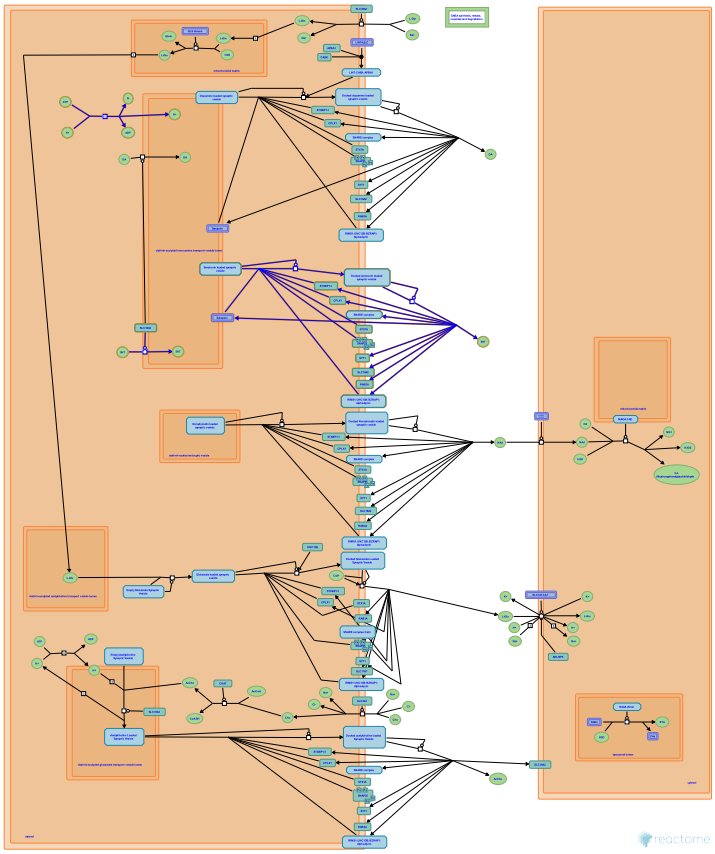
Serotonin Neurotransmitter Release Cycle



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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.

03/10/2024

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. ↗

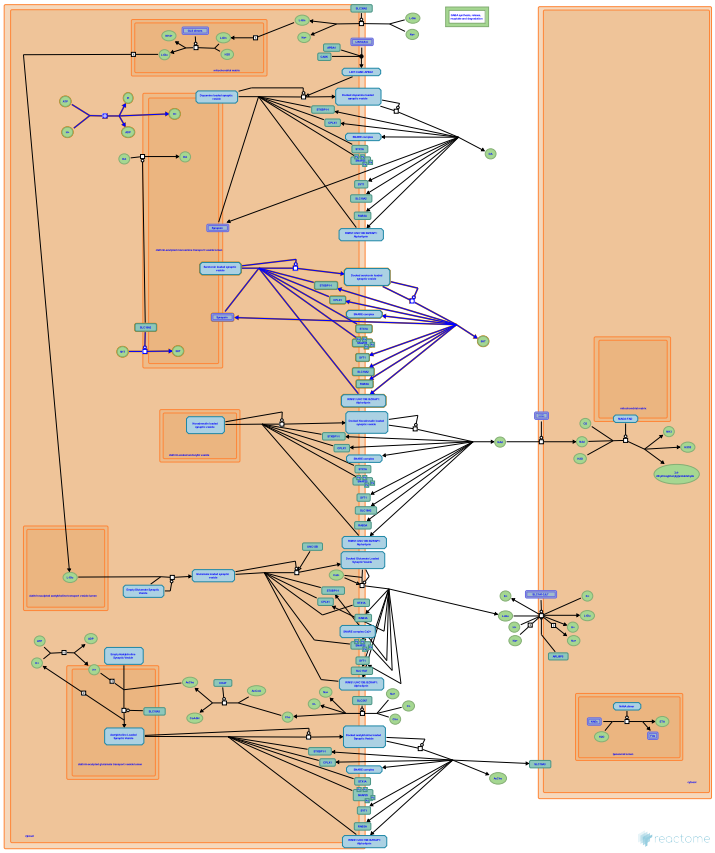
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Serotonin Neurotransmitter Release Cycle ↗

