Beta-catenin binds SOX proteins

Garapati, P V., Harley, V., Zorn, AM.

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

16/10/2024

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. ↗

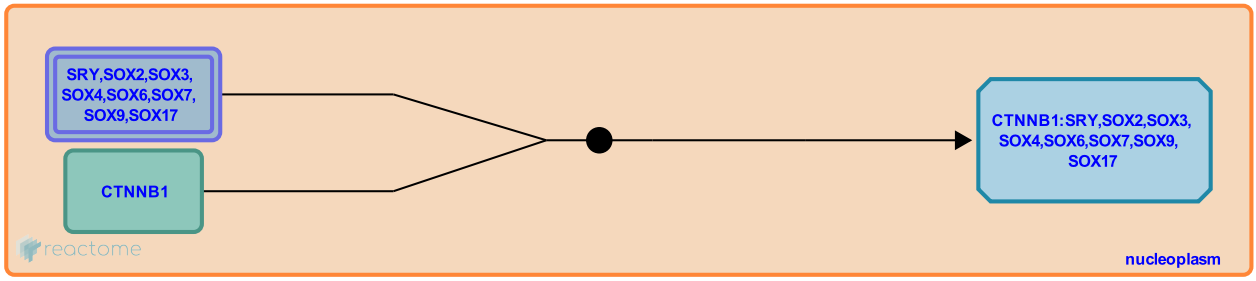
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Beta-catenin binds SOX proteins ↗

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).

Literature references

Zhang, Y., Yang, X., Yu, W., Shi, L., Li, R., Zhang, L. et al. (2008). The molecular mechanism governing the oncogenic potential of SOX2 in breast cancer. *J. Biol. Chem., 283*, 17969-78. ↗

Darido, C., Marty-Double, C., Hollande, F., Scherer, G., Kist, R., Bibeau, F. et al. (2007). Sox9 regulates cell proliferation and is required for Paneth cell differentiation in the intestinal epithelium. *J. Cell Biol., 178*, 635-48. ↗

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. ↗

Sakai, J., Tanaka, T., Inagaki, Y., Iguchi, H., Ikeda, Y., Yamamoto, TT. et al. (2007). SOX6 suppresses cyclin D1 promoter activity by interacting with beta-catenin and histone deacetylase 1, and its down-regulation induces pancreatic beta-cell proliferation. *J. Biol. Chem., 282*, 19052-61. ↗

Bonneaud, N., Poulat, F., Berta, P., Jay, P., Takash, W., Mattei, MG. et al. (2001). SOX7 transcription factor: sequence, chromosomal localisation, expression, transactivation and interference with Wnt signalling. *Nucleic Acids Res., 29*, 4274-83. ↗

Editions

2014-10-08	Authored, Edited	Garapati, P V.
2015-02-11	Reviewed	Zorn, AM., Harley, V.