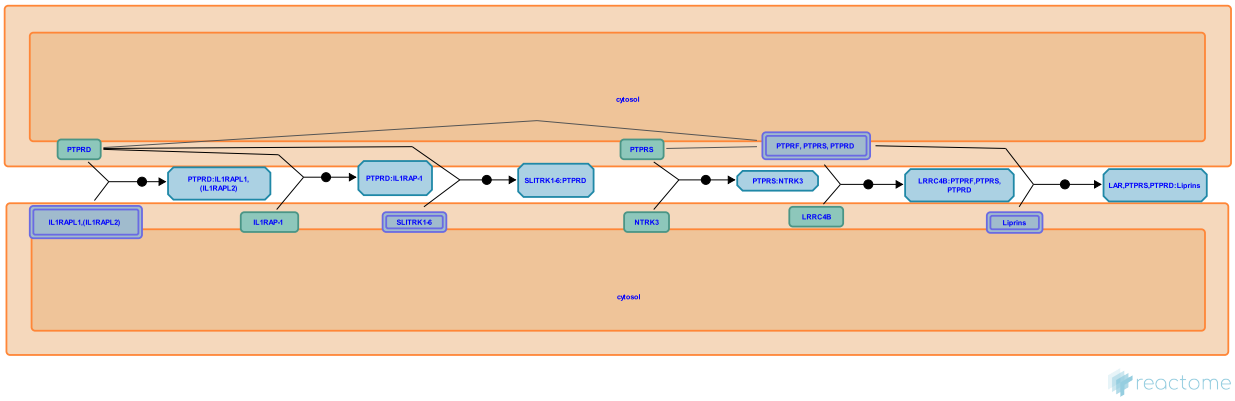
Receptor-type tyrosine-protein phosphatases



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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

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

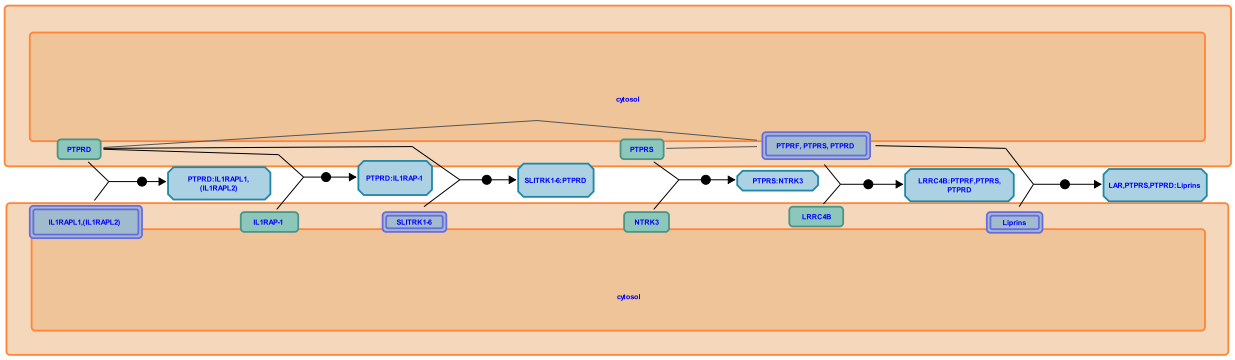
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Receptor-type tyrosine-protein phosphatases ↗

Stable identifier: R-HSA-388844

Compartments: plasma membrane



Like neurexins, Receptor-like protein tyrosine phosphatases (RPTPs) make trans-synaptic adhesion complexes with multiple postsynaptic binding partners to regulate synapse organization. The type IIa RPTPs include three members, Receptor-type tyrosine-protein phosphatase F (PTPRF) sometimes referred to as leukocyte common antigen-related (LAR), Receptor-type tyrosine-protein phosphatase sigma (PTPRS) and Receptor-type tyrosine-protein phosphatase delta (PTPRD). These proteins contain typical cell adhesion immunoglobulin-like (Ig) and fibronectin III (FNIII) domains, suggesting the involvement of RPTPs in cell-cell and cell-matrix interactions. To date, six different types of postsynaptic organizers for type-IIa RPTPs have been reported: interleukin-1 receptor accessory protein (IL1RAP, IL-1RAcP) (Yoshida et al. 2012), IL-1RAcP-like-1 (IL1RAPL1) (Yoshida et al. 2011), Neurotrophin receptor tyrosine kinase 3 (NTRK3, TrkC) (Takahashi et al. 2011), Leucine-rich repeat-containing protein 4B (LRRC4B, Netrin-G ligand-3, NGL-3) (Woo et al. 2009, Kwon et al. 2010), the Slit- and Trk-like (Slitrk) family proteins (Takahashi et al. 2012, Yim et al. 2013, Yamagata et al. 2015) and the liprins (Serra-Pagès et al. 1998, Dunah et al. 2005).

