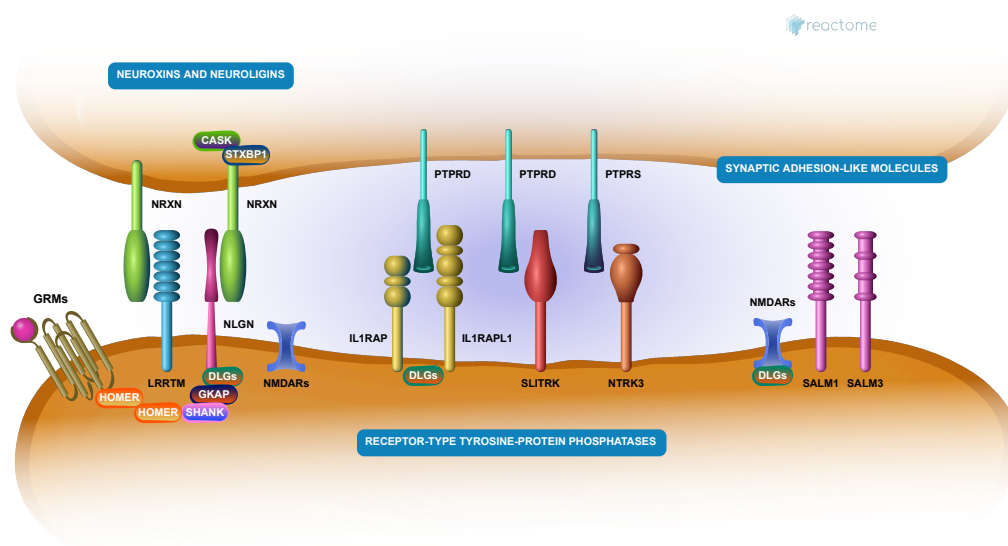


Protein-protein interactions at synapses



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](#).

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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.

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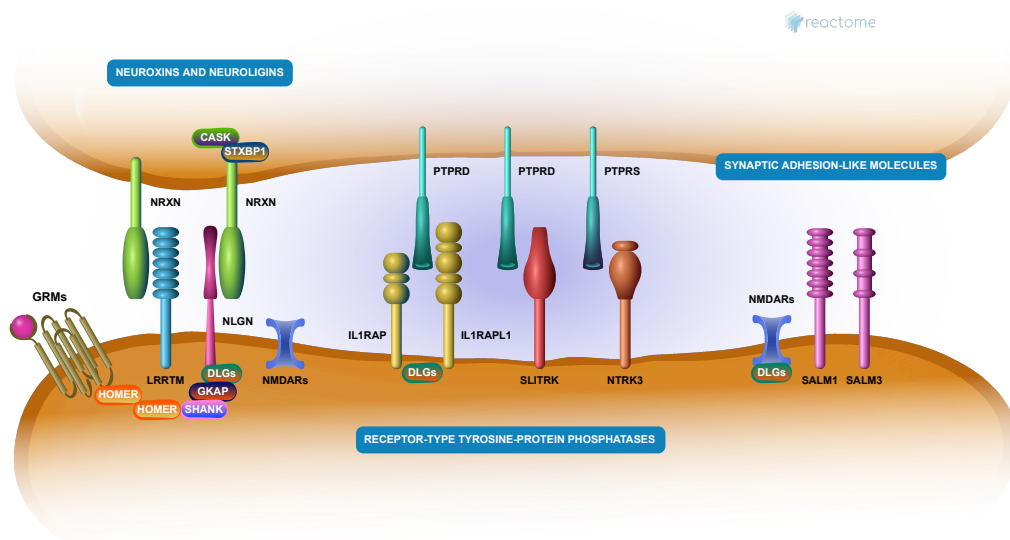
Reactome database release: 88

This document contains 4 pathways ([see Table of Contents](#))

Protein-protein interactions at synapses ↗

Stable identifier: R-HSA-6794362

Compartments: plasma membrane, cytosol



Synapses constitute highly specialized sites of asymmetric cell-cell adhesion and intercellular communication. Its formation involves the recruitment of presynaptic and postsynaptic molecules at newly formed contacts. Synapse assembly and maintenance invokes heterophilic presynaptic and postsynaptic transmembrane proteins that bind each other in the extracellular space and recruit additional proteins via their intracellular domains. Members of the cadherin and immunoglobulin (Ig) superfamilies are thought to mediate this function. Several molecules, including synaptic cell-adhesion molecule (SynCAM), N-cadherin, neural cell-adhesion molecule (NCAM), Eph receptor tyrosine kinases, and neuroligins and neurexins, have been implicated in synapse formation and maintenance (Dean & Dresbach 2006, Craig et al. 2006, Craig & Kang 2007, Südhof 2008).

