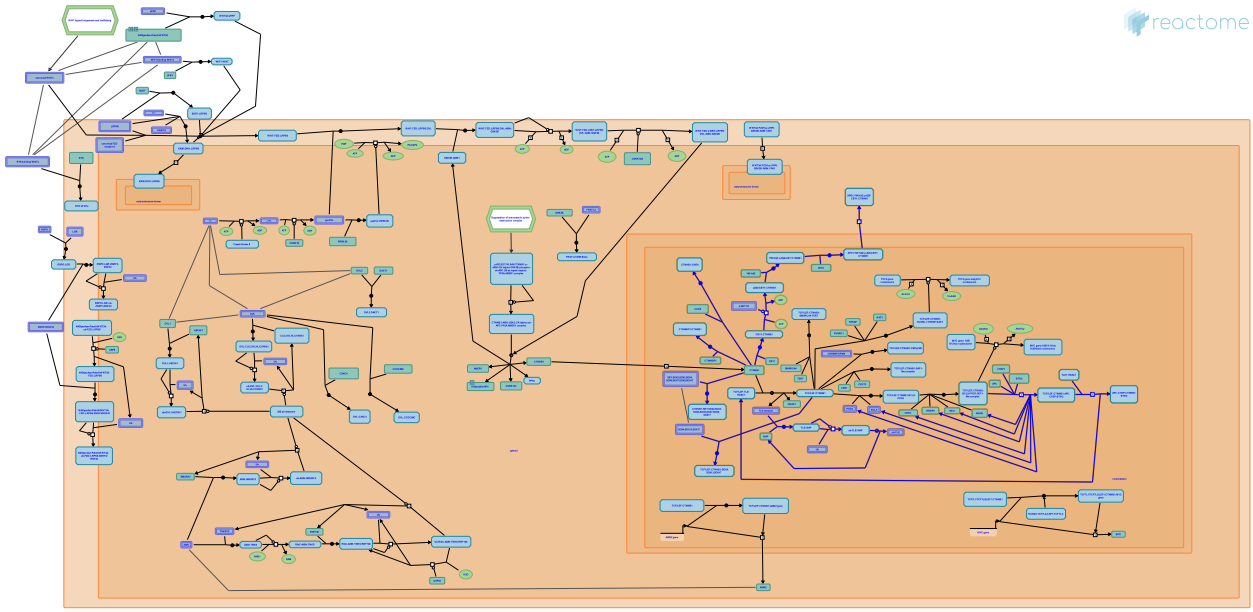
Deactivation of the beta-catenin trans-activating complex



Garapati, P V., Gillespie, ME., Harley, V., Kikuchi, A., Matthews, L., Rajakulendran, N., Rothfels, K., Zorn, AM., van Amerongen, R.

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

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05/05/2024

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.

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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. ↗

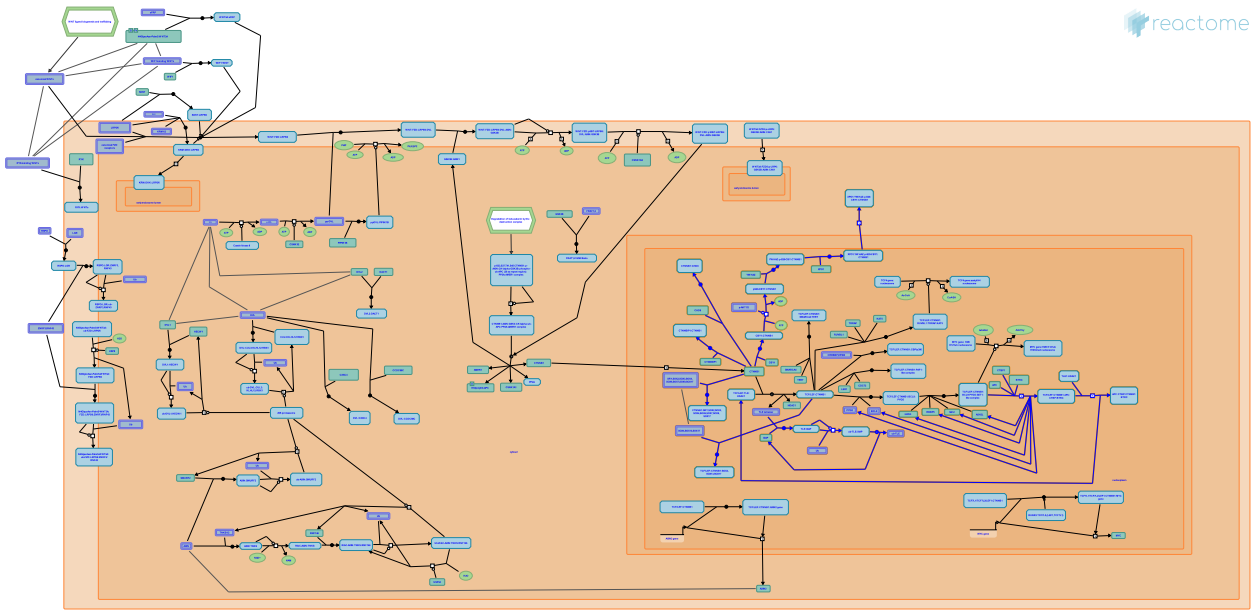
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Deactivation of the beta-catenin transactivating complex ↗

Stable identifier: R-HSA-3769402



The mechanisms involved in downregulation of TCF-dependent transcription are not yet very well understood. beta-catenin is known to recruit a number of transcriptional repressors, including Reptin, SMRT and NCoR, to the TCF/LEF complex, allowing the transition from activation to repression (Bauer et al, 2000; Weiske et al, 2007; Song and Gelmann, 2008). CTNNBIP1 (also known as ICAT) and Chibby are inhibitors of TCF-dependent signaling that function by binding directly to beta-catenin and preventing interactions with critical components of the transactivation machinery (Takemaru et al, 2003; Li et al, 2008; Tago et al, 2000; Graham et al, 2002; Daniels and Weiss, 2002). Chibby additionally promotes the nuclear export of beta-catenin in conjunction with 14-3-3/YWHAZ proteins (Takemura et al, 2003; Li et al, 2008). A couple of recent studies have also suggested a role for nuclear APC in the disassembly of the beta-catenin activation complex (Hamada and Bienz, 2004; Sierra et al, 2006). It is worth noting that while some of the players involved in the disassembly of the beta-catenin transactivating complex are beginning to be worked out in vitro, the significance of their role in vivo is not yet fully understood, and some can be knocked out with little effect on endogenous WNT signaling (see for instance Voronina et al, 2009).

