Downregulation of ERBB2 signaling

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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**


Reactome database release: 79

This document contains 2 pathways and 6 reactions (see Table of Contents)
Downregulation of ERBB2 signaling

Stable identifier: R-HSA-8863795

Signaling by ERBB2 can be downregulated by ubiquitination and subsequent proteasome-dependent degradation of ERBB2 or activated ERBB2 heterodimers. In addition, protein tyrosine phosphatases that dephosphorylate tyrosine residues in the C-terminus of ERBB2 prevent the recruitment of adapter proteins involved in signal transduction, thus attenuating ERBB2 signaling.

STUB1 (CHIP) and CUL5 are E3 ubiquitin ligases that can target non-activated ERBB2 for proteasome-dependent degradation (Xu et al. 2002, Ehrlich et al. 2009). RNF41 (NRDP1) is an E3 ubiquitin ligase that targets ERBB3 and activated heterodimers of ERBB2 and ERBB3 for proteasome-dependent degradation by ubiquitinating ERBB3 (Cao et al. 2007).

Two protein tyrosine phosphatases of the PEST family, PTPN12 and PTPN18, dephosphorylate tyrosine residues in the C-terminus of ERBB2, thus preventing signal transduction to RAS and PI3K effectors (Sun et al. 2011, Wang et al. 2014).

Literature references


Editions

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CHIP (STUB1) mediates ubiquitination of ERBB2

**Location:** Downregulation of ERBB2 signaling

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