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Role of intracellular trafficking of AMPAR during LTP

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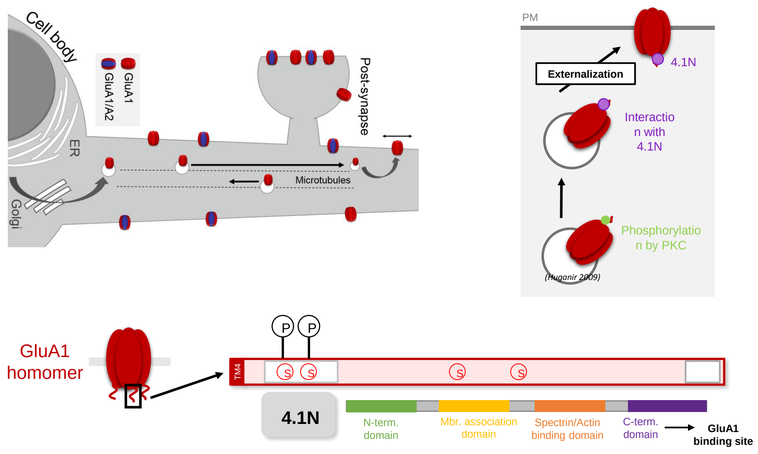
Introduction

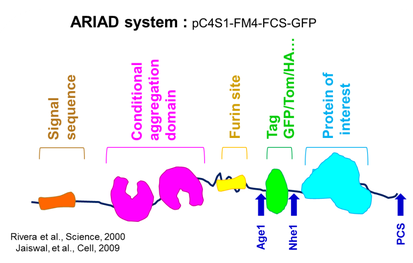
Abundance of AMPA receptors (AMPAR) at synapse is essential for the establishment and maintenance of synaptic function. Their synaptic localization is dependent on a highly dynamic exocytosis, endocytosis and plasma membrane mobility events.

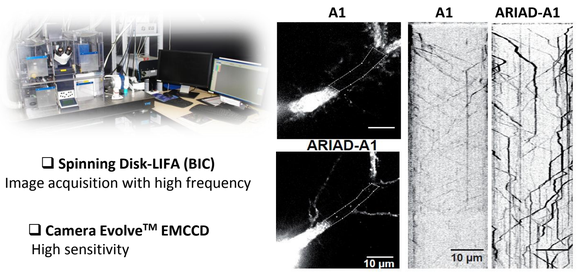
Using our new biochemical tool combined with photonic live imaging, we controlled and followed the intracellular transport of tagged GluA1 containing receptors in cultured rat hippocampal neurons. Analyzes are performed for GluA1 WT and mutants of GluA1 C-terminus domain in basal condition and during LTP. In organotypic hippocampal slices we combine imaging and electrophysiology experiments to analyze the impact of intracellular transport of AMPAR on LTP.

Localization of AMPAR is regulated by their intracellular trafficking thru interaction of their C-terminus domains with different intracellular partners. These interactions play a major role in the exocytosis and localization of the receptor at the plasma membrane both in basal condition of during cLTP. In hippocampal slice intracellular transport of AMPAR plays a major role during LTP.



Biomolecular & Imaging Tools



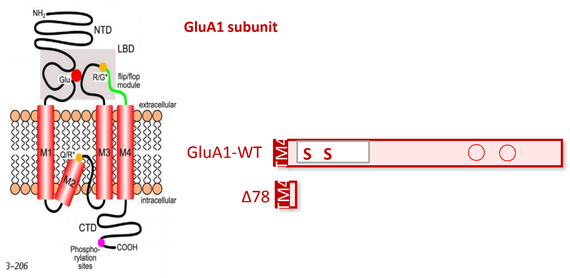


- Spinning Disk-LIFA (BIC)
  Image acquisition with high frequency
- Camera Evolve™ EMCCD
  High sensitivity

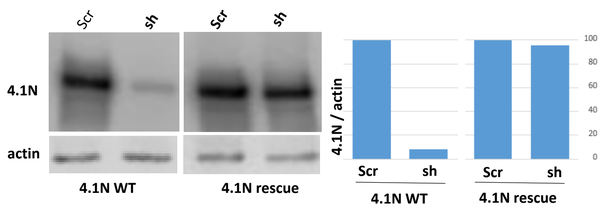
Combine Video-spinning microscopy after FRAP photobleaching to visualize GluA1 transport.

Role of the interaction between 4.1N and the C-terminal domain of GluA1 in the intracellular transport of GluA1 during basal transmission and LTP

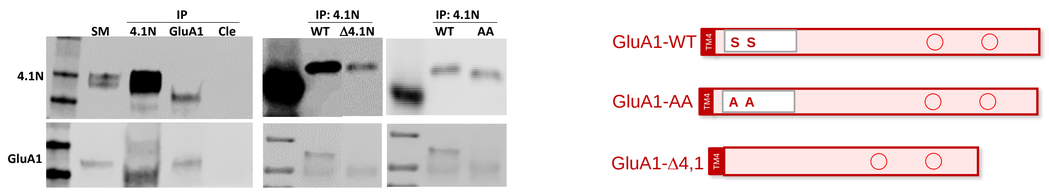
GluA1 C-term. domain and IT



4.1N and GluA1 IT

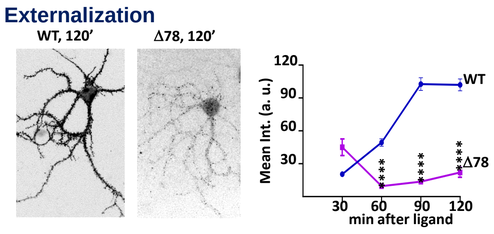


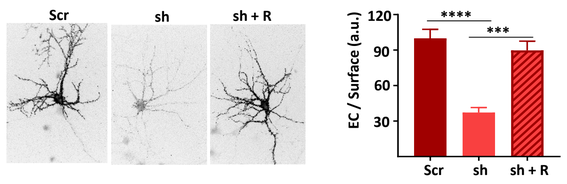
Binding GluA1 / 4.1N and GluA1 IT

