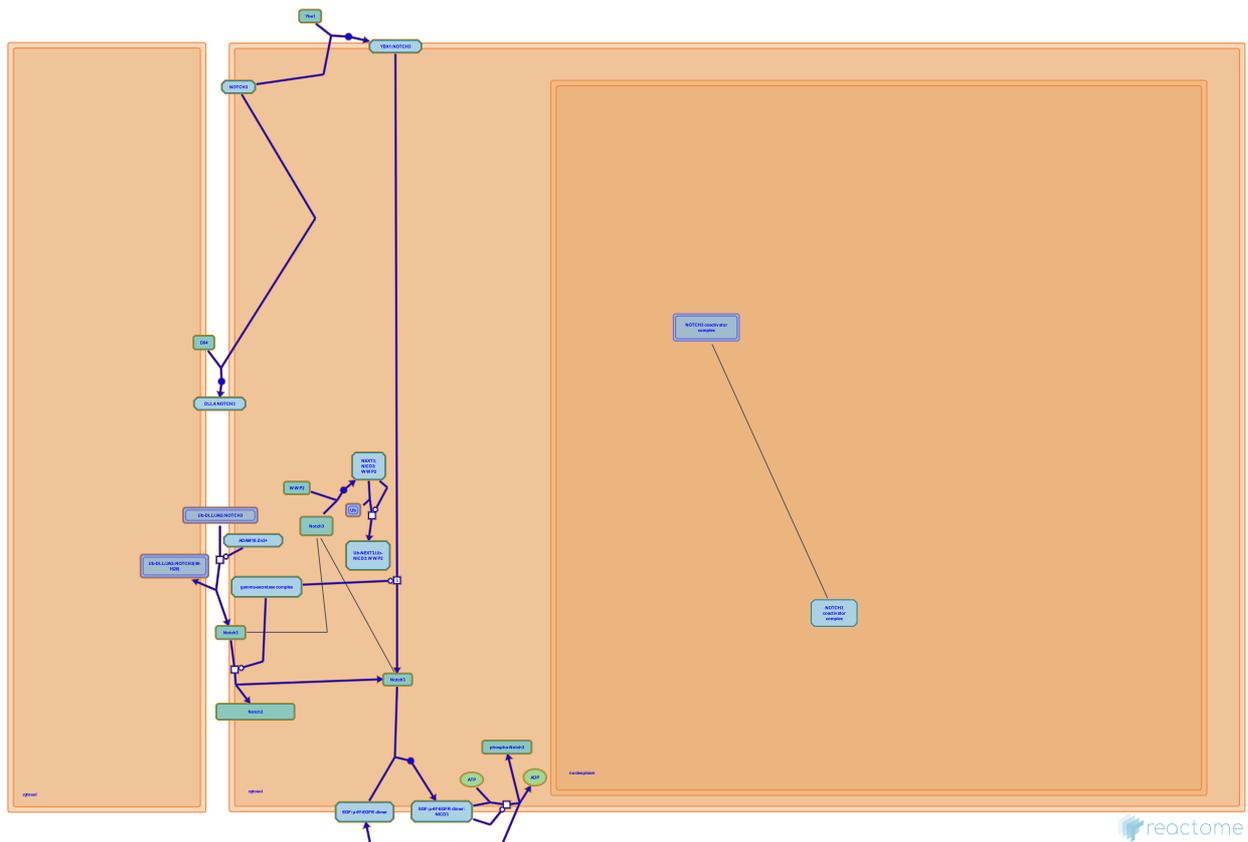


NOTCH3 Activation and Transmission of Signal to the Nucleus



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://www.reactome.org/textbook/).