Literature references

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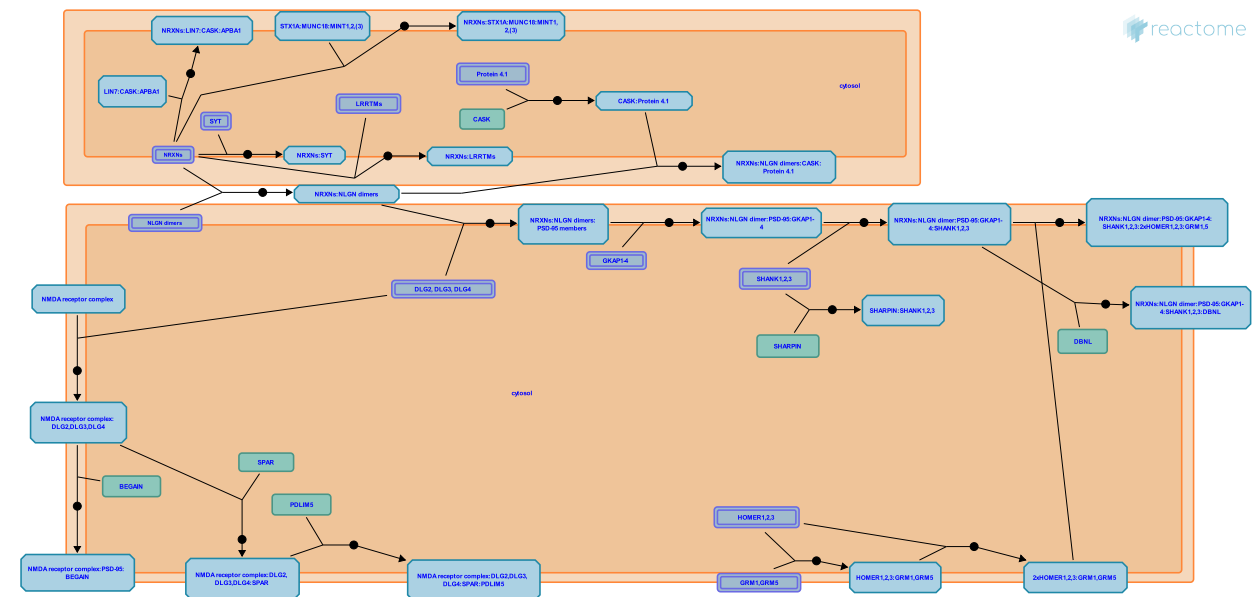
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Neurexins and neuroligins ↗

Location: Protein-protein interactions at synapses

Stable identifier: R-HSA-6794361



Neurexins (NRXNs) and neuroligins (NLGNs) are best characterized synaptic cell-adhesion molecules. They are part of excitatory glutamatergic and inhibitory GABAergic synapses in mammalian brain, mediate trans-synaptic signaling, and shape neural network properties by specifying synaptic functions. As cell-adhesion molecules, NRXNs and NLGNs probably function by binding to each other and by interacting with intracellular PDZ-domain proteins, but the precise mechanisms involved and their relation to synaptic transmission remain unclear. The binding of NRXNs and NLGNs to their partners, helps to align the pre-synaptic release machinery and post-synaptic receptors. The importance of neurexins and neuroligins for synaptic function is evident from the dramatic deficits in synaptic transmission in mice lacking Nrnxn or Nlgn. In humans, alterations in NRXNs or NLGNs genes are implicated in autism and other cognitive diseases, connecting synaptic cell adhesion to cognition and its disorders (Sudhof 2008, Craig et al. 2006, Craig & Kang 2007).

