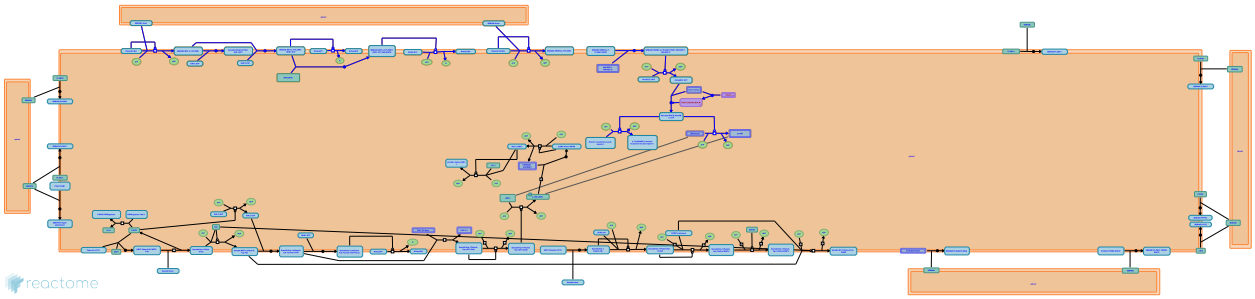
Sema4D in semaphorin signaling



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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.
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. ↗

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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. ↗

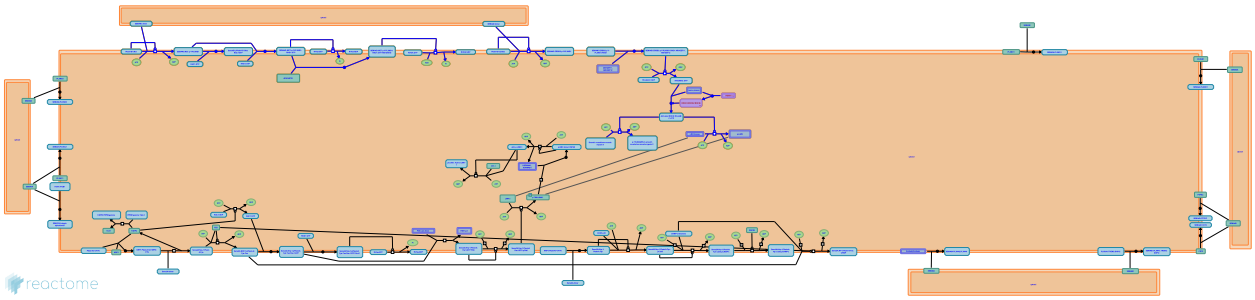
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

Sema4D in semaphorin signaling ↗

Stable identifier: R-HSA-400685



Semaphorin 4D (Sema 4D/CD100) is an axon guidance molecule with two disulfide-linked 150-kDa subunits. SEMA4D is structurally defined by a conserved 500-amino acid extracellular domain with 16 cysteines (sema domain) and also an Ig-like domain C-terminal to the sema domain. Sema4D is expressed on the cell surface as a homodimer; cysteine 679 within the sema domain is required for this dimerization.
The main receptors for Sema4D are plexin-B1 and CD72. The activation of plexins by semaphorins initiates a variety of signaling processes that involve several small GTPases of the Ras and Rho families. Sema4D-Plexin-B1 interaction appears to mediate different and sometimes opposite effects depending on the cellular context. Plexin-B1 activation inhibits integrin-mediated cell attachment and cell migration through the activation of the R-RasGAP activity inherent to plexin-B1 or through the inhibition of RhoA. However, activation of plexin-B1 by Sema4D stimulates the migration of endothelial cells by mediating the activation of RhoA.

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Kumanogoh, A., Kikutani, H. (2004). Biological functions and signaling of a transmembrane semaphorin, CD100/Sema4D. *Cell Mol Life Sci, 61*, 292-300. ↗

Katoh, H., Oinuma, I., Negishi, M. (2005). Plexins: axon guidance and signal transduction. *Cell Mol Life Sci, 62*, 1363-71. ↗

Guan, KL., Aurandt, J., Kruger, RP. (2005). Semaphorins command cells to move. *Nat Rev Mol Cell Biol, 6*, 789-800. ↗