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Daniels, DL., Weis, WI. (2002). ICAT inhibits beta-catenin binding to Tcf/Lef-family transcription factors and the general coactivator p300 using independent structural modules. *Mol. Cell, 10*, 573-84. ↗

Bienz, M., Hamada, F. (2004). The APC tumor suppressor binds to C-terminal binding protein to divert nuclear beta-catenin from TCF. *Dev. Cell, 7*, 677-85. ↗

Gelmann, EP., Song, LN. (2008). Silencing mediator for retinoid and thyroid hormone receptor and nuclear receptor corepressor attenuate transcriptional activation by the beta-catenin-TCF4 complex. *J. Biol. Chem., 283*, 25988-99. ↗

Morishita, Y., Shibuya, H., Hyodo, J., Tago, K., Akiyama, T., Ohwada, S. et al. (2000). Inhibition of Wnt signaling by ICAT, a novel beta-catenin-interacting protein. *Genes Dev., 14*, 1741-9. ↗

Yoshida, T., Jones, KA., Sierra, J., Joazeiro, CA. (2006). The APC tumor suppressor counteracts beta-catenin activation and H3K4 methylation at Wnt target genes. *Genes Dev., 20*, 586-600. ↗

Editions

2007-09-04	Edited	Matthews, L.
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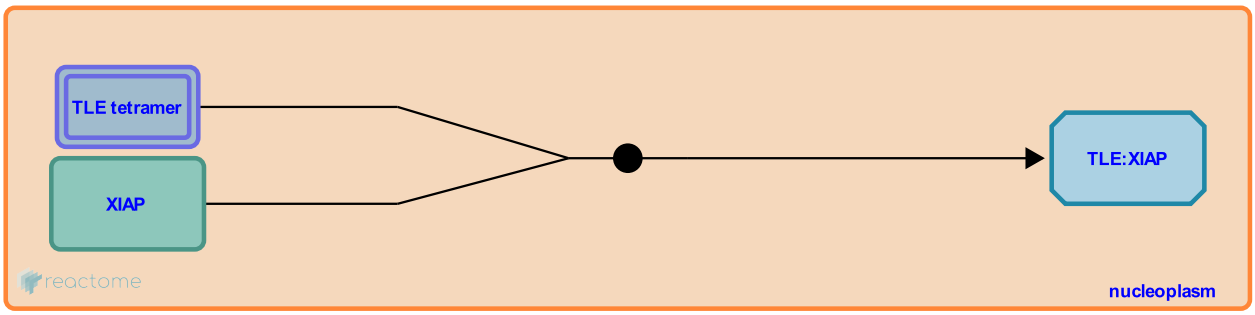
XIAP binds TLE ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3322431

Type: binding

Compartments: nucleoplasm



XIAP (X-linked inhibitor of apoptosis) has three BIR domains with known roles in the degradation of caspases and a C-terminal E3 ligase domain with both anti-apoptotic and non-apoptotic roles (Galban and Duckett, 2010; Burstein et al, 2004). The Drosophila homologue DAIP1 was recently identified in a screen in S2 cells for regulators of Wg signalling (Hanson et al, 2012). Knockdown of XIAP in HEK293 cells reduces WNT3a-induced reporter activity and expression of endogenous WNT target genes without affecting beta-catenin levels or localization. In vitro studies show that XIAP can ubiquitinate all human TLE isoforms, including the truncated isoform Amino-terminal enhancer of split (AES). TLE3 co-immunoprecipitates with XIAP from HEK293 cells in both the presence and absence of WNT signalling, consistent with a constitutive role for XIAP in TLE regulation. XIAP may act either by ubiquitinating free nuclear TLE to reduce the amount available to interact with TCF/LEFs or by ubiquitinating TLE in the context of TCF/LEF transcriptional complexes to promote its dissociation, or both. In support of the latter model, XIAP is pulled down with TCF7L2 (TCF4) in a WNT-dependent manner, and knockdown of XIAP reduces the amount of beta-catenin that co-immunoprecipitates with TCF7L2 (TCF4) upon WNT pathway activation (Hanson et al, 2012).

Followed by: XIAP monoubiquinates TLE

Literature references

Beauchamp, RD., Freeman, TJ., Wallace, HA., Hanson, AJ., Lee, E., Lee, LA. (2012). XIAP monoubiquitylates Groucho/TLE to promote canonical Wnt signaling. *Mol. Cell, 45*, 619-28. ↗

Klomp, LW., Duckett, CS., Wilkinson, JC., Nabel, GJ., van De Sluis, B., Ganesh, L. et al. (2004). A novel role for XIAP in copper homeostasis through regulation of MURR1. *EMBO J., 23*, 244-54. ↗

Duckett, CS., Galbán, S. (2010). XIAP as a ubiquitin ligase in cellular signaling. *Cell Death Differ., 17*, 54-60. ↗

