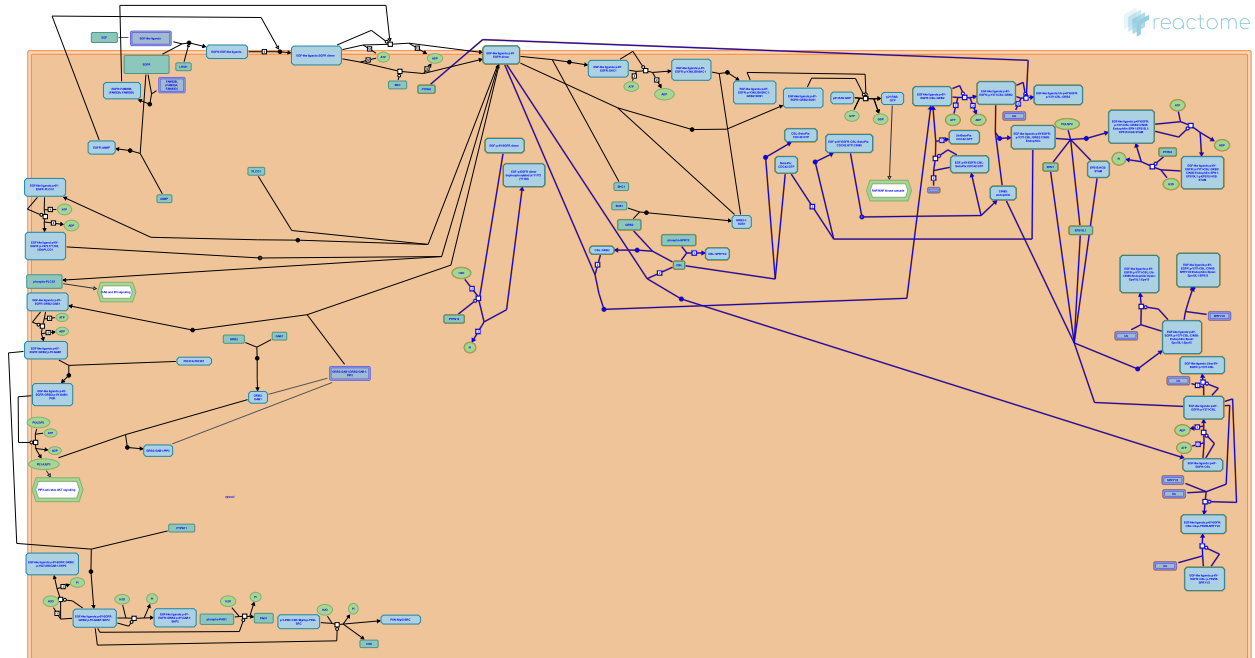


# EGFR downregulation



European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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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](https://reactome.org/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

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- 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. [↗](#)

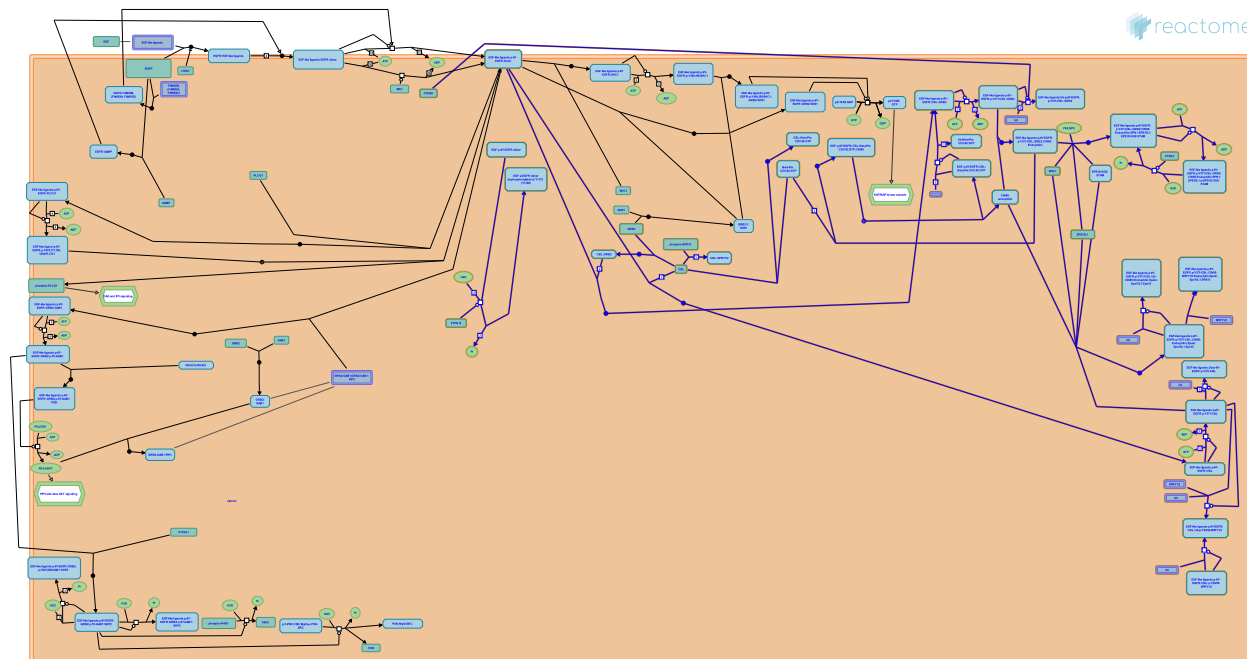
Reactome database release: 88

This document contains 1 pathway and 22 reactions ([see Table of Contents](#))

