SMURF1/2 bind PTCH1

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14/08/2021

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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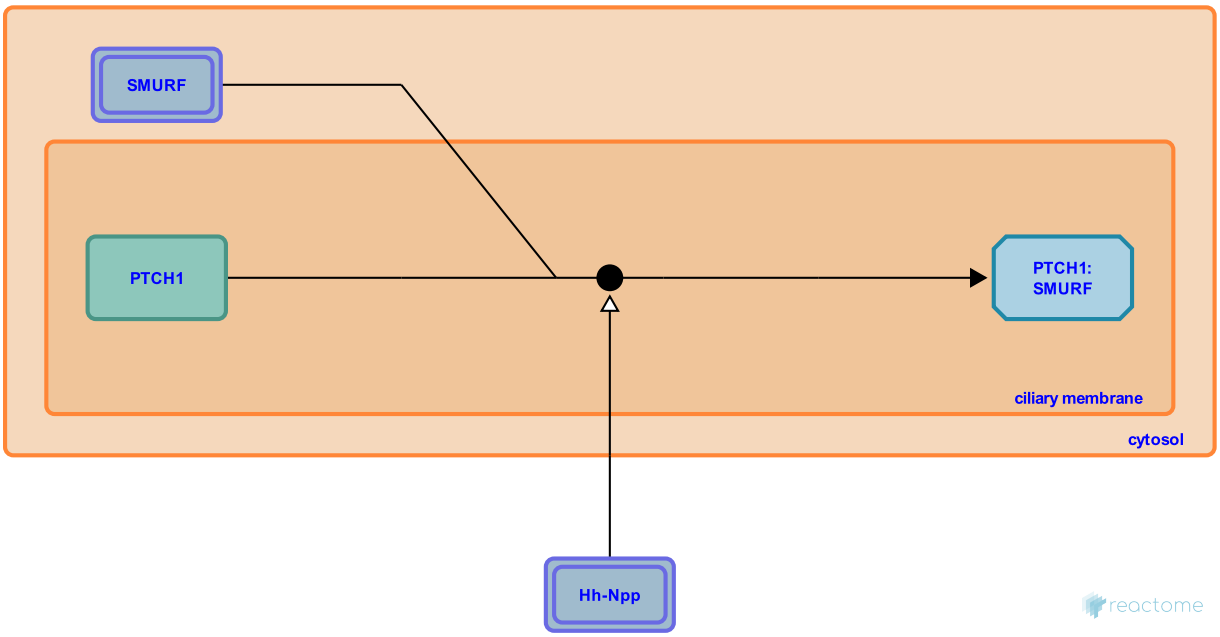
SMURF1/2 bind PTCH1 ↗

Stable identifier: R-HSA-5632646

Type: binding

Compartments: ciliary membrane

Inferred from: Smurf1/2 bind Ptch1 (Mus musculus)



Hh stimulation promotes PTCH1 clearance from the primary cilium to endocytic compartments (Rohatgi et al, 2007; reviewed in Nowaza et al, 2013). Receptor internalization is required for pathway activation, and additionally limits the duration and range of Hh signaling by sequestering the ligand inside the cell (Rohatgi et al, 2007; Incardona et al, 2000; Incardona et al, 2002; Denef et al, 2000; Huang et al, 2013; Yue et al, 2014). Upon Hh pathway activation, the E3 ligases SMURF1 and SMURF2 bind to two PPXY motifs in the C-terminal tail of PTCH1 to promote its ubiquination, endocytosis and degradation. In Drosophila, SMURF-mediated ubiquitination of PTCH is depends on an interaction between SMURF and activated SMO, but this does not appear to be true in vertebrates where PTCH1 turnover is SMO-independent (Yue et al, 2014; Huang et al, 2013; Lu et al, 2006). In flies, SMURF-dependent ubiquitination preferentially downregulates ligand-unbound receptor and is thus believed to regulate downstream signaling by altering the ratio of bound to unbound receptor on the cell surface; this aspect of PTCH1 downregulation has not been examined in detail in vertebrate cells (Huang et al, 2013; Casali and Struhl, 2004; Yue et al, 2014).

Literature references

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Editions

2014-10-20	Authored	Rothfels, K.
2014-10-31	Edited	Gillespie, ME.
2014-11-09	Reviewed	Liu, Y C.