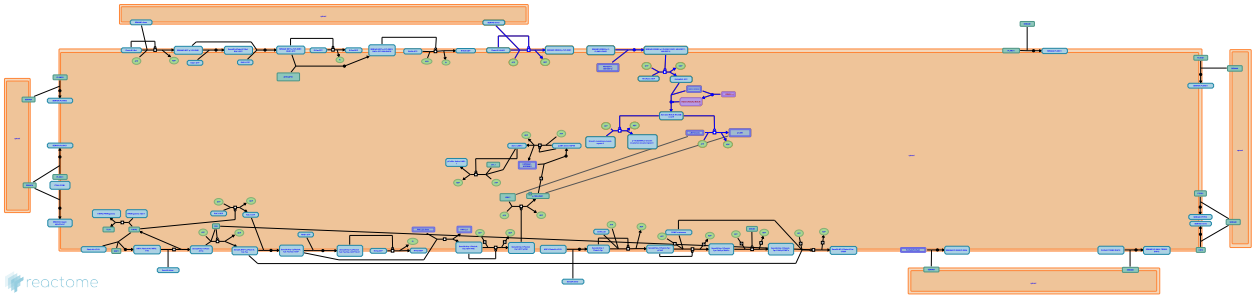
Sema4D induced cell migration and growth-cone collapse



Akkerman, JW., Garapati, P V., Jassal, B., Jupe, S., Kikutani, H., Kumanogoh, A., Orlic-Milacic, M., Rivero Crespo, F., Shoichet, BK.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

19/05/2024

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. ↗

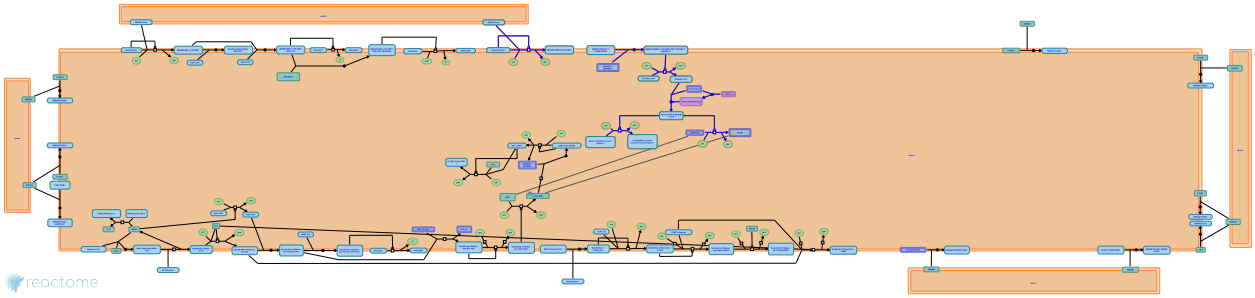
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Sema4D induced cell migration and growth-cone collapse ↗

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.

Literature references

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

Offermanns, S., Kuner, R., Swiercz, JM. (2004). Plexin-B1/RhoGEF-mediated RhoA activation involves the receptor tyrosine kinase ErbB-2. *J Cell Biol, 165*, 869-80. ↗

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

Furuyama, T., Kogo, M., Matsuya, T., Inagaki, S., Yamamoto, T., Hirotani, M. et al. (2002). Interaction of plexin-B1 with PDZ domain-containing Rho guanine nucleotide exchange factors. *Biochem Biophys Res Commun, 297*, 32-7. ↗