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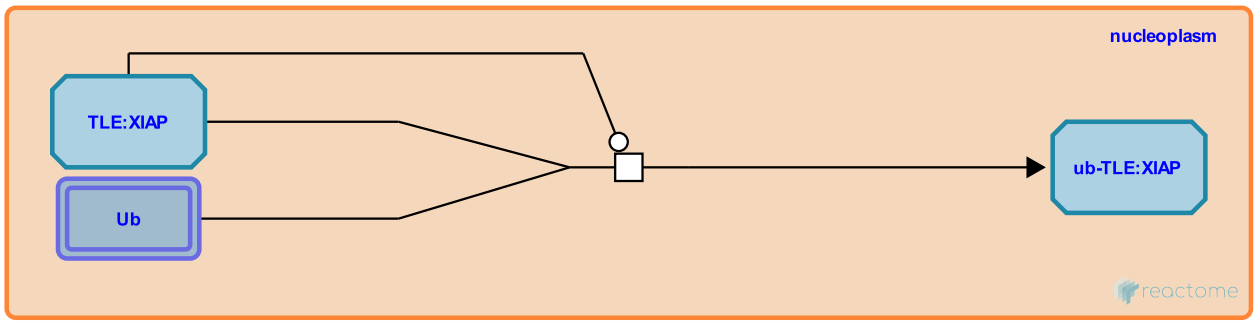
XIAP monoubiquinates TLE ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3322429

Type: transition

Compartments: nucleoplasm



XIAP has been shown to ubiquitinate all human isoforms of TLE in vitro, likely in the conserved Q domain. Ubiquitination does not appear to affect the stability, localization or tetramerization of TLE; rather ubiquitination affects the interaction with TCF/LEF. Ubiquitinated TLE3 is not able to bind TCF7L2 (TCF4) in vitro and addition of XIAP to TLE3-TCF7L2 complexes promotes the dissociation of TLE from TCF7L2. Although XIAP ubiquitinates TLE in a constitutive manner, XIAP only co-immunoprecipitates with TCF7L2 upon activation of the WNT signalling pathway. These data support a model where XIAP regulates the interaction between TLE and TCF/LEF by limiting the pool of free nuclear TLE that is available for binding, and by potentially disrupting existing repression complexes at WNT-responsive promoters. By disrupting the interaction between TLE and TCF/LEF, XIAP may facilitate the recruitment of beta-catenin and the establishment of an activation complex at WNT-responsive promoters (Hanson et al, 2012)

Preceded by: XIAP binds TLE

Followed by: XIAP dissociates from ub-TLE

Literature references

Beauchamp, RD., Freeman, TJ., Wallace, HA., Hanson, AJ., Lee, E., Lee, LA. (2012). XIAP monoubiquitylates Groucho/TLE to promote canonical Wnt signaling. *Mol. Cell, 45*, 619-28. ↗

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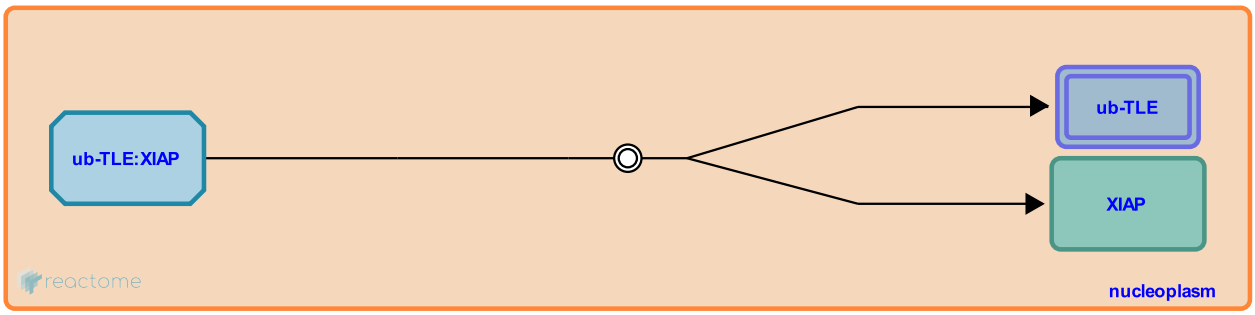
XIAP dissociates from ub-TLE ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3322434

Type: dissociation

Compartments: nucleoplasm



After ubiquitinating TLE, XIAP presumably dissociates. The model proposed by Hanson et al suggests the existence of an as-yet unidentified deubiquitinase that removes the ubiquitin from TLE to allow it to rebind to TCF/LEF.

Preceded by: XIAP monoubiquinates TLE

Literature references

Beauchamp, RD., Freeman, TJ., Wallace, HA., Hanson, AJ., Lee, E., Lee, LA. (2012). XIAP monoubiquitylates Groucho/TLE to promote canonical Wnt signaling. *Mol. Cell, 45*, 619-28. ↗

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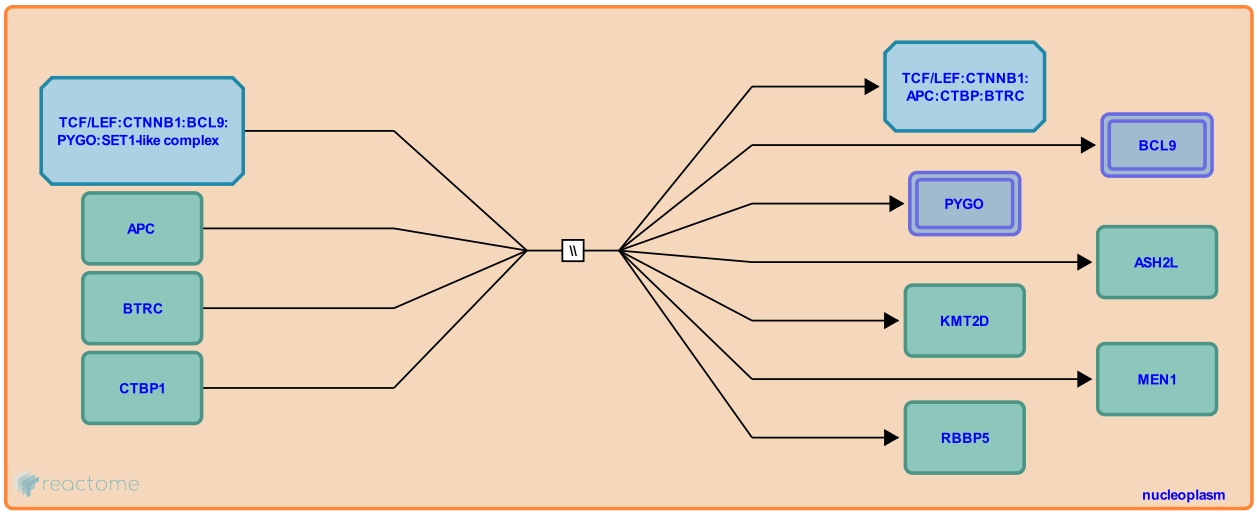
APC promotes disassembly of beta-catenin transactivation complex ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3364042

