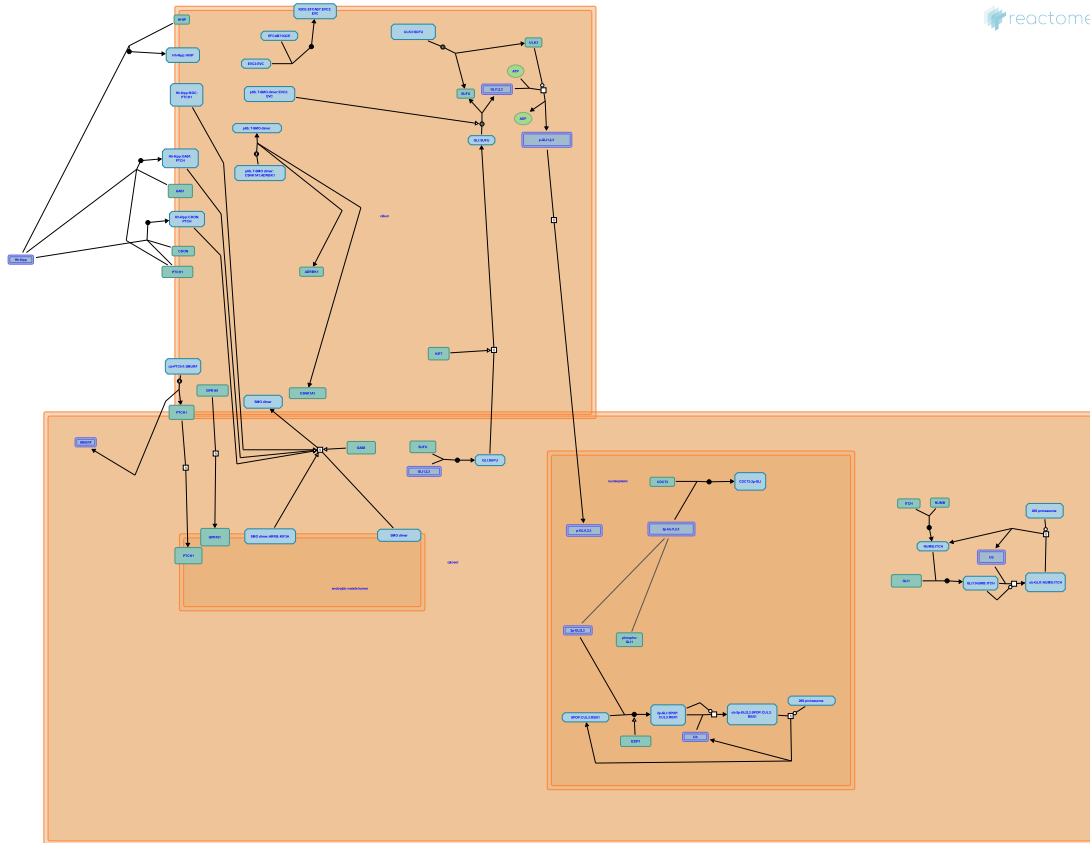


Hedgehog 'on' state



European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/textbook/).

01/04/2024

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

- 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. [↗](#)

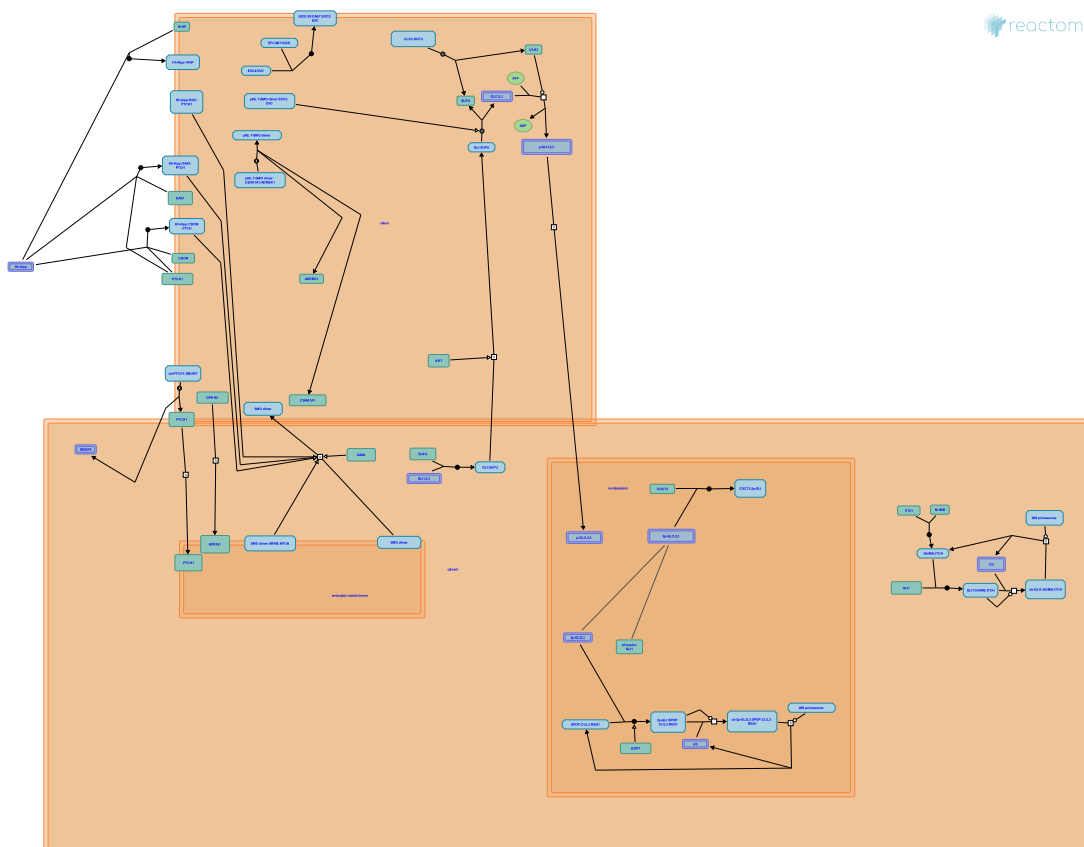
Reactome database release: 88

This document contains 3 pathways and 17 reactions ([see Table of Contents](#))