Editions

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

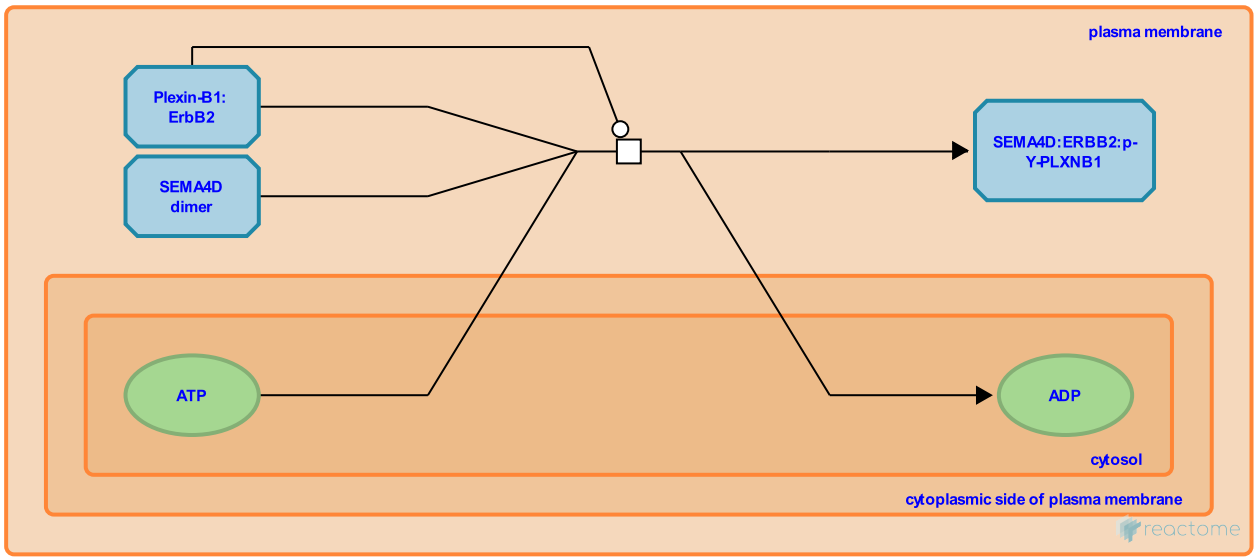
SEMA4D interacts with Plexin-B1:ErbB2 ↗

Location: Sema4D induced cell migration and growth-cone collapse

Stable identifier: R-HSA-373750

Type: transition

Compartments: plasma membrane, cytosol



Sema4D binds Plexin-B1 to induce repulsive or attractive effects in neuronal and nonneuronal cells. Plexins constitute a large family of transmembrane proteins that function as receptors for semaphorins and their interaction governs cell adhesion and migration in a variety of tissues. All B-class plexins can interact with the receptor tyrosine kinases Met and ErbB2. Upon binding of Sema4D to plexin-B1, the kinase activity of ErbB2 is increased resulting in tyrosine phosphorylation of both Plexin-B1 and ErbB2. ErbB2 has been shown to mediate Sema4D-induced growth cone collapse in hippocampal neurons by the activation of RhoA via plexinB1 and PDZRhoGEF/LARG.
Sequence alignment reveals the presence of 13 conserved tyrosine residues (highly conserved sites 1918, 1953, 2038) but the specific tyrosine residues phosphorylated in the cytoplasmic domain of plexins in response to semaphorin stimulation have not yet been identified.

Followed by: LARG and PDZ-RhoGEF binds to Plexin-B1

Literature references

Offermanns, S., Kuner, R., Swiercz, JM. (2004). Plexin-B1/RhoGEF-mediated RhoA activation involves the receptor tyrosine kinase ErbB-2. *J Cell Biol, 165*, 869-80. ↗

Offermanns, S., Worzfeld, T., Swiercz, JM. (2008). ErbB-2 and met reciprocally regulate cellular signaling via plexin-B1. *J Biol Chem, 283*, 1893-901. ↗

