Dopamine synaptic vesicle docking and priming

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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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Literature references

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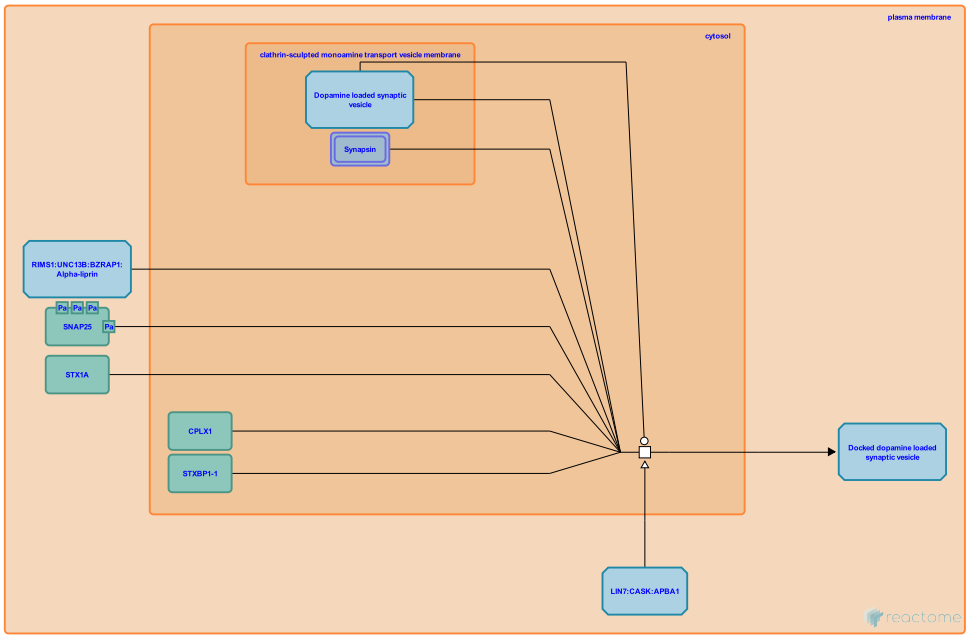
Stable identifier: R-HSA-380574

Type: transition

Compartments: cytosol, clathrin-sculpted monoamine transport vesicle membrane, plasma membrane



Dopamine loaded synaptic vesicles are docked, inside the synapse in the presynaptic cell, close to the plasma membrane. The docking brings the vesicles in close proximity to the release site to facilitate the release of dopamine. Some of the molecules involved in the docking process are STXBP1 (Munc 18), RAB3A (Rab3), RIMS1 (Rab 3 interacting molecule, RIM), BZRAP1 (RIM-binding protein), UNC13B (Munc13) and alpha-liprins.

STXBP1 is an SM (Sec1/Munc18-like) protein that probably functions by wrapping around the trans-SNARE complex to catalyze membrane fusion. It binds to the amino-terminus of STX1A (syntaxin-1A) (D-ulubova et al. 1999) and though it's exact role is unclear (Sudhof & Riso 2011), it is essential for membrane fusion in vivo (Khvotchev et al. 2007).

During synaptic exocytosis synaptic vesicles dock with an electron-dense structure called the presynaptic active zone. This has at least four key protein components: UNC13B, RIMS1, BZRAP1 and alpha-liprins. UNC13B is essential for synaptic priming (Augustin et al. 1999). The amino-terminal zinc-finger domain of RIMS1 interacts with the amino-terminal C2a-domain of UNC13B (Lu et al. 2006). A proline-rich domain in RIMS1 interacts with an SH3 domain in BZRAP1 (Wang et al. 2000). Alpha-liprins bind the C2B domain of RIMS1 (Schoch et al. 2002). RIMS1 binds to synaptic vesicle-bound RAB3A (Lu et al. 2006) and possibly SYT1 (synaptotagmin). RIMS1 and BZRAP1 bind to N and P/Q-type calcium channels in the plasma membrane (Kaeser et al. 2011).

The priming reaction brings docked but unprimed synaptic vesicles into a releasable pool. Priming involves formation of the trimeric SNARE complex between two plasma membrane proteins SNAP25 and Syntaxin and vesicular membrane protein, VAMP2.

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Editions

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