Stable identifier: R-HSA-181429



Serotonin is synthesized in the serotonergic neurons in the central nervous system and the enterochrommaffin cells of the gastroinetstinal system. Serotonin is loaded into the clathrin sculpted monoamine transport vesicles. The vesicles are docked, primed and release after the change in the membrane potential that activates voltage gated calcium channels and the reponse by several proetins to the changes in intracellular Ca2+ increase leads to fusion of the vesicle and release of serotonin into the synapse.

Editions

2008-01-14	Authored	Mahajan, SS.
2008-04-24	Reviewed	Kavalali, E.
2008-11-18	Edited	Mahajan, SS.

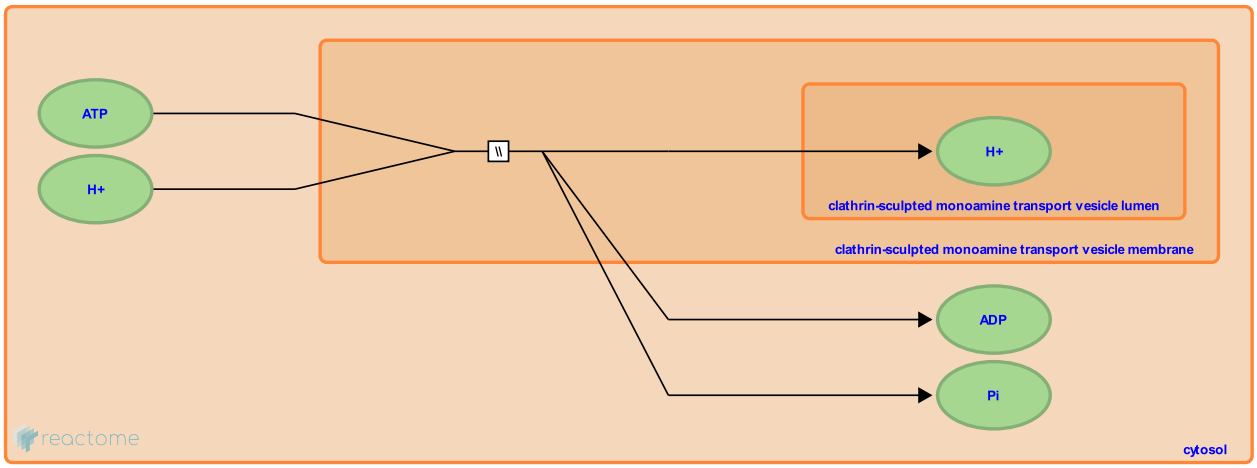
Re-acidification of clathrin sculpted monoamine transport vesicle lumen ↗

Location: Serotonin Neurotransmitter Release Cycle

Stable identifier: R-HSA-374916

Type: omitted

Compartments: clathrin-sculpted monoamine transport vesicle membrane, cytosol



Loading of the monoamine vesicle is preceded by acidifcation of the vesicle by ATPase.

Followed by: loading of Serotonin in synaptic vesicles

Literature references

Jahn, R., Takamori, S., Riedel, D. (2000). Immunoisolation of GABA-specific synaptic vesicles defines a functionally distinct subset of synaptic vesicles. *J Neurosci, 20*, 4904-11. ↗

Editions

2008-06-26	Authored	Mahajan, SS.
2008-11-27	Reviewed	Restituito, S.
2009-11-19	Edited	Gillespie, ME.