## EGFR downregulation ↗

**Stable identifier:** R-CFA-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 ↗

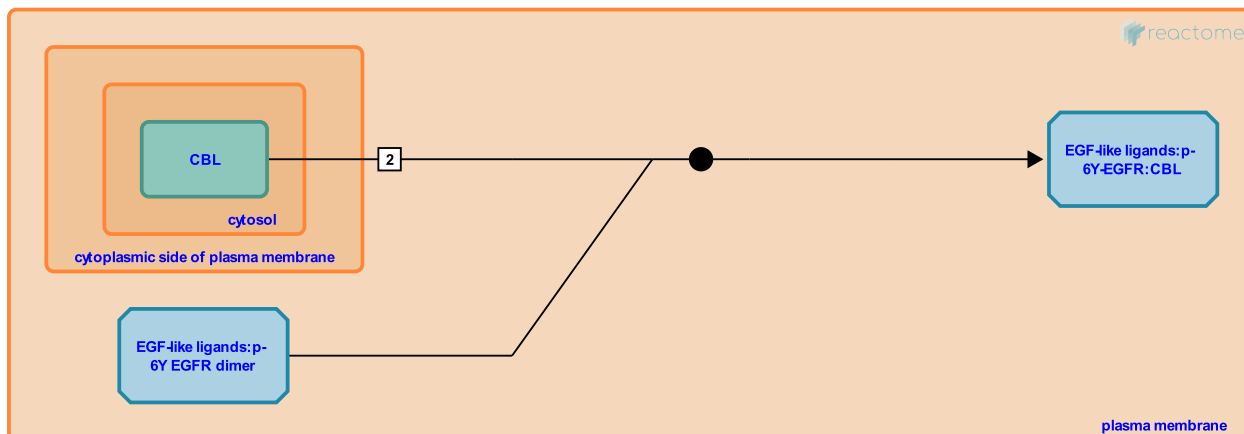
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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) ↗

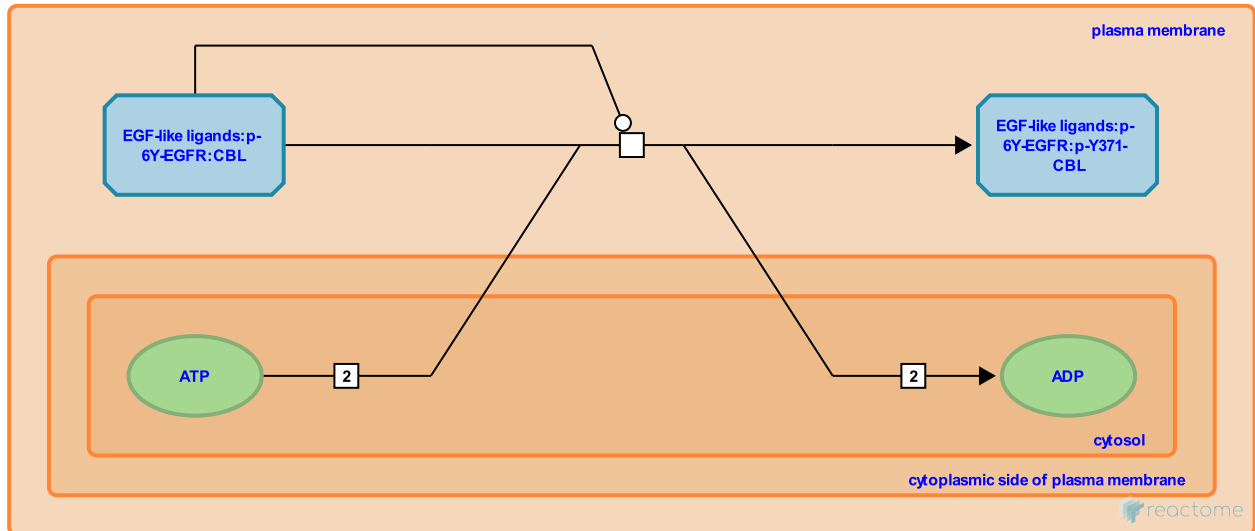
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

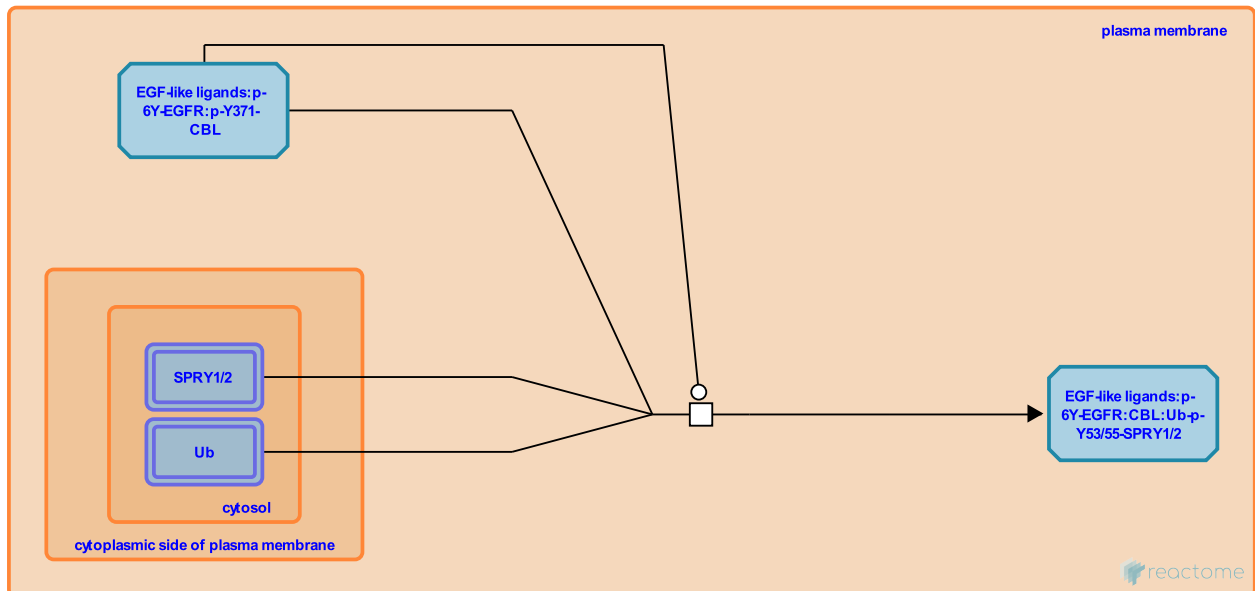
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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) ↗