Editions

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

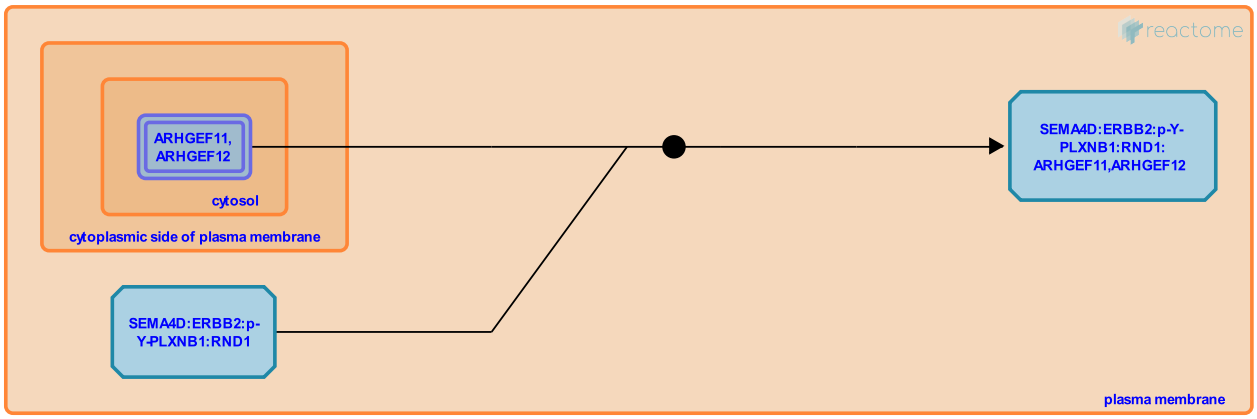
LARG and PDZ-RhoGEF binds to Plexin-B1 ↗

Location: Sema4D induced cell migration and growth-cone collapse

Stable identifier: R-HSA-416594

Type: binding

Compartments: plasma membrane, cytosol



Plexin-B1 activates RhoA and induces growth cone collapse and and cytoskeletal reorganization through Rho-specific guanine nucleotide exchange factors PDZ-RhoGEF (ARHGEF11) and leukemia-associated RhoGEF (LARG, ARHGEF12). Plexin-B1 directly interacts with PDZ-RhoGEF through its c-terminal PDZ domain binding motif. It has been suggested that Rnd1, which binds to the cytoplasmic part of plexin-B1, can promote the interaction between plexin-B1 and PDZ-RhoGEF. The PDZ domain of LARG is directly involved in the interaction with the c-terminal sequence of Plexin-B1.

Preceded by: SEMA4D interacts with Plexin-B1:ErbB2

Followed by: Activation of Rho by LARG and PDZ-RhoGEF

Literature references

Guan, KL., Vikis, HG., Aurandt, J., Ahn, N., Gutkind, JS. (2002). The semaphorin receptor plexin-B1 signals through a direct interaction with the Rho-specific nucleotide exchange factor, LARG. *Proc Natl Acad Sci U S A, 99*, 12085-90. ↗

Offermanns, S., Kuner, R., Swiercz, JM. (2004). Plexin-B1/RhoGEF-mediated RhoA activation involves the receptor tyrosine kinase ErbB-2. *J Cell Biol, 165*, 869-80. ↗

Katoh, H., Oinuma, I., Negishi, M., Harada, A. (2003). Direct interaction of Rnd1 with Plexin-B1 regulates PDZ-RhoGEF-mediated Rho activation by Plexin-B1 and induces cell contraction in COS-7 cells. *J Biol Chem, 278*, 25671-7. ↗

Furuyama, T., Kogo, M., Matsuya, T., Inagaki, S., Yamamoto, T., Hirotani, M. et al. (2002). Interaction of plexin-B1 with PDZ domain-containing Rho guanine nucleotide exchange factors. *Biochem Biophys Res Commun, 297*, 32-7. ↗