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Editions

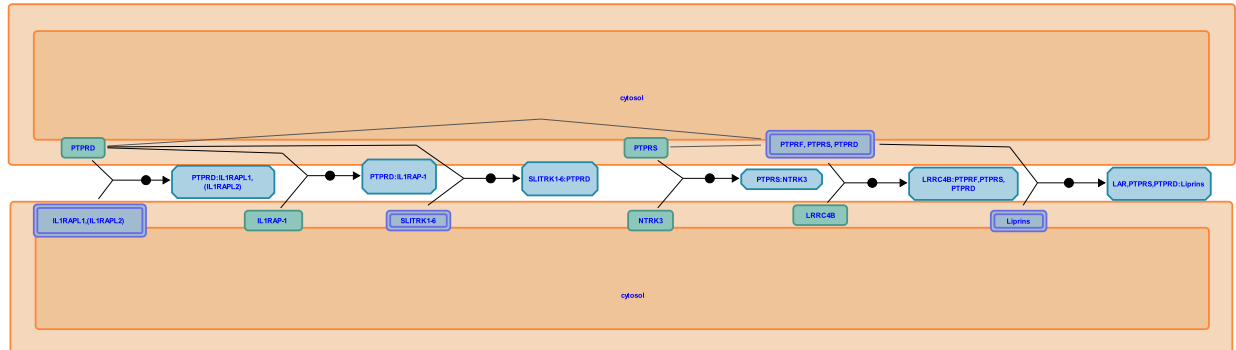
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Receptor-type tyrosine-protein phosphatases ↗

Location: Protein-protein interactions at synapses

Stable identifier: R-HSA-388844

Compartments: plasma membrane



reactome

Like neuroligins, Receptor-like protein tyrosine phosphatases (RTPs) make trans-synaptic adhesion complexes with multiple postsynaptic binding partners to regulate synapse organization. The type IIa RTPs 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 RTPs in cell-cell and cell-matrix interactions. To date, six different types of postsynaptic organizers for type-IIa RTPs 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).

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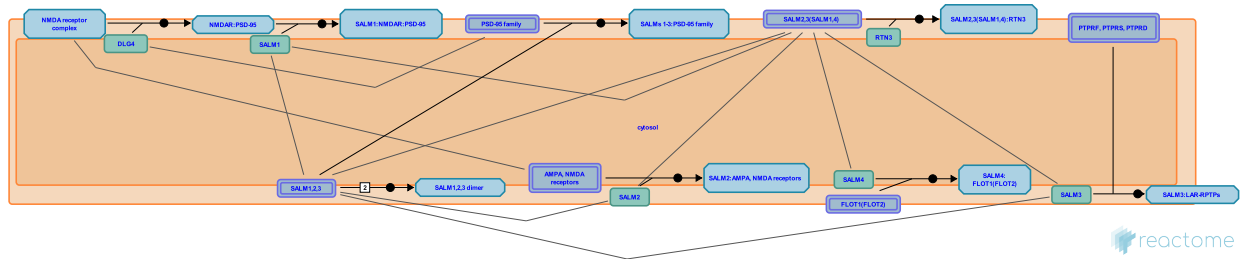
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Synaptic adhesion-like molecules ↗

Location: Protein-protein interactions at synapses

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Recruitment of receptors and ion channels to the postsynaptic membrane is the last step in synapse formation. Many of these proteins interact directly or indirectly with postsynaptic density-95 (PSD95)/Discs large/zona occludens-1 (PDZ) proteins, thus linking them to the postsynaptic scaffold and providing a mechanism for both retaining the protein at the synapse and keeping its proximity to signaling molecules known to associate with PDZ proteins (Wang et al. 2006, Morimura et al. 2006, Ko et al. 2006, Nourry et al. 2003, Kim & Sheng 2004, Montgomery et al. 2004, Sheng and Kim 2011). The synaptic adhesion-like molecules (SALM) family belongs to the superfamily of leucine-rich repeat (LRR)-containing adhesion molecules, alternatively referred to as LRFN (leucine-rich repeat and fibronectin III domain-containing) is synapse adhesion molecule linked to NMDA and AMPA receptors. It includes five known members (SALMs 1-5 or LRFN1-5), which have been implicated in the regulation of neurite outgrowth and branching, and synapse formation and maturation. SALM proteins are distributed to both dendrites and axons in neurons (Ko et al. 2006, Wang et al. 2006, Sebold et al. 2012). The family members, SALM1-SALM5, have a single transmembrane (TM) domain and contain extracellular leucine-rich repeats, an Ig C2 type domain, a fibronectin type III domain, and an intracellular postsynaptic density-95 (PSD-95)/Discs large/zona occludens-1 (PDZ) binding domain, which is present on all members except SALM4 and SALM5 (Ko et al. 2006, Wang et al. 2006, Morimura et al. 2006).

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