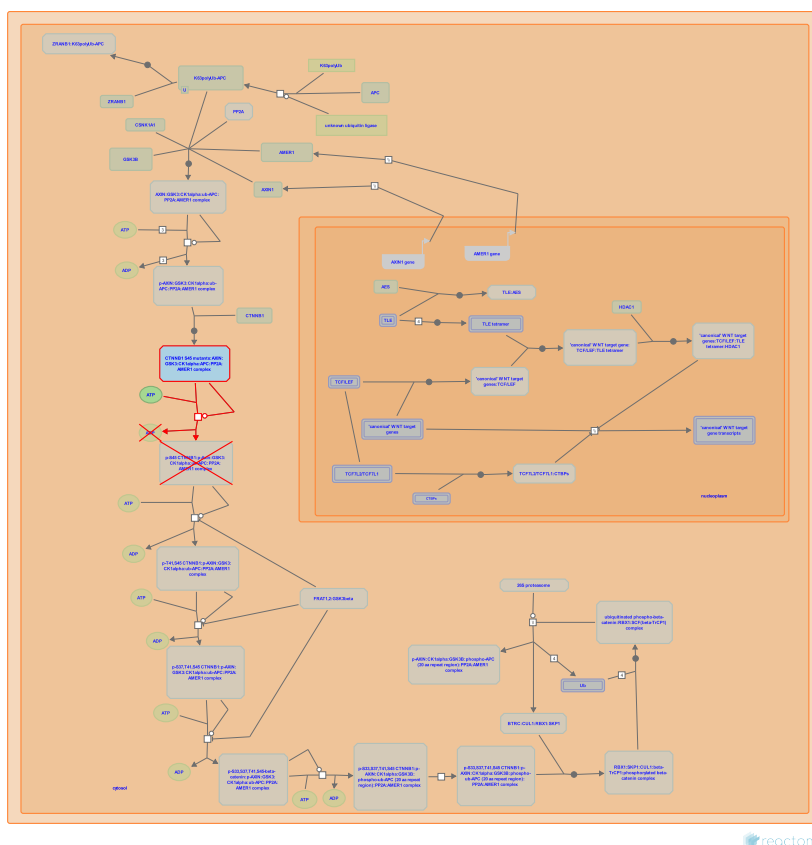


CTNNB1 S45 mutants aren't phosphorylated



Matthews, L., Rothfels, K., Salahshor, S., Woodgett, J.

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://reactome.org/faq).

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/faq).

15/05/2024

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

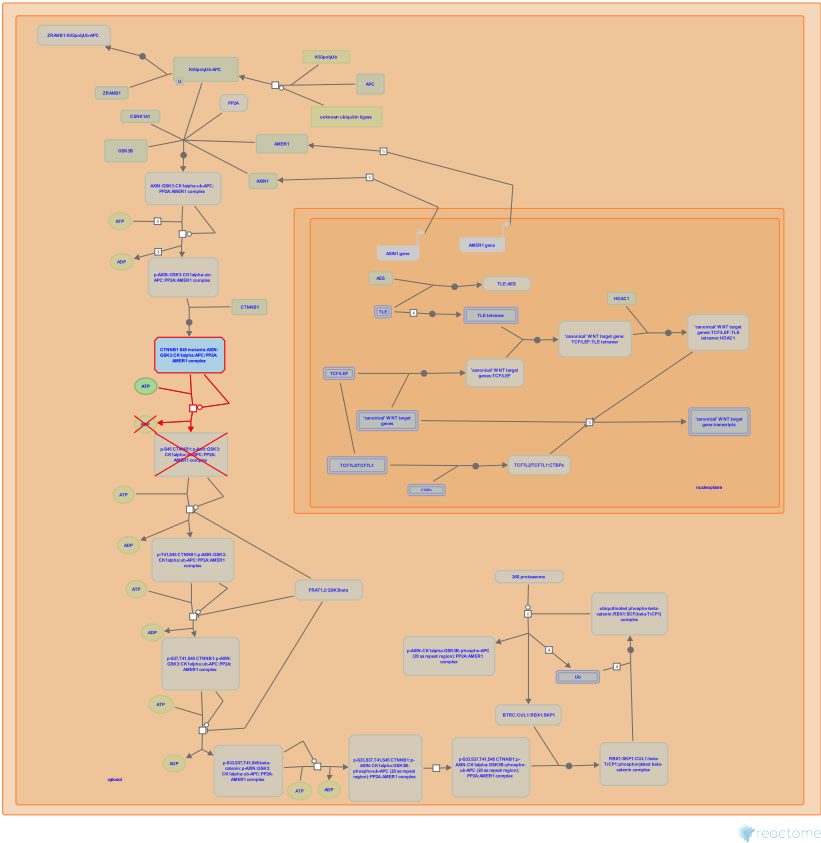
This document contains 1 pathway and 1 reaction ([see Table of Contents](#))

CTNNB1 S45 mutants aren't phosphorylated ↗

Stable identifier: R-HSA-5358751

Compartments: cytosol

Diseases: cancer



S45 mutants of beta-catenin have been identified in colorectal and hepatocellular carcinomas, soft tissue cancer and Wilms Tumors, among others (reviewed in Polakis, 2000). These mutations abolish the CK1alpha phosphorylation site of beta-catenin which acts as a critical priming site for GSK3 phosphorylation of T41(and subsequently S37 and S33) thus preventing its ubiquitin-mediated degradation (Morin et al, 1997; Amit et al, 2002).

