

# CBL ubiquitinates FRS2 and FGFR4

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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

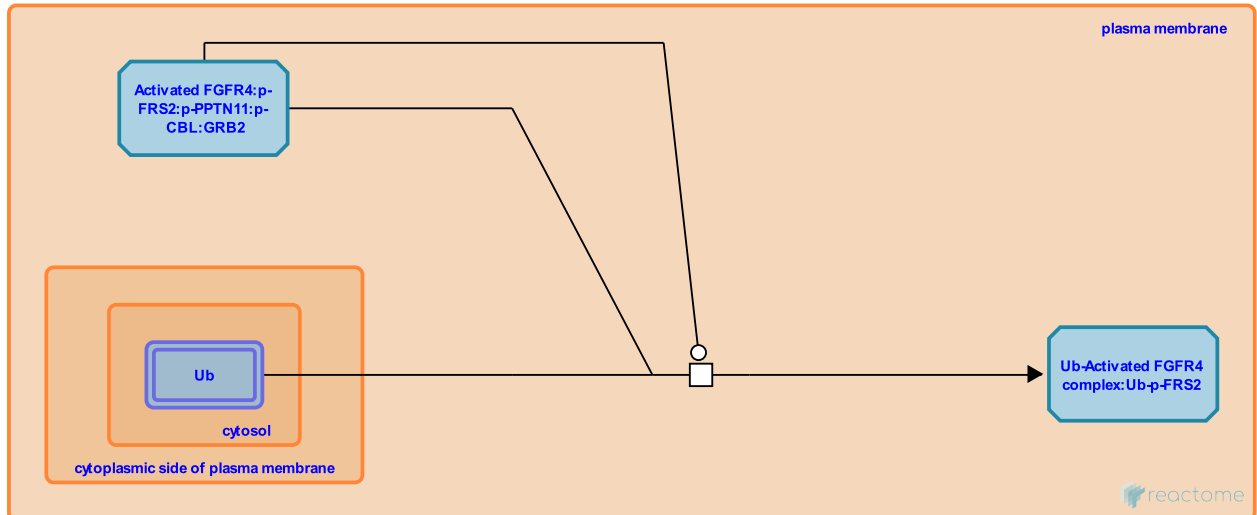
This document contains 1 reaction ([see Table of Contents](#))

## CBL ubiquitinates FRS2 and FGFR4 [↗](#)

**Stable identifier:** R-HSA-5654684

**Type:** transition

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



Grb2 bound to tyrosine phosphorylated FRS2 forms a ternary complex with Cbl through the binding of the SH3 domains of Grb2 to a proline rich region in Cbl. Grb2-mediated recruitment of Cbl results in ubiquitination of FGFR and FRS2. Cbl is a multidomain protein that possesses an intrinsic ubiquitin ligase activity and also functions as a platform for recruitment of a variety of signaling proteins. Multiple mechanisms appear to be required for downregulation of FGFR, as internalization of the receptor is reduced but not abolished if recruitment of CBL to FRS2 is compromised by mutation of GRB2-binding sites.

### Literature references

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### Editions

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