05/12/2022

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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Reactome database release: 82

This document contains 2 pathways and 7 reactions ([see Table of Contents](#))

NOTCH3 binds DLL4 ↗

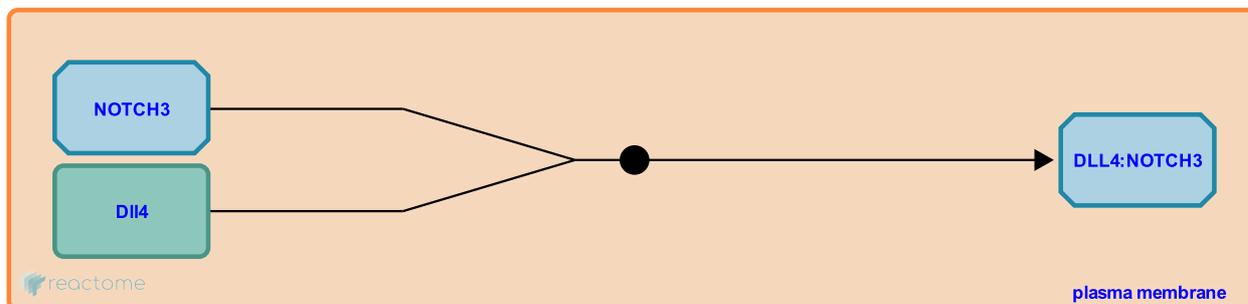
Location: [NOTCH3 Activation and Transmission of Signal to the Nucleus](#)

Stable identifier: R-RNO-2168136

Type: binding

Compartments: plasma membrane

Inferred from: [NOTCH3 binds DLL4 \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

NOTCH3-ligand complex is cleaved to produce NEXT3 ↗

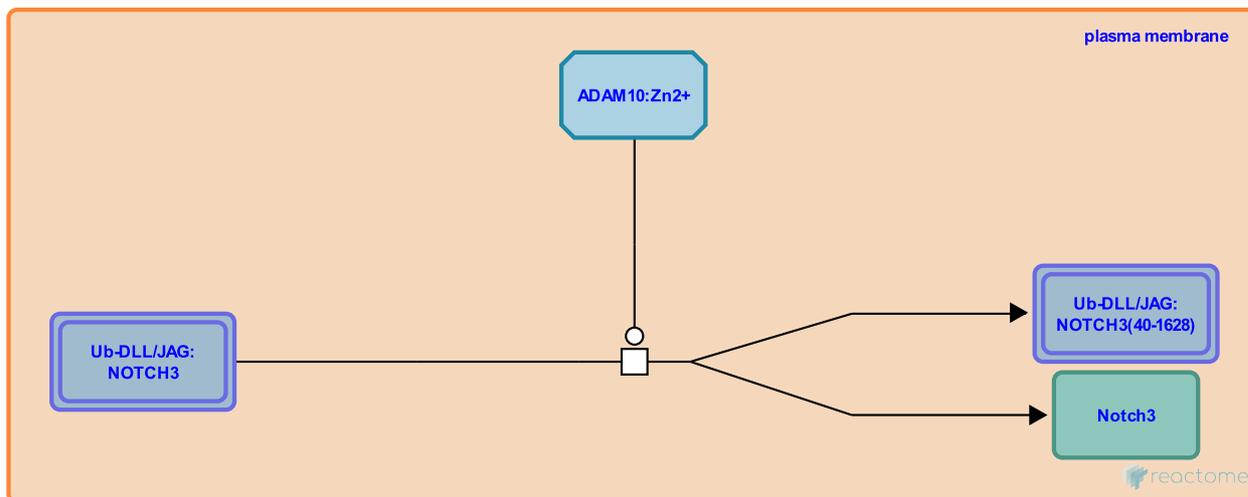
Location: [NOTCH3 Activation and Transmission of Signal to the Nucleus](#)

Stable identifier: R-RNO-9013284

Type: transition

Compartments: plasma membrane, extracellular region

Inferred from: [NOTCH3-ligand complex is cleaved to produce NEXT3 \(Homo sapiens\)](#)



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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.

