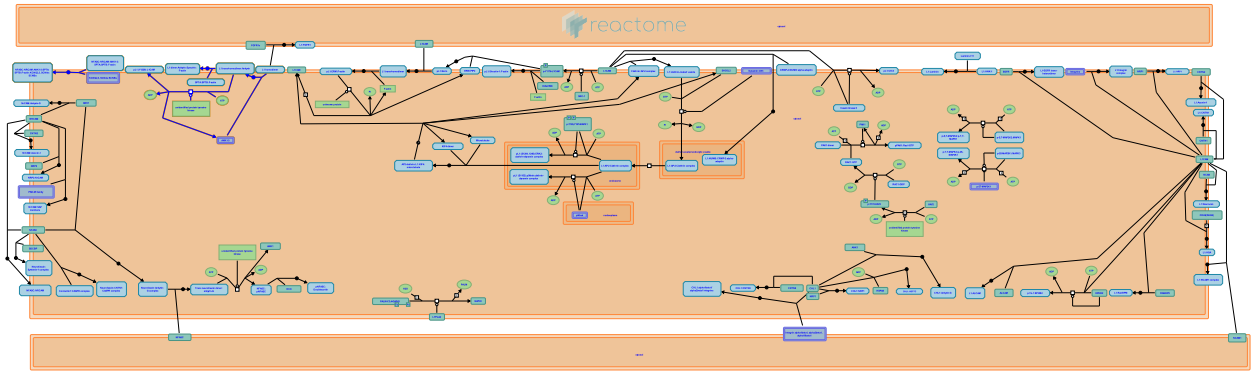
Interaction between L1 and Ankyrins



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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. ↗

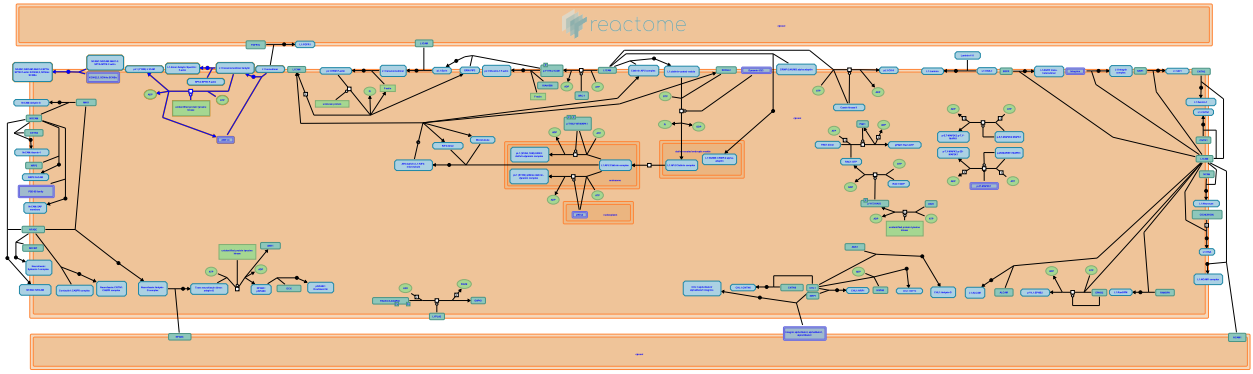
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Interaction between L1 and Ankyrins ↗

Stable identifier: R-HSA-445095



Ankyrins are a family of adaptor proteins that couple membrane proteins such as voltage gated Na+ channels and the Na+/K+ anion exchanger to the spectrin actin cytoskeleton. Ankyrins are encoded by three genes (ankyrin-G, -B and -R) of which ankyrin-G and -B are the major forms expressed in the developing nervous system. Ankyrins bind to the cytoplasmic domain of L1 CAMs and couple them and ion channel proteins, to the spectrin cytoskeleton. This binding enhances the homophilic adhesive activity of L1 and reduces its mobility within the plasma membrane. L1 interaction with ankyrin mediates branching and synaptogenesis of cortical inhibitory neurons.