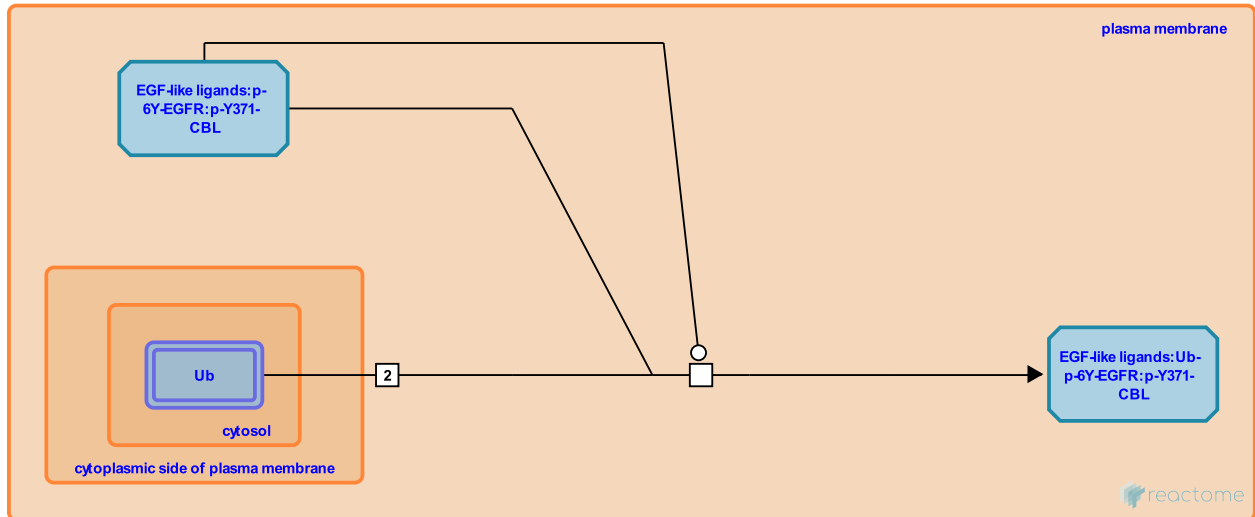
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

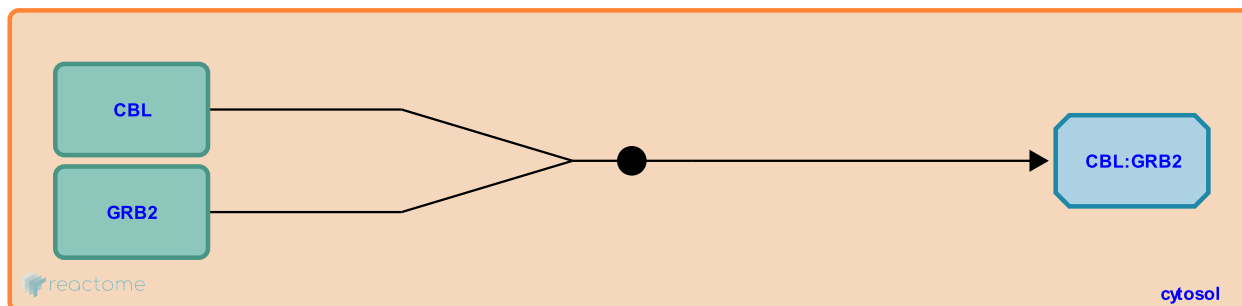
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

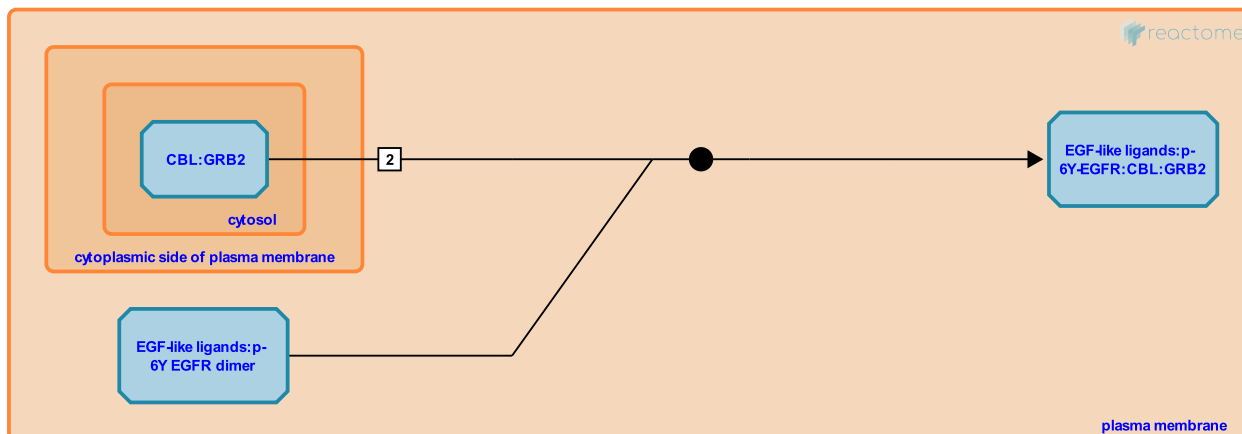
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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) ↗

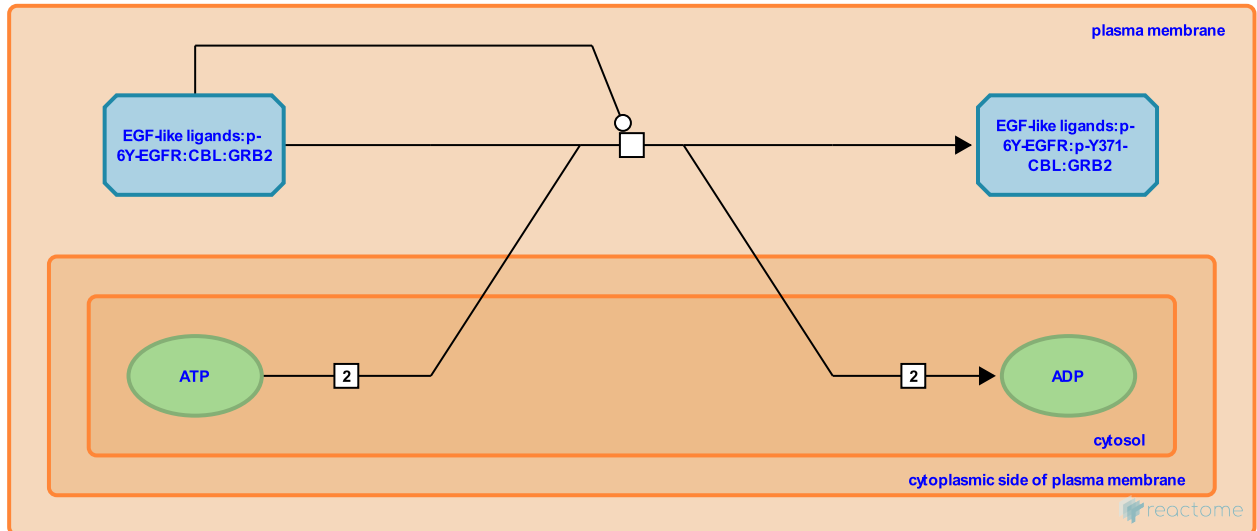
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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) ↗