Type: omitted

Compartments: nucleoplasm



Studies in mouse myoblast and colorectal cancer cell lines show that APC, beta-TrCP and the CTBP corepressor are present at the MYC enhancer at times when beta-catenin and its associated coactivators are also present. Binding of APC is correlated with dissociation of the activator complex and precedes recruitment of TLE1 and HDAC1, suggesting that APC may promote the exchange between activator and repressor complexes at the enhancer (Sierra et al, 2006). CSNK1gamma phosphorylation of APC strongly increases its affinity for beta-catenin, and a phosphorylated APC fragment disrupts the formation of a DNA:LEF1:beta-catenin complex by EMSA, consistent with previous reports (Xing et al, 2003; Xing et al, 2004; Sierra et al, 2006). Because beta-catenin is unable to simultaneously bind APC and TCF/LEF, however, the mechanism of APC recruitment to the enhancer complex is unclear (Sierra et al, 2006). Full-length APC associates with CTBP in vitro and in vivo (Hamada and Bienz, 2004; Sierra et al, 2006) while Class I and Class II mutant APC proteins, which are commonly found in colorectal cancers, do not (Sierra et al, 2006; reviewed in Neufeld, 2009). CTBP repressor functions may therefore include facilitating the exchange of coactivator and corepressor complexes at WNT target genes.

Followed by: beta-catenin is replaced by repression complexes at the promoter

Literature references

Xu, W., Xing, Y., Clements, WK., Kimelman, D. (2003). Crystal structure of a beta-catenin/axin complex suggests a mechanism for the beta-catenin destruction complex. *Genes Dev., 17*, 2753-64. ↗

Yoshida, T., Jones, KA., Sierra, J., Joazeiro, CA. (2006). The APC tumor suppressor counteracts beta-catenin activation and H3K4 methylation at Wnt target genes. *Genes Dev., 20*, 586-600. ↗

Neufeld, KL. (2009). Nuclear APC. *Adv. Exp. Med. Biol., 656*, 13-29. ↗

Kimelman, D., Stenkamp, R., Hinds, TR., Xing, Y., Clements, WK., Le Trong, I. et al. (2004). Crystal structure of a beta-catenin/APC complex reveals a critical role for APC phosphorylation in APC function. *Mol Cell, 15*, 523-33. ↗

Bienz, M., Hamada, F. (2004). The APC tumor suppressor binds to C-terminal binding protein to divert nuclear beta-catenin from TCF. *Dev. Cell, 7*, 677-85. ↗

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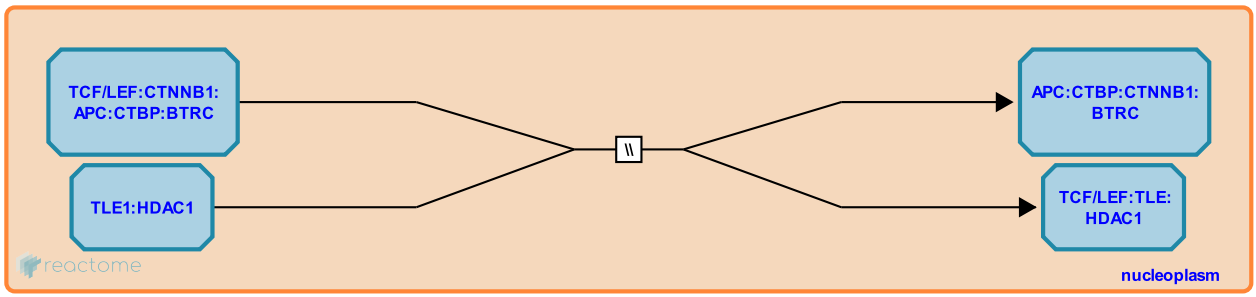
beta-catenin is replaced by repression complexes at the promoter ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3361751

Type: omitted

Compartments: nucleoplasm



Displacement of the APC:CTBP:beta-catenin:betaTrCP complex allows subsequent recruitment of TLE:HDAC1 to TCF/LEF, re-establishing a repression complex (Sierra et al, 2006)

Preceded by: APC promotes disassembly of beta-catenin transactivation complex

Literature references

Yoshida, T., Jones, KA., Sierra, J., Joazeiro, CA. (2006). The APC tumor suppressor counteracts beta-catenin activation and H3K4 methylation at Wnt target genes. *Genes Dev., 20*, 586-600. ↗

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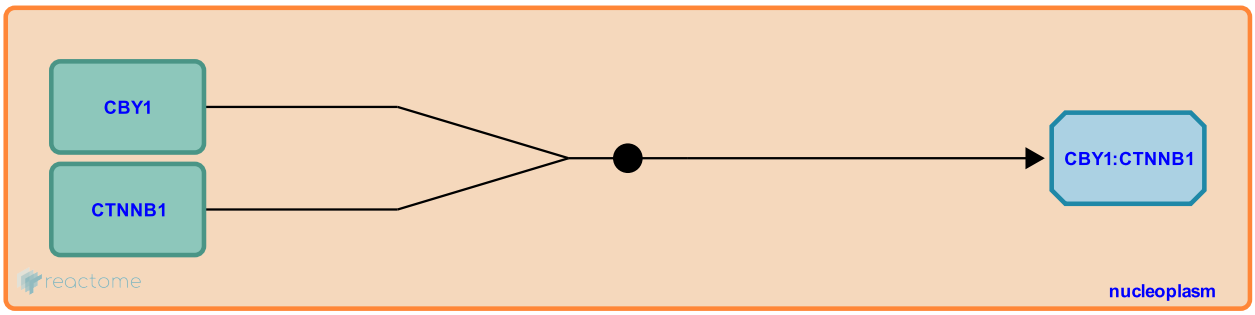
CBY1 binds beta-catenin ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3769383

