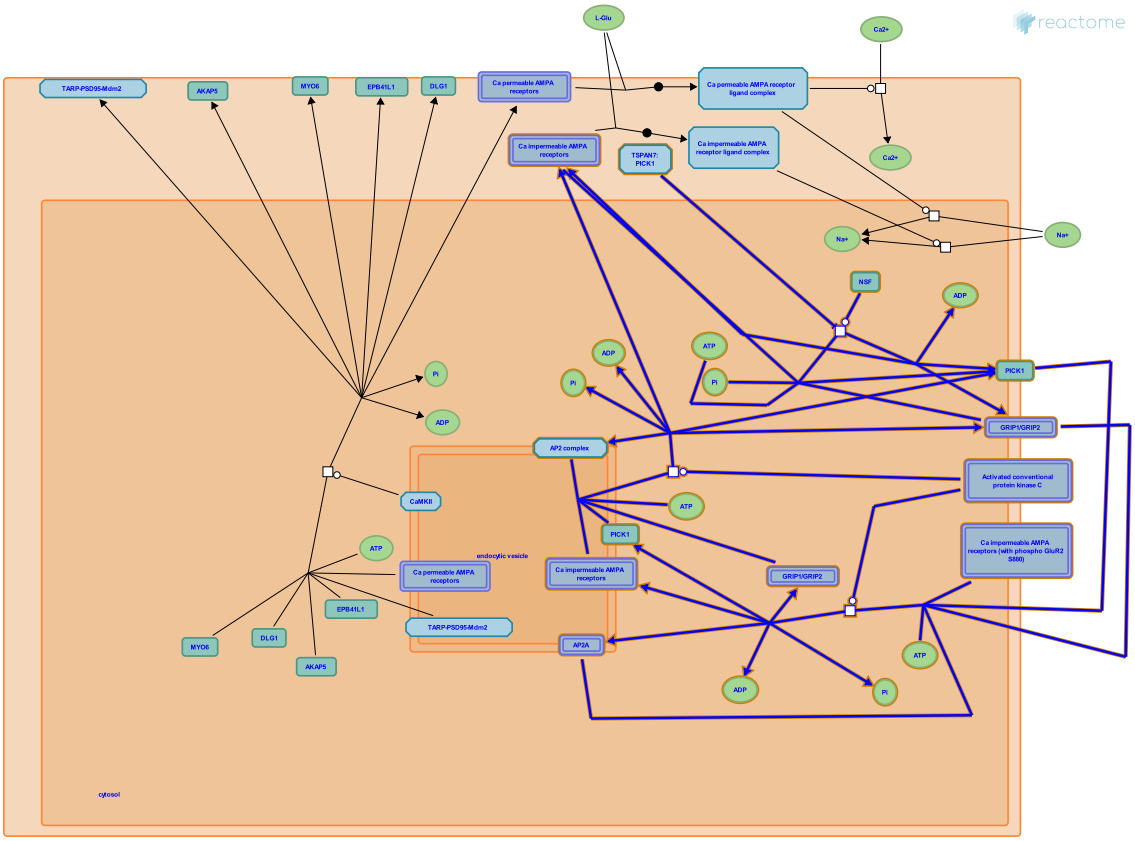
Trafficking of GluR2-containing AMPA receptors



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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. ↗