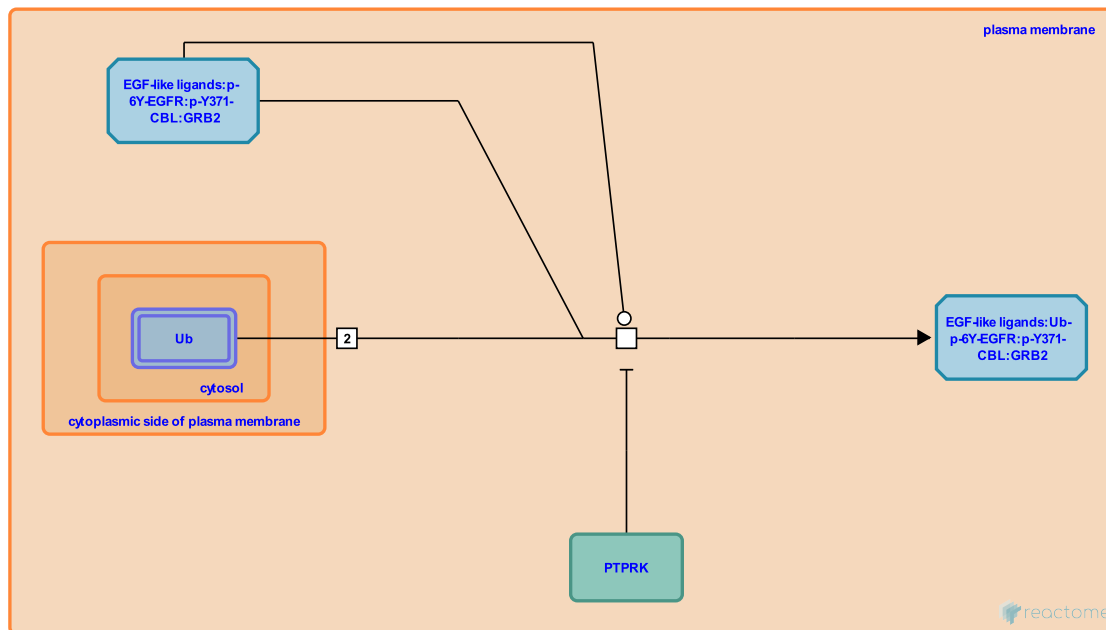
**Location:** EGFR downregulation

**Stable identifier:** R-CFA-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.](http://www.pantherdb.org/about.jsp) 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 ↗

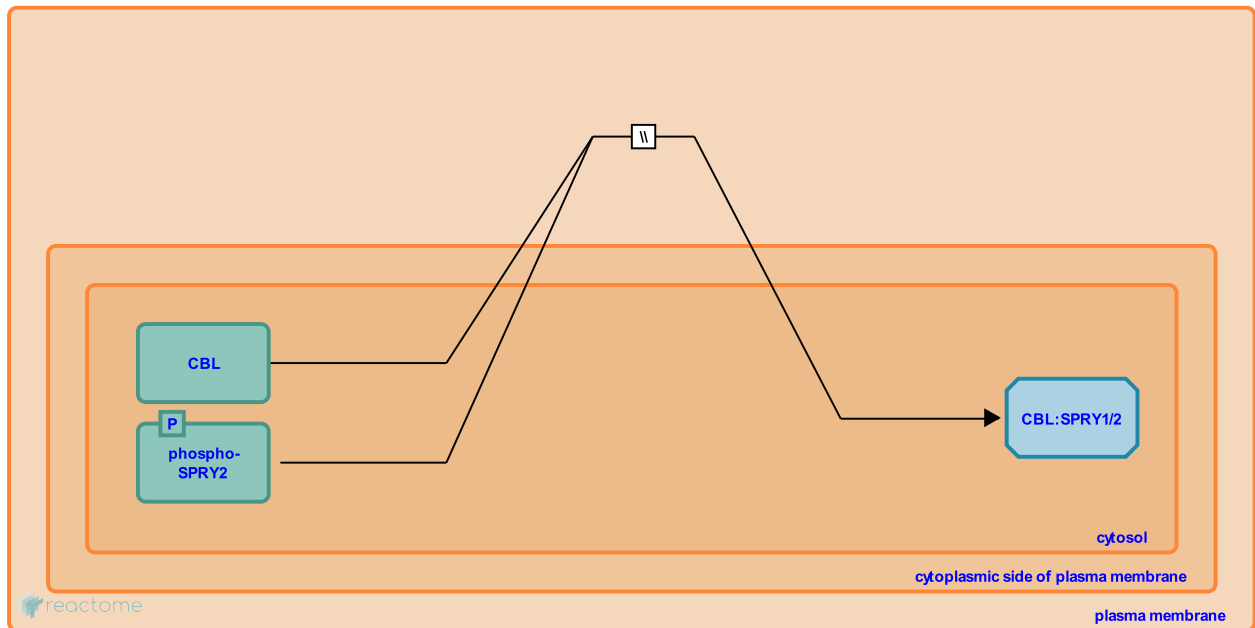
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

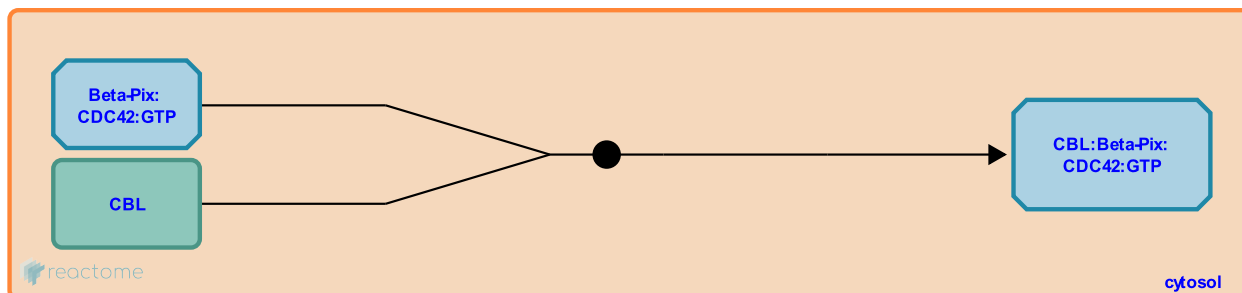
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

