Proteolytic processing of SLIT

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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. ↗

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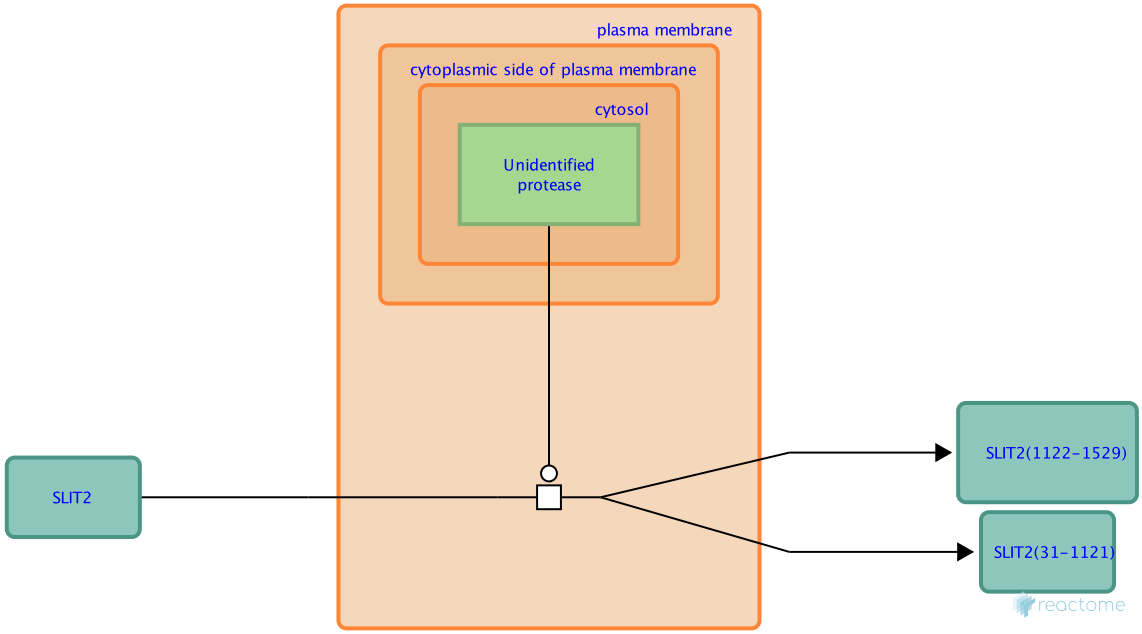
Stable identifier: R-HSA-376149

Type: transition

Compartments: plasma membrane



The full length SLIT proteins are secreted and, when not bound to ROBO receptors, are indirectly associated with the plasma membrane via the extracellular matrix proteins. These full length SLITs undergo posttranslational modification and proteolytic processing to generate an N-terminal fragment (SLIT2-N) and a corresponding C-terminal fragment (SLIT2-C). SLIT2 is cleaved within the EGF repeats, between EGF5 and EGF6, by unknown proteases. Cleavage of SLIT proteins is evolutionarily conserved, although the molecular biological significance is unknown. The N-terminal fragment of SLIT2 stimulates growth and branching of dorsal root ganglia (DRG) axons, and this activity is opposed by un-cleaved SLIT. The stimulation of axon branching is mediated by ROBO receptors. Additional functional differences between the full-length and N-terminal forms have been discovered in their abilities to repel different populations of axons and dendrites. Finally, SLIT can attract migrating muscles in the fly, and also human endothelial cells, both via ROBO receptors (Brose et al. 1999, Wang et al. 1999).

SLIT C-terminal fragments may transduce signaling independently of ROBO receptors and Neuropilins (semaphorin receptors) by directly binding to Plexin A1 (Delloye-Bourgeois et al. 2015).

Literature references

Wang, KH., Brose, K., Arnott, D., Kidd, T., Goodman, CS., Henzel, W. et al. (1999). Biochemical purification of a mammalian slit protein as a positive regulator of sensory axon elongation and branching. *Cell, 96*, 771-84. ↗

Brose, K., Bland, KS., Wang, KH., Arnott, D., Henzel, W., Goodman, CS. et al. (1999). Slit proteins bind Robo receptors and have an evolutionarily conserved role in repulsive axon guidance. *Cell, 96*, 795-806. ↗

Editions

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