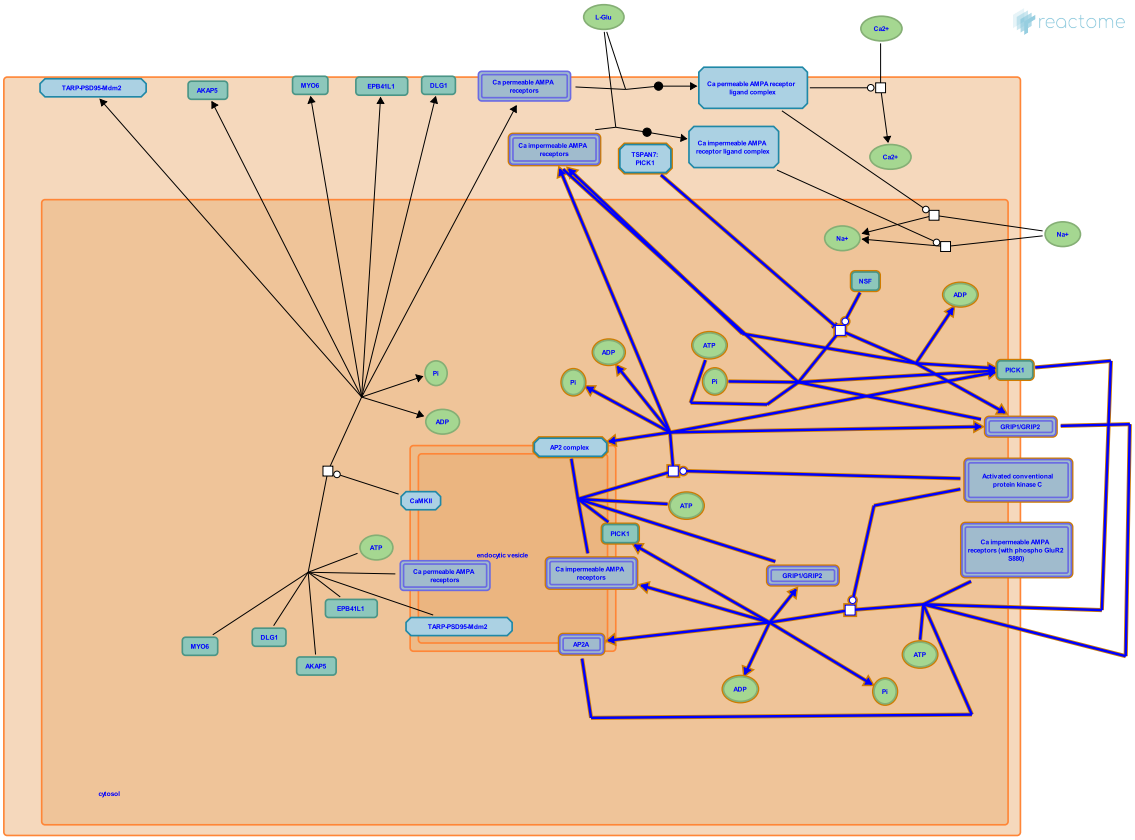
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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 GluR2-containing 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.

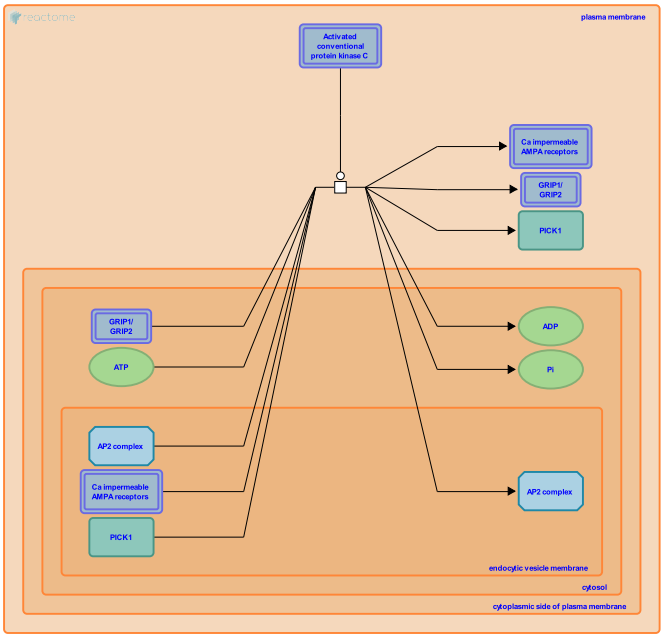
Trafficking of GluR2-containing AMPA receptors to extrasynaptic sites ↗

Location: Trafficking of GluR2-containing AMPA receptors

Stable identifier: R-HSA-416639

Type: transition

Compartments: plasma membrane



GluR2 containing AMPA receptors are trafficked to the plasmamembrane by the activation of Ca activated PKC that binds PICK.The PICK interaction delivers GluR2 containing AMPA receptors to the Plasmamembrane. This reaction is a part of constitutive recycling of AMPA receptor that delivers the AMPA receptors from the endosome to the plasmamembrane and back to endosome from the plasmamembrane.

Preceded by: Endocytosis of Ca impermeable AMPA receptors

Followed by: Endocytosis of Ca impermeable AMPA receptors, Trafficking of GluR2-containing AMPA receptors to synapse

Literature references

Ziff, EB., Lu, W. (2005). PICK1 interacts with ABP/GRIP to regulate AMPA receptor trafficking. *Neuron, 47*, 407-21. ↗

Editions

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

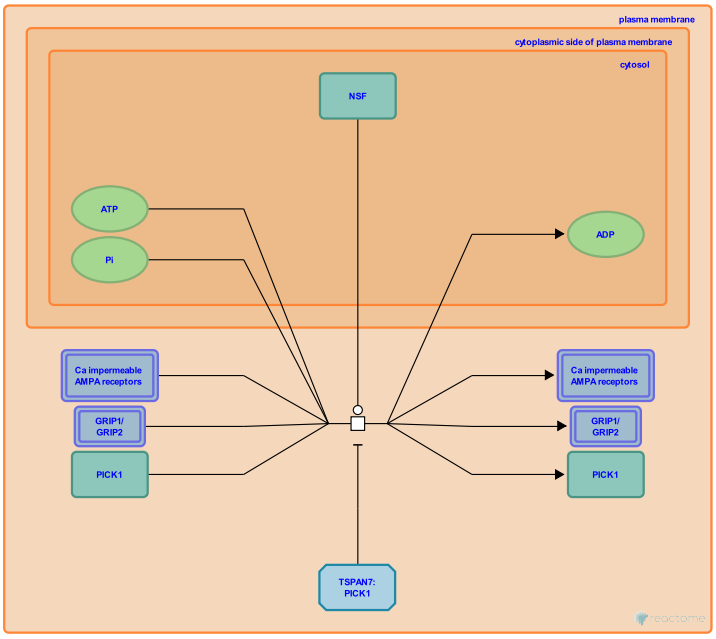
Trafficking of GluR2-containing AMPA receptors to synapse ↗