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Followed by: [NOTCH3 binds WWP2, NEXT3 is cleaved to produce NICD3](#)

NEXT3 is cleaved to produce NICD3 ↗

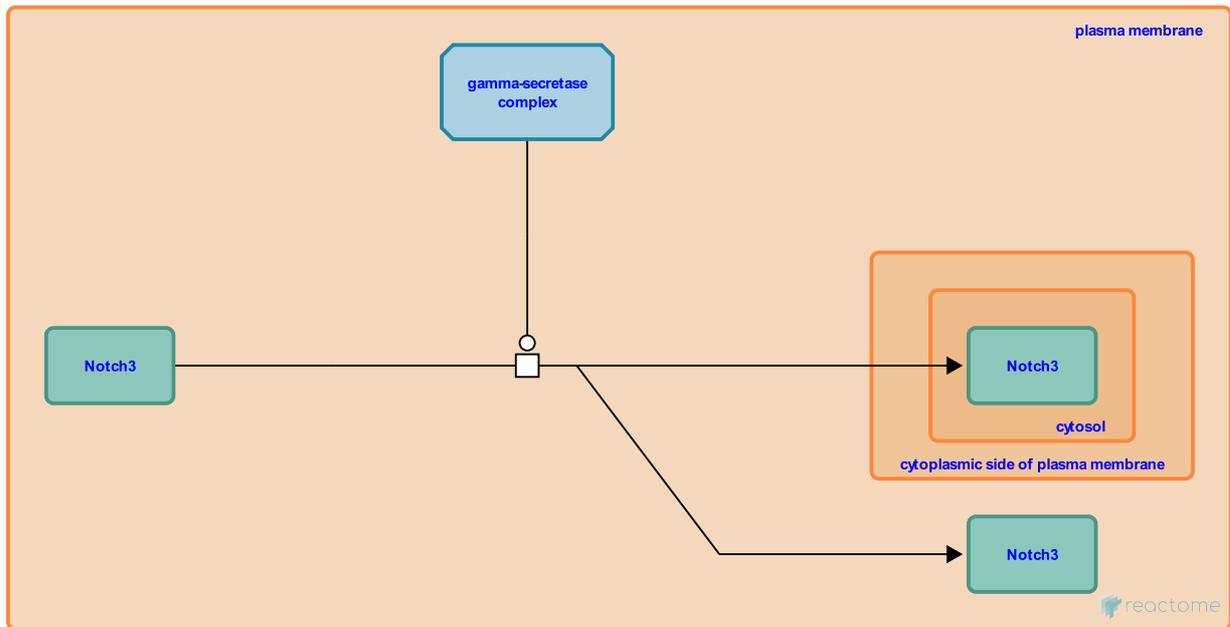
Location: [NOTCH3 Activation and Transmission of Signal to the Nucleus](#)

Stable identifier: R-RNO-9013361

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: [NEXT3 is cleaved to produce NICD3 \(Homo sapiens\)](#)



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

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Preceded by: [NOTCH3-ligand complex is cleaved to produce NEXT3](#)