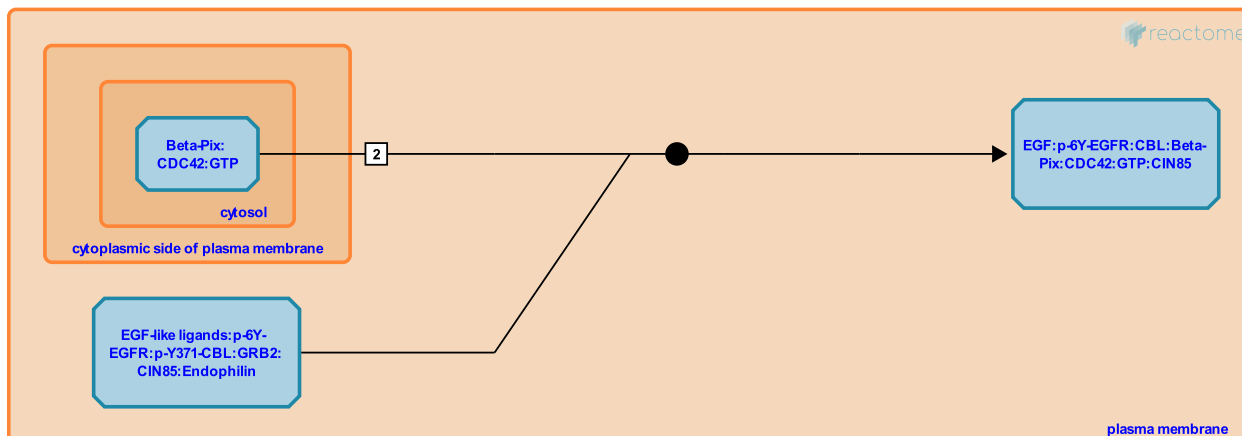
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

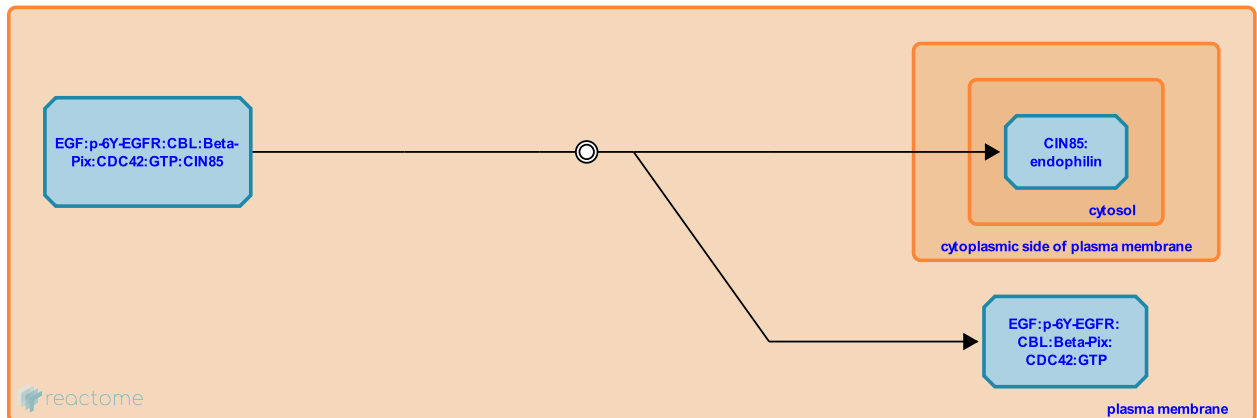
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

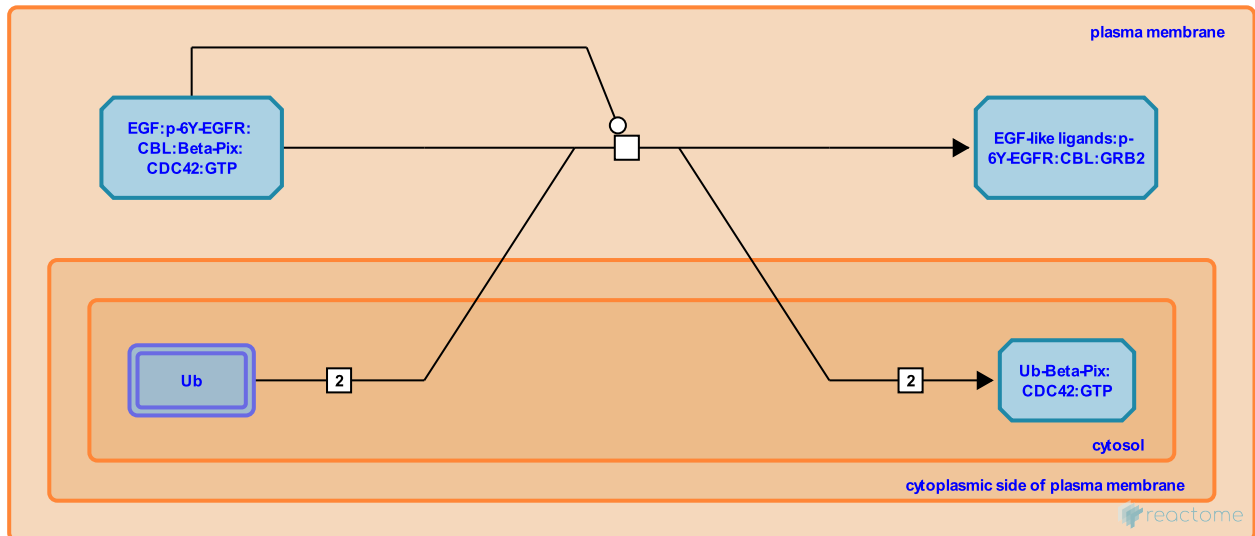
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