Hedgehog 'on' state ↗

Stable identifier: R-SSC-5632684

Inferred from: Hedgehog 'on' state (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

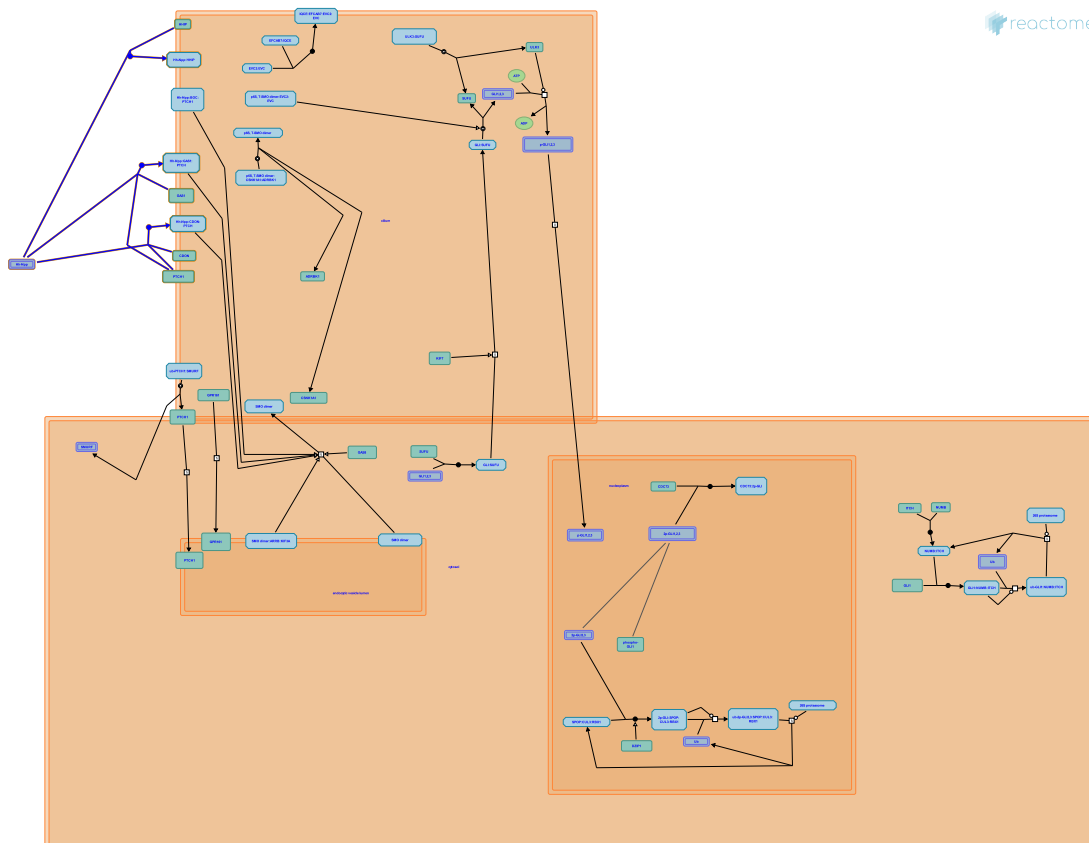
[More details and caveats of the event inference in Reactome.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Ligand-receptor interactions ↗

Location: Hedgehog 'on' state

Stable identifier: R-SSC-5632681

Inferred from: Ligand-receptor interactions (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

SMURF1/2 dissociates from ub-PTCH1 ↗

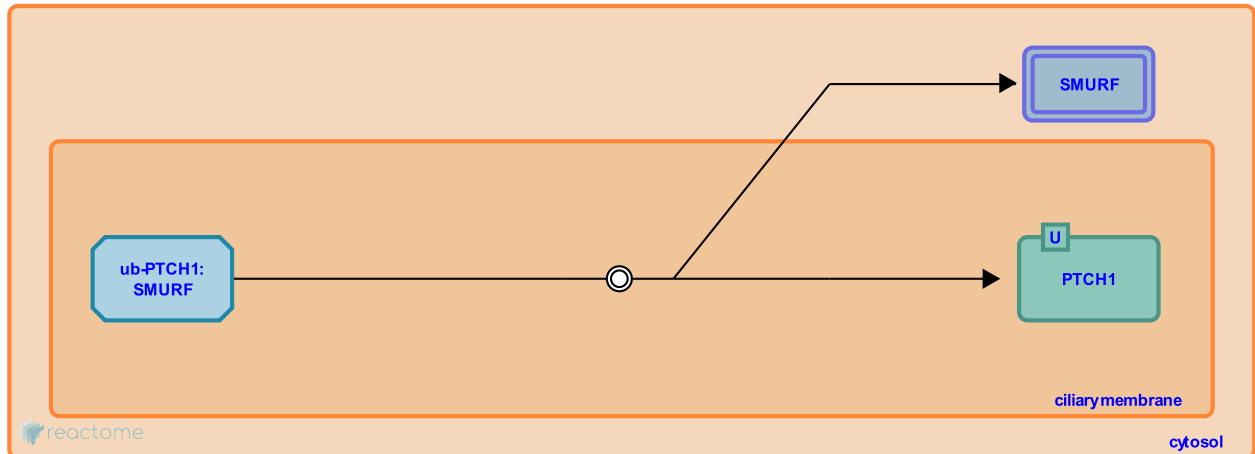
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635865