Literature references

Craig, AM., Takahashi, H. (2013). Protein tyrosine phosphatases PTPÎ´, PTPÏƒ, and LAR: presynaptic hubs for synapse organization. *Trends Neurosci., 36*, 522-34. ↗

Editions

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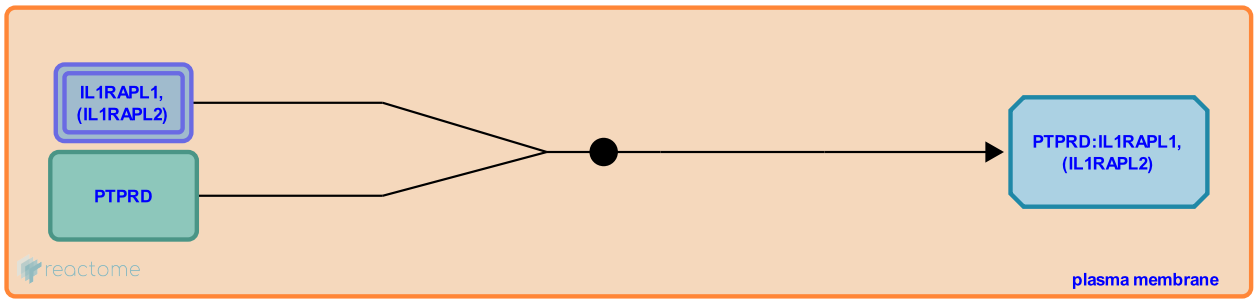
PTPRD binds IL1RAPL1 ↗

Location: Receptor-type tyrosine-protein phosphatases

Stable identifier: R-HSA-6797810

Type: binding

Compartments: plasma membrane



Interleukin-1 receptor accessory protein-like 1 (IL1RAPL1) belongs to the interleukin-1/Toll receptor family. It has extracellular Ig-like domains and an intracellular Toll/IL1R (TIR) domain. It regulates synapse formation of cortical neurons. Trans-synaptic interaction between postsynaptic IL1RAPL1 and presynaptic Receptor-type tyrosine-protein phosphatase delta (PTPRD) bidirectionally regulates excitatory synapse development. IL1RAPL2 is related to IL1RAPL1 and may also function in excitatory synapse organization although with less potency than IL1RAPL1 (Yoshida et al. 2011, Valnegri et al. 2011). IL1RAPL1 is associated with cognitive diseases ranging from nonsyndromic X-linked mental retardation to autism (Hayashi et al. 2013, Piton et al. 2008, Carrie et al. 1999).

Literature references

Ra, M., Mishina, M., Taguchi, R., Lee, SJ., Uemura, T., Yasumura, M. et al. (2011). IL-1 receptor accessory protein-like 1 associated with mental retardation and autism mediates synapse formation by trans-synaptic interaction with protein tyrosine phosphatase δ. *J. Neurosci., 31*, 13485-99. ↗

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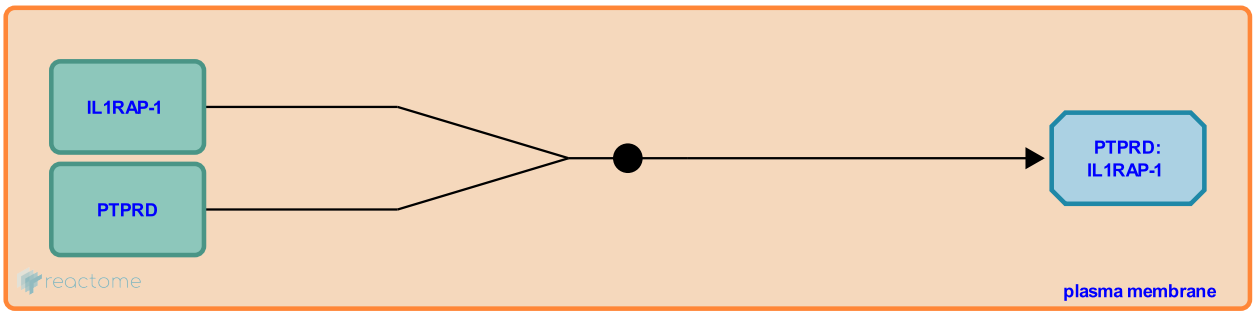
PTPRD binds IL1RAP-1 ↗

