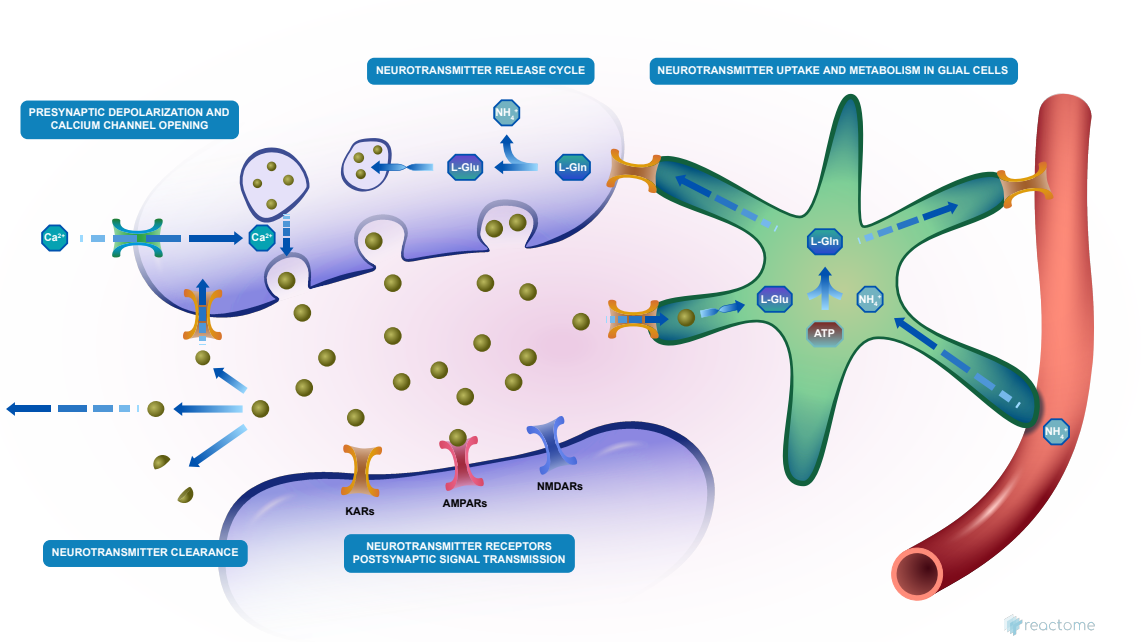
Transmission across Chemical Synapses



Kavalali, E., Mahajan, SS., Restituito, S., Wen, H.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

04/05/2024

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. ↗

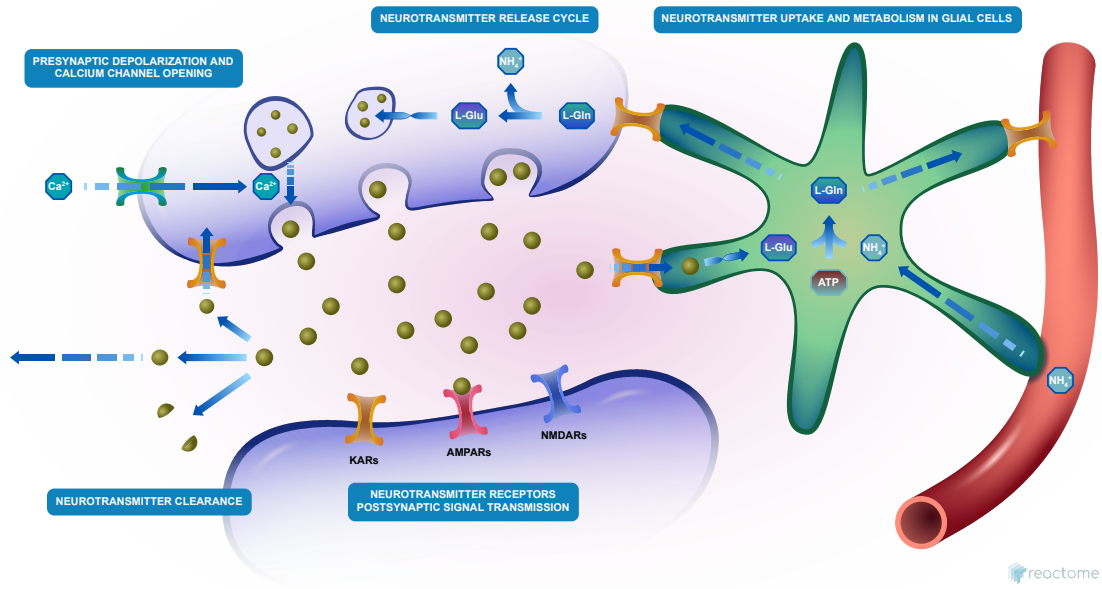
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 88