Literature references

Nagaraj, K., Hortsch, M., Godenschwege, TA. (2009). The interaction between L1-type proteins and ankyrins--a master switch for L1-type CAM function. *Cell Mol Biol Lett, 14*, 57-69. ↗

Nagaraj, K., Hortsch, M. (2006). Phosphorylation of L1-type cell-adhesion molecules--ankyrins away!. *Trends Biochem Sci, 31*, 544-6. ↗

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Gunn-Moore, FJ., Hill, M., Herron, LR., Davey, F. (2009). The intracellular interactions of the L1 family of cell adhesion molecules. *Biochem J, 419*, 519-31. ↗

Editions

2008-07-30	Authored, Edited	Garapati, P V.
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L1 dimer binds Ankyrin ↗

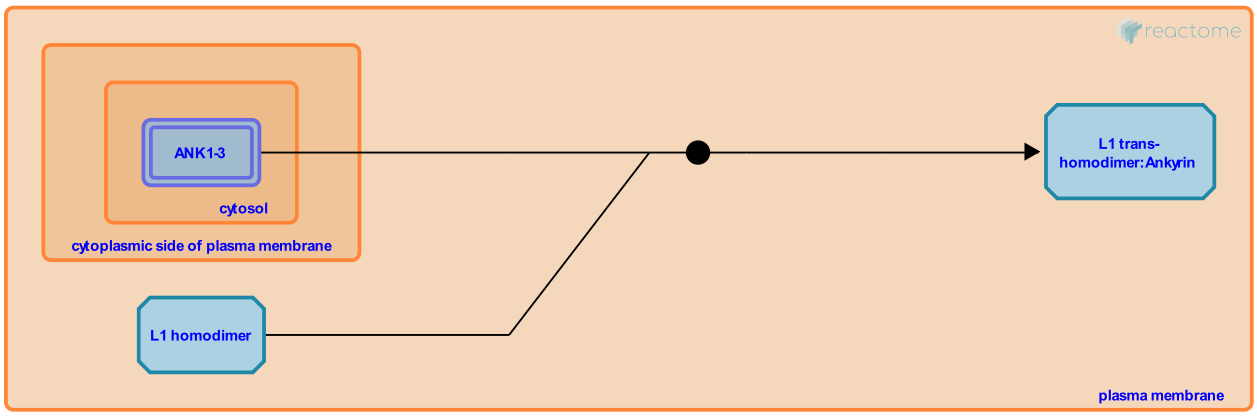
Location: Interaction between L1 and Ankyrins

Stable identifier: R-HSA-374675

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: L1 dimer binds Ankyrin (Homo sapiens)



L1 recruits membrane skeletal component ankyrin to cell to cell contact sites in response to cis interaction with homophilic axonin 1/TAG 1 or trans L1 L1 homophilic interaction although in mammalian cells trans binding interactions are not required. L1 interacts with ankyrin proteins through two highly conserved amino acid sequence motifs, LADY and FIGQY.
Ankyrin binding immobilizes L1 molecules in the neuronal plasma membrane. This interaction is required for axon maintenance. L1 also elevates cyclic AMP levels in neurons via ankyrin B and mediates Ca+2 dependent attraction.The L1/ankyrin interaction is a vital determinant of synaptic targeting of retinal axons to the superior colliculus and cooperates with EphrinB/EphB signaling to induce axon branch attraction.