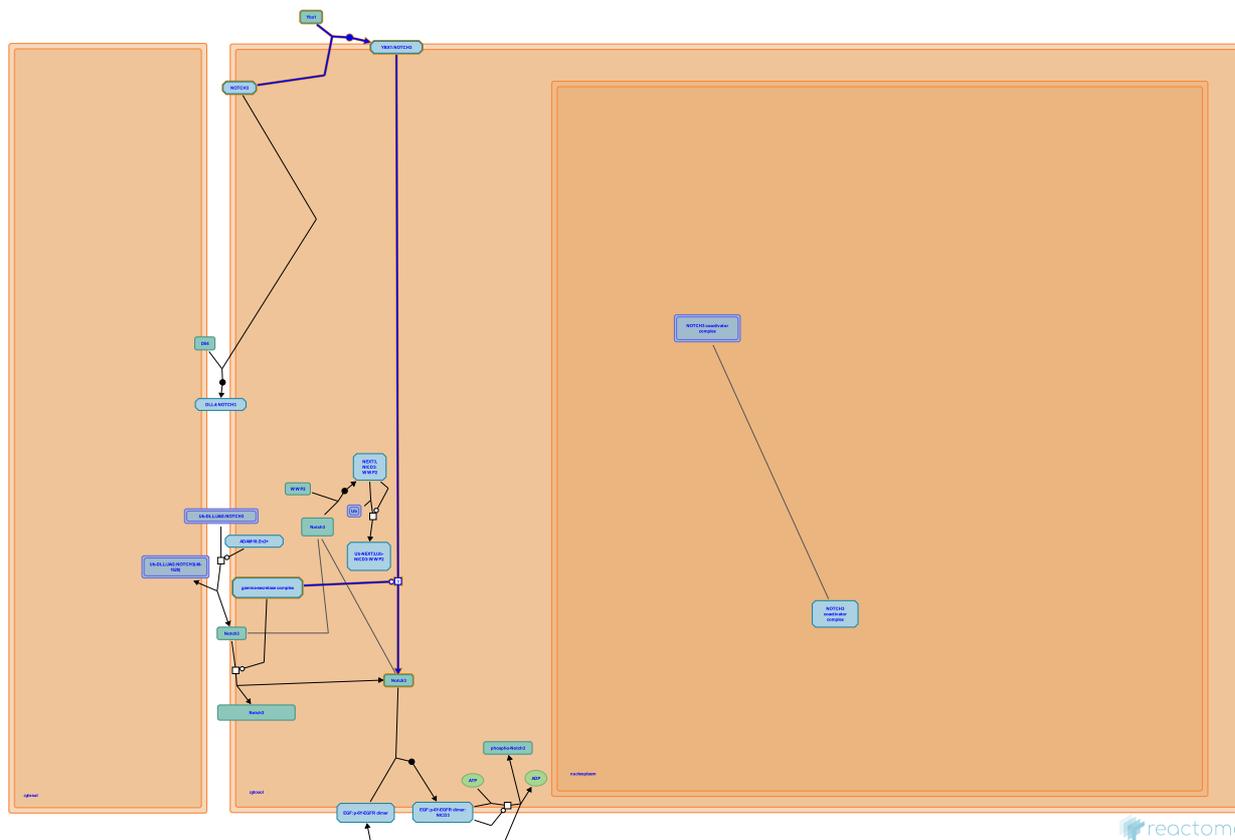
Followed by: [NOTCH3 binds WWP2](#), [NOTCH3 binds activated EGFR](#)

Noncanonical activation of NOTCH3 ↗

Location: NOTCH3 Activation and Transmission of Signal to the Nucleus

Stable identifier: R-RNO-9017802

Inferred from: Noncanonical activation of NOTCH3 (Homo sapiens)



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

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NOTCH3 binds activated EGFR ↗

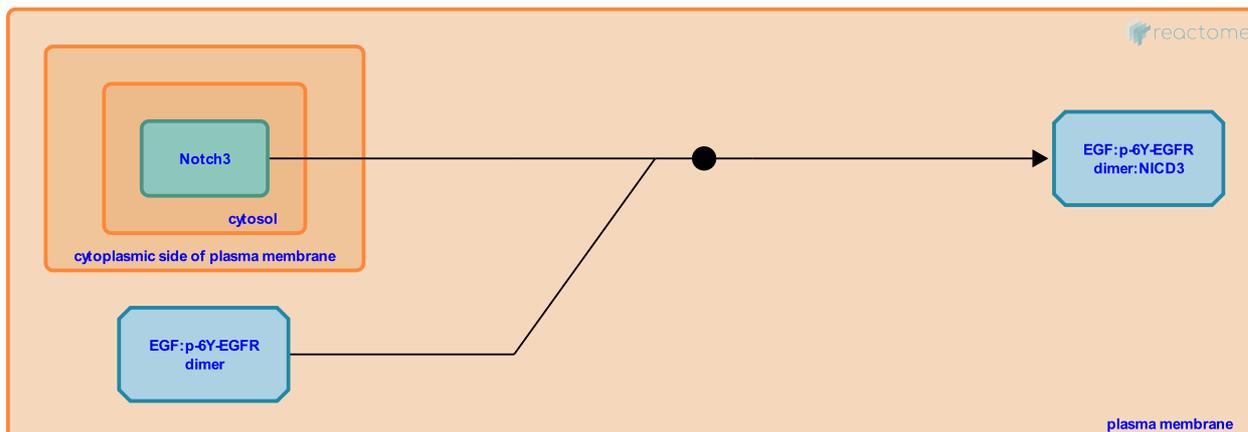
Location: [NOTCH3 Activation and Transmission of Signal to the Nucleus](#)

