Murine Axin1 is dephosphorylated by PP2A leading to reduced binding affinity with beta-catenin

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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

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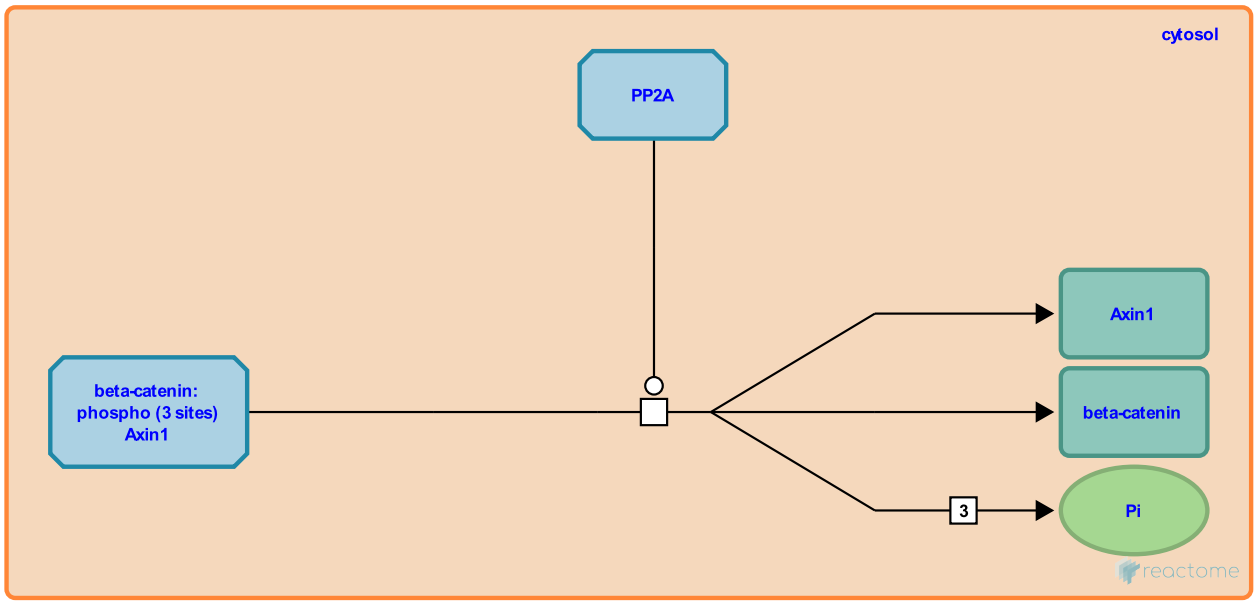
Stable identifier: R-MMU-209096

Type: transition

Compartments: cytosol



AXIN is believed to be dephosphorylated upon WNT pathway stimulation, decreasing its affinity for beta-catenin (Willert et al, 1999; Jho et al 1999). AXIN has been shown to be a direct target of GSK3beta in vitro (Ikeda et al, 1998; Jho et al, 1999). In the absence of a WNT signal AXIN is phosphorylated at Thr519 and Ser524 by GSK3beta and at Ser531 by an unknown kinase. Mutation of these sites decreases the binding to beta-catenin and results in increased TCF-dependent signaling (Jho et al, 1999).

The destruction complex phosphatase PP2A has been implicated as both a positive and negative regulator of WNT and is a candidate for the WNT-dependent dephosphorylation of AXIN (Willert et al, 1999; reviewed in Kimelman and Xu, 2006; MacDonald et al, 2009). Stimulation of the WNT pathway leads to changes in AXIN mobility that are reproduced in vitro by dephosphorylation of immunoprecipitated AXIN by PP2A. Consistent with this, treatment of cells with the PP2A inhibitor okadaic acid blocks the dephosphorylation of AXIN upon treatment with WNT3A (Willert et al, 1999). Stimulation of the WNT pathway results in the recovery of less AXIN in a beta-catenin pulldown, and the AXIN that is isolated in this way is exclusively the phosphorylated form (Willert et al, 1999). In addition to dephosphorylating AXIN, PP2A has also been shown to dephosphorylate beta-catenin itself, as well as APC (Su et al, 2008; Ikeda et al, 2000).

Another candidate for the dephosphorylation of AXIN is PP1. PP1 interacts with AXIN and PP1-dependent dephosphorylation of AXIN decreases the AXIN-GSK3beta interaction and inhibits beta-catenin phosphorylation (Luo et al, 2007).

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Editions

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