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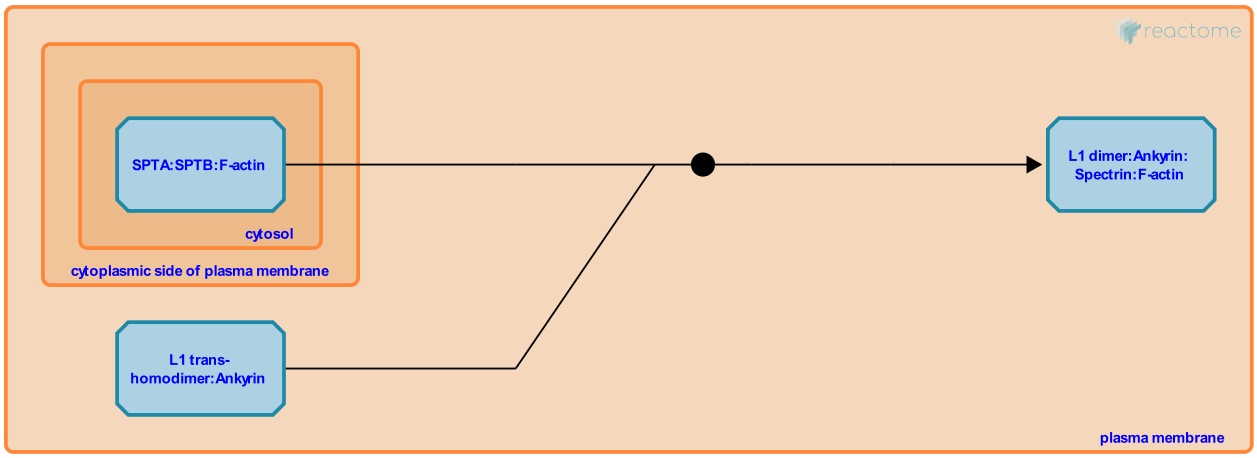
L1 linked to actin cytoskeleton by ankyrin ↗

Location: Interaction between L1 and Ankyrins

Stable identifier: R-HSA-392751

Type: binding

Compartments: plasma membrane, cytosol



Ankyrins are bifunctional linker proteins that tether L1 to the membrane associated, spectrin based actin cytoskeleton. Spectrin is a tetramer of two alpha- and two beta-chains. The spectrin alpha chain has 21 and the beta chain has 16 (conventional beta) or 30 (heavy beta) successive triple helix repeats. At the N-terminus of beta spectrin, there is a pair of CH (calponin homology) domains which together form an actin binding domain, while the triple helical repeats 14-15 bind ankyrin.
Interaction with spectrin bound F-actin blocks the mobility of L1 and this immobilization mediates adjacent neuron adhesions.

Literature references

Nagaraj, K., Hortsch, M. (2006). Phosphorylation of L1-type cell-adhesion molecules--ankyrins away!. *Trends Biochem Sci, 31*, 544-6. ↗

Thelen, K., Needham, LK., Maness, PF. (2001). Cytoplasmic domain mutations of the L1 cell adhesion molecule reduce L1-ankyrin interactions. *J Neurosci, 21*, 1490-500. ↗

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Editions

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Ankyrins link voltage-gated sodium and potassium channels to spectrin and L1 ↗

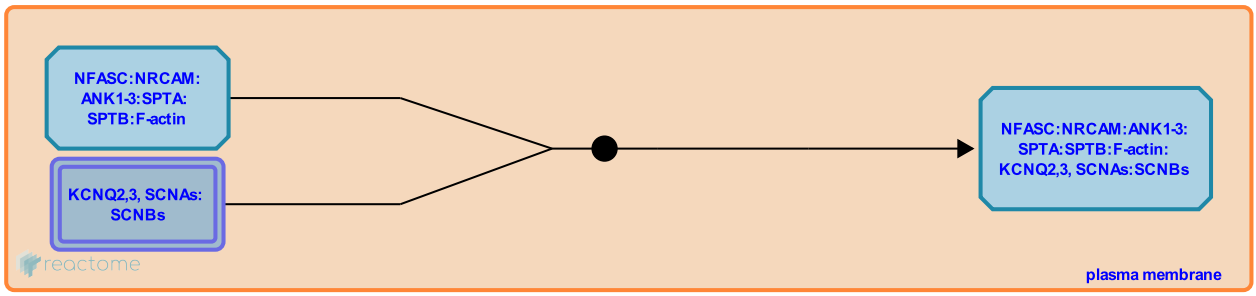
Location: Interaction between L1 and Ankyrins