Stable identifier: R-RNO-9018573

Type: binding

Compartments: plasma membrane

Inferred from: [NOTCH3 binds activated EGFR \(Homo sapiens\)](#)



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Preceded by: [NEXT3 is cleaved to produce NICD3](#)

Followed by: [EGFR phosphorylates NOTCH3](#)

EGFR phosphorylates NOTCH3 ↗

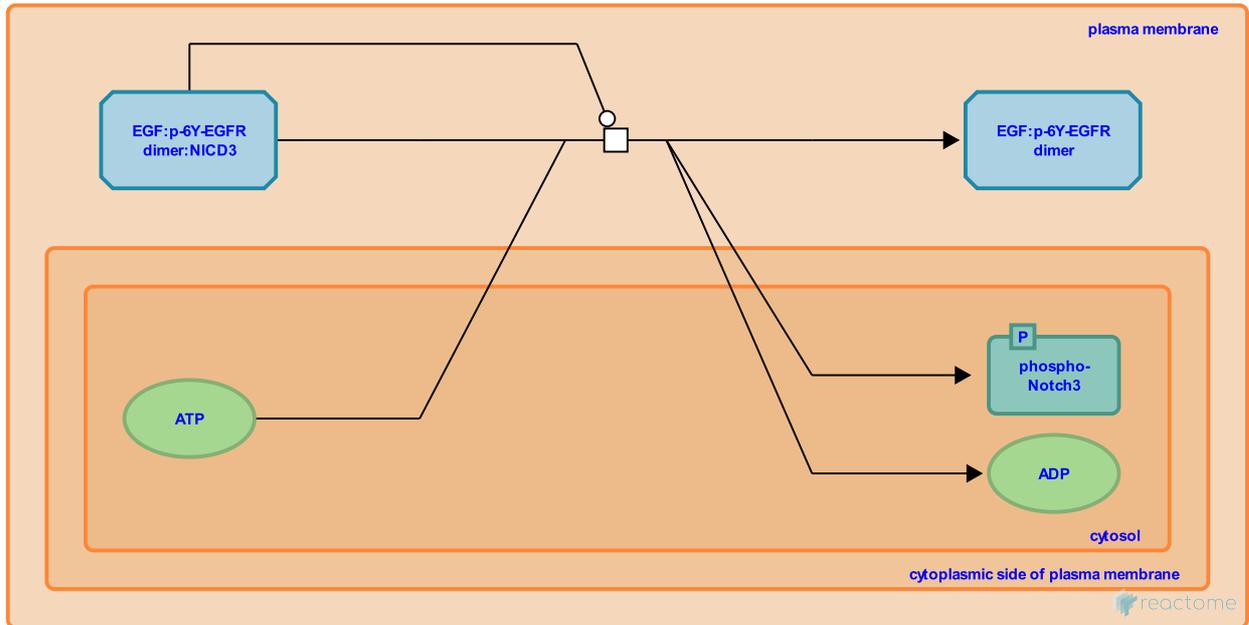
Location: [NOTCH3 Activation and Transmission of Signal to the Nucleus](#)

Stable identifier: R-RNO-9018572

Type: transition

Compartments: plasma membrane

Inferred from: [EGFR phosphorylates NOTCH3 \(Homo sapiens\)](#)



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

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Preceded by: [NOTCH3 binds activated EGFR](#)

