

# Ubiquitination of stimulated EGFR (CBL:GRB2)

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## 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.

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## Literature references

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Reactome database release: 88

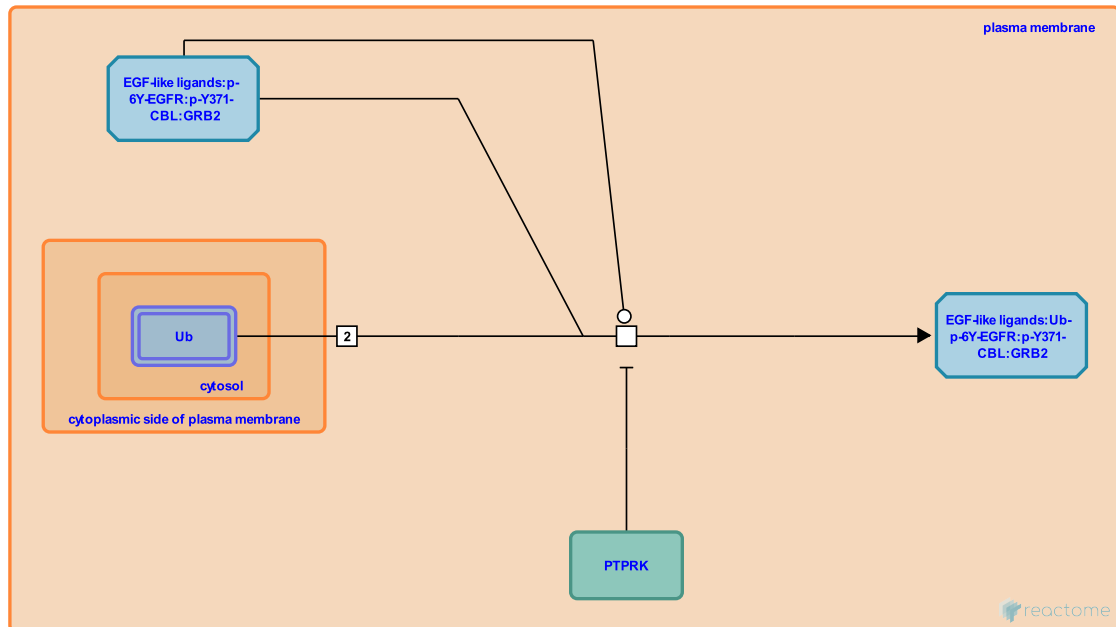
This document contains 1 reaction ([see Table of Contents](#))

## Ubiquitination of stimulated EGFR (CBL:GRB2) ↗

**Stable identifier:** R-HSA-183036

**Type:** transition

**Compartments:** cytosol, plasma membrane



CBL down-regulates receptor tyrosine kinases by conjugating ubiquitin to them. This leads to receptor internalization and degradation. The ubiquitin protein ligase activity of CBL (abbreviated as E3 activity) is mediated by its RING finger domain. Receptor-type tyrosine-protein phosphatase kappa (PTPRK/RPTPk/DEP1) dephosphorylates EGFR, thereby inhibiting receptor ubiquitylation (Ub) by c-CBL, which decelerates the rate of receptor internalization and diminishes MAPK signals generated at the membrane and in endosomes. PTPRK disrupts physical association of ubiquitin ligase complex with EGFR and impairs its internalization (Tarcic et al. 2009, Xu et al. 2005).

### Literature references

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Huang, H., Liu, YC., Hunter, T., Levenson, JD., Wing, SS., Joazeiro, CA. (1999). The tyrosine kinase negative regulator c-Cbl as a RING-type, E2-dependent ubiquitin-protein ligase. *Science*, 286, 309-12. ↗

### Editions

2006-10-10	Authored	Castagnoli, L.
2008-02-12	Reviewed	Heldin, CH.
2011-08-25	Edited	Orlic-Milacic, M.