Editions

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

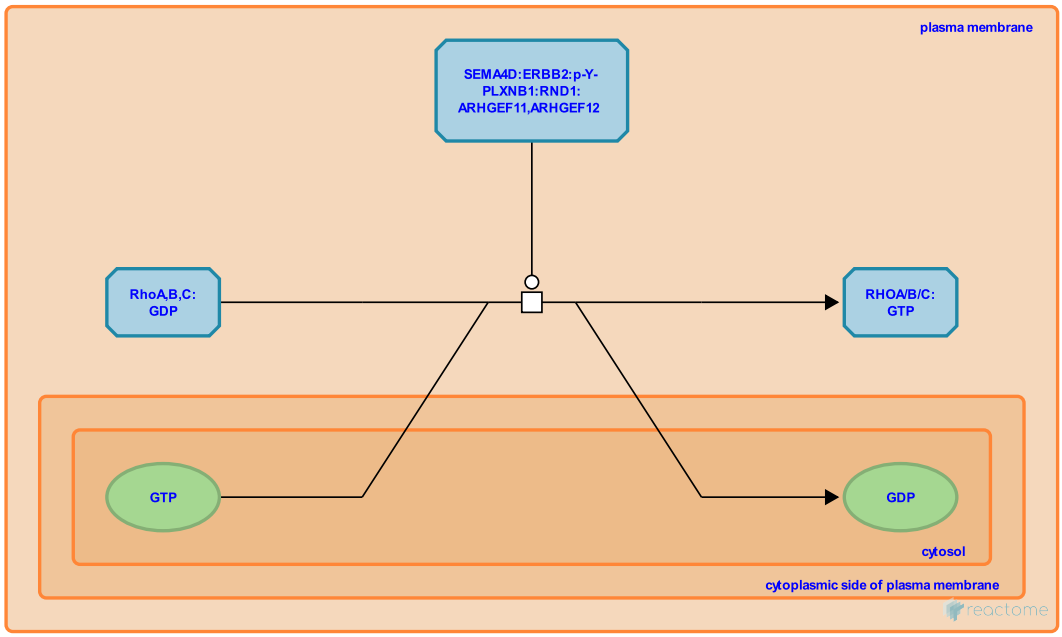
Activation of Rho by LARG and PDZ-RhoGEF ↗

Location: Sema4D induced cell migration and growth-cone collapse

Stable identifier: R-HSA-416588

Type: transition

Compartments: plasma membrane, cytosol



The RhoGEFs LARG and PDZ-RhoGEF complexed with Plexin-B1 stimulate the exchange of GDP for GTP on RhoA through their DH and PH domains.

Preceded by: LARG and PDZ-RhoGEF binds to Plexin-B1

Followed by: ROCK activation by RHO

Literature references

Offermanns, S., Kuner, R., Swiercz, JM. (2004). Plexin-B1/RhoGEF-mediated RhoA activation involves the receptor tyrosine kinase ErbB-2. *J Cell Biol, 165*, 869-80. ↗

Katoh, H., Oinuma, I., Negishi, M., Harada, A. (2003). Direct interaction of Rnd1 with Plexin-B1 regulates PDZ-RhoGEF-mediated Rho activation by Plexin-B1 and induces cell contraction in COS-7 cells. *J Biol Chem, 278*, 25671-7. ↗

Furuyama, T., Kogo, M., Matsuya, T., Inagaki, S., Yamamoto, T., Hirotani, M. et al. (2002). Interaction of plexin-B1 with PDZ domain-containing Rho guanine nucleotide exchange factors. *Biochem Biophys Res Commun, 297*, 32-7. ↗

