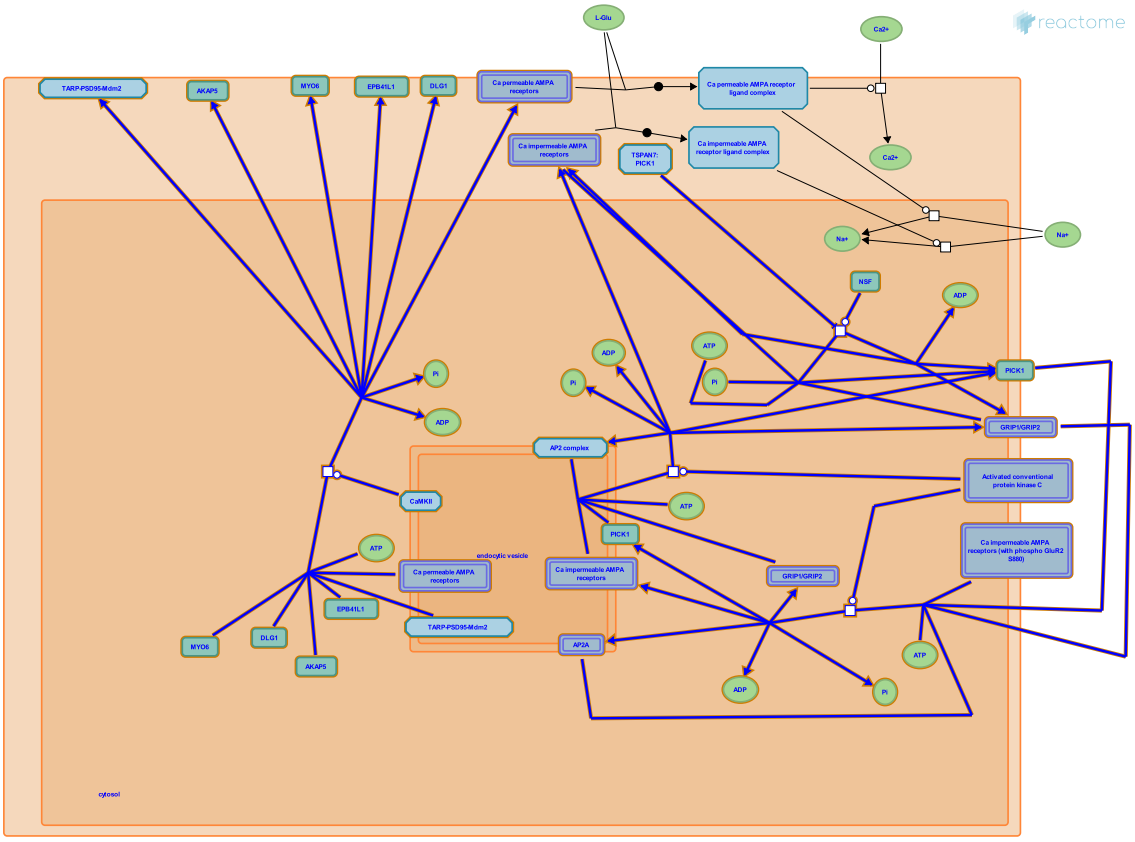
Trafficking of AMPA receptors



Mahajan, SS., Ziff, EB.

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

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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.

07/05/2024

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. ↗

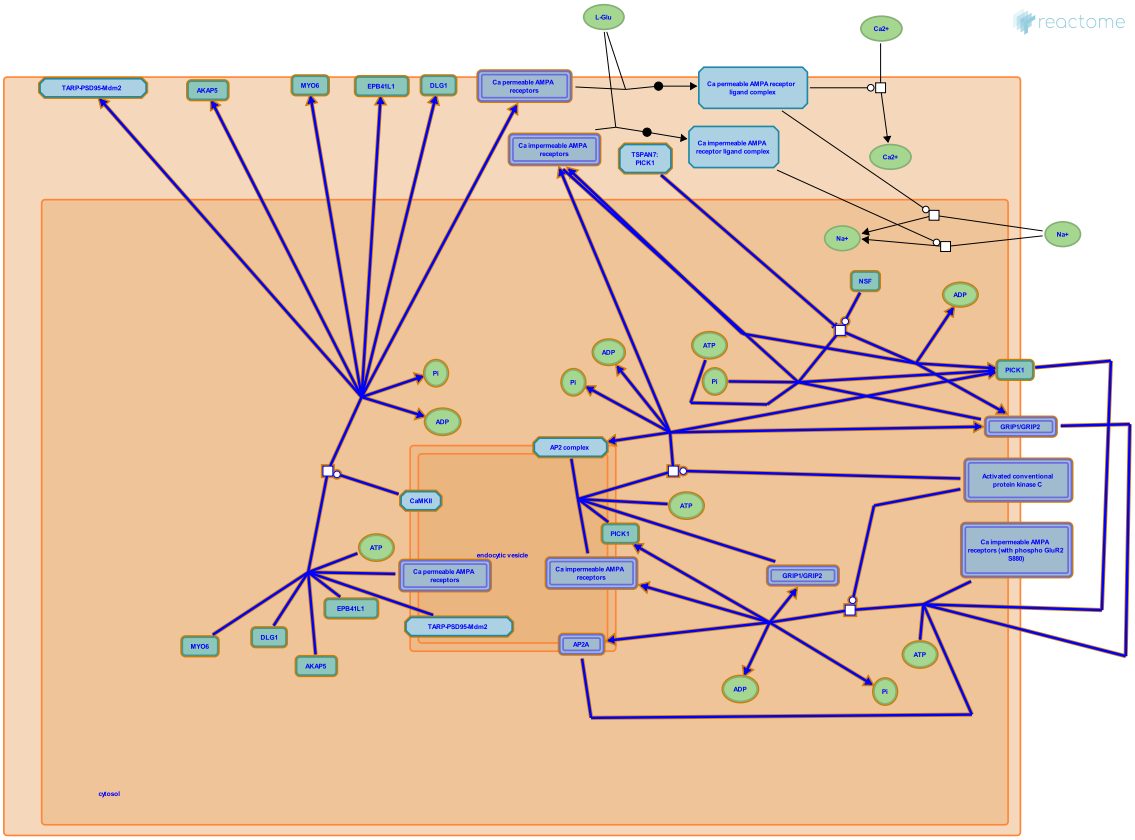
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Trafficking of AMPA receptors ↗

