

SMURF1/2 bind PTCH1

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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

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- 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: 78

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

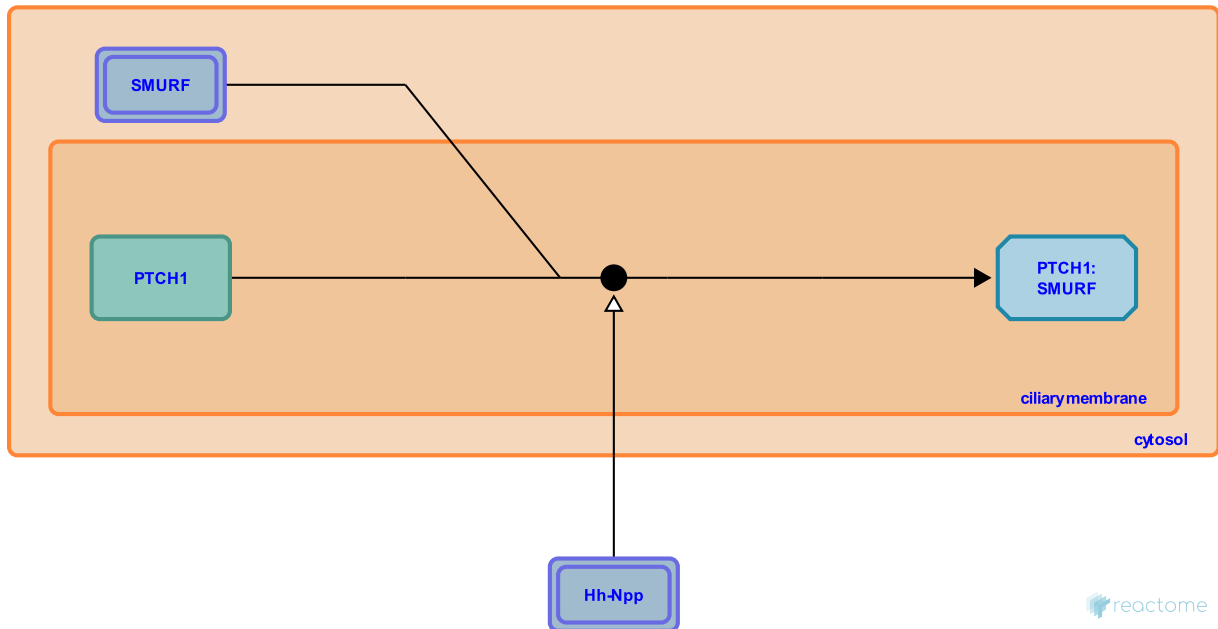
SMURF1/2 bind PTCH1 [↗](#)

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; Deneff 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 ubiquitination, endocytosis and degradation. In *Drosophila*, SMURF-mediated ubiquitination of PTCH1 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

- Kapur, RP., Robertson, CP., Roelink, H., Incardona, JP., Lee, JH., Enga, K. (2000). Receptor-mediated endocytosis of soluble and membrane-tethered Sonic hedgehog by Patched-1. *Proc. Natl. Acad. Sci. U.S.A.*, 97, 12044-9. [↗](#)
- Lin, C., Chuang, PT., Nozawa, YI. (2013). Hedgehog signaling from the primary cilium to the nucleus: an emerging picture of ciliary localization, trafficking and transduction. *Curr. Opin. Genet. Dev.*, 23, 429-37. [↗](#)
- Cohen, SM., Deneff, N., Neubüser, D., Perez, L. (2000). Hedgehog induces opposite changes in turnover and subcellular localization of patched and smoothened. *Cell*, 102, 521-31. [↗](#)
- Milenkovic, L., Rohatgi, R., Scott, MP. (2007). Patched1 regulates hedgehog signaling at the primary cilium. *Science*, 317, 372-6. [↗](#)

Gruenberg, J., Roelink, H., Incardona, JP. (2002). Sonic hedgehog induces the segregation of patched and smoothed in endosomes. *Curr. Biol.*, 12, 983-95. [↗](#)

Editions

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