Type: dissociation

Compartments: ciliary membrane

Inferred from: [SMURF1/2 dissociates from ub-PTCH1 \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Followed by: [PTCH1 is internalized](#)

PTCH is internalized ↗

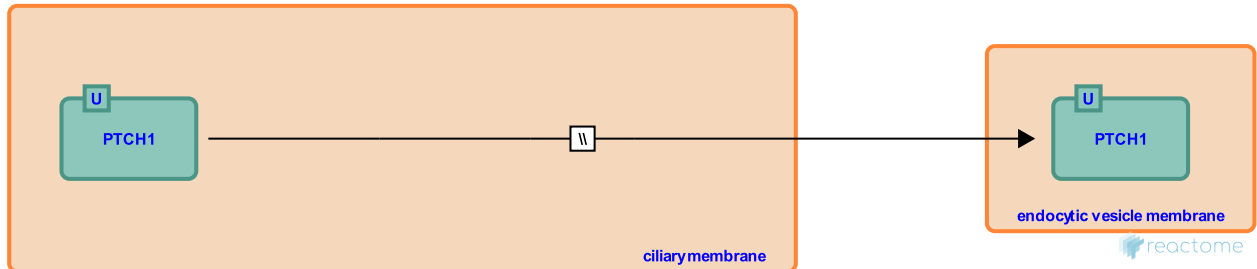
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5632677

Type: omitted

Compartments: ciliary membrane

Inferred from: [PTCH is internalized \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [SMURF1/2 dissociates from ub-PTCH1](#)

GPR161 is internalized ↗

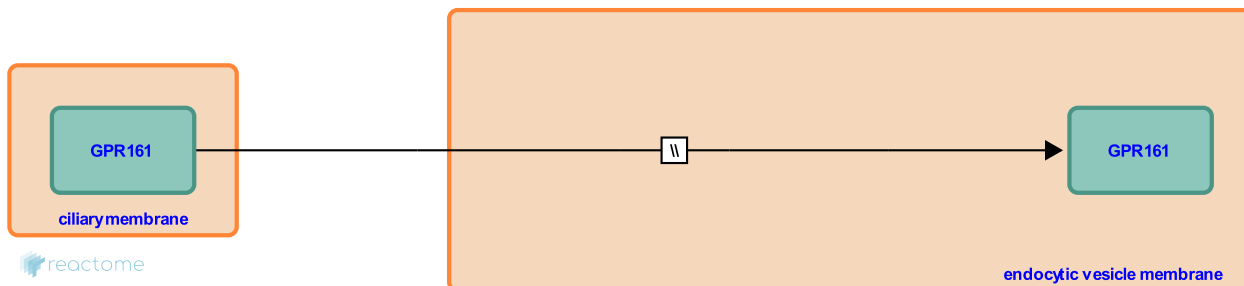
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635102

Type: omitted

Compartments: endocytic vesicle membrane, ciliary membrane

Inferred from: [GPR161 is internalized \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

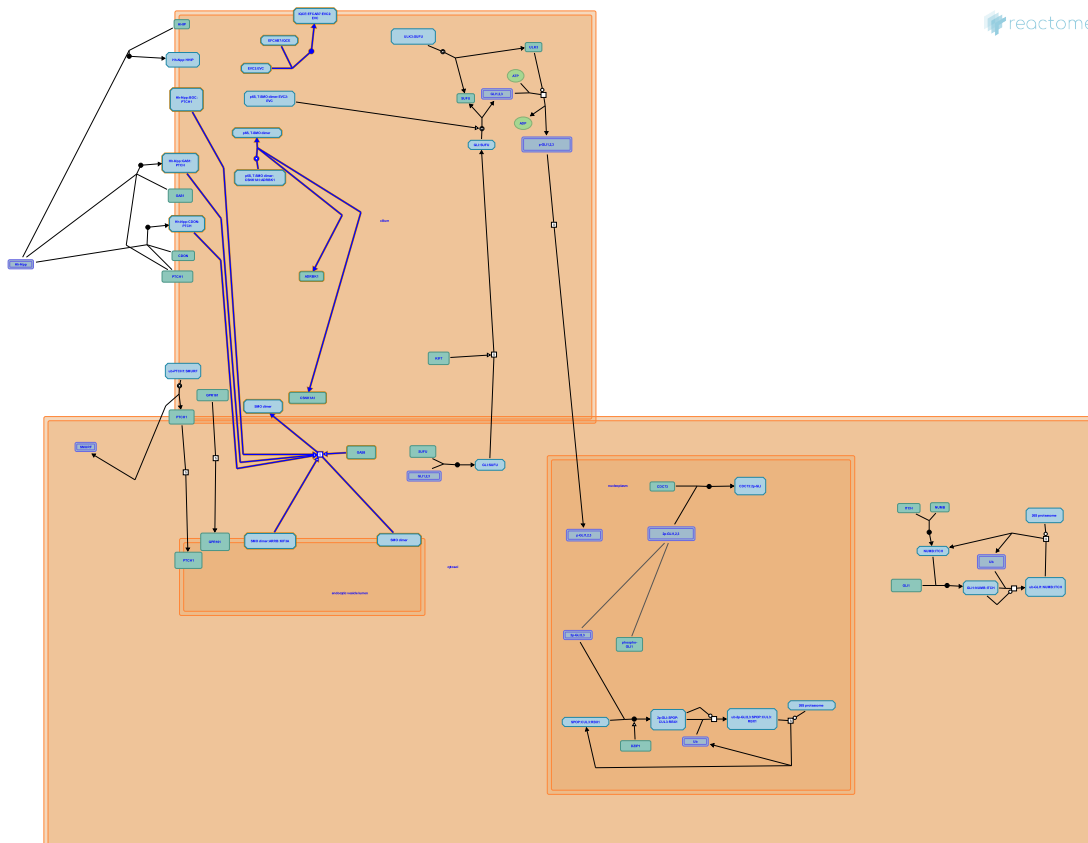
[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Activation of SMO ↗