This document contains 6 pathways (see Table of Contents)

Transmission across Chemical Synapses ↗

Stable identifier: R-HSA-112315



Chemical synapses are specialized junctions that are used for communication between neurons, neurons and muscle or gland cells. The synapse involves a presynaptic neuron and a postsynaptic neuron, muscle cell or glad cell. The pre and the postsynaptic cell are separated by a gap (space) of 20 to 40 nm called the synaptic cleft. The signals pass in a single direction from the presynaptic to postsynaptic neuron (cell). The presynaptic neuron communicates via the release of neurotransmitter which bind the receptors on the postsynaptic cell. The process is initiated when an action potential invades the terminal membrane of the presynaptic neuron.
Action potentials occur in electrically excitable cells such as neurons and muscles and endocrine cells. They are initiated by the transient opening of voltage dependent sodium channels, causing a rapid, large depolarization of membrane potentials that spread along the axon membrane.
When action potentials arrive at the synaptic terminals, depolarization in membrane potential leads to the opening of voltage gated calcium channels located on the presynaptic membrane. The external Ca2+ concentration is approximately 10-3 M while the internal Ca2+ concentration is approximately 10-7 M. Opening of calcium channels causes a rapid influx of Ca2+ into the presynaptic terminal. The elevated presynaptic Ca2+ concentration allows synaptic vesicles to fuse with the plasma membrane of the presynaptic neuron and release their contents, neurotransmitters, into the synaptic cleft. These diffuse across the synaptic cleft and bind to specific receptors on the membrane of the postsynaptic cells. Activation of postsynaptic receptors upon neurotransmitter binding can lead to a multitude of effects in the postsynaptic cell, such as changing the membrane potential and excitability, and triggering intracellular signaling cascades.

Literature references

Fitzpatrick, D., Augustine, DJ., Katz, LC., Williams, JM., Purves, D., McNamara, JO. et al. (2001). Neuroscience 2nd Edition. *Oxford University Press.*