Stable identifier: R-HSA-399719



Repetitive presynaptic activity causes long lasting changes in the postsynaptic transmission by changing the type and the number of AMPA receptors. These changes are brought about by trafficking mechanisms that are mainly controlled by activity dependent phosphorylation/desphosphorylation of the GluR1/GluR2 subunits.

Literature references

Kessels, HW., Malinow, R. (2009). Synaptic AMPA receptor plasticity and behavior. *Neuron, 61*, 340-50. ↗

Editions

2008-01-14	Authored, Edited	Mahajan, SS.
2009-05-15	Reviewed	Ziff, EB.

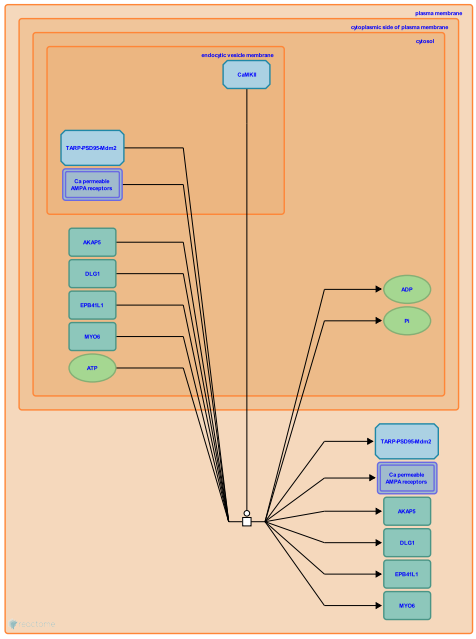
Trafficking of GluR1-containing AMPA receptors ↗

Location: Trafficking of AMPA receptors

Stable identifier: R-HSA-416320

Type: transition

Compartments: plasma membrane



GluR1-containing AMPA receptors are delivered to the synapses in an activity dependent manner. GluR1 trafficking is controlled by protein- protein interactions with 4.1N/G protein, SAP97 and by intricate regulation of phosphorylation of GluR1 at several phosphorylation sites in the C tail. GluR1 has four phosphorylation sites; serine 818 (S818) is phosphorylated by PKC, necessary for LTP, serine 831 (S831) is phosphorylated by CaMKII and increases the delivery of receptors to the synapse and also increases their single channel conductance, Threonine (T840) is implicated in LTP and serine 845 (S845) phosphorylated by PKA regulates open channel probability and also by cGKII, a cyclic GMP activated kinase, that increases the surface expression of GluR1. GluR1 insertion into synapse by CaMKII may induce LTP. CaMKII is a Ca/calmodulin dependent kinase that is activated upon increases in the Ca ion concentration during postsynaptic activity through NMDA receptors. The increase in GluR1-containing AMPA receptor population at the synapse results in enhancement of excitatory post synaptic potential (EPSC) which forms the basis of Long term potentiation (LTP). LTP is one form of synaptic plasticity that is involved in memory and learning. The increase in the GluR1 containing AMPA receptors and their activity leads to rise in intracellular Ca which induces signaling pathways that in turn promote switch in the type of AMPA receptors (Ca impermeable) thereby limiting the Ca increase and preventing cell death.