Literature references

Andersen, JS., Birman, Y., Mann, M., Ben-Shushan, E., Alkalay, I., Hatzubai, A. et al. (2002). Axin-mediated CKI phosphorylation of beta-catenin at Ser 45: a molecular switch for the Wnt pathway. *Genes Dev*, 16, 1066-76. ↗

Barker, N., Clevers, HC., Morin, PJ., Kinzler, KW., Vogelstein, B., Korinek, V. et al. (1997). Activation of beta-catenin-Tcf signaling in colon cancer by mutations in beta-catenin or APC. *Science*, 275, 1787-90. ↗

Polakis, P. (2000). Wnt signaling and cancer. *Genes Dev.*, 14, 1837-51. ↗

Editions

2014-04-02	Authored	Rothfels, K.
2014-04-03	Edited	Matthews, L.
2014-05-12	Reviewed	Salahshor, S.
2014-05-22	Reviewed	Woodgett, J.

CTNNB1 S45 mutants aren't phosphorylated by CK1alpha ↗

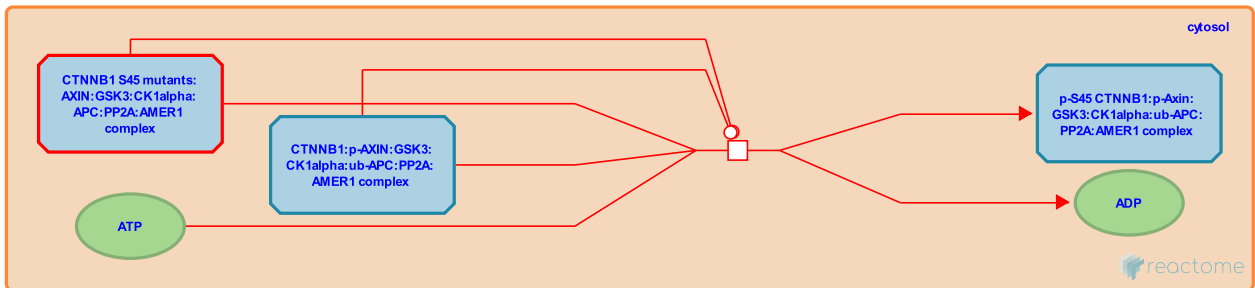
Location: [CTNNB1 S45 mutants aren't phosphorylated](#)

Stable identifier: R-HSA-4827388

Type: transition

Compartments: cytosol

Diseases: cancer



Missense or deletion mutations at Ser45 abolish the CK1alpha phosphorylation site of beta-catenin, which, via its critical role in providing a priming site for GSK3 phosphorylation of three other residues, prevents its ubiquitin-mediated degradation (Morin et al, 1997; Amit et al, 2002). S45 mutant forms of beta-catenin show enhanced nuclear localization, supershift TCF-DNA complexes in vitro and support enhanced transcriptional activity as assessed by reporter assay (Morin et al, 1997; Koesters et al, 2003; Laurent-Puig et al, 2003). Nuclear accumulation of mutant beta-catenin is also associated with increased cell proliferation (Nhieu et al, 1999). S45 gain-of-function mutants of beta-catenin have been identified in colorectal and hepatocellular carcinomas, soft tissue cancer and Wilms Tumors, among others (reviewed in Polakis, 2000).

Literature references

Andersen, JS., Birman, Y., Mann, M., Ben-Shushan, E., Alkalay, I., Hatzubai, A. et al. (2002). Axin-mediated CKI phosphorylation of beta-catenin at Ser 45: a molecular switch for the Wnt pathway. *Genes Dev*, 16, 1066-76. ↗

Bluteau, O., Monges, G., Bioulac-Sage, P., Binot, F., Franco, D., Thomas, G. et al. (2001). Genetic alterations associated with hepatocellular carcinomas define distinct pathways of hepatocarcinogenesis. *Gastroenterology*, 120, 1763-73. ↗

Barker, N., Clevers, HC., Morin, PJ., Kinzler, KW., Vogelstein, B., Korinek, V. et al. (1997). Activation of beta-catenin-Tcf signaling in colon cancer by mutations in beta-catenin or APC. *Science*, 275, 1787-90. ↗

Zafrani, ES., Renard, CA., Wei, Y., Cherqui, D., Nhieu, JT., Buendia, MA. (1999). Nuclear accumulation of mutated beta-catenin in hepatocellular carcinoma is associated with increased cell proliferation. *Am. J. Pathol.*, 155, 703-10. ↗

Polakis, P. (2000). Wnt signaling and cancer. *Genes Dev.*, 14, 1837-51. ↗

Editions

2014-04-03	Edited	Matthews, L.
2014-04-03	Authored	Rothfels, K.
2014-05-12	Reviewed	Salahshor, S.
2014-05-22	Reviewed	Woodgett, J.

Table of Contents

Introduction	1
CTNNB1 S45 mutants aren't phosphorylated	2
CTNNB1 S45 mutants aren't phosphorylated by CK1alpha	3
Table of Contents	4