Type: binding

Compartments: nucleoplasm



Chibby (CBY1) is a conserved 126 amino acid protein that acts as an antagonist to the canonical WNT signaling pathway. CBY1 binds to the C-terminal region of beta-catenin and inhibits beta-catenin-dependent signaling by competing for the TCF/LEF binding sites and by promoting beta-catenin nuclear export (Takemaru et al, 2003; Li et al, 2008; Li et al, 2010). Endogenous CBY1 and beta-catenin co-immunoprecipitate from HEK293 cells and overexpression of CBY1 reduces expression of a beta-catenin dependent reporter gene, supporting a functional role for the CBY1-beta-catenin interaction in vivo (Takemaru et al, 2003). Studies with CBY1 knockout mice show only a slight effect on expression of WNT-dependent target genes, however; more work will be required to fully elucidate the role of CBY1 in regulating endogenous WNT signaling (Veronina et al, 2009).

Followed by: AKT phosphorylates CBY1

Literature references

Yamaguchi, S., Zhang, Y., Moon, RT., Takemaru, K., Lee, YS., Carthew, RW. (2003). Chibby, a nuclear beta-catenin-associated antagonist of the Wnt/Wingless pathway. *Nature, 422*, 905-9. ↗

Adams, A., Hajjar, AM., Voronina, VA., Takemaru, K., Li, FQ., Treuting, P. et al. (2009). Inactivation of Chibby affects function of motile airway cilia. *J. Cell Biol., 185*, 225-33. ↗

Mofunanya, A., Harris, K., Takemaru, K., Li, FQ. (2008). Chibby cooperates with 14-3-3 to regulate beta-catenin sub-cellular distribution and signaling activity. *J. Cell Biol., 181*, 1141-54. ↗

Hall, J., Mofunanya, A., Fischer, V., Takemaru, K., Li, FQ. (2010). Nuclear-cytoplasmic shuttling of Chibby controls beta-catenin signaling. *Mol. Biol. Cell, 21*, 311-22. ↗

Editions

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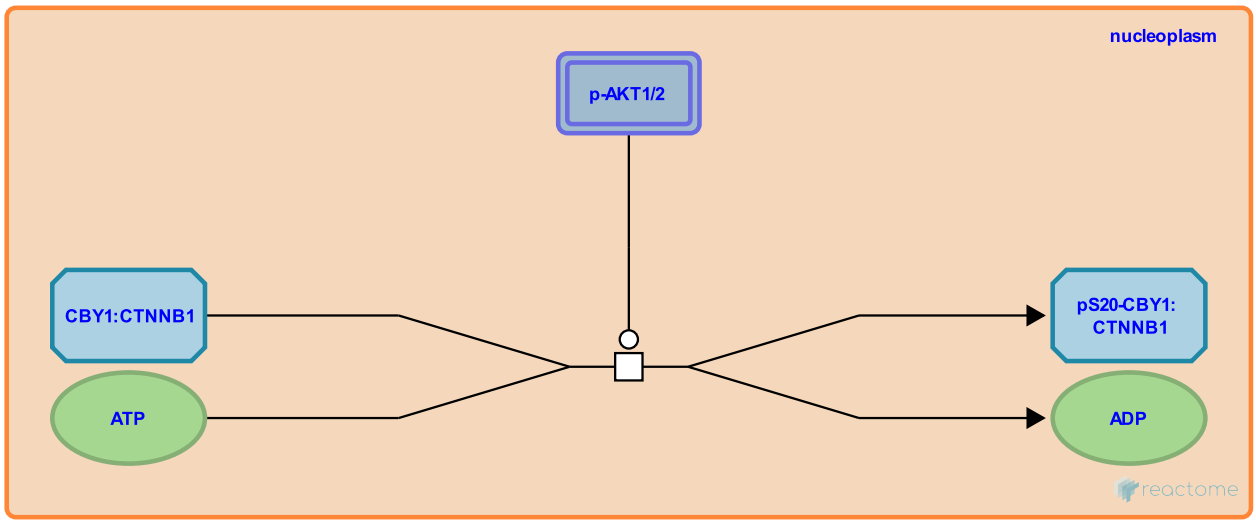
AKT phosphorylates CBY1 ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3769394

Type: transition

Compartments: nucleoplasm



CBY1 is phosphorylated in vitro at serine 20 by AKT1 and AKT2. In vivo, this phosphorylation is required for the export of beta-catenin from the nucleus, facilitated by the binding of 14-3-3/YWHAZ proteins to the pS20 residue of CBY1 (Li et al, 2008).

Preceded by: CBY1 binds beta-catenin

Followed by: YWHAZ binds p-CBY:CTNNB1

Literature references

Mofunanya, A., Harris, K., Takemaru, K., Li, FQ. (2008). Chibby cooperates with 14-3-3 to regulate beta-catenin subcellular distribution and signaling activity. *J. Cell Biol., 181*, 1141-54. ↗

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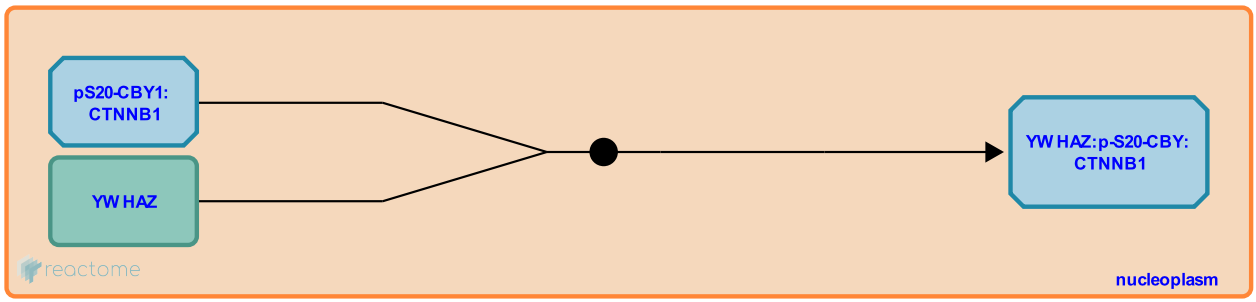
YWHAZ binds p-CBY:CTNNB1 ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3769393

Type: binding

Compartments: nucleoplasm



14-3-3 proteins, represented here as YWHAZ, bind directly to CBY1 after AKT-dependent phosphorylation of CBY1 serine 20. Tagged versions of beta-catenin, CBY1 and 14-3-3/YWHAZ expressed in HEK293 cells co-immunoprecipitate in a CBY1-phosphorylation dependent manner. 14-3-3/YWHAZ binding promotes sequestration of CBY1 and beta-catenin in the cytoplasm, thus antagonizing beta-catenin-dependent transcription (Li et al, 2008).