Literature references

Bassani, S., El-Husseini, A., Passafaro, M., Correia, SS., Brown, TC., Esteban, JA. et al. (2008). Motor protein-dependent transport of AMPA receptors into spines during long-term potentiation. *Nat Neurosci, 11*, 457-66. ↗

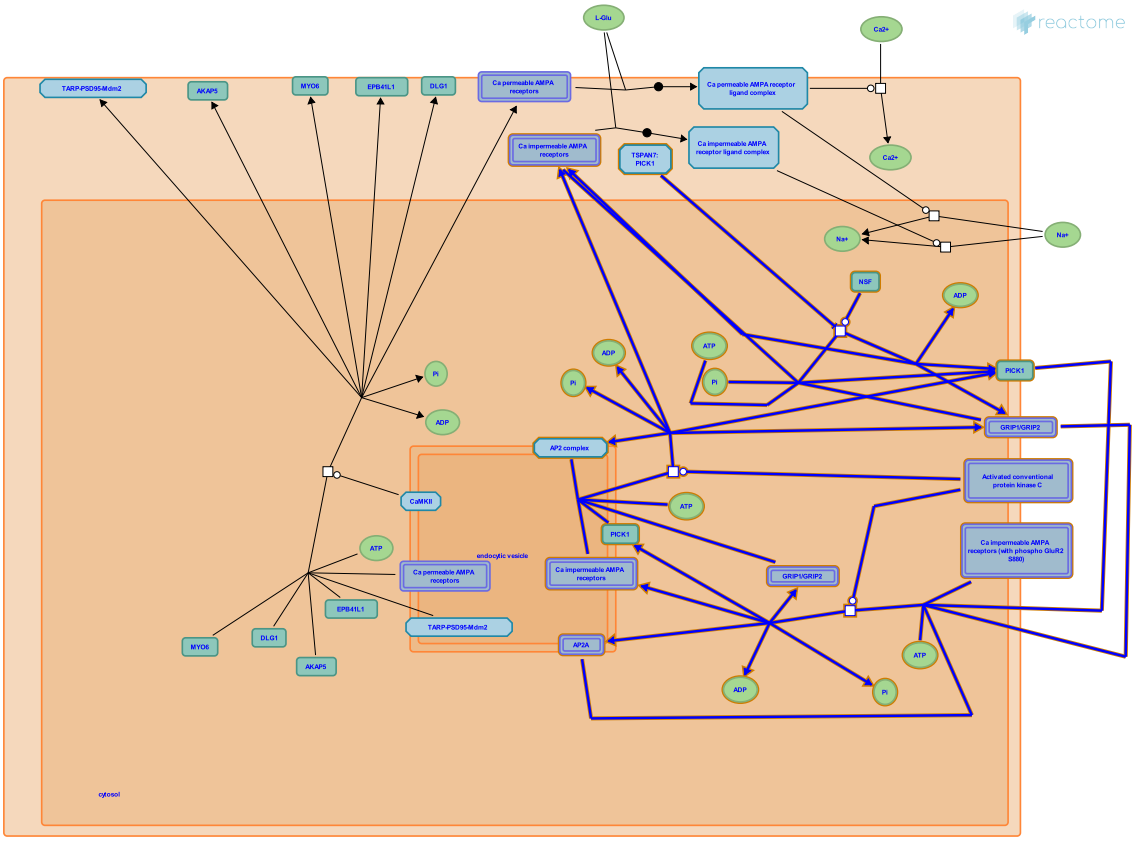
Editions

2008-01-14	Authored	Mahajan, SS.
2009-05-15	Reviewed	Ziff, EB.
2009-05-31	Edited	Mahajan, SS.

Trafficking of GluR2-containing AMPA receptors ↗

Location: Trafficking of AMPA receptors

Stable identifier: R-HSA-416993



Trafficking of GluR2-containing receptors is governed by protein protein interactions that are regulated by phosphorylation events. GluR2 binds NSF and AP2 in the proximal C terminal region and binds PICK and GRIP1/2 in the extreme C terminal region. GluR2 interaction with NSF is necessary to maintain the synaptic levels of GluR2-containing AMPA receptors both at basal levels and under conditions of synaptic activity. GluR2 interaction with GRIP helps anchor AMPA receptors at the synapse. Phosphorylation of GluR2 at S880 disrupts GRIP interaction but allows binding of PICK. PICK is activated by Ca sensitive Protein kinase C (PKC). Under basal conditions, in hippocampal synapse, GluR2-containing AMPA receptors (GluR2/GluR3) constitutively recycle between the synapse and the endosome by endocytosis and exocytosis. GRIP anchors the receptors at the synapse while PICK interaction internalizes the receptors and NSF helps maintain the synaptic receptors. Cerebellar stellate cells mainly contain GluR3 homomers as Ca permeable receptors. The interaction of GluR3 and GRIP is disrupted by PICK interaction by phosphorylation of equivalent of S880 residue in GluR3. Under conditions of repetitive presynaptic activity, there is PICK dependent removal of GluR2-lacking AMPA receptors and selective incorporation of GluR2-containing AMPA receptors at the synapse. The GluR2-containing AMPA receptors are first delivered to the surface by PICK and mobilized to the synapse by NSF dependent mechanism (Liu SJ and Cull-Candy SG Nat Neurosci. 2005 Jun;8(6):768-75)

Literature references

Glauser, L., Kropf, M., Johnsson, K., Rey, G., Hirling, H., Kulangara, K. (2008). Subunit-specific surface mobility of differentially labeled AMPA receptor subunits. *Eur J Cell Biol, 87*, 763-78. ↗

Editions

2008-01-14	Authored, Edited	Mahajan, SS.
2009-05-15	Reviewed	Ziff, EB.

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