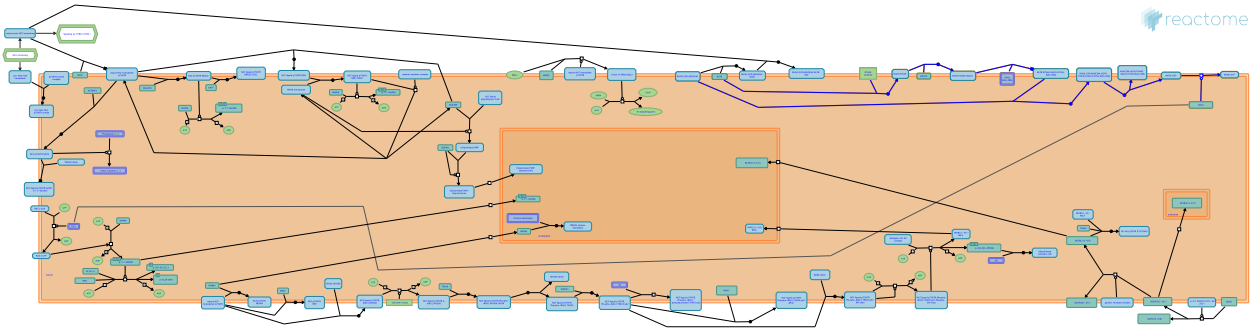
Axonal growth inhibition (RHOA activation)



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27/09/2021

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. ↗

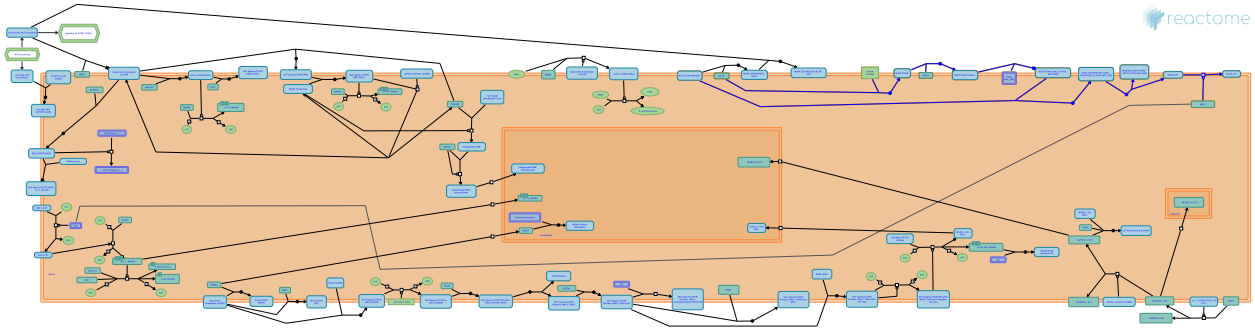
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Axonal growth inhibition (RHOA activation) ↗

Stable identifier: R-HSA-193634



p75NTR can also form a receptor complex with the Nogo receptor (NgR). Such complexes mediates axonal outgrowth inhibitory signals of MDGIs (myelin-derived growth-inhibitors), such as Nogo66, myelin-associated glycoprotein (MAG), and oligodendrocyte myelin glycoprotein (OMGP).

Literature references

Filbin, MT. (2003). Myelin-associated inhibitors of axonal regeneration in the adult mammalian CNS. *Nat Rev Neurosci, 4*, 703-13. ↗

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
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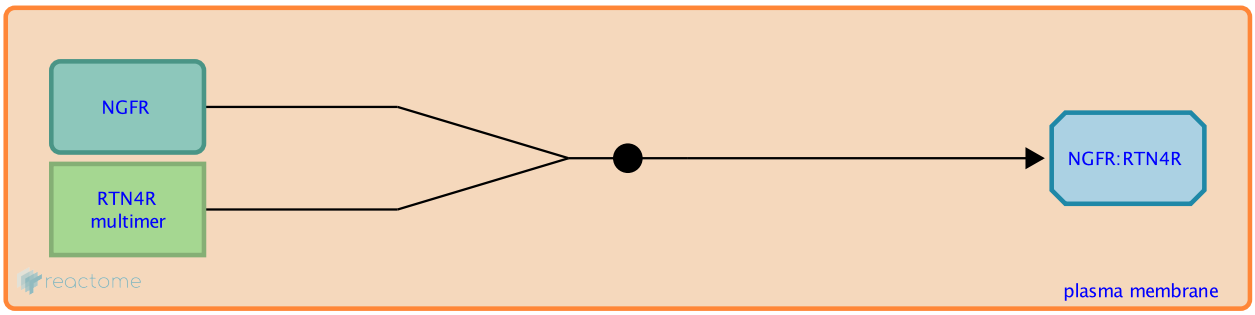
p75NTR interacts with the NOGO receptor ↗

Location: Axonal growth inhibition (RHOA activation)

Stable identifier: R-HSA-193636

Type: binding

Compartments: plasma membrane



The p75NTR extracellular domain interacts with NOGO receptor (NgR), a glycosyl phosphatidylinositol (GPI)-anchored protein present as a homomultimer at the cell surface. As NgR lacks an intracellular domain, it utilizes p75NTR as a co-receptor for intracellular signalling.