Editions

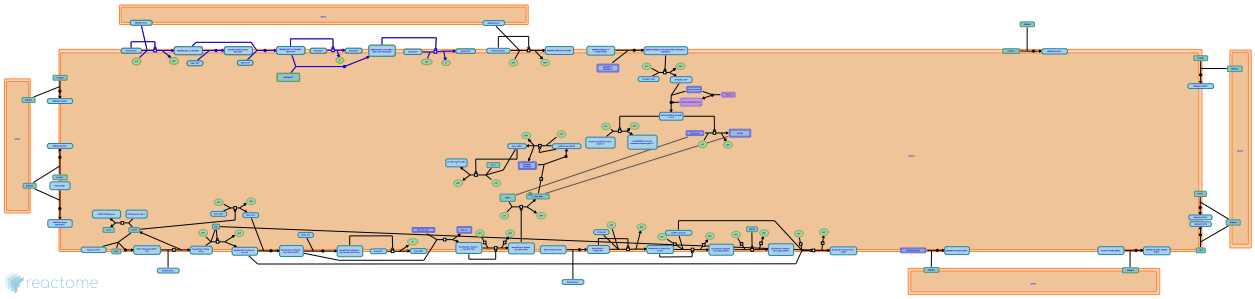
2009-03-23	Authored, Edited	Garapati, P V.
2009-09-02	Reviewed	Kikutani, H., Kumanogoh, A.

Sema4D mediated inhibition of cell attachment and migration ↗

Location: Sema4D in semaphorin signaling

Stable identifier: R-HSA-416550

Compartments: plasma membrane



Repulsive Sema4D-Plexin-B1 signaling involves four GTPases, Rnd1, R-Ras, Rho and Rac1. Sema4D-Plexin-B1 binding promotes Rnd1-dependent activation of the plexin-B1 GAP domain and transient suppression of R-Ras activity. R-Ras inactivation promotes PI3K and Akt inactivation followed by GSK-3beta activation and CRMP2 inactivation. Plexin-B1 also transiently associates with and activates p190Rho-GAP, triggering a transient decrease in activated Rho.

Literature references

Kumanogoh, A., Kikutani, H. (2004). Biological functions and signaling of a transmembrane semaphorin, CD100/Sema4D. *Cell Mol Life Sci, 61*, 292-300. ↗

Guan, KL., Aurandt, J., Kruger, RP. (2005). Semaphorins command cells to move. *Nat Rev Mol Cell Biol, 6*, 789-800. ↗

Zhou, Y., Pasterkamp, RJ., Gunput, RA. (2008). Semaphorin signaling: progress made and promises ahead. *Trends Biochem Sci, 33*, 161-70. ↗

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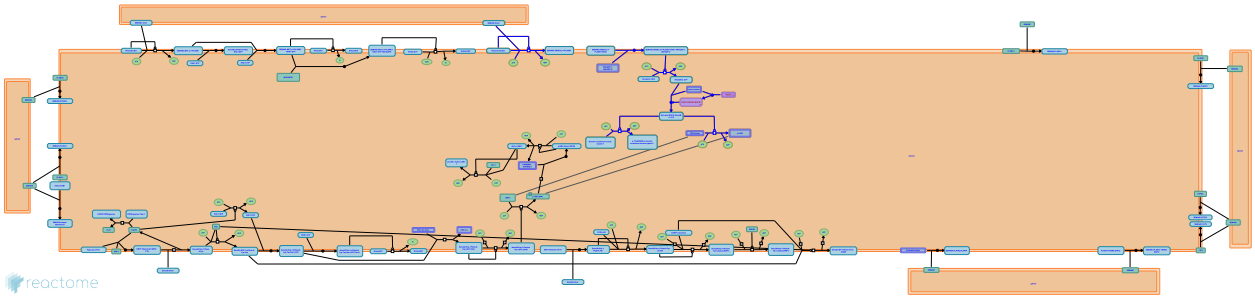
Sema4D induced cell migration and growth-cone collapse ↗

Location: Sema4D in semaphorin signaling

Stable identifier: R-HSA-416572

Compartments: plasma membrane



Sema4D-mediated attraction of endothelial cells requires Rho, but not R-Ras, signaling. Sema4D-mediated plexinB1 activation activates Rho and its downstream effector ROCK. ROCK then phosphorylates MLC to induce actomyosin stress fiber contraction and to direct the assembly of focal adhesion complexes and integrin-mediated adhesion.

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