Location: Receptor-type tyrosine-protein phosphatases

Stable identifier: R-HSA-6800380

Type: binding

Compartments: plasma membrane



Receptor protein tyrosine phosphatase delta (PTPRD) can bidirectionally induce pre- and postsynaptic differentiation of neurons by trans-synaptically binding to interleukin-1 receptor accessory protein (IL1RAP) (Yoshida et al. 2012, Yamagata et al. 2015). IL1RAP has two distinct functions, one in immune regulation and inflammation by associating with IL1 and IL1R1 and another with PTPRD in synaptic adhesion and synapse organization (Dunne & O'Neill 2003).

Literature references

Mishina, M., Chen, X., Lee, SJ., Uemura, T., Yasumura, M., Shiroshima, T. et al. (2012). Interleukin-1 receptor accessory protein organizes neuronal synaptogenesis as a cell adhesion molecule. *J. Neurosci., 32*, 2588-600. ↗

Mishina, M., Maeda, A., Goto-Ito, S., Shiroshima, T., Uemura, T., Mori, H. et al. (2015). Mechanisms of splicing-dependent trans-synaptic adhesion by PTPÎ´-IL1RAPL1/IL-1RAcP for synaptic differentiation. *Nat Commun, 6*, 6926. ↗

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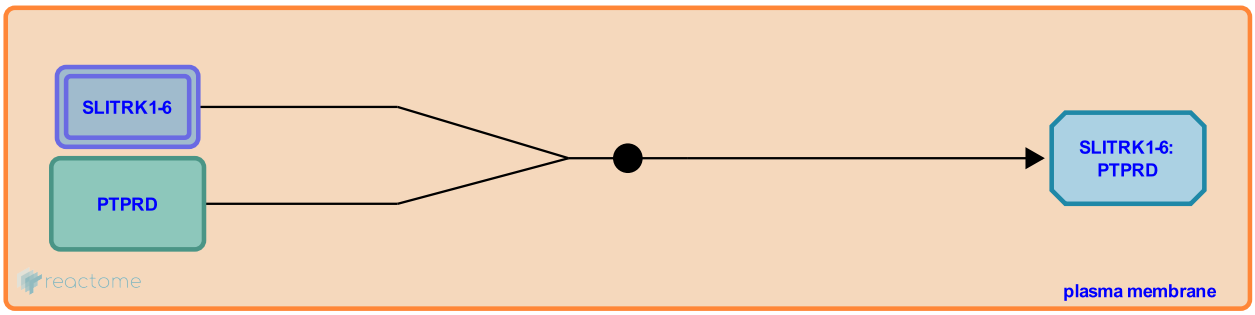
PTPRD binds SLITRK1-6 ↗

Location: Receptor-type tyrosine-protein phosphatases

Stable identifier: R-HSA-6797803

Type: binding

Compartments: plasma membrane



The SLIT and NTRK-like protein (SLITRK) family consists of six brain-specific transmembrane proteins (SLITRK1–6) that possess extracellular LRR domains homologous to the axon guidance molecule Slit and intracellular C-terminal tyrosine residues with surrounding sequences homologous to the Trk family (Aruga & Mikoshiba 2003). SLITRKs have been implicated in the modulation of neuronal process outgrowth promoting neuronal survival and in synapse formation (Linhoff et al. 2009). They exhibit synaptogenic activities through their interactions with specific LAR-RPTP members. All SLITRKs can interact with Receptor-type tyrosine-protein phosphatase delta (PTPRD), and SLIK1-3 at least can also interact with PTPRS (Meyer et al. 2004). SLITRK3 can induce inhibitory, but not excitatory, presynaptic differentiation whereas other family members induce both excitatory and inhibitory presynapses (Takahashi et al. 2012).
SLITRK1 variants are associated with Tourette's syndrome (Abelson et al. 2005) and Trichotillomania (Zuchner et al. 2006) and obsessive compulsive disorders (OCDs). SLITRK2 is a candidate gene for schizophrenia (Piton et al. 2011) and bipolar disorder.