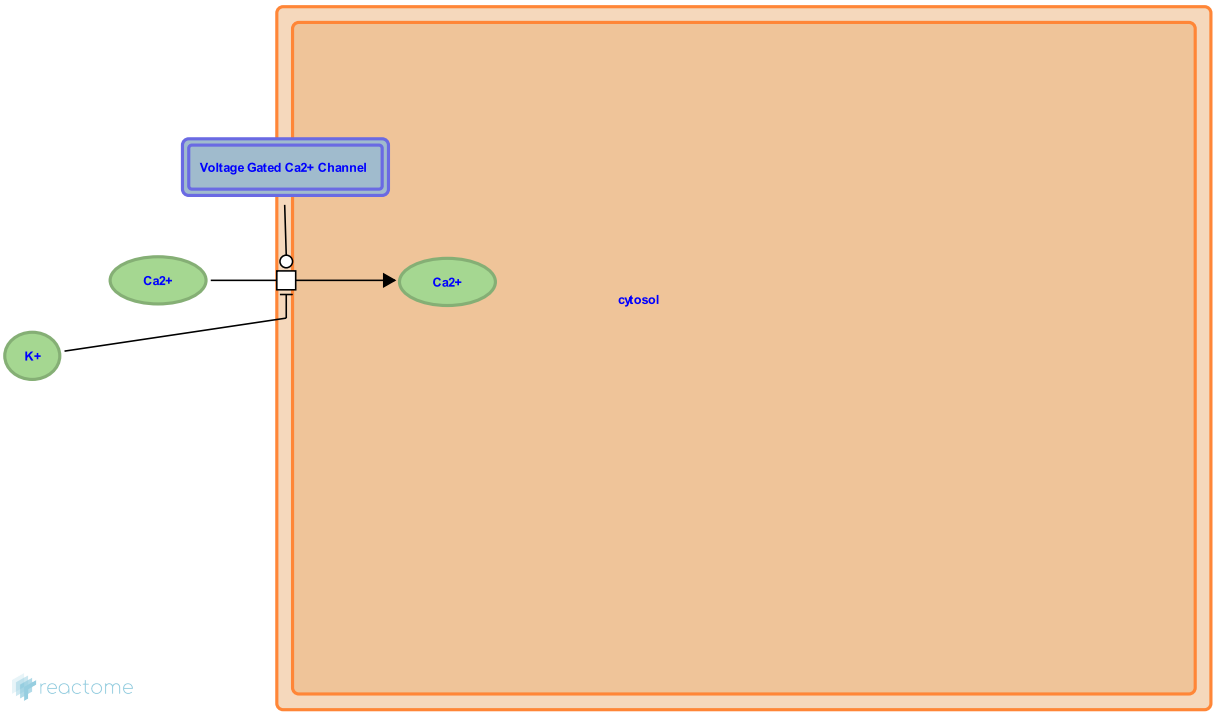
Editions

2008-01-14	Authored, Edited	Mahajan, SS.
2008-12-02	Reviewed	Kavalali, E., Restituito, S.
2020-01-24	Reviewed	Wen, H.

Presynaptic depolarization and calcium channel opening ↗

Location: Transmission across Chemical Synapses

Stable identifier: R-HSA-112308



Action potentials occur in electrically excitable cells such as neurons, muscles, and endocrine cells. They are initiated by transient opening of voltage dependent sodium channels, causing a rapid, large depolarization of membrane potentials that spread along the axon membrane.
The action potential travels down the axon and reaches the presynaptic terminal depolarizing the membrane in the pre synaptic terminal. The depolarization causes the voltage gated Ca2+ channels to open allowing the influx of Ca2+ that signals the release of neurotransmitter into the synaptic cleft.

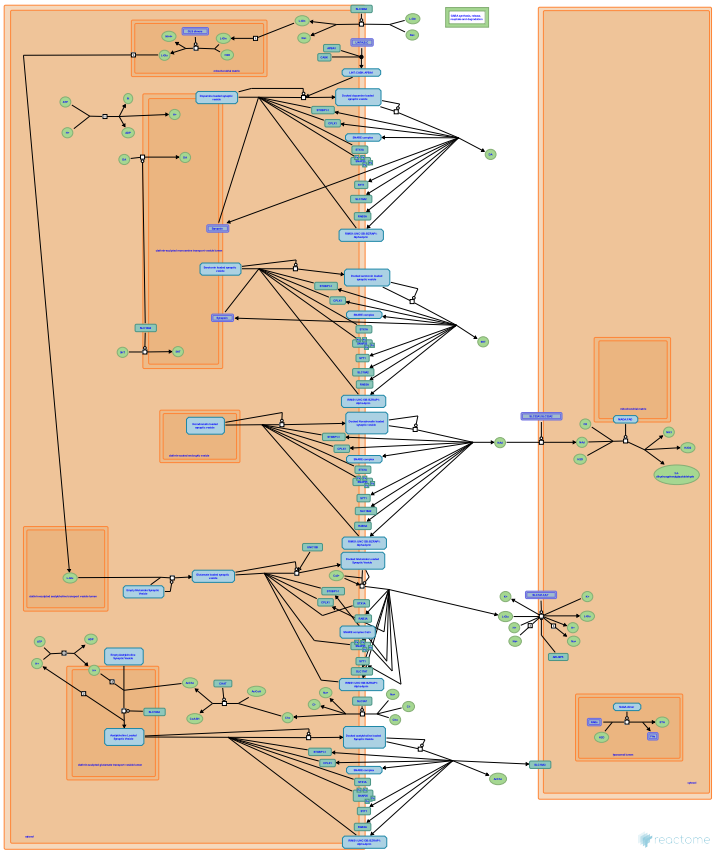
Editions

2008-01-14	Authored, Edited	Mahajan, SS.
2008-04-24	Reviewed	Kavalali, E.
2020-01-24	Reviewed	Wen, H.