Followed by: p75NTR:NgR complex interacts with the axonal inhibitor LINGO1

Literature references

Fournier, AE., GrandPre, T., Strittmatter, SM. (2001). Identification of a receptor mediating Nogo-66 inhibition of axonal regeneration. *Nature, 409*, 341-6. ↗

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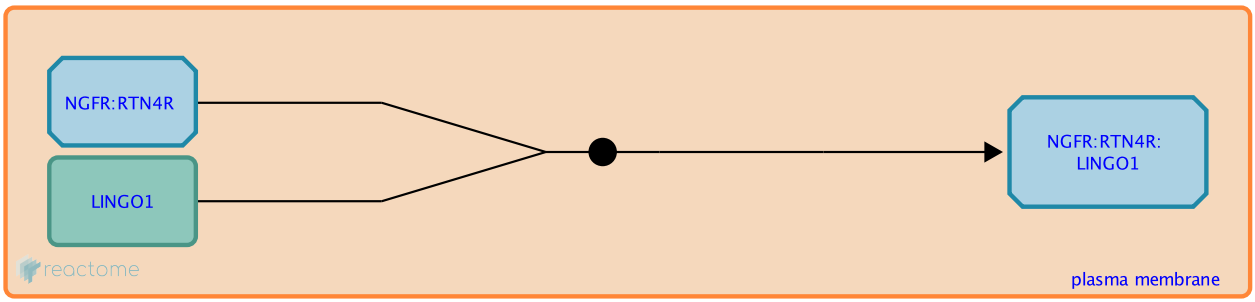
p75NTR:NgR complex interacts with the axonal inhibitor LINGO1 ↗

Location: Axonal growth inhibition (RHOA activation)

Stable identifier: R-HSA-209573

Type: binding

Compartments: plasma membrane



The NgR1:p75NTR complex also interacts with LINGO1, a nervous system-specific transmembrane protein. LINGO1 is a potent axonal inhibitor of oligodendrocyte differentiation and myelination, and is regulated by NGF and its receptor TRKA .

Preceded by: p75NTR interacts with the NOGO receptor

Followed by: Myelin components can interact with p75NTR:NgR:LINGO1

Literature references

Mi, S., Lee, X., Shao, Z., Thill, G., Ji, B., Relton, J. et al. (2004). LINGO-1 is a component of the Nogo-66 receptor/p75 signaling complex. *Nat Neurosci, 7*, 221-8. ↗

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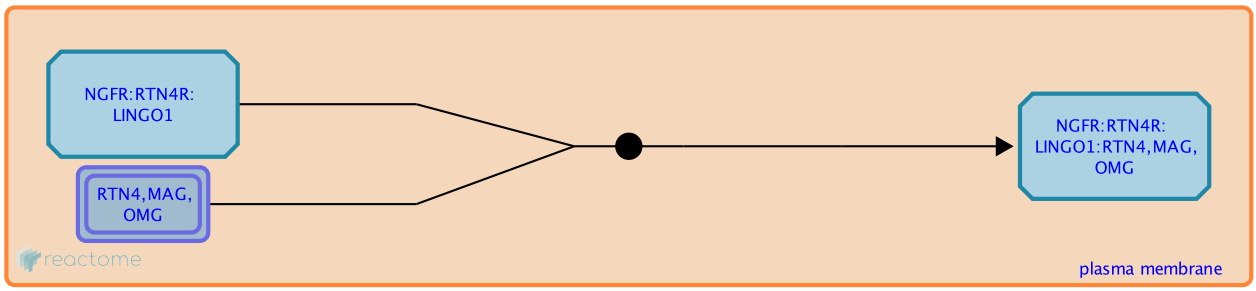
Myelin components can interact with p75NTR:NgR:LINGO1 ↗

Location: Axonal growth inhibition (RHOA activation)

Stable identifier: R-HSA-193655

Type: binding

Compartments: plasma membrane



A group of myelin components named MDGIs (myelin-derived growth-inhibitors), bind to NgR and inhibit neurite outgrowth. Examples of such components are NOGO, OMGP (oligodendrocyte myelin glycoprotein) and MAG (myelin-associated glycoprotein). The amino-terminal region of NgR, covering eight leucine-rich repeats (LRR) and the LRR carboxy-terminal domain (LRRCT) is sufficient to interact with MAG, OMGP and NOGO. Their binding to NgR enhances the NgR-p75 interaction.These inhibitors bind to a receptor complex made up of the NOGO receptor, NgR, and p75NTR. Such complexes then activate RHOA, thereby inhibiting axonal growth.