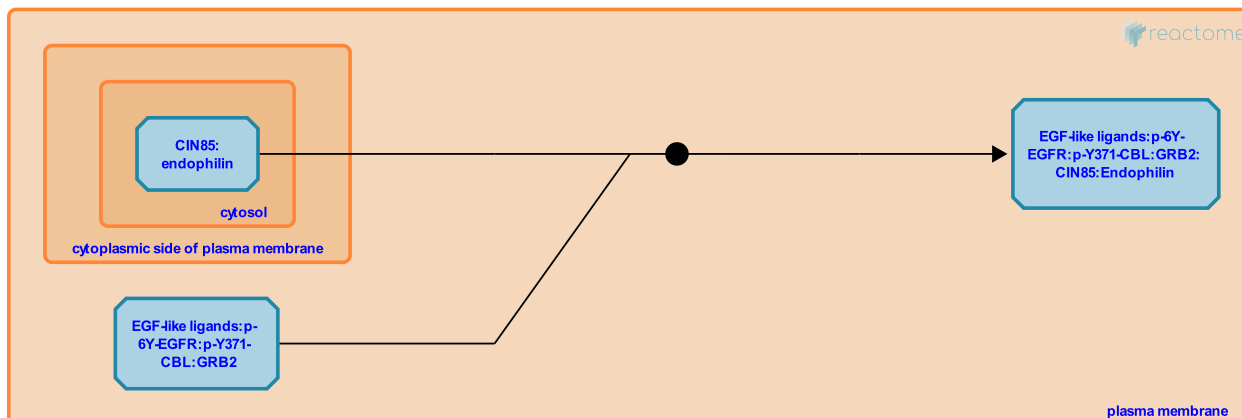
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

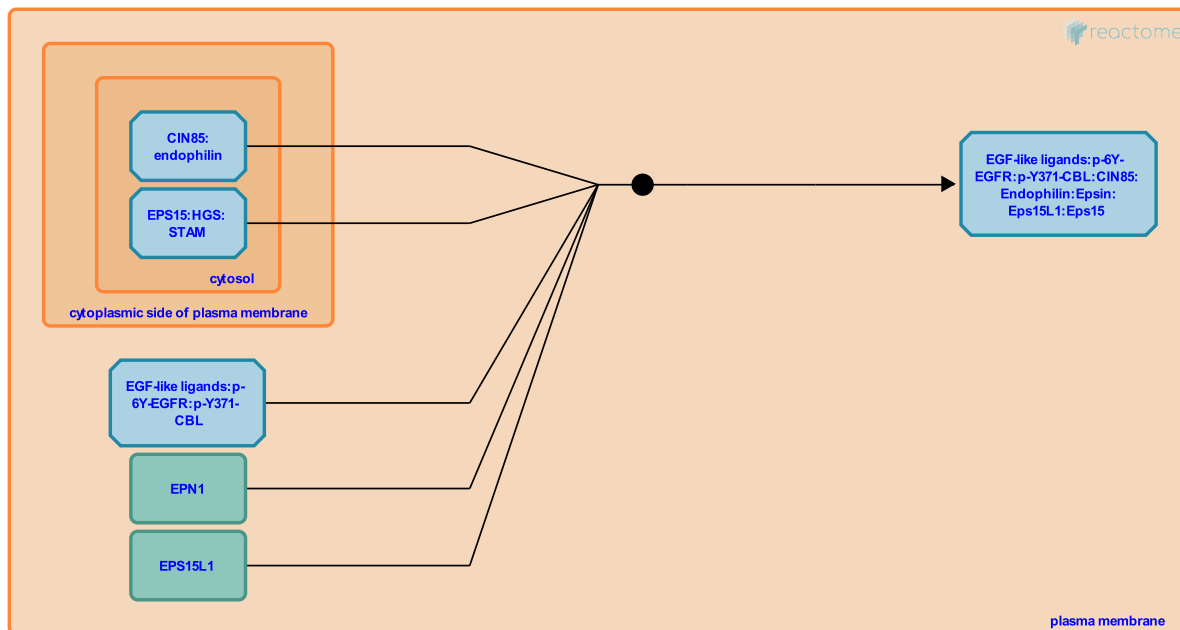
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 [↗](#)

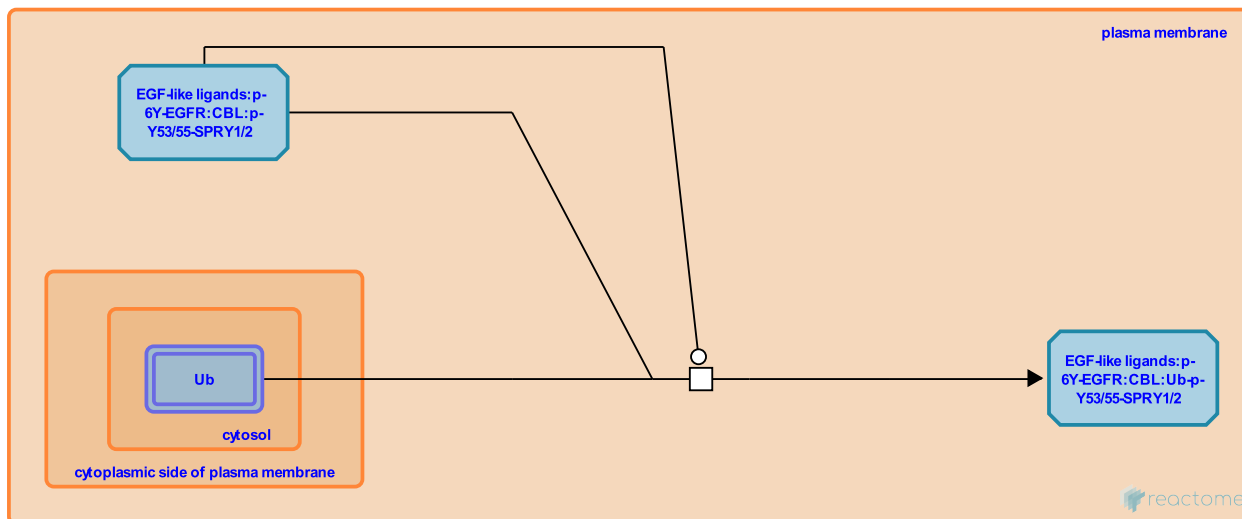
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