Editions

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

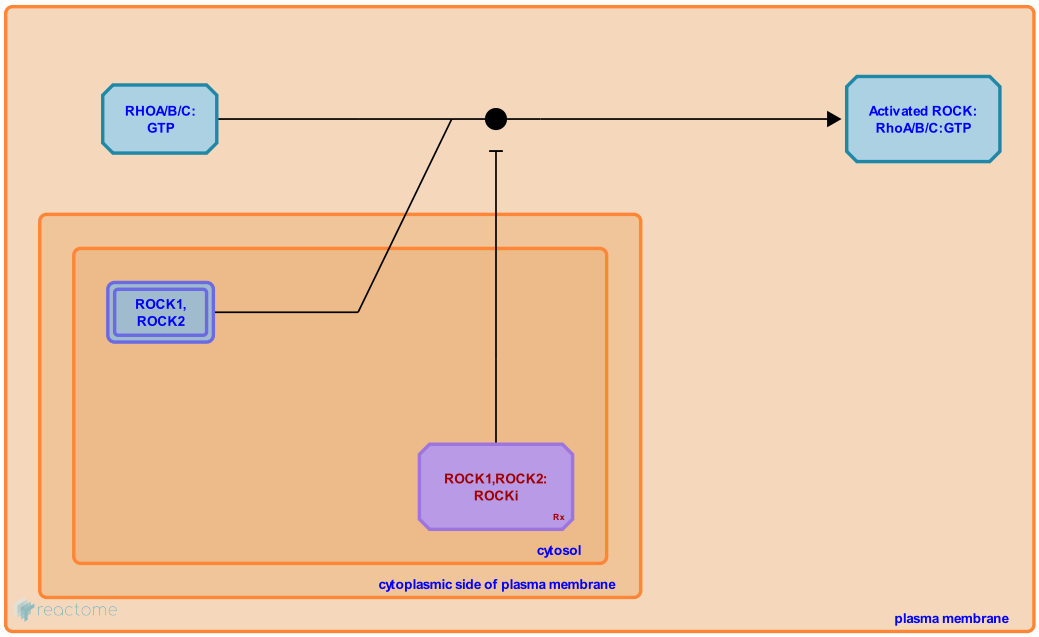
ROCK activation by RHO ↗

Location: Sema4D induced cell migration and growth-cone collapse

Stable identifier: R-HSA-419049

Type: binding

Compartments: plasma membrane, cytosol



ROCKs are primarily known as downstream effectors of RHO, but they can also be activated by arachidonic acid, which binds to the pleckstrin homology domain, releasing an autoinhibitory loop within ROCK and allowing catalytic activity (Araki et al. 2001). Proteolytic cleavage at the C-terminus by caspase-3 and granzyme B also activates ROCK1 and ROCK2, causing plasma membrane blebbing during apoptosis (Coleman et al. 2001, Sebbagh et al. 2005). Multiple targets of ROCK contribute to the stabilization of actin filaments and the generation of actin-myosin contractile force.

Preceded by: Activation of Rho by LARG and PDZ-RhoGEF

Followed by: LIM kinase phosphorylation by ROCK, Myosin regulatory light chain phosphorylation by ROCK

Literature references

Isaka, N., Hartshorne, DJ., Kaibuchi, K., Kureishi, Y., Ito, M., Feng, J. et al. (2001). Arachidonic acid-induced Ca2+ sensitization of smooth muscle contraction through activation of Rho-kinase. *Pflugers Arch., 441*, 596-603. ↗

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Saito, Y., Fujita, A., Narumiya, S., Okawa, K., Iwamatsu, A., Morii, N. et al. (1996). The small GTP-binding protein Rho binds to and activates a 160 kDa Ser/Thr protein kinase homologous to myotonic dystrophy kinase. *EMBO J, 15*, 1885-93. ↗

Olson, MF., Coleman, ML., Yeo, M., Dewar, A., Sahai, EA., Bosch, M. (2001). Membrane blebbing during apoptosis results from caspase-mediated activation of ROCK I. *Nat. Cell Biol., 3*, 339-45. ↗

Bertoglio, J., Breard, J., Hamelin, J., Solary, E., Sebbagh, M. (2005). Direct cleavage of ROCK II by granzyme B induces target cell membrane blebbing in a caspase-independent manner. *J. Exp. Med., 201*, 465-71. ↗

Editions

2009-05-20	Edited	Jupe, S.
2009-06-03	Authored	Akkerman, JW.
2009-09-02	Reviewed	Kikutani, H., Kumanogoh, A.
2014-12-26	Reviewed	Rivero Crespo, F.
2015-01-28	Revised	Orlic-Milacic, M.