Preceded by: AKT phosphorylates CBY1

Followed by: XPO1 binds the beta-catenin:CBY complex

Literature references

Mofunanya, A., Harris, K., Takemaru, K., Li, FQ. (2008). Chibby cooperates with 14-3-3 to regulate beta-catenin subcellular distribution and signaling activity. *J. Cell Biol., 181*, 1141-54. ↗

Editions

2013-05-30	Authored	Rothfels, K.
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2014-04-22	Reviewed	Kikuchi, A.

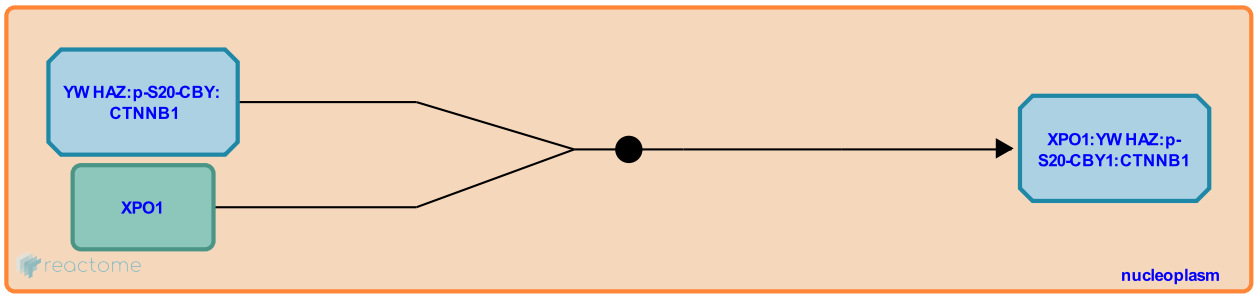
XPO1 binds the beta-catenin:CBY complex ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3769391

Type: binding

Compartments: nucleoplasm



CBY1 contains both NLS and NES sequences and continuously shuttles between the cytoplasm and the nucleus. Treatment of cells with leptomycin B (LMB), an inhibitor of XPO1-mediated nuclear export, results in nuclear accumulation of both CBY1 and 14-3-3/YWHAZ proteins (Li et al, 2008; Li et al, 2010). Consistent with this, CBY1 binds to XPO1 in an NES-dependent manner. 14-3-3/YWHAZ enhances the CBY1-XPO1 interaction, possibly by inducing a conformational change that exposes the adjacent NES sequence. Binding of 14-3-3/YWHAZ also inhibits the interaction of CBY1 with alpha-importin, additionally favouring its cytoplasmic localization. CBY1 NES mutants that are incapable of nuclear export show reduced ability to repress a beta-catenin-dependent reporter, and knockdown of endogenous CBY1 causes an accumulation of beta-catenin in the nucleus. These data support a role for CBY1 in the nuclear export of beta-catenin (Li et al, 2010). Despite growing evidence for a role for CBY1 in regulating WNT signaling, a formal requirement for CBY1 in vivo is still lacking.

Preceded by: YWHAZ binds p-CBY:CTNNB1

Followed by: YWHAZ and XPO1 mediate the nuclear export of beta-catenin

Literature references

Hall, J., Mofunanya, A., Fischer, V., Takemaru, K., Li, FQ. (2010). Nuclear-cytoplasmic shuttling of Chibby controls beta-catenin signaling. *Mol. Biol. Cell, 21*, 311-22. ↗

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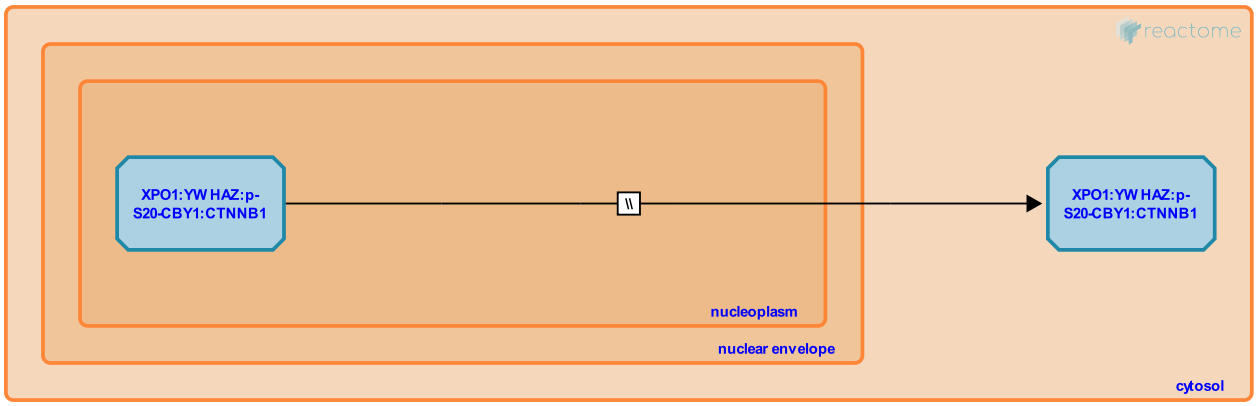
YWHAZ and XPO1 mediate the nuclear export of beta-catenin ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3769392

Type: omitted

Compartments: nucleoplasm, cytosol



14-3-3/YWHAZ and XPO1 both contribute to the CBY1-mediated nuclear export of beta-catenin (Li et al, 2008; Li et al, 2010). The fate of the tripartite beta-catenin:CBY1:14-3-3/YWHAZ complex in the cytoplasm is unknown, although it may represent a reservoir of beta-catenin available for further signaling. CBY1 may remain associated with 14-3-3/YWHAZ in the cytoplasm, as 14-3-3/YWHAZ binding inhibits binding of alpha-importin to CBY1 (Li et al, 2010) . This suggests the presence of a phosphatase that dephosphorylates S20 on CBY1 to allow binding with alpha-importin and reimport into the nucleus.

