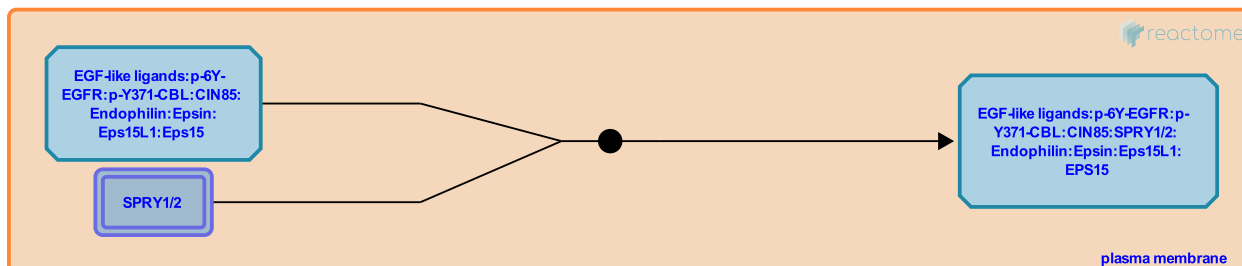
Location: EGFR downregulation

Stable identifier: R-BTA-182990

Type: binding

Compartments: plasma membrane

Inferred from: Sprouty sequesters CBL away from active EGFR (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: EGFR non-clathrin mediated endocytosis
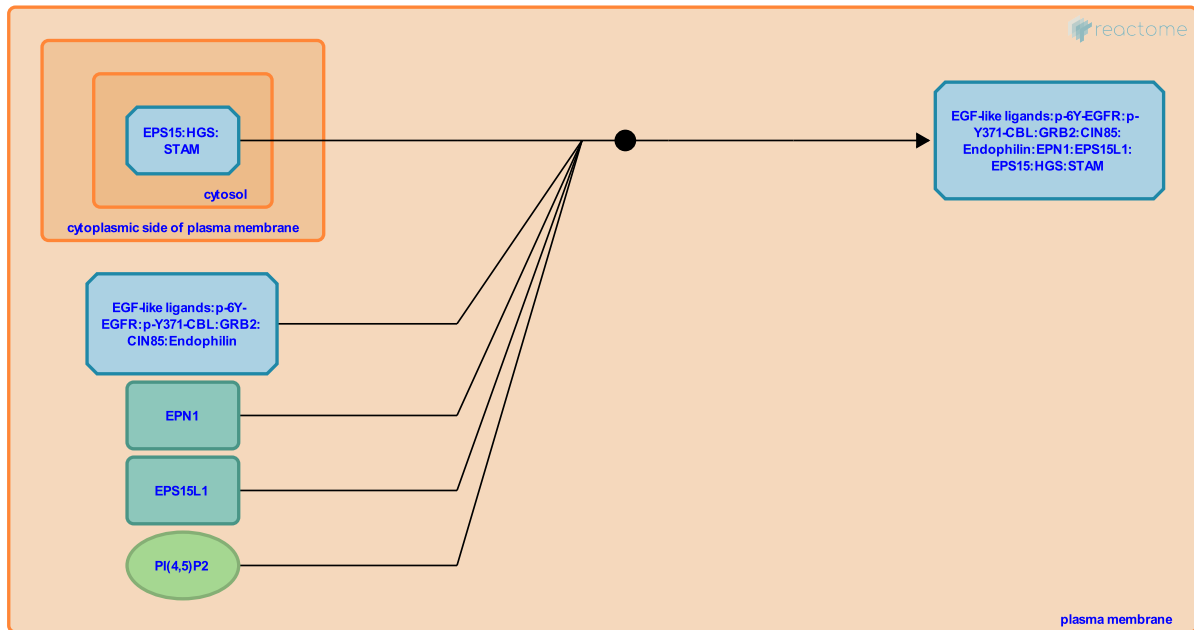
EGFR binds EPS15, EPN1, EPS15L1 ↗

Location: EGFR downregulation

Stable identifier: R-BTA-8867044

Type: binding

Compartments: plasma membrane

Inferred from: EGFR binds EPS15, EPN1, EPS15L1 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: Assembly of EGFR complex in clathrin-coated vesicles