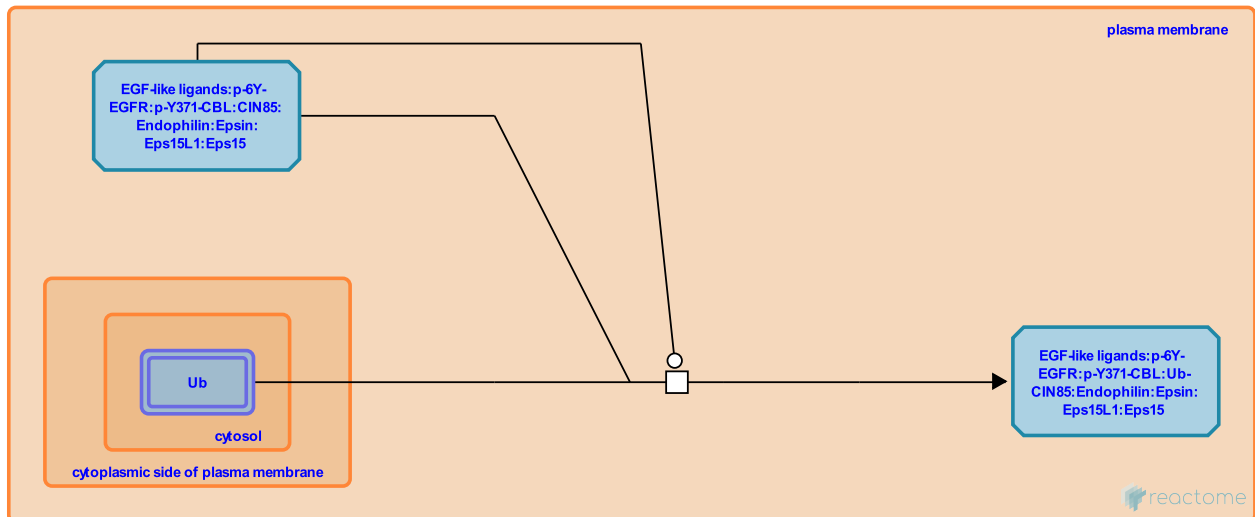
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

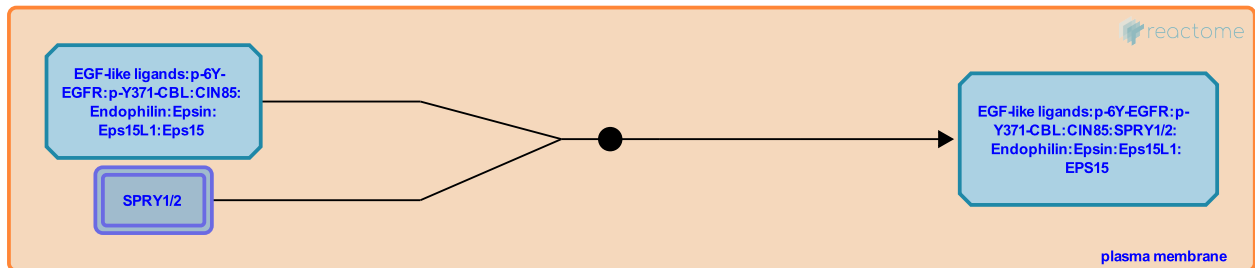
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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](#)

## PTPN12 dephosphorylates EGFR at Y1172 (Y1148) ↗

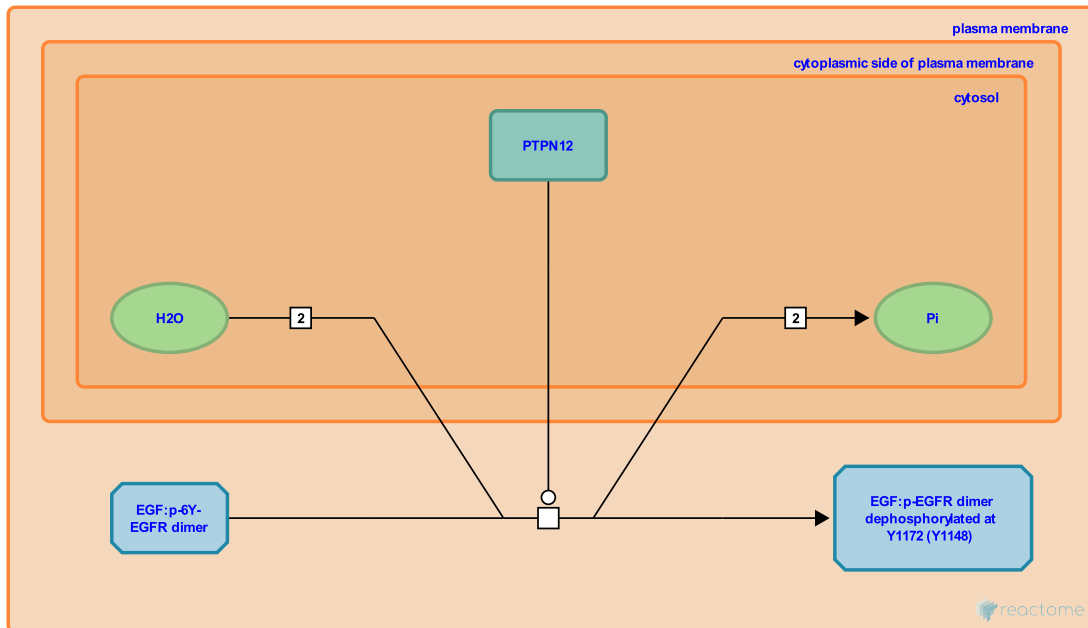
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-8864029