Literature references

Aruga, J., Craig, AM., Takahashi, H., Ota, M., Sohya, K., Matsumoto, Y. et al. (2012). Selective control of inhibitory synapse development by Slitrk3-PTPδ trans-synaptic interaction. *Nat. Neurosci., 15*, 389-98, S1-2. ↗

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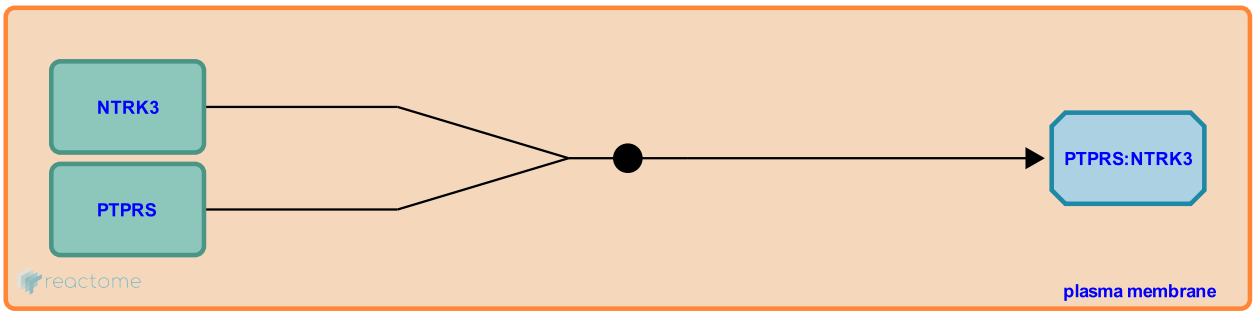
PTPRS binds NTRK3 ↗

Location: Receptor-type tyrosine-protein phosphatases

Stable identifier: R-HSA-6798257

Type: binding

Compartments: plasma membrane



Neurotrophin receptor 3 (NTRK3, TrkC) non-catalytic form acts as a synaptogenic adhesion molecule by binding to axonal Protein receptor-type tyrosine-protein phosphatase sigma (PTPRS). Transsynaptic interaction between dendritic NTRK3 and axonal PTPRS generates bidirectional non-catalytic signaling essential for excitatory pre- and postsynaptic differentiation in neural network development (Takahashi et al. 2011). The interaction between pre-synaptic PTPRS and post-synaptic NTRK3 involves extracellular domains of both proteins (Coles et al. 2014).

Literature references

Craig, AM., Murphy, TH., Takahashi, H., Arstikaitis, P., Wang, YT., Bartlett, TE. et al. (2011). Postsynaptic TrkC and presynaptic PTPσ function as a bidirectional excitatory synaptic organizing complex. *Neuron, 69*, 287-303. ↗

Zhang, P., Craig, AM., Elegheert, J., Nakagawa, T., Stoker, AW., Aricescu, AR. et al. (2014). Structural basis for extracellular cis and trans RPTPσ signal competition in synaptogenesis. *Nat Commun, 5*, 5209. ↗

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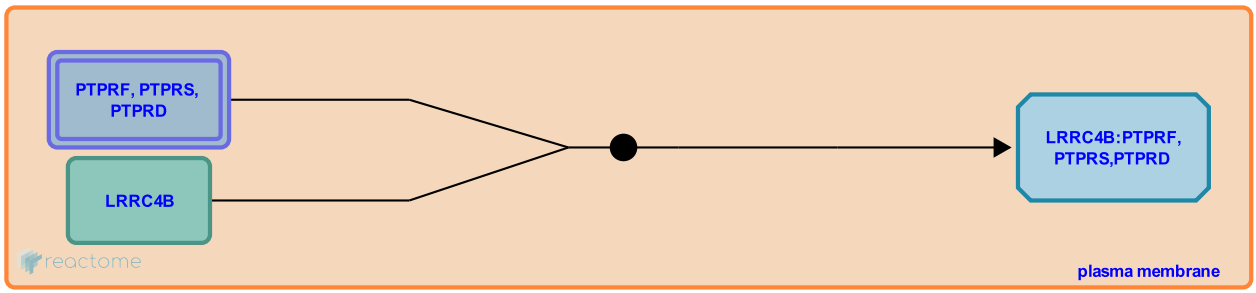
PRTPRF, PTPRS, PTPRD bind LRRC4B ↗

