Phosphorylation of LRP5/6 cytoplasmic domain by membrane-associated GSK3beta

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03/05/2024

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. ↗

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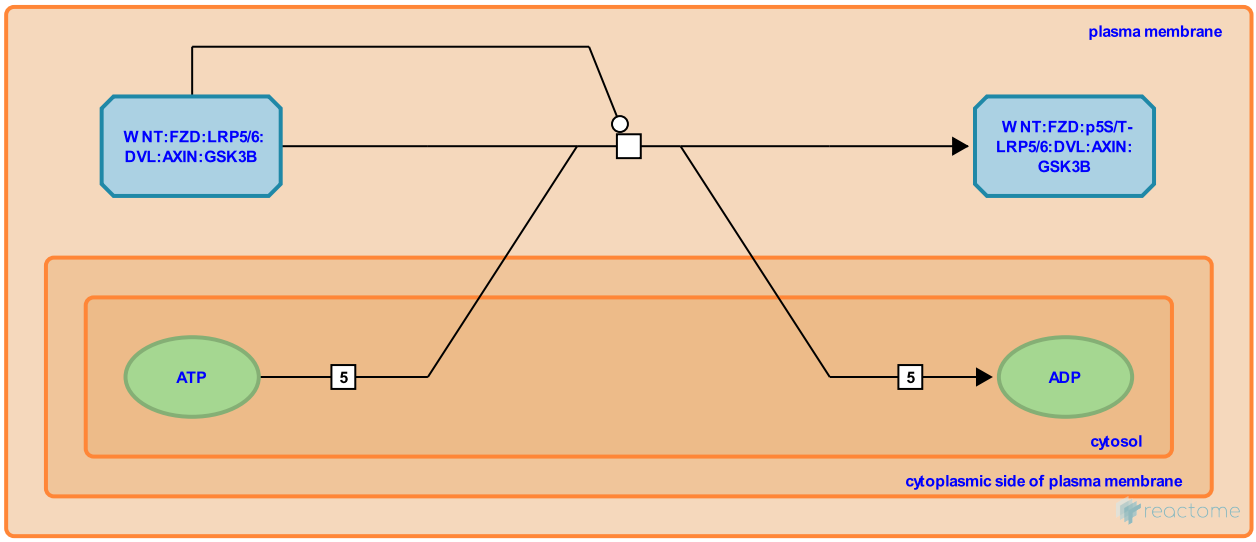
Stable identifier: R-HSA-201677

Type: transition

Compartments: plasma membrane, cytosol, extracellular region



LRP5/6 contains 5 PPP(S/T)PxS motifs in its intracellular domain which have been shown to be phosphorylated by a membrane-associated pool of GSK3beta. Individual phosphorylation of each of these motifs promotes interaction with AXIN and stimulates WNT signaling as assessed by activation of a TCF/beta-catenin responsive reporter (Tamai et al, 2004; Zeng et al, 2005; MacDonald et al, 2008). In the context of full length LRP6, phosphorylation of the five motifs shows cooperative stimulation of AXIN binding and WNT signaling. GSK3beta-mediated phosphorylation of LRP6 is thought to prime the receptor for subsequent phosphorylation by CSNK1 (Zeng et al, 2005; reviewed in He et al, 2004).

Literature references

Tamai, K., Zeng, X., Semenov, M., He, X. (2004). LDL receptor-related proteins 5 and 6 in Wnt/beta-catenin signaling: arrows point the way. *Development, 131*, 1663-77. ↗

MacDonald, BT., Tamai, K., Yokota, C., Zeng, X., He, X. (2008). Wnt signal amplification via activity, cooperativity, and regulation of multiple intracellular PPPSP motifs in the Wnt co-receptor LRP6. *J Biol Chem, 283*, 16115-23. ↗

Tamai, K., Woodgett, J., Okamura, H., Doble, B., Li, S., Huang, H. et al. (2005). A dual-kinase mechanism for Wnt co-receptor phosphorylation and activation. *Nature, 438*, 873-7. ↗

Zhang, X., Tamai, K., Chang, Z., Harada, Y., Zeng, X., He, X. et al. (2004). A mechanism for Wnt coreceptor activation . *Mol Cell, 13*, 149-56. ↗

Editions

2007-09-10	Edited	Matthews, L.
2013-08-24	Authored	Rothfels, K.
2013-10-03	Edited	Gillespie, ME.
2014-01-22	Reviewed	Rajakulendran, N.
2014-02-15	Reviewed	van Amerongen, R.
2014-04-22	Reviewed	Kikuchi, A.