NOTCH3 binds WWP2 ↗

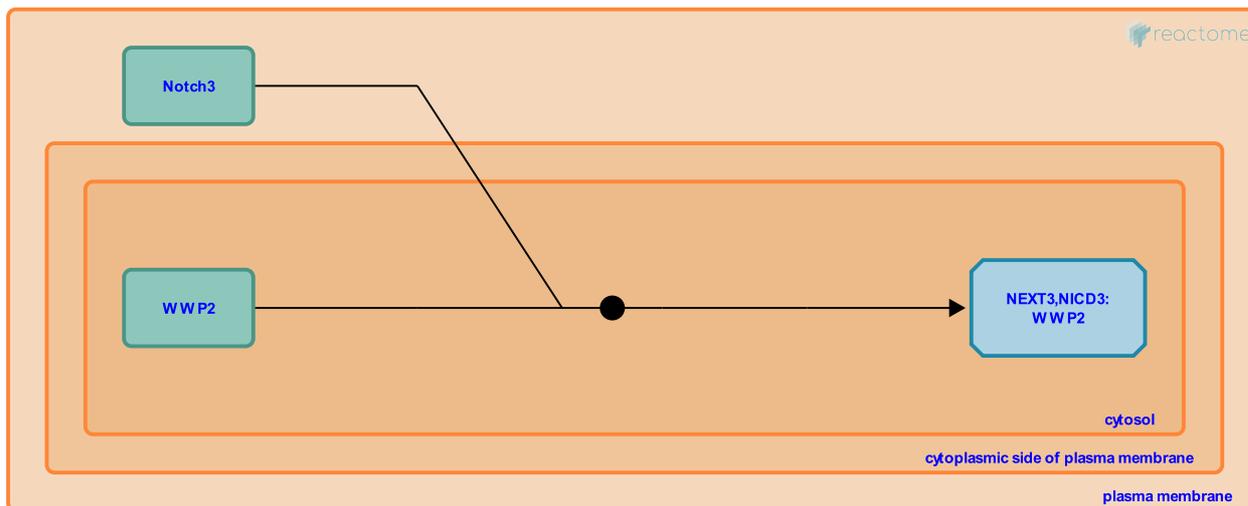
Location: [NOTCH3 Activation and Transmission of Signal to the Nucleus](#)

Stable identifier: R-RNO-9021520

Type: binding

Compartments: cytosol

Inferred from: [NOTCH3 binds WWP2 \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [NOTCH3-ligand complex is cleaved to produce NEXT3, NEXT3 is cleaved to produce NICD3](#)

Followed by: [WWP2 ubiquitinates NOTCH3](#)

WWP2 ubiquitinates NOTCH3 ↗

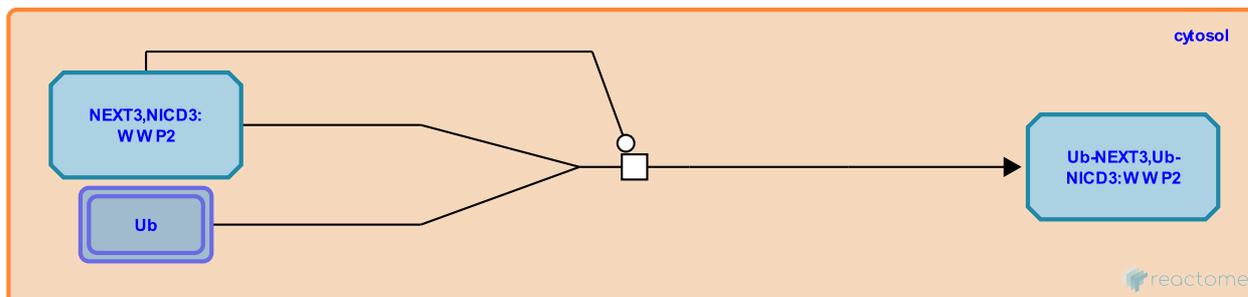
Location: [NOTCH3 Activation and Transmission of Signal to the Nucleus](#)

Stable identifier: R-RNO-9021523

Type: transition

Compartments: cytosol

Inferred from: [WWP2 ubiquitinates NOTCH3 \(Homo sapiens\)](#)



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.

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Preceded by: [NOTCH3 binds WWP2](#)

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