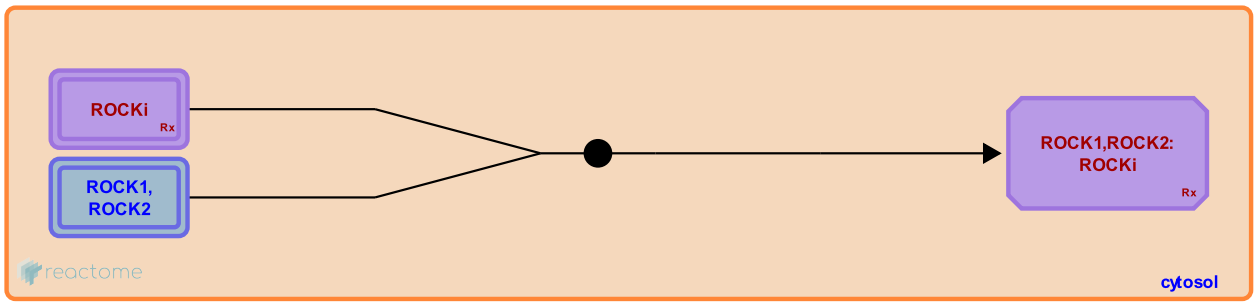
ROCK1,2 bind ROCKi ↗

Location: Sema4D induced cell migration and growth-cone collapse

Stable identifier: R-HSA-9680443

Type: binding

Compartments: cytosol



Ripasudil (Glanatec), as its hydrochloride hydrate (K-115), is a specifc Rho-associated coiled-coil containing protein kinase (ROCK) inhibitor (ROCKi) used for the treatment of glaucoma and ocular hypertension in Japan (Garnock-Jones 2014). Netarsudil is a USA-approved ROCKi used to treat glaucoma and ocular hypertenstion (Sturdivant et al. 2016, Tanna & Johnson 2018).

Literature references

Sturdivant, JM., Royalty, SM., Laethem, CL., Lin, CW., Moore, LA., Sherman, B. et al. (2016). Discovery of the ROCK inhibitor netarsudil for the treatment of open-angle glaucoma. *Bioorg. Med. Chem. Lett., 26*, 2475-2480. ↗

Tanna, AP., Johnson, M. (2018). Rho Kinase Inhibitors as a Novel Treatment for Glaucoma and Ocular Hypertension. *Ophthalmology, 125*, 1741-1756. ↗

Garnock-Jones, KP. (2014). Ripasudil: first global approval. *Drugs, 74*, 2211-5. ↗

Editions

2020-03-27	Authored, Edited	Jassal, B.
2020-05-14	Reviewed	Shoichet, BK.

Myosin regulatory light chain phosphorylation by ROCK ↗

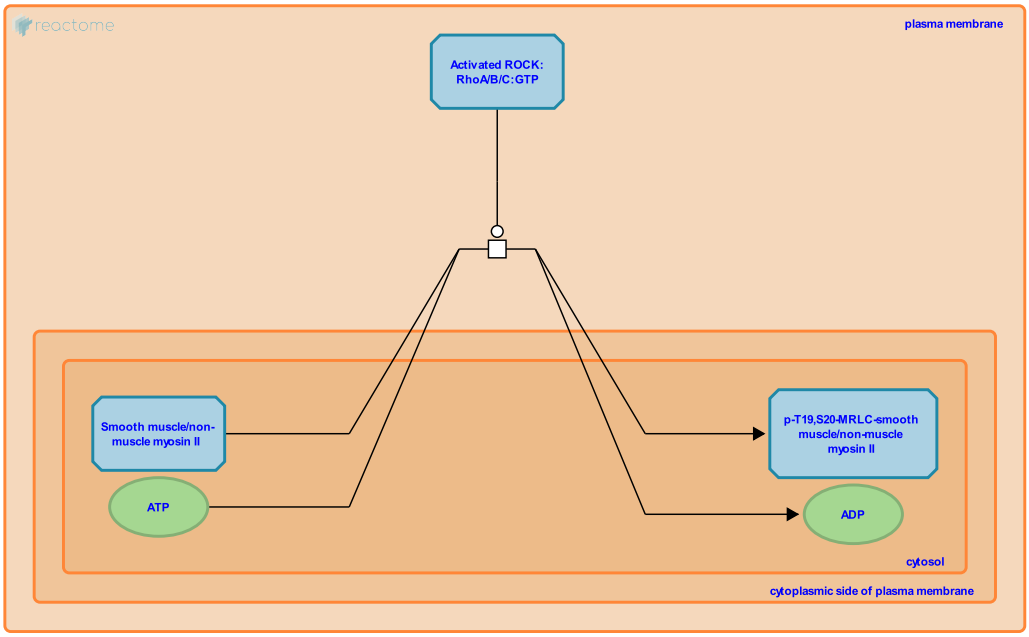
Location: Sema4D induced cell migration and growth-cone collapse