Location: Hedgehog 'on' state

Stable identifier: R-SSC-5635838

Inferred from: Activation of SMO (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

GLI proteins bind SUFU ↗

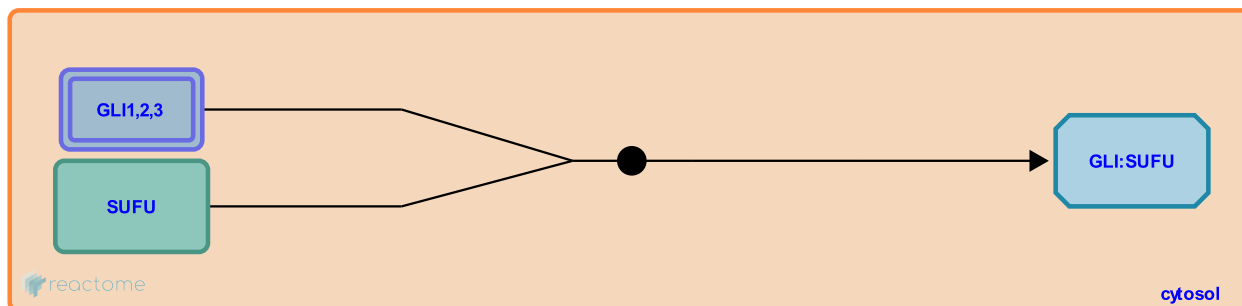
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5610723

Type: binding

Compartments: cytosol

Inferred from: [GLI proteins bind SUFU \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Followed by: [GLI:SUFU translocates to the ciliary tip in response to Hh signaling](#)

GLI:SUFU translocates to the ciliary tip in response to Hh signaling ↗

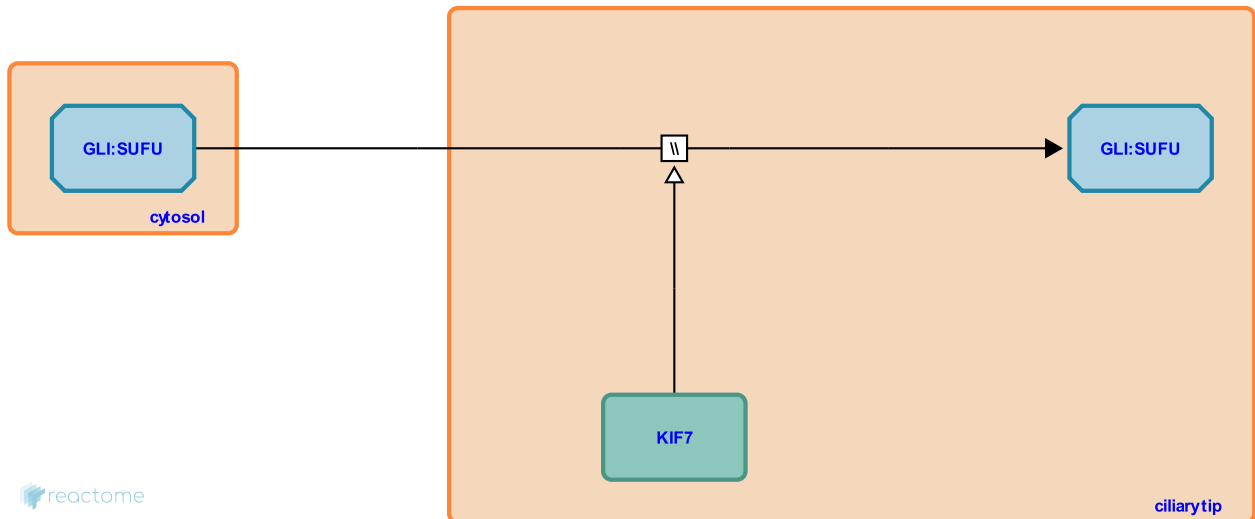
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635860

Type: omitted

Compartments: ciliary tip

Inferred from: [GLI:SUFU translocates to the ciliary tip in response to Hh signaling \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [GLI proteins bind SUFU](#)

Followed by: [GLI:SUFU dissociates](#)

GLI:SUFU dissociates ↗

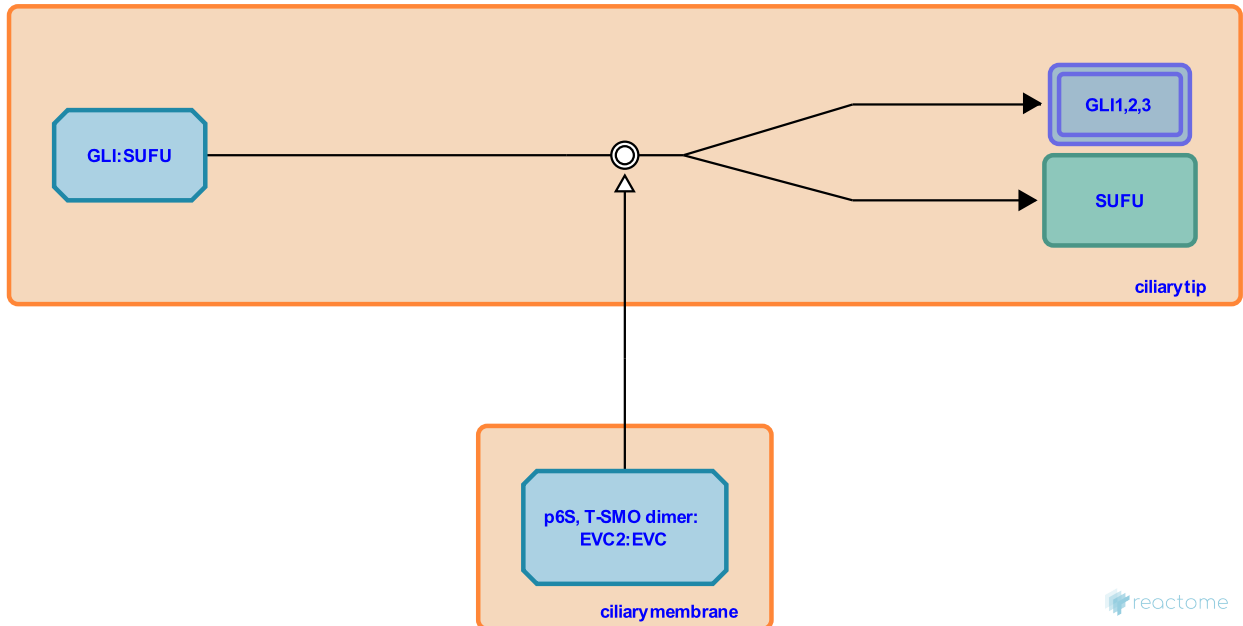
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635859