Neurotransmitter release cycle ↗

Location: Transmission across Chemical Synapses

Stable identifier: R-HSA-112310



Neurotransmitter is stored in the synaptic vesicle in the pre-synaptic terminal prior to its release in the synaptic cleft upon depolarization of the pre-synaptic membrane. The release of the neurotransmitter is a multi-step process that is controlled by electrical signals passing through the axons in form of action potential. Neurotransmitters include glutamate, acetylcholine, nor-epinephrine, dopamine and seratonin. Each of the neurotransmitter cycle is independently described.

Literature references

Edwards, RH. (2007). The neurotransmitter cycle and quantal size. *Neuron, 55*, 835-58. ↗

Südhof, TC. (2004). The synaptic vesicle cycle. *Annu Rev Neurosci, 27*, 509-47. ↗

Schoch, S., Gundelfinger, ED. (2006). Molecular organization of the presynaptic active zone. *Cell Tissue Res, 326*, 379-91. ↗

Rettig, J., Becherer, U. (2006). Vesicle pools, docking, priming, and release. *Cell Tissue Res, 326*, 393-407. ↗

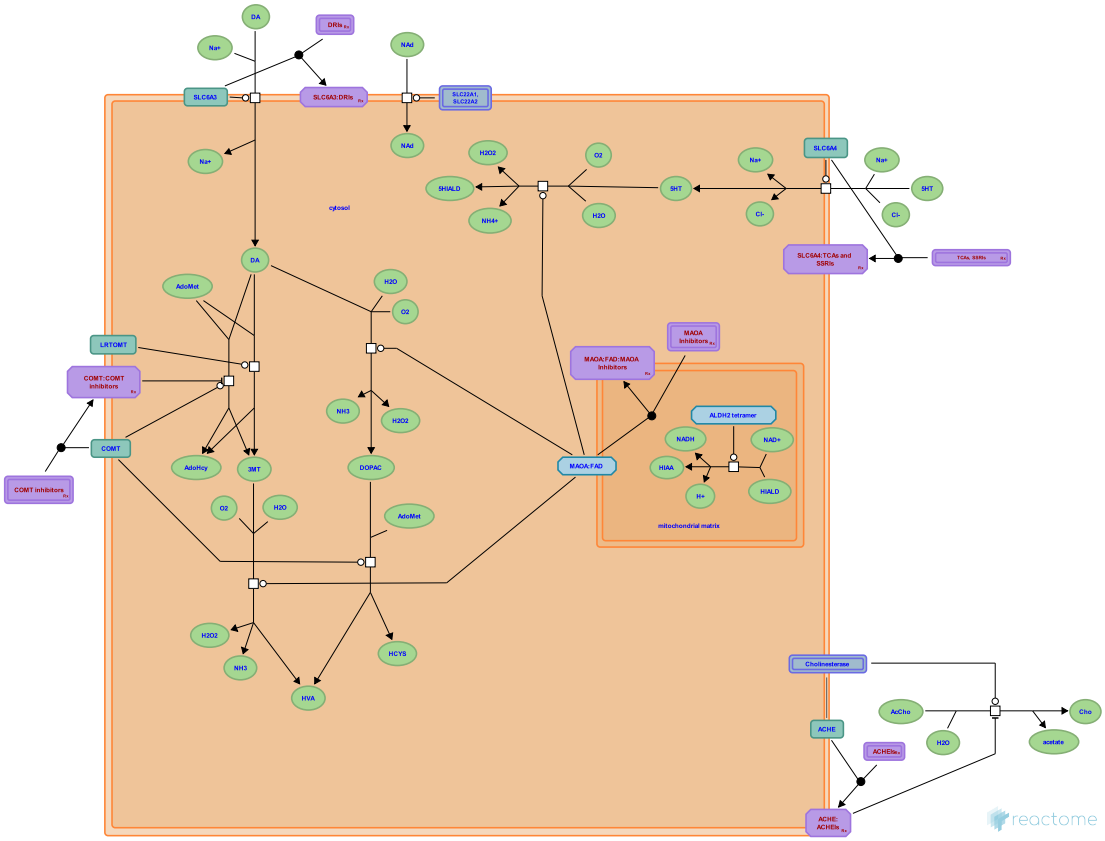
Editions

2008-01-14	Authored, Edited	Mahajan, SS.
2008-12-02	Reviewed	Kavalali, E., Restituito, S.