Stable identifier: R-HSA-419197

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Myosin regulatory light chain phosphorylation by Rock2 (Gallus gallus)



Nonmuscle myosin II (NMM2) is an actin-based motor protein that plays a crucial role in a variety of cellular processes, including smooth muscle contraction, cell migration, polarity formation, and cytokinesis. NMM2 consists of two myosin heavy chains encoded by MYH9, MYH10, MYH14 (NMHC-IIA, B and C) or MYH11, two copies of MYL6 essential light chain protein, and two regulatory light chains (MRLCs), MYL9 and MYL12B. Myosin II activity is stimulated by phosphorylation of MRLC. Diphosphorylation at Thr-19 and Ser-20 (commonly referred in the literature as Thr-18 and Ser-19) increases both actin-activated Mg2+ ATPase activity and the stability of myosin II filaments; monophosphorylation at Ser-20 is less effective (Ikebe and Hartshorne 1985, Ikebe et al. 1988). Kinases responsible for the phosphorylation include myosin light chain kinase (MLCK), ROCK kinase, citron kinase, myotonic dystrophy kinase-related CDC42-binding protein kinase, and Zipper-interacting protein (ZIP) kinase. ROCK activity has been shown to regulate MRLC phosphorylation by directly mono- or diphosphorylating MRLC (Amano et al., 1996, Ueda et al., 2002, Watanabe et al. 2007).

Preceded by: ROCK activation by RHO

Literature references

Matsuura, Y., Amano, M., Kaibuchi, K., Ito, M., Nakano, T., Fukata, Y. et al. (1996). Phosphorylation and activation of myosin by Rho-associated kinase (Rho-kinase). *J Biol Chem, 271*, 20246-9. ↗

Hartshorne, DJ., Ikebe, M. (1985). Phosphorylation of smooth muscle myosin at two distinct sites by myosin light chain kinase. *J. Biol. Chem., 260*, 10027-31. ↗

Hartshorne, DJ., Koretz, J., Ikebe, M. (1988). Effects of phosphorylation of light chain residues threonine 18 and serine 19 on the properties and conformation of smooth muscle myosin. *J. Biol. Chem., 263*, 6432-7. ↗

Watanabe, T., Hosoya, H., Yonemura, S. (2007). Regulation of myosin II dynamics by phosphorylation and dephosphorylation of its light chain in epithelial cells. *Mol Biol Cell, 18*, 605-16. ↗

Tatsuka, M., Murata-Hori, M., Hosoya, H., Ueda, K. (2002). Rho-kinase contributes to diphosphorylation of myosin II regulatory light chain in nonmuscle cells. *Oncogene, 21*, 5852-60. ↗

Editions

2009-05-20	Edited	Jupe, S.
2009-06-03	Authored	Akkerman, JW.
2009-09-02	Reviewed	Kikutani, H., Kumanogoh, A.
2014-12-26	Reviewed	Rivero Crespo, F.
2015-01-28	Revised	Orlic-Milacic, M.