**Type:** transition

**Compartments:** plasma membrane, cytosol

**Inferred from:** [PTPN12 dephosphorylates EGFR at Y1172 \(Y1148\) \(Homo sapiens\)](#)



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>

## EGFR binds EPS15, EPN1, EPS15L1 ↗

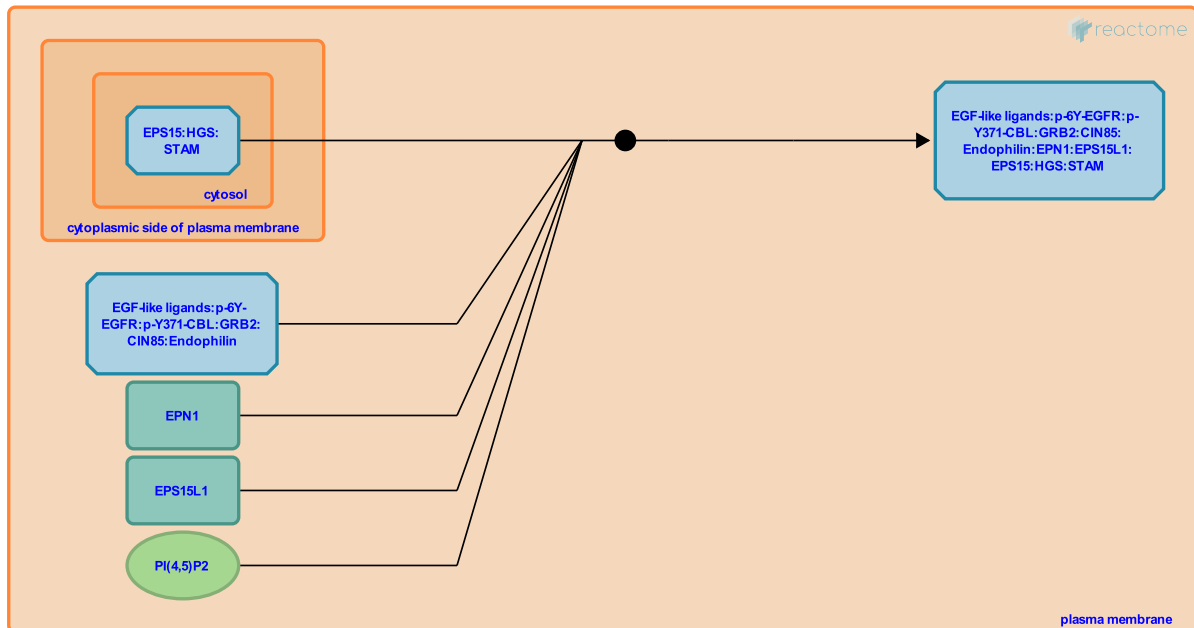
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

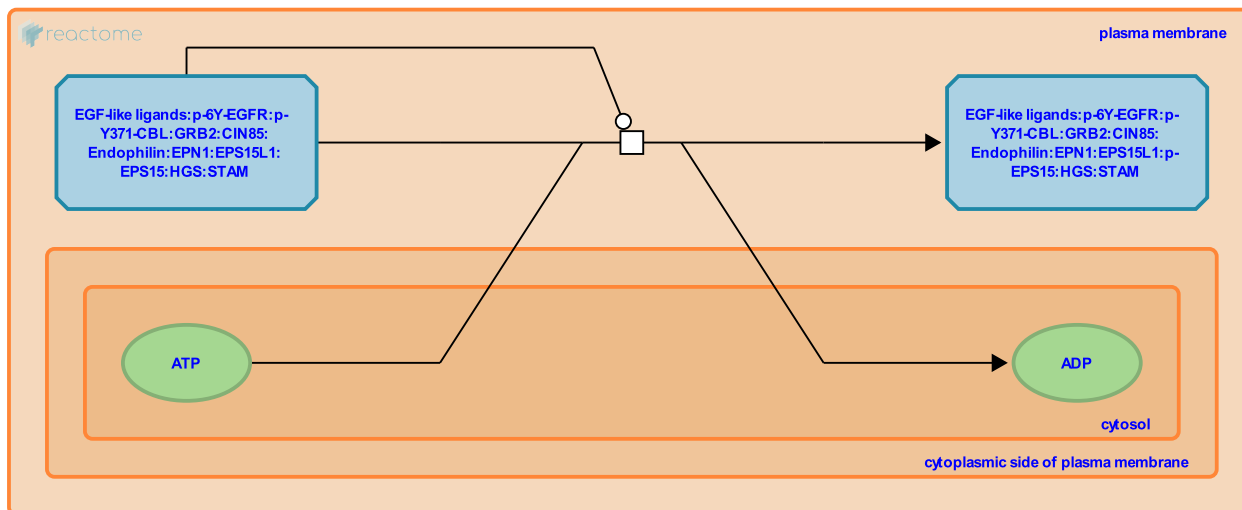
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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 ↗

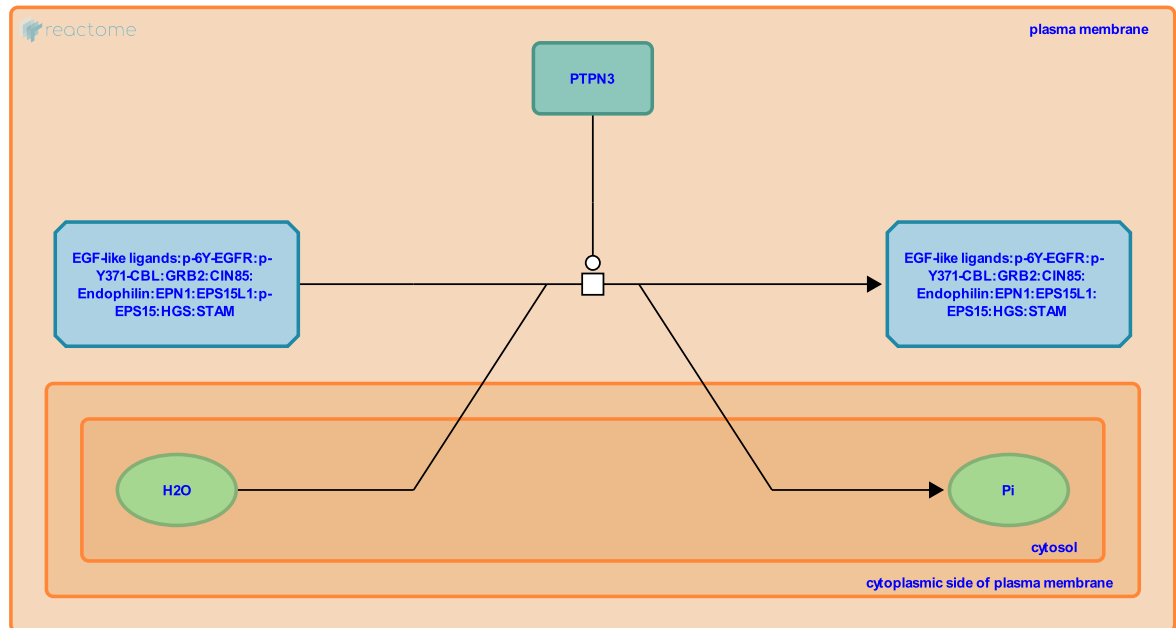
**Location:** [EGFR downregulation](#)

**Stable identifier:** R-CFA-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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