Type: dissociation

Compartments: ciliary tip

Inferred from: [GLI:SUFU dissociates \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [GLI:SUFU translocates to the ciliary tip in response to Hh signaling](#)

Followed by: [ULK3 phosphorylates GLI](#)

ULK3:SUFU dissociates ↗

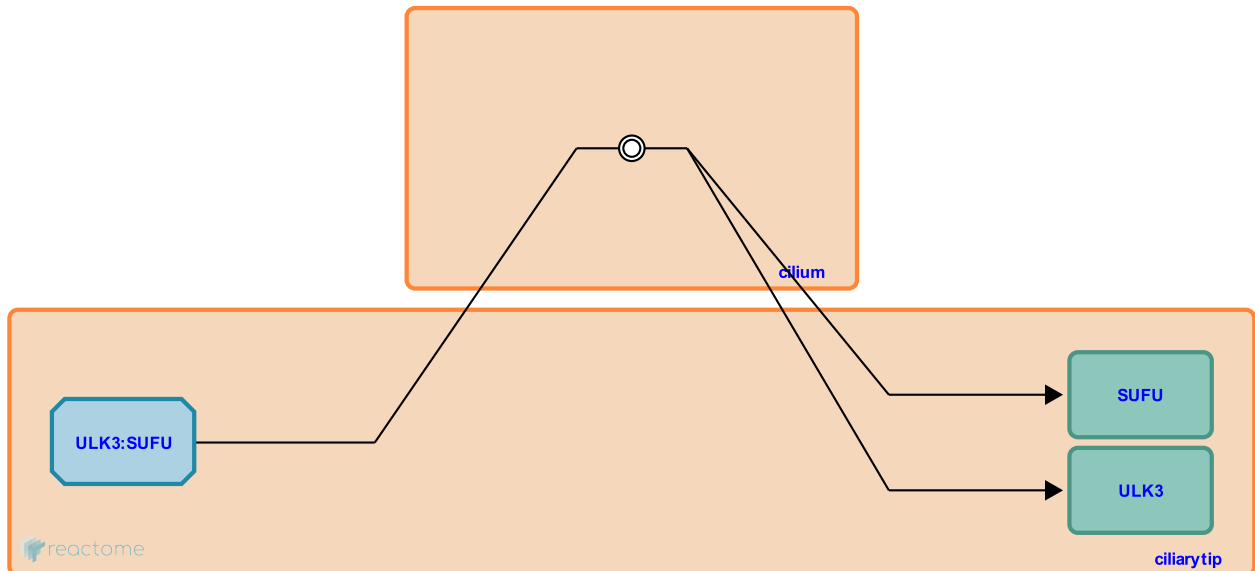
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635839

Type: dissociation

Compartments: cilium

Inferred from: [ULK3:SUFU dissociates \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Followed by: [ULK3 phosphorylates GLI](#)

ULK3 phosphorylates GLI ↗

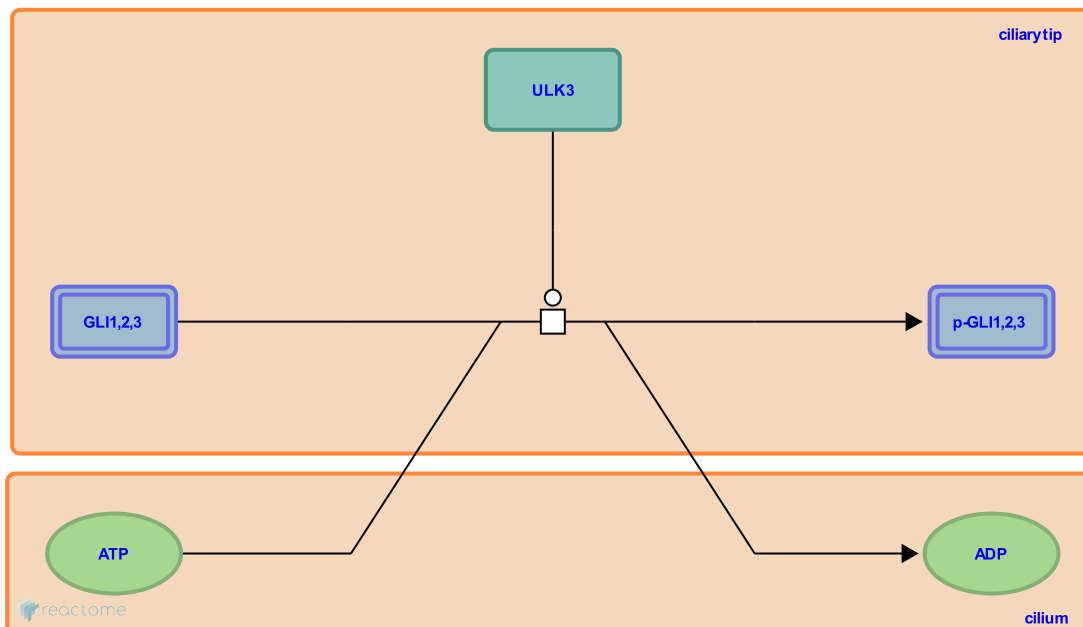
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635842