Location: Trafficking of GluR2-containing AMPA receptors

Stable identifier: R-HSA-416985

Type: transition

Compartments: plasma membrane, cytosol



Tetraspanin 7 (TSPAN7) a member of the tetraspanin superfamily associates dynamically with numerous partner proteins in tetraspanin-enriched microdomains (TEMs) of the plasma membrane (Boucheix and Rubinstein, 2001). TSPAN7 promotes filopodia and dendritic spine formation in cultured hippocampal neurons, and is required for spine stability and normal synaptic transmission. Via its C-terminus, TSPAN7 interacts with the PDZ domain of protein interacting with C kinase 1 (PICK1), to regulate PICK1 and GluR2/3 association and AMPA receptor trafficking (Bassani et al. 2012). PICK1 is involved in the internalization and recycling of AMPA receptors (AMPARs) (Perez et al. 2001). In hippocampal neurons, TSPAN7 may regulate AMPA receptor trafficking by limiting PICK1 accessibility to AMPA receptors and suggest an additional mechanism for the functional maturation of glutamatergic synapses, whose impairment is implicated in intellectual disability (Bassani et al. 2012).
Constitutively recycling GluR2 containing AMPA receptors in the plasma membrane are stabilized by the action of NSF ATPase activity which disassociates PICK from GluR2 thereby retaining AMPA receptors in the plasma membrane.

Preceded by: Trafficking of GluR2-containing AMPA receptors to extrasynaptic sites

Followed by: Endocytosis of Ca impermeable AMPA receptors

Literature references

Ziff, EB., Lu, W. (2005). PICK1 interacts with ABP/GRIP to regulate AMPA receptor trafficking. *Neuron, 47*, 407-21. ↗

Editions

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

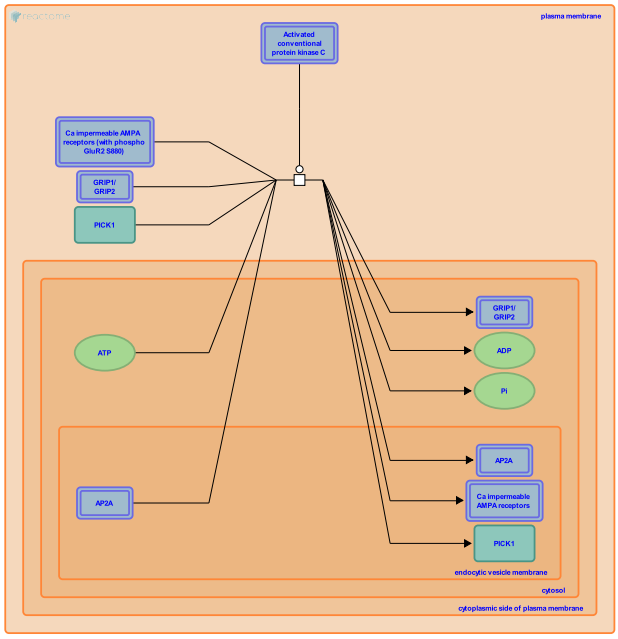
Endocytosis of Ca impermeable AMPA receptors ↗

Location: Trafficking of GluR2-containing AMPA receptors

Stable identifier: R-HSA-421007

Type: transition

Compartments: plasma membrane



GluR2 containing AMPA receptors are constitutively recycled between the endosome membrane and the plasma membrane. GRIP and PICK compete for the binding to the C tail of GluR2. Once the GluR2 containing AMPA receptors are in the plasmamembrane, phosphorylation of GluR2 at S880 by PKC causes disruption of GRIP interaction, but not PICK interaction which facilitates internalization of GluR2 containing AMPA receptors into endosomes.

Preceded by: Trafficking of GluR2-containing AMPA receptors to synapse, Trafficking of GluR2-containing AMPA receptors to extrasynaptic sites

Followed by: Trafficking of GluR2-containing AMPA receptors to extrasynaptic sites

Literature references

Ziff, EB., Lu, W. (2005). PICK1 interacts with ABP/GRIP to regulate AMPA receptor trafficking. *Neuron, 47,* 407-21. ↗

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