LIM kinase phosphorylation by ROCK ↗

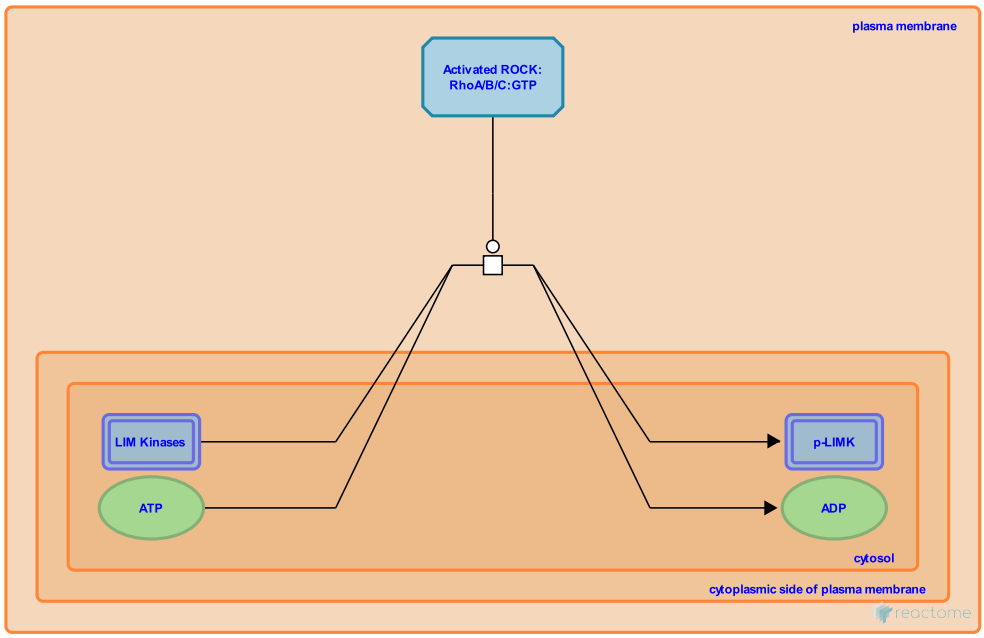
Location: Sema4D induced cell migration and growth-cone collapse

Stable identifier: R-HSA-419087

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: ROCK1 phosphorylates LIMK2 (rat) (Homo sapiens)



LIM kinases are serine protein kinases with a unique combination of two N-terminal LIM motifs, a central PDZ domain, and a C-terminal protein kinase domain. ROCK1 and ROCK2 phosphorylate and activate LIM kinases LIMK1 and LIMK2 at Thr508 and Thr505, respectively (Ohashi et al. 2000, Sumi et al. 2001). These threonine residues lay within the activation loop of the kinase domain. LIMKs phosphorylate and inactivate cofilin, an actin depolymerizing factor, resulting in stabilization of the actin cytoskeleton (Pandey et al. 2006).

Preceded by: ROCK activation by RHO

Literature references

Nakamura, T., Matsumoto, K., Sumi, T. (2001). Specific activation of LIM kinase 2 via phosphorylation of threonine 505 by ROCK, a Rho-dependent protein kinase. *J Biol Chem, 276*, 670-6. ↗

Siess, W., Bamburg, JR., Pandey, D., Goyal, P. (2006). Regulation of LIM-kinase 1 and cofilin in thrombin-stimulated platelets. *Blood, 107*, 575-83. ↗

Ohashi, K., Narumiya, S., Mizuno, K., Ishizaki, T., Nagata, K., Maekawa, M. (2000). Rho-associated kinase ROCK activates LIM-kinase 1 by phosphorylation at threonine 508 within the activation loop. *J Biol Chem, 275*, 3577-82. ↗

Editions

2009-04-28	Edited	Jupe, S.
2009-06-03	Authored	Akkerman, JW.
2009-09-02	Reviewed	Kikutani, H., Kumanogoh, A.
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Table of Contents