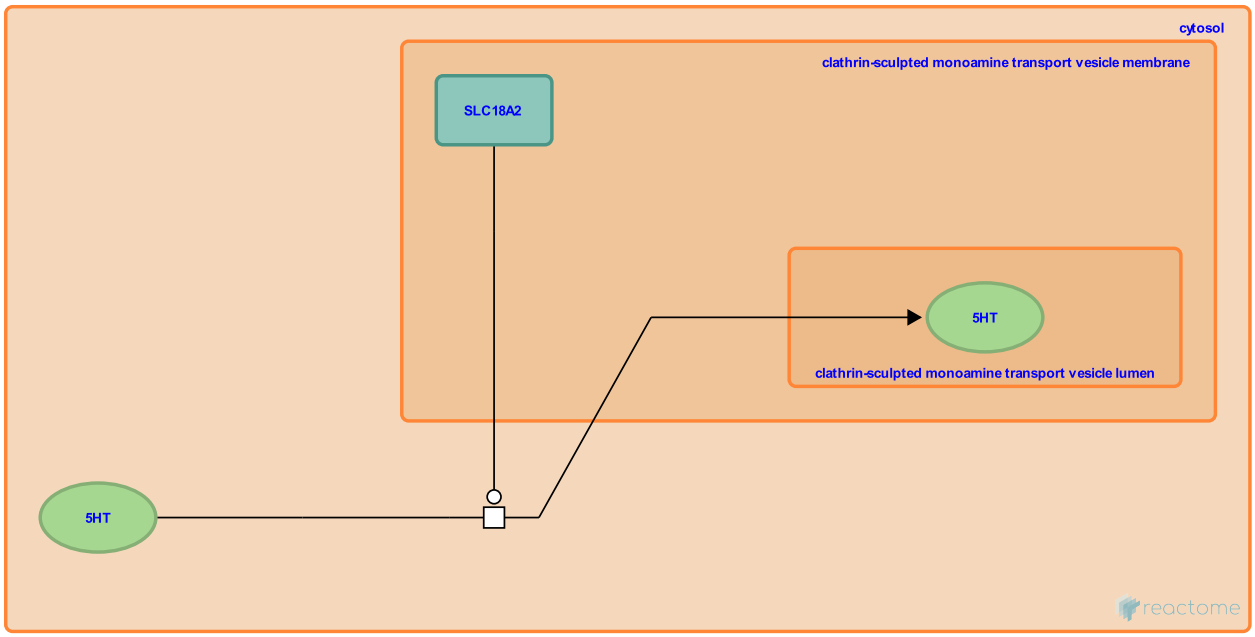
loading of Serotonin in synaptic vesicles ↗

Location: Serotonin Neurotransmitter Release Cycle

Stable identifier: R-HSA-380586

Type: transition

Compartments: cytosol, clathrin-sculpted monoamine transport vesicle lumen



Serotonin is loaded into the clathrin sculpted monoamine transport vesicle by vesicular monoamine transporter (Johnssom 1998, Henry et al. 1994).

Preceded by: Re-acidification of clathrin sculpted monoamine transport vesicle lumen

Followed by: Serotonin loaded synaptic vesicle docking and priming

Literature references

Massoulie, J., Henry, JP., Gasnier, B., Raisman-Vozari, R., Krejci, E., Isambert, MF. et al. (1994). Biochemistry and molecular biology of the vesicular monoamine transporter from chromaffin granules. *J. Exp. Biol., 196*, 251-62. ↗

Johnson, RG. (1988). Accumulation of biological amines into chromaffin granules: a model for hormone and neurotransmitter transport. *Physiol. Rev., 68*, 232-307. ↗

Alkhater, RA., Rilstone, JJ., Minassian, BA. (2013). Brain dopamine-serotonin vesicular transport disease and its treatment. *N. Engl. J. Med., 368*, 543-50. ↗

Editions

2008-08-06	Authored	Mahajan, SS.
2008-11-27	Reviewed	Restituito, S.
2009-11-19	Edited	Gillespie, ME.