Neurotransmitter clearance ↗

Location: Transmission across Chemical Synapses

Stable identifier: R-HSA-112311



Neurotransmitter released in the synaptic cleft binds to specific receptors on the post-synaptic cell and the excess of the neurotransmitter is cleared to prevent over activation of the post-synaptic cell. The neurotransmitter is cleared by either re-uptake by the pre-synaptic neuron, diffusion in the perisynaptic area, uptake by astrocytes surrounding the synaptic cleft or enzymatic degradation of the neurotransmitter.

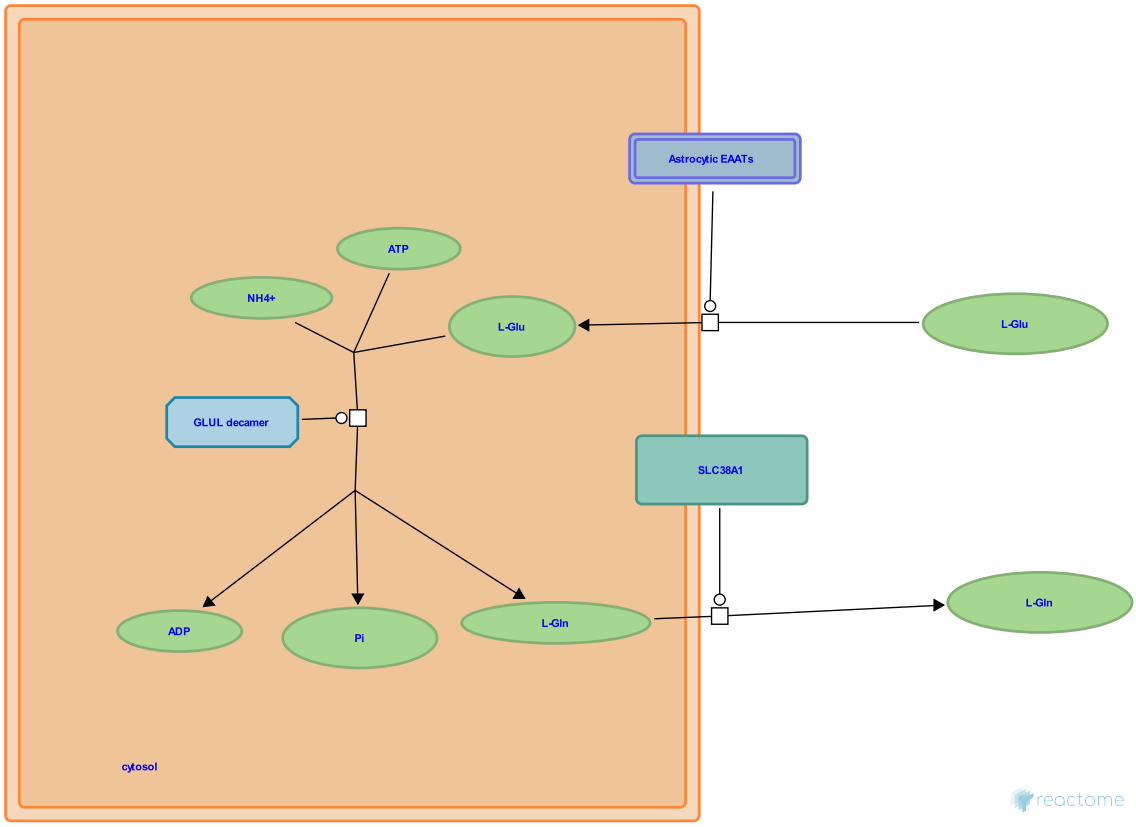
Editions

2008-01-14	Authored, Edited	Mahajan, SS.
2008-11-27	Reviewed	Restituito, S.