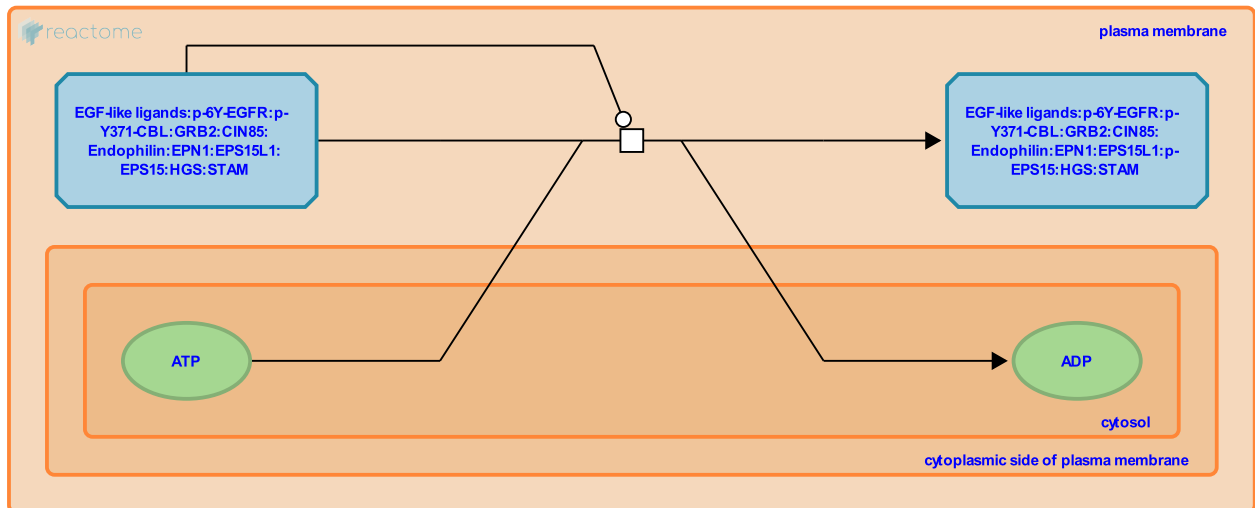**Followed by:** EGFR phosphorylates EPS15

EGFR phosphorylates EPS15 ↗

Location: EGFR downregulation

Stable identifier: R-BTA-8867041

Type: transition

Compartments: plasma membrane

Inferred from: EGFR phosphorylates EPS15 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: EGFR binds EPS15, EPN1, EPS15L1

Followed by: PTPN3 dephosphorylates EPS15
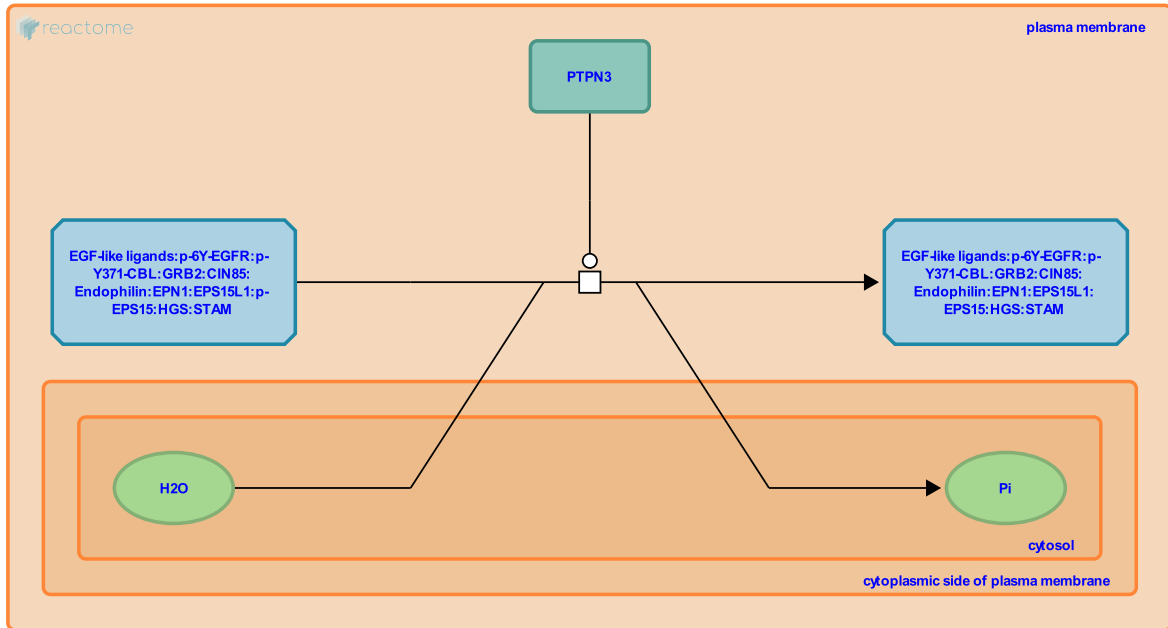
PTPN3 dephosphorylates EPS15 ↗

Location: EGFR downregulation

Stable identifier: R-BTA-8867047

Type: transition

Compartments: plasma membrane

Inferred from: PTPN3 dephosphorylates EPS15 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: EGFR phosphorylates EPS15

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