NOTCH1 binds DLK1

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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. ↗

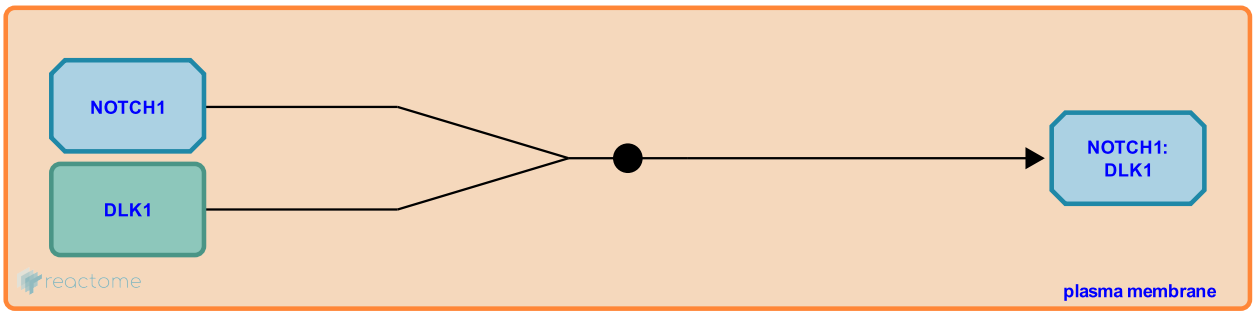
NOTCH1 binds DLK1 ↗

Stable identifier: R-HSA-1980130

Type: binding

Compartments: plasma membrane

Inferred from: Notch1 binds Dlk1 (Mus musculus)



DLK1 is a Delta-like transmembrane protein with six extracellular EGF repeats and a short intracellular tail. DLK1 is encoded by a paternally imprinted gene and, based on mouse studies, is implicated in many developmental processes, such as adipogenesis, hematopoiesis, differentiation of adrenal gland and other neuroendocrine cells, as well as development of the central nervous system. Mice lacking Dlk1 exhibit growth retardation and obesity. Based on studies done in mice and flies, NOTCH1 and DLK1 interact to form a complex, most likely in cis, which results in the inhibition of NOTCH1 signaling by preventing NOTCH1 interaction with DLL and JAG ligands (Baladron et al. 2005, Bray et al. 2008). Besides its inhibitory role, DLK1 may function as a coactivator for NOTCH receptors. DLK1 possesses a Delta and OSM-11 motif (DOS), which has been found in C. elegans proteins that facilitate Notch activation in trans by DSL family ligands. The mammalian DLK1 can substitute for OSM-11 protein in C. elegans development (Komatsu et al. 2008).

Literature references

Komatsu, H., Chao, MY., Larkins-Ford, J., Corkins, ME., Somers, GA., Tucey, T. et al. (2008). OSM-11 facilitates LIN-12 Notch signaling during Caenorhabditis elegans vulval development. *PLoS Biol, 6*, e196. ↗

Baladrón, V., Ruiz-Hidalgo, MJ., Nueda, ML., Díaz-Guerra, MJM., García-Ramírez, JJ., Bonvini, E. et al. (2005). dlk acts as a negative regulator of Notch1 activation through interactions with specific EGF-like repeats. *Exp Cell Res, 303*, 343-59. ↗

Bray, SJ., Takada, S., Harrison, E., Shen, SC., Ferguson-Smith, AC. (2008). The atypical mammalian ligand Delta-like homologue 1 (Dlk1) can regulate Notch signalling in Drosophila. *BMC Dev Biol, 8*, 11. ↗

Editions

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