Neurotransmitter uptake and metabolism In glial cells ↗

Location: Transmission across Chemical Synapses

Stable identifier: R-HSA-112313



Neuotransmitter uptake by astrocytes is mediated by a specific transporter located on the astrocytic membrane. The imported neurotransmitter is metabolized and transported back to the neuron.

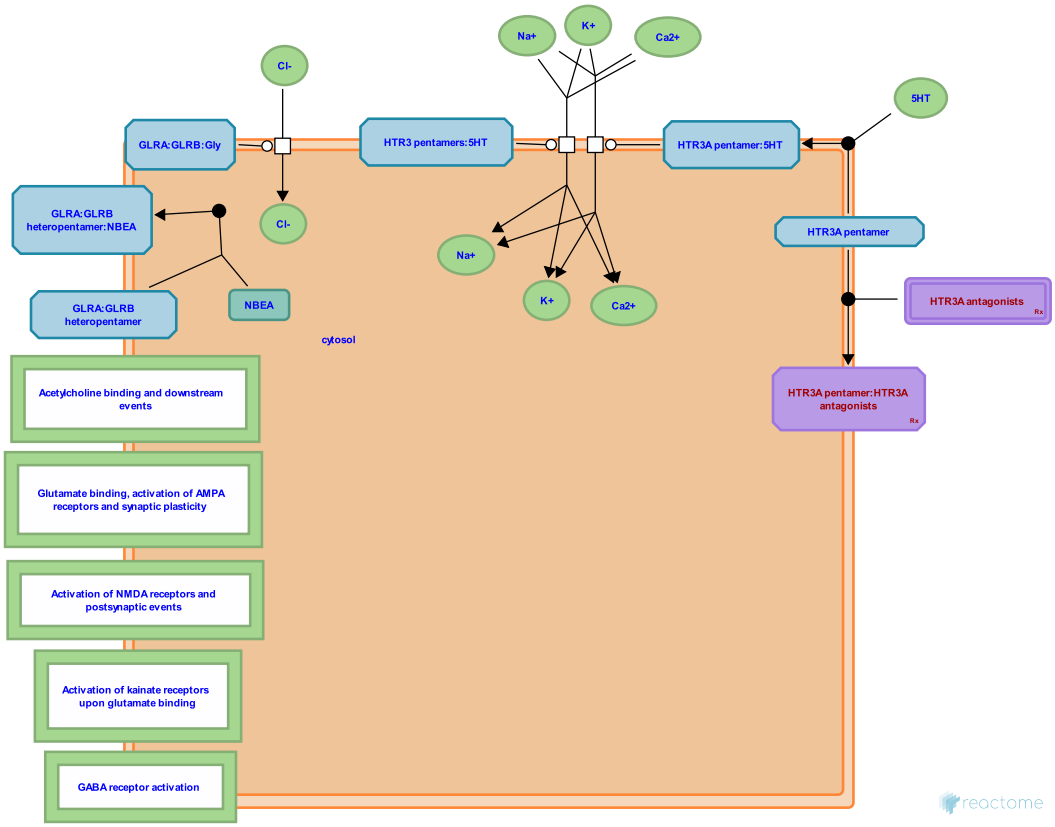
Editions

2008-01-14	Authored, Edited	Mahajan, SS.
2008-12-02	Reviewed	Kavalali, E., Restituito, S.

Neurotransmitter receptors and postsynaptic signal transmission ↗

Location: Transmission across Chemical Synapses

Stable identifier: R-HSA-112314



The neurotransmitter in the synaptic cleft released by the pre-synaptic neuron binds specific receptors located on the post-synaptic terminal. These receptors are either ion channels or G protein coupled receptors that function to transmit the signals from the post-synaptic membrane to the cell body.

Editions

2008-01-14	Authored	Mahajan, SS.
2008-12-02	Reviewed	Kavalali, E., Restituito, S.

Table of Contents

Introduction 1

Transmission across Chemical Synapses 2

- Presynaptic depolarization and calcium channel opening 3
- Neurotransmitter release cycle 4
- Neurotransmitter clearance 5
- Neurotransmitter uptake and metabolism In glial cells 6
- Neurotransmitter receptors and postsynaptic signal transmission 7

Table of Contents 8