Preceded by: XPO1 binds the beta-catenin:CBY complex

Literature references

Mofunanya, A., Harris, K., Takemaru, K., Li, FQ. (2008). Chibby cooperates with 14-3-3 to regulate beta-catenin subcellular distribution and signaling activity. *J. Cell Biol., 181*, 1141-54. ↗

Hall, J., Mofunanya, A., Fischer, V., Takemaru, K., Li, FQ. (2010). Nuclear-cytoplasmic shuttling of Chibby controls beta-catenin signaling. *Mol. Biol. Cell, 21*, 311-22. ↗

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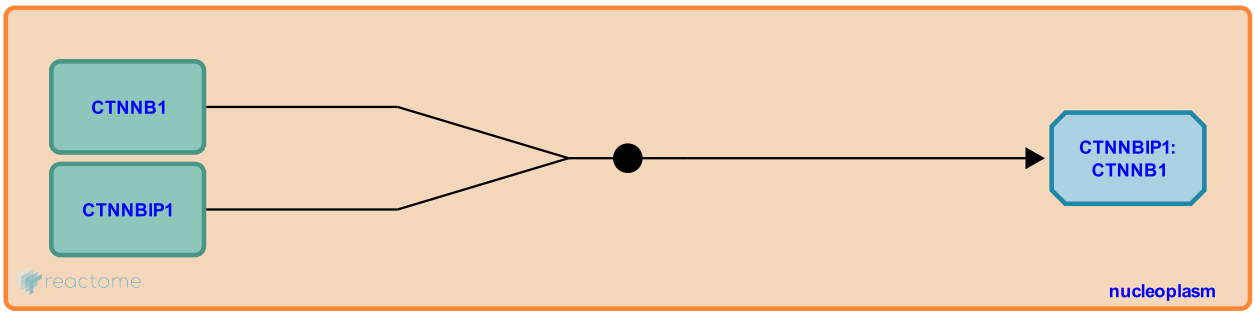
CTNNBIP1 binds beta-catenin ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-3772430

Type: binding

Compartments: nucleoplasm



CTNNBIP1 (also known as ICAT) is an 81 amino-acid protein that was identified in a two-hybrid screen to identify beta-catenin interacting partners (Tago et al, 2000). CTNNBIP1 binds directly to beta-catenin in vitro and in vivo and interferes with the formation of a TCF/LEF:beta-catenin complex (Tago et al, 2000; Daniels and Weiss et al, 2002; Graham et al, 2002). Expression of CTNNBIP1 abrogates expression of a WNT-dependent reporter gene (Tago et al, 2000).

Literature references

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Editions

2013-05-30	Authored	Rothfels, K.
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2014-01-22	Reviewed	Rajakulendran, N.
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2014-04-22	Reviewed	Kikuchi, A.

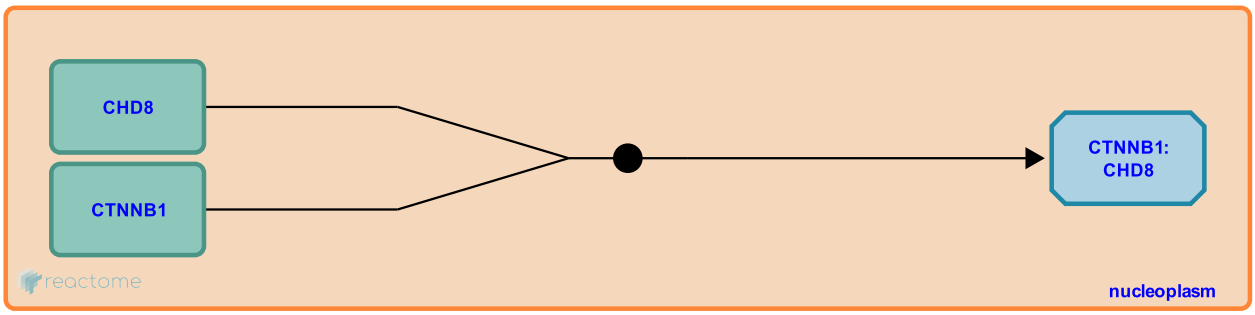
CHD8 binds beta-catenin to negatively regulate WNT-dependent gene expression ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-5368580

Type: binding

Compartments: nucleoplasm



CHD8 is a ATP-dependent chromatin remodeling factor that binds directly to beta-catenin to repress transcription of WNT target genes (Thompson et al, 2008; Sakamoto et al, 2000). ChIP studies show that CHD8 is recruited to the promoters of several beta-catenin-responsive targets, and knockdown of CHD8 results in induction of these target genes in vivo (Thompson et al, 2008). An N-terminal fragment of CHD was independently identified as the rat protein Duplin. Duplin was shown to negatively regulate WNT target gene expression by competing with TCF7L2 for beta-catenin binding (Sakamoto et al, 2000; Kobayashi et al, 2002). A corresponding fragment of CHD8 has not been identified in human cells and its significance is not clear.

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Kishida, M., Kikuchi, A., Asashima, M., Sakamoto, I., Takada, S., Hino, S. et al. (2000). A novel beta-catenin-binding protein inhibits beta-catenin-dependent Tcf activation and axis formation. *J. Biol. Chem., 275*, 32871-8. ↗

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Editions

2014-04-22	Authored	Kikuchi, A.
2014-05-07	Edited	Matthews, L.

