ADRBK1 phosphorylates SMO dimer

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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

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. ↗

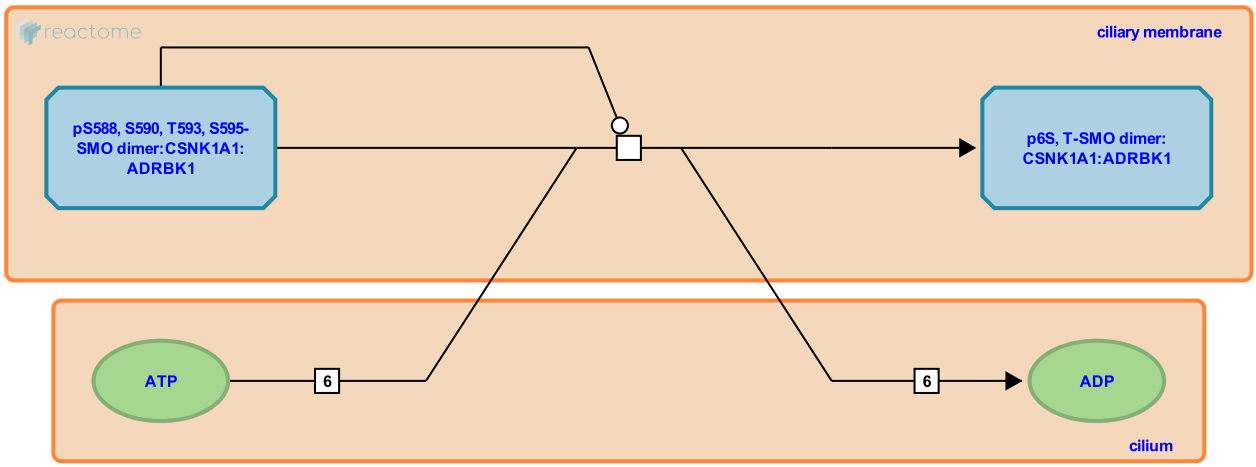
ADRBK1 phosphorylates SMO dimer ↗

Stable identifier: R-HSA-5632672

Type: transition

Compartments: ciliary membrane

Inferred from: Adrbk1 phosphorylates Smo dimer (Mus musculus)



ADRBK1 phosphorylates the SMO C-terminal tail after initial phosphorylation by CSNK1A1. Phosphorylation promotes an open, activated conformation of the C-terminal tails, allowing an intramolecular interaction between tails of adjacent monomers in the SMO dimer. This Hh-dependent conformational change is required for downstream signal propagation (Chen et al, 2011; Chen et al, 2010; Zhao et al, 2007; Meloni et al, 2006; Philipp et al, 2008; reviewed in Briscoe and Therond, 2013). In Drosophila, Smo C-terminal tail phosphorylation promotes an association with the Hedgehog signaling complex (HSC) through interaction with the scaffolding kinesin-2 like protein Cos2, and ultimately results in the release of full-length Ci from the complex (Zhang et al, 2005; Ogden et al, 2003; Lum et al, 2003; reviewed in Mukhopadhyay and Rohatgi, 2014). How Hh signal is transmitted from activated SMO to downstream components in vertebrate cells is not fully established

Literature references

Zhao, Y., Tong, C., Jiang, J. (2007). Hedgehog regulates smoothened activity by inducing a conformational switch. *Nature, 450*, 252-8. ↗

Mukhopadhyay, S., Rohatgi, R. (2014). G-protein-coupled receptors, Hedgehog signaling and primary cilia. *Semin. Cell Dev. Biol.*. ↗

Briscoe, J., Thérond, PP. (2013). The mechanisms of Hedgehog signalling and its roles in development and disease. *Nat. Rev. Mol. Cell Biol., 14*, 416-29. ↗

Philipp, M., Fralish, GB., Meloni, AR., Chen, W., MacInnes, AW., Barak, LS. et al. (2008). Smoothened signaling in vertebrates is facilitated by a G protein-coupled receptor kinase. *Mol. Biol. Cell, 19*, 5478-89. ↗

Yue, S., Tang, LY., Tang, Y., Tang, Y., Shen, QH., Ding, J. et al. (2014). Requirement of Smurf-mediated endocytosis of Patched1 in Sonic Hedgehog signal reception. *Elife*, e02555. ↗

Editions

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