Location: Receptor-type tyrosine-protein phosphatases

Stable identifier: R-HSA-6798258

Type: binding

Compartments: plasma membrane



Leucine-rich repeat-containing protein 4B (LRRC4B, NGL-3) is a member of the netrin-G ligand (NGL, LRRC4) family that is widely expressed in the brain. LRRC4B binds with high affinity to Protein tyrosine Receptor-type tyrosine-protein phosphatase F (PTPRF, LAR), Protein tyrosine Receptor-type tyrosine-protein phosphatase sigma (PTPRS) and Protein tyrosine Receptor-type tyrosine-protein phosphatase delta (PTPRD). It binds to the first two fibronectin III (FnIII) domains of the PTPRs, thus it is likely to interact with all PTPRs splice variants. LRRC4B may induce both excitatory and inhibitory presynaptic differentiation in contacting axons (Woo et al. 2009, 2010).

Literature references

Kim, H., Kim, E., Kim, SY., Woo, J., Kwon, SK. (2010). Trans-synaptic adhesions between netrin-G ligand-3 (NGL-3) and receptor tyrosine phosphatases LAR, protein-tyrosine phosphatase delta (PTPdelta), and PTPsigma via specific domains regulate excitatory synapse formation. *J. Biol. Chem., 285*, 13966-78. ↗

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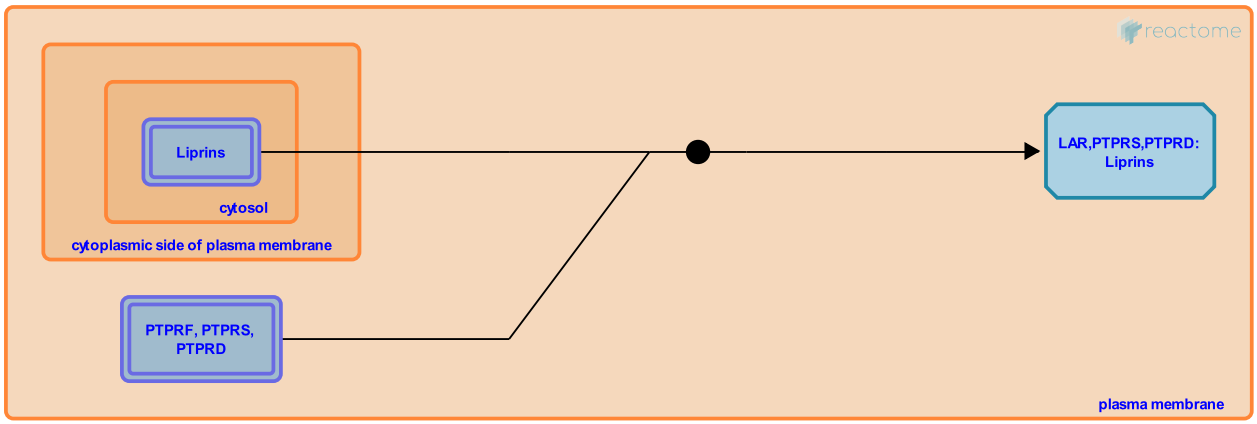
PTPRF, PTPRS, PTPRD bind Liprins ↗

Location: Receptor-type tyrosine-protein phosphatases

Stable identifier: R-HSA-388824

Type: binding

Compartments: plasma membrane, cytosol



All the three LAR-RPTP transmembrane tyrosine phosphatases associate with liprin proteins and colocalize with liprin-alpha1 at the proximal edges of focal adhesions. Based on sequence similarities and binding characteristics, liprins are subdivided into alpha-type and beta-type liprins. The C-terminal, non-coiled coil regions of alpha-liprins bind to the membrane-distal phosphatase domains of LAR family members, as well as to the C-terminal, non-coiled coil region of beta-liprins. Liprin is required for normal presynaptic differentiation in C. elegans and controls synapse morphogenesis in Drosophila. In mammalian synapses the functional significance of liprin and LAR-RPTP interaction is unknown (Pages et al. 1998, Dunah et al. 2005).

Literature references

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