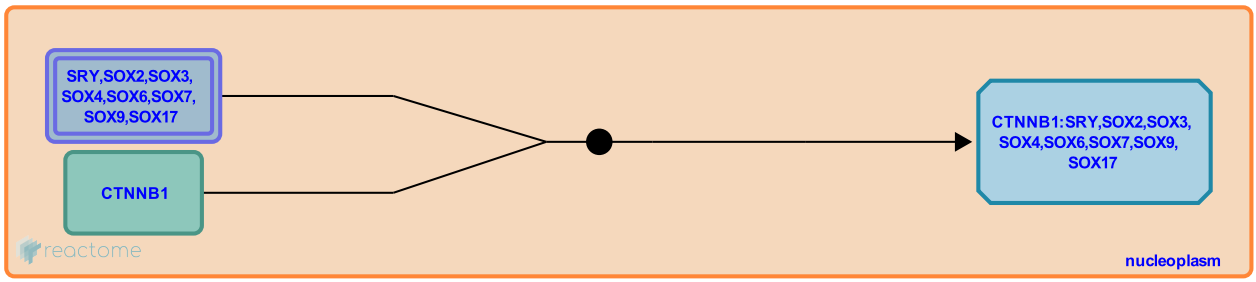
Beta-catenin binds SOX proteins ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-5626938

Type: binding

Compartments: nucleoplasm



SOX protein family members are the transcription factors that regulate many different development processes and also control homeostasis in adult tissues. SOX proteins can be either transcriptional activators or repressors depending on the cellular context and their associated interacting proteins (Kormish et al. 2010). There are over twenty SOX proteins encoded in mammalian genome of which many of these can physically interact with beta-catenin and TCF (T-cell factor) transcription factors and modulate the Wnt signaling. Evidences suggest that SOX proteins have widespread role in modulating Wnt signaling in development and disease. In most cases SOX proteins repress WNT transcriptional responses, however some SOX proteins appear to enhance WNT-regulated gene expression. The precise mechanism by which SOX proteins regulate beta-catenin/TCF activity are still unclear. Differential recruitment of transcriptional co-activators or co-repressors is one mechanism by which SOX factors can either enhance or repress Wnt-target gene transcription. Another mechanism by which some SOX proteins repress Wnt signaling is by promoting proteosome-mediated beta-catenin degradation (Kormish et al. 2010).
Human SRY binds beta-catenin through a N-terminal domain (Bernard et al. 2008), SOX6 interacts via a centrally located leucine zipper (LZ/Q) element (Iguchi et al. 2007), and mammalian SOX7, SOX9 and SOX17 all bind beta-catenin via their C-terminal regions (Zorn et al., 1999; Takash et al., 2001; Akiyama et al., 2004; Sinner et al., 2007, Kormish et al. 2010). SRY and SOX9 function in part by suppressing canonical Wnt signaling by promoting beta-catenin phosphorylation in the nucleus (Topol et al. 2009). SOX9 and SRY are involved in the regulation of mammalian sex determination and mutation in human SRY and SOX9 results in sex reversal, with female development in XY individuals (Bernard et al. 2008). SOX2 binds beta-catenin and promotes cell proliferation by transcriptionally activating the Wnt target Cyclin D1 gene in breast cancer cells (Chen et al., 2008), whereas SOX6 represses Cyclin D1 transcription in pancreatic cells (Iguchi et al., 2007). SOX7 and SOX17 reduce cyclin-D1 expression and repress proliferation by stimulating beta-catenin degradation (Sinner et al. 2007, Zhang et al. 2008, 2009).

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Editions

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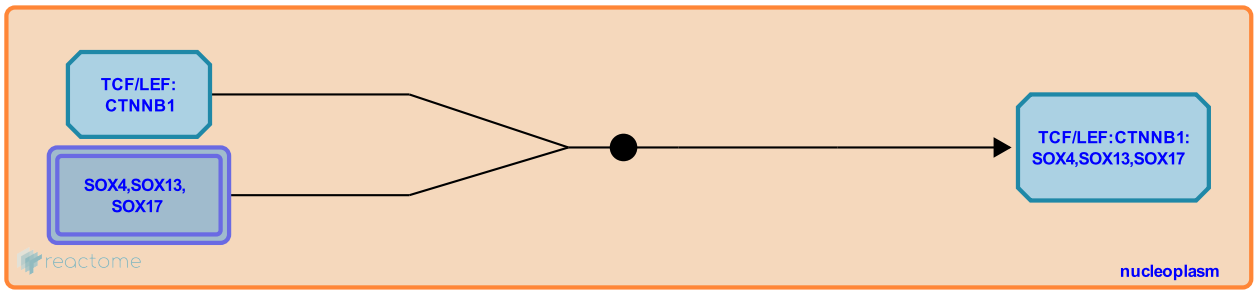
TCF:Beta-catenin binds SOX proteins ↗

Location: Deactivation of the beta-catenin transactivating complex

Stable identifier: R-HSA-5665608

Type: binding

Compartments: nucleoplasm



In vitro protein binding experiments have shown that mammalian SOX4, SOX13 and SOX17 can directly interact with TCF (T-cell factor) (Sinner at al. 2007). SOX4 and SOX17 can interact with either TCF or beta-catenin protein. They have opposite effects on Wnt signalling, SOX4 enhances while SOX17 represses Wnt activity (Sinner et al. 2007). SOX13 is known to repress Wnt signaling by interacting and sequestering TCF1 from the Wnt transcriptionally active complex (Melichar et al. 2007). SOX and TCF proteins interact with overlapping armadillo repeats with in beta-catenin and thus might compete for beta-catenin binding (Kormish et al. 2010).

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Lin, SC., Opoka, R., Kordich, JJ., Zorn, AM., Spence, JR., Rankin, S. et al. (2007). Sox17 and Sox4 differentially regulate beta-catenin/T-cell factor activity and proliferation of colon carcinoma cells. *Mol. Cell. Biol., 27*, 7802-15. ↗

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Editions

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2015-02-11	Reviewed	Zorn, AM., Harley, V.

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