Preceded by: p75NTR:NgR complex interacts with the axonal inhibitor LINGO1

Literature references

Wong, ST., Henley, JR., Kanning, KC., Huang, KH., Bothwell, M., Poo, MM. (2002). A p75(NTR) and Nogo receptor complex mediates repulsive signaling by myelin-associated glycoprotein. *Nat Neurosci, 5*, 1302-8. ↗

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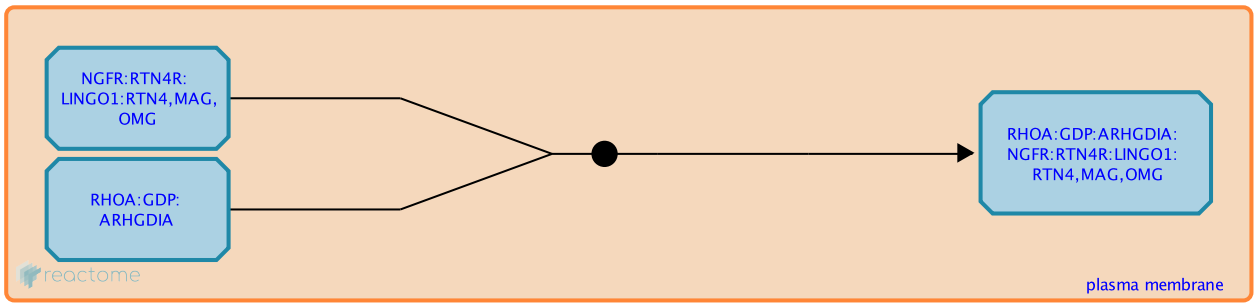
The p75NTR:NgR:MDGI binds RHOA-GDI ↗

Location: Axonal growth inhibition (RHOA activation)

Stable identifier: R-HSA-9012761

Type: binding

Compartments: plasma membrane



In the presence of a myelin component (GMDI), such as MAG, NOGO or OMG, bound to a complex of the NOGO receptor (RTN4R, also known as NgR) and NGFR (p75NTR), binding of NGFR to ARHGDIA, a RHO-GDI, associated with RHOA:GDP, is strengthened (Yamashita and Tohyama 2003). The presence of LINGO1 in the complex of NGFR, RTN4R and MAG, NOGO or OMG is needed for NGFR-dependent activation of RHOA (Mi et al. 2004).

Followed by: The p75NTR:NgR:MDGI complex reduces RHOA-GDI activity, displacing RHOA

Literature references

Yamashita, T., Tohyama, M. (2003). The p75 receptor acts as a displacement factor that releases Rho from Rho-GDI. *Nat Neurosci, 6*, 461-7. ↗

Mi, S., Lee, X., Shao, Z., Thill, G., Ji, B., Relton, J. et al. (2004). LINGO-1 is a component of the Nogo-66 receptor/p75 signaling complex. *Nat Neurosci, 7*, 221-8. ↗

Editions

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2008-05-20	Edited	Jassal, B.
2008-05-28	Reviewed	Chao, MV.

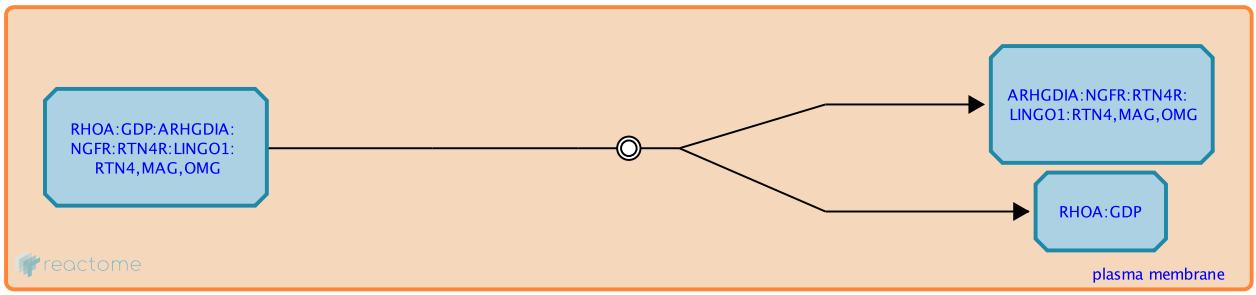
The p75NTR:NgR:MDGI complex reduces RHOA-GDI activity, displacing RHOA ↗