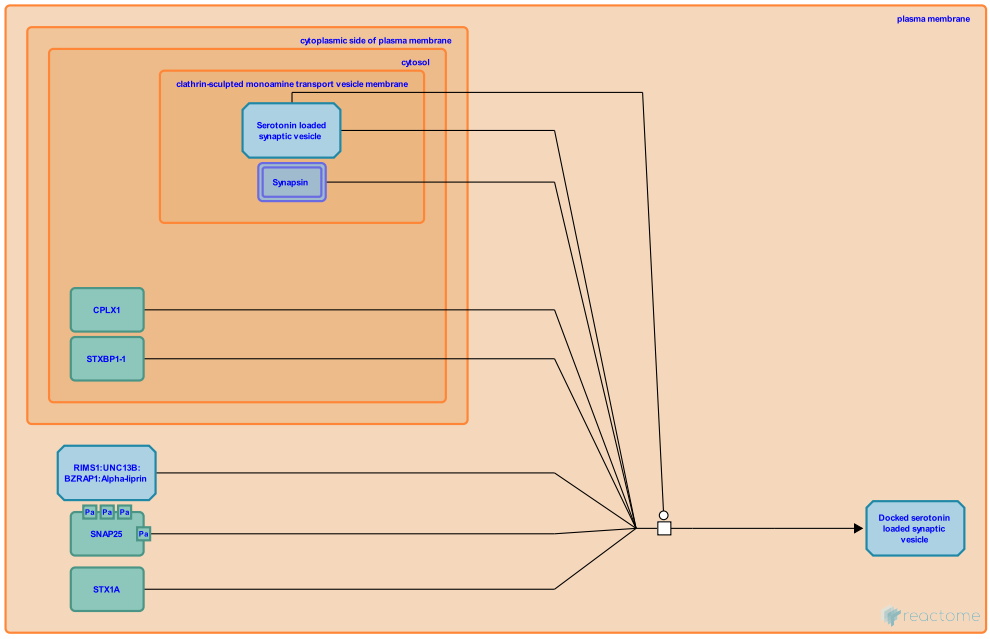
Serotonin loaded synaptic vesicle docking and priming ↗

Location: Serotonin Neurotransmitter Release Cycle

Stable identifier: R-HSA-380905

Type: transition

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



Serotonin loaded synaptic vesicles are docked, inside the synapse in the presynaptic cell, close to the plasmamembrane. The docking brings the vesicles in close proximity to the release site to fascilitate the release of serotonin. Some of the molecules involved in the docking process are Munc 18, Rab3a, Rab 3 interacting molecule (RIM). The priming reaction brings docked but unprimed synaptic vesicles into a releaseable pool. Priming involes formation of the trimeric SNARE complex between two plasmamembrane proteins SNAP25 and Syntaxin and vesicular membrane protein, VAMP2.

Preceded by: loading of Serotonin in synaptic vesicles

Followed by: Release of docked serotonin loaded synaptic vesicle

Literature references

Olkkonen, VM., Galli, T., Riento, K., Ehnholm, C., Lehtonen, E., Jansson, S. (1998). Interaction of Munc-18-2 with syntaxin 3 controls the association of apical SNAREs in epithelial cells. *J Cell Sci, 111*, 2681-8. ↗

de Vries, KJ., Zalm, R., Südhof, TC., Verhage, M., Toonen, RF. (2005). Munc18-1 stabilizes syntaxin 1, but is not essential for syntaxin 1 targeting and SNARE complex formation. *J Neurochem, 93*, 1393-400. ↗

Dai, H., Sun, J., Rizo, J., Südhof, TC., Dulubova, I., Khvotchev, M. (2007). Dual modes of Munc18-1/SNARE interactions are coupled by functionally critical binding to syntaxin-1 N terminus. *J Neurosci, 27*, 12147-55. ↗

Editions

2008-10-30	Authored	Mahajan, SS.
2008-11-27	Reviewed	Restituito, S.
2009-11-19	Edited	Gillespie, ME.