Stable identifier: R-HSA-373739

Type: binding

Compartments: plasma membrane

Inferred from: Ankyrins link voltage-gated sodium and pottasium channels to spectrin and L1 (Rattus norvegicus)



Ankyrins link both L1 and ion channel proteins, coupling them to the spectrin actin cytoskeleton. In the nervous system ankyrins interact with voltage gated channels and cluster them in axon initial segments to generate action potentials. At these points the actin spectrin network is linked via ankyrins to voltage gated sodium channels, L1, and the voltage gated potassium ion channel subunits, KCNQ2 and KCNQ3.

Editions

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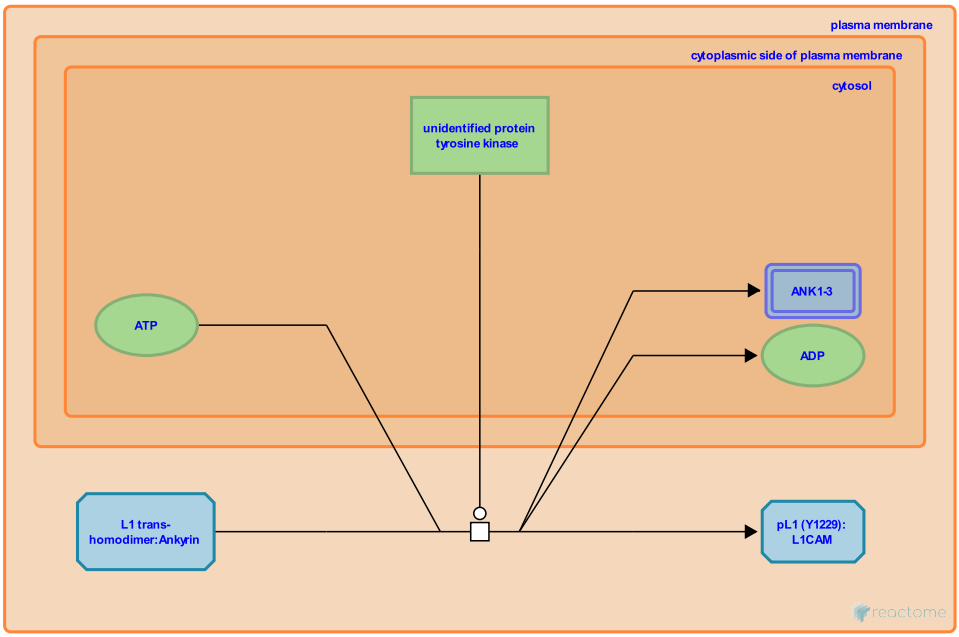
Phosphorylation of Y1229 in L1 ↗

Location: Interaction between L1 and Ankyrins

Stable identifier: R-HSA-445076

Type: transition

Compartments: plasma membrane, cytosol



Binding of ankyrins is dependent on the phosphorylation and dephosphorylation state of the tyrosine in the L1 FIGQY motif. In the dephosphorylated state ankyrins bind to L1 and in the phosphorylated state L1 releases from ankyrins and binds to doublecortin.
The specific kinase that is responsible for the phosphorylation of this tyrosine residue is still unknown, but components of the MAP kinase pathway may regulate this event. Tyrosine phosphorylation abolishes ankyrin binding and also increases L1 lateral mobility and neurite growth

Literature references

Gazdoiu, M., Sakurai, T., Felsenfeld, DP., Cassella, MR., Whittard, JD. (2006). MAP kinase pathway-dependent phosphorylation of the L1-CAM ankyrin binding site regulates neuronal growth. *Mol Biol Cell, 17*, 2696-706. ↗

Editions

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