Location: Axonal growth inhibition (RHOA activation)

Stable identifier: R-HSA-193696

Type: dissociation

Compartments: plasma membrane



In the presence of a myelin component (GMDI), such as MAG, NOGO or OMG, bound to a complex of the NOGO receptor (RTN4R, also known as NgR) and NGFR (p75NTR), binding of NGFR to ARHGDIA, a RHO-GDI, associated with RHOA:GDP, is strengthened (Yamashita and Tohyama 2003). The presence of LINGO1 in the complex of NGFR, RTN4R and MAG, NOGO or OMG is needed for NGFR-dependent activation of RHOA (Mi et al. 2004).

Preceded by: The p75NTR:NgR:MDGI binds RHOA-GDI

Followed by: RhoA is activated by nucleotide exchange and inhibits axonal growth

Literature references

Yamashita, T., Tohyama, M. (2003). The p75 receptor acts as a displacement factor that releases Rho from Rho-GDI. *Nat Neurosci, 6*, 461-7. ↗

Editions

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2008-05-28	Reviewed	Chao, MV.

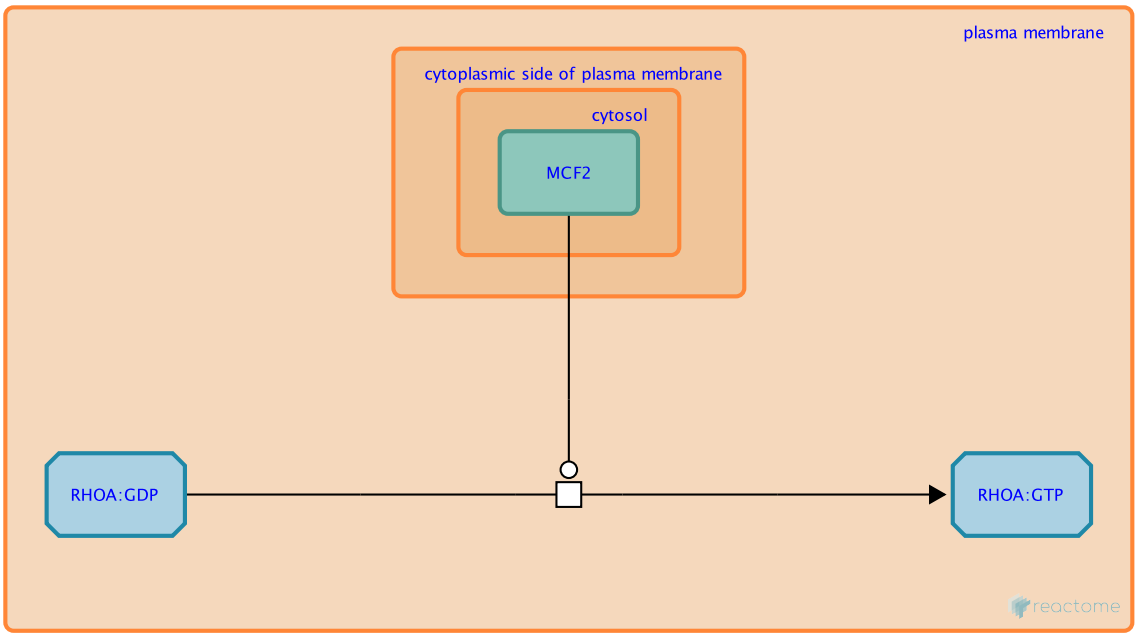
RhoA is activated by nucleotide exchange and inhibits axonal growth ↗

Location: Axonal growth inhibition (RHOA activation)

Stable identifier: R-HSA-194518

Type: transition

Compartments: plasma membrane



RHOA is activated by guanine nucleotide exchange factors (RhoGEFs), exchanging GDP for GTP. RHOA, activated following binding of MDGIs (RTN4, MAG or OMG) to the complex of NOGO receptor (RTN4R, also known as NgR) and NGFR (p75NTR), rigidifies the actin cytoskeleton, thereby inhibiting axonal elongation and causing growth cone collapse. MCF2 (Dbl) RHO GEF was used to demonstrate activation of RHOA downstream of NGFR and RTN4R-mediated sequestration of ARHGDIA, a RHO-GDI, but other RHO GEFs may also be involved in RHOA activation (Yamashita and Tohyama 2003).

Preceded by: The p75NTR:NgR:MDGI complex reduces RHOA-GDI activity, displacing RHOA

Literature references

Yamashita, T., Tohyama, M. (2003). The p75 receptor acts as a displacement factor that releases Rho from Rho-GDI. *Nat Neurosci, 6*, 461-7. ↗

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