Type: transition

Compartments: ciliary tip

Inferred from: [ULK3 phosphorylates GLI \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [ULK3:SUFU dissociates](#), [GLI:SUFU dissociates](#)

Followed by: [GLI translocates to the nucleus](#)

GLI translocates to the nucleus ↗

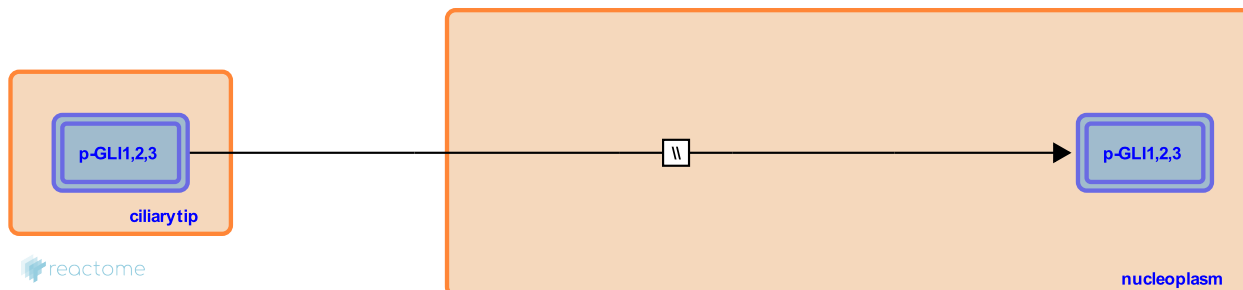
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635843

Type: omitted

Compartments: nucleoplasm, ciliary tip

Inferred from: [GLI translocates to the nucleus \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [ULK3 phosphorylates GLI](#)

GLI proteins bind CDC73 [↗](#)

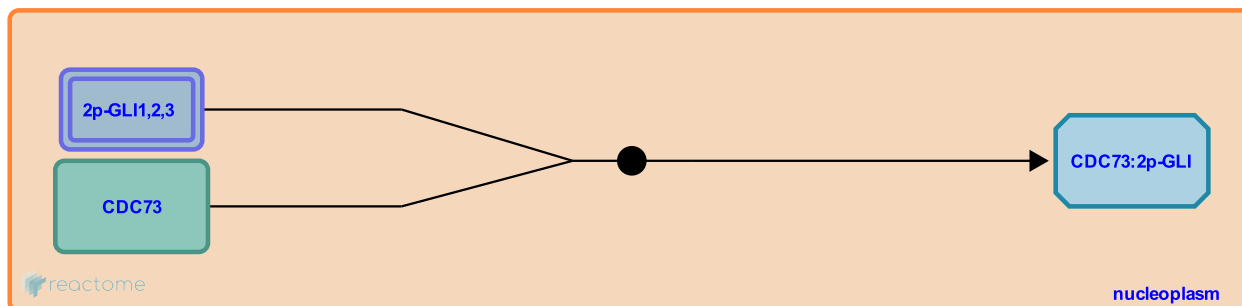
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635845

Type: binding

Compartments: nucleoplasm

Inferred from: [GLI proteins bind CDC73 \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

phosphorylated GLI proteins bind SPOP:CUL3:RBX1 ↗

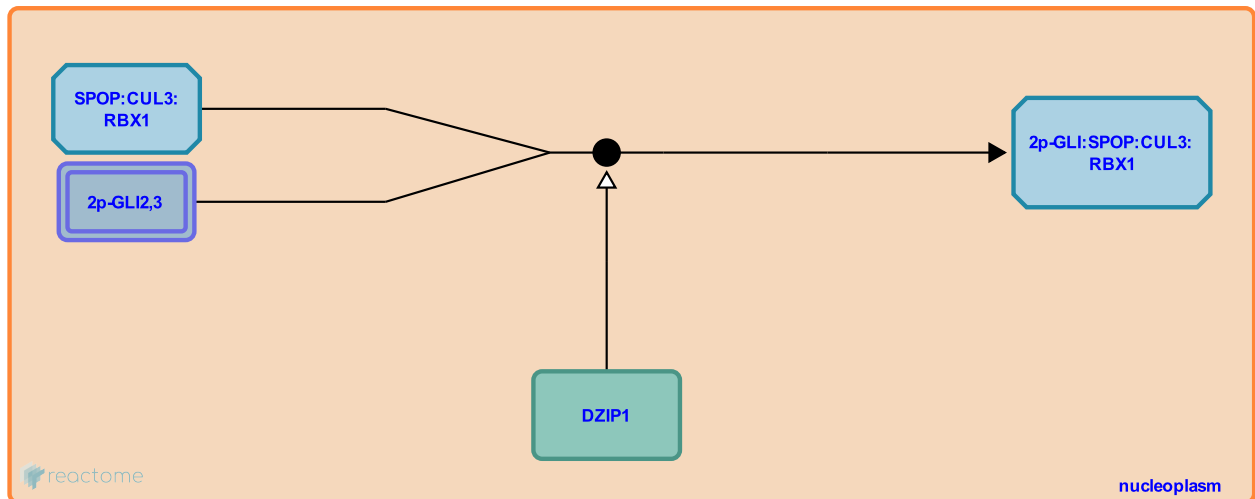
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635855

Type: binding

Compartments: nucleoplasm

Inferred from: [phosphorylated GLI proteins bind SPOP:CUL3:RBX1 \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Followed by: [SPOP:CUL3:RBX1 ubiquitinates GLI2,3](#)