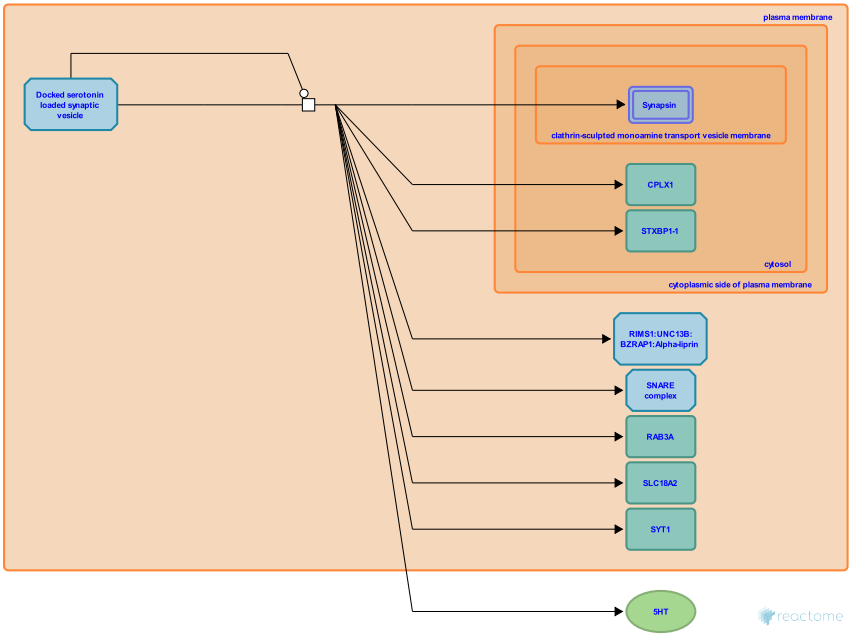
Release of docked serotonin loaded synaptic vesicle ↗

Location: Serotonin Neurotransmitter Release Cycle

Stable identifier: R-HSA-380901

Type: transition

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



The trimeric complex formed between V-SNARE (VAMP) and the T-SNAREs (syntaxin and SNAP 25) after priming step is called transSNARE complex because the members of each group lie on the opposide side of the membrane, plasmamembrane side and the vesicular membrane side. Ca2+ influx through the Voltage gated Calcium Channels (VGCC) initaites the process of fusion of the synaptic vesicle in the presynaptic cell. The rise in Ca2+ leads to the activation of Protein Kinase A through rise in cAMP. Synaptotagmin, a Ca2+ sensor proetin also plays a role in the fusion process. Following fusion the members of V and T SNARES lie on the same membrane formin the cis-SNARES. The fusion of release causes the release of the neurotransmitter into the synaptic cleft.

Preceded by: Serotonin loaded synaptic vesicle docking and priming

Literature references

Fisher, RJ., Craig, TJ., Burgoyne, RD., Morgan, A., Evans, GJ., Ciufo, LF. et al. (2003). Phosphorylation of Munc18 by protein kinase C regulates the kinetics of exocytosis. *J Biol Chem, 278*, 10538-45. ↗

Martens, S., McMahon, HT., Kozlov, MM. (2007). How synaptotagmin promotes membrane fusion. *Science, 316*, 1205-8. ↗

Jahn, R., Radhakrishnan, A., Stein, A., Fasshauer, D., Riedel, D. (2007). Synaptotagmin activates membrane fusion through a Ca2+-dependent trans interaction with phospholipids. *Nat Struct Mol Biol, 14*, 904-11. ↗

Editions

2008-06-26	Authored	Mahajan, SS.
2008-11-27	Reviewed	Restituito, S.
2009-11-19	Edited	Gillespie, ME.

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