SPOP:CUL3:RBX1 ubiquitinates GLI2,3 ↗

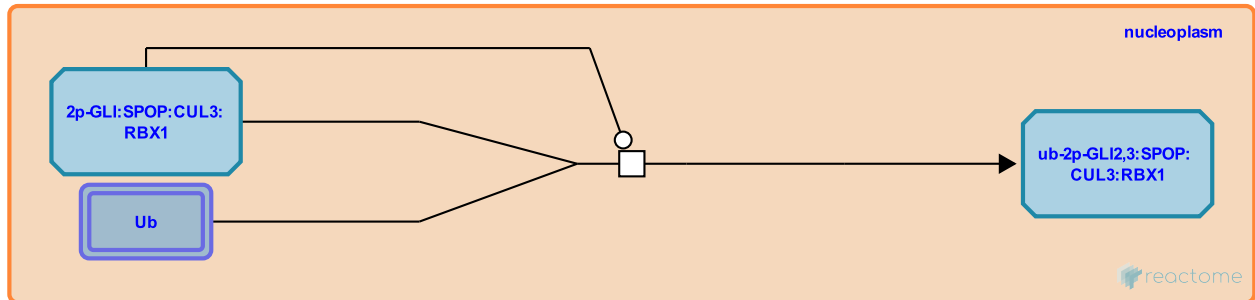
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635856

Type: transition

Compartments: nucleoplasm

Inferred from: [SPOP:CUL3:RBX1 ubiquitinates GLI2,3 \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [phosphorylated GLI proteins bind SPOP:CUL3:RBX1](#)

Followed by: [GLI2,3 are degraded by the proteasome](#)

GLI2,3 are degraded by the proteasome ↗

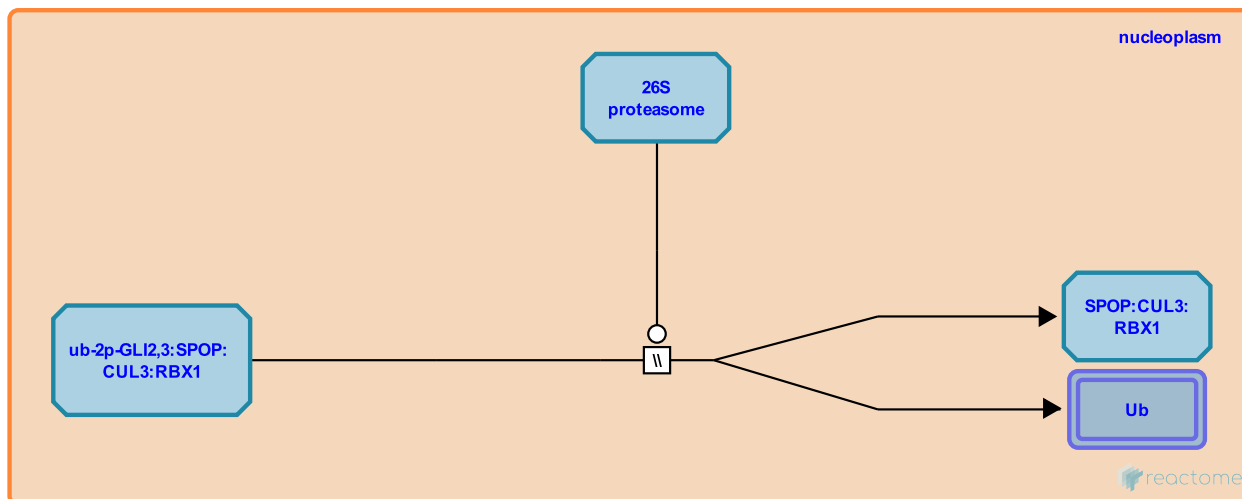
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635854

Type: omitted

Compartments: nucleoplasm

Inferred from: [GLI2,3 are degraded by the proteasome \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [SPOP:CUL3:RBX1 ubiquitinates GLI2,3](#)

NUMB binds ITCH ↗

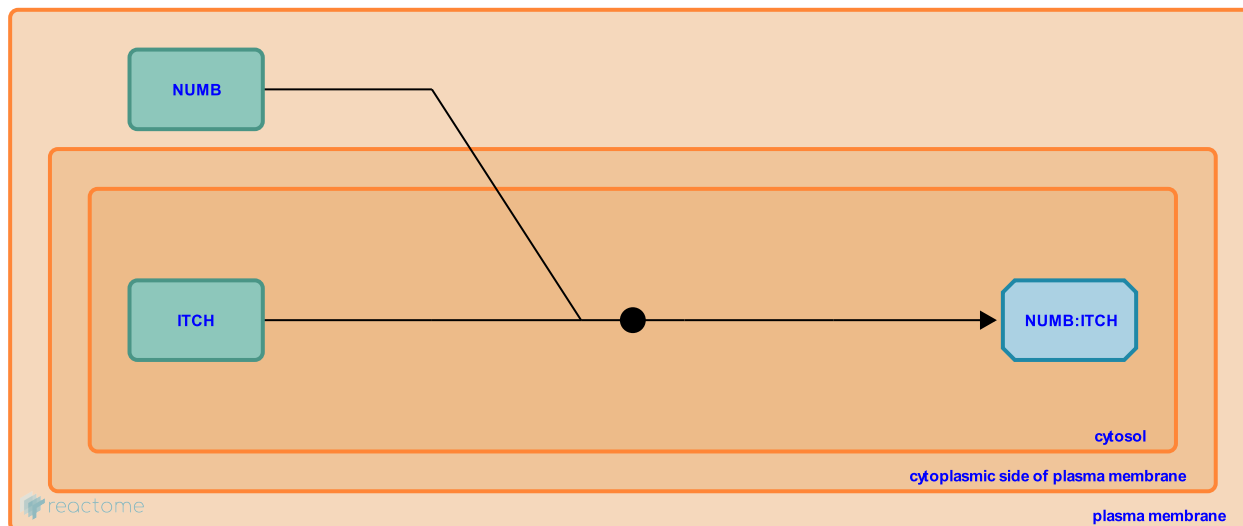
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5610735

Type: binding

Compartments: cytosol

Inferred from: [NUMB binds ITCH \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Followed by: [NUMB:ITCH binds GLI1](#)

NUMB:ITCH binds GLI1 [↗](#)

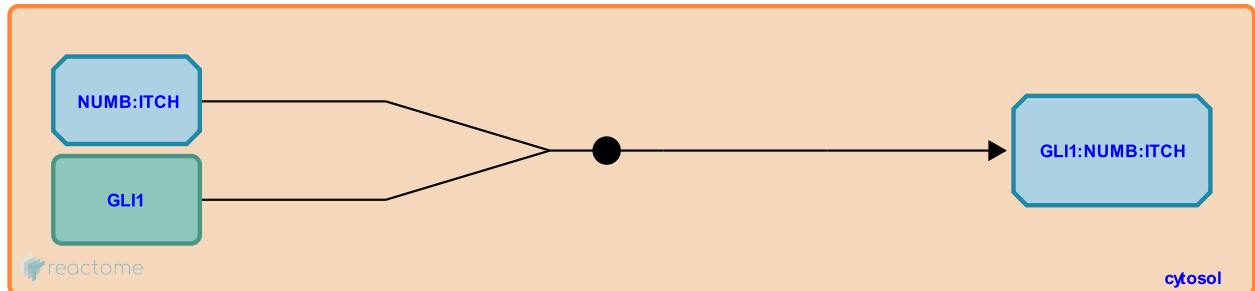
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635861

Type: binding

Compartments: cytosol

Inferred from: [NUMB:ITCH binds GLI1 \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [NUMB binds ITCH](#)

Followed by: [NUMB:ITCH ubiquitinates GLI1](#)

NUMB:ITCH ubiquitinates GLI1 ↗

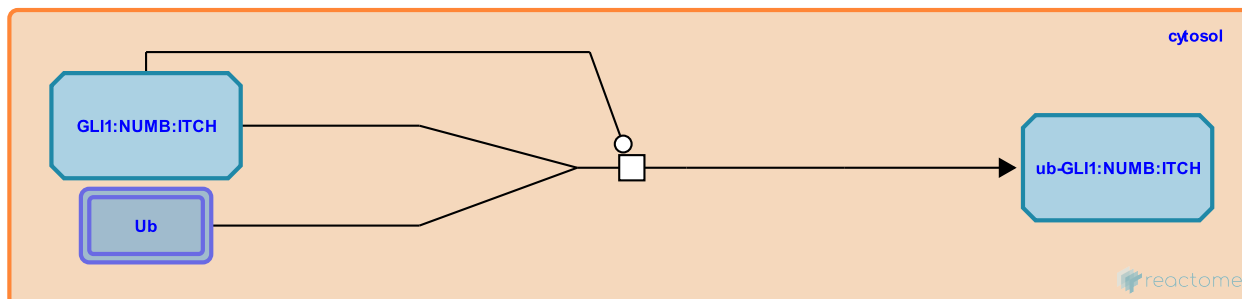
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635864

Type: transition

Compartments: cytosol

Inferred from: [NUMB:ITCH ubiquitinates GLI1 \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [NUMB:ITCH binds GLI1](#)

Followed by: [ub-GLI1 is degraded by the proteasome](#)

ub-GLI is degraded by the proteasome ↗

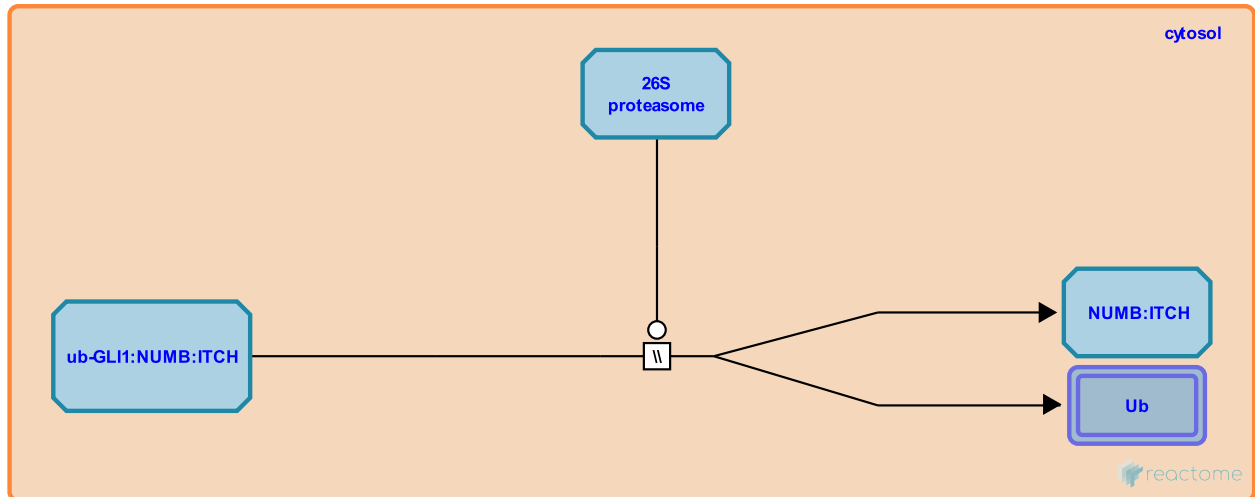
Location: [Hedgehog 'on' state](#)

Stable identifier: R-SSC-5635868

Type: omitted

Compartments: cytosol

Inferred from: [ub-GLI is degraded by the proteasome \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](#) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [NUMB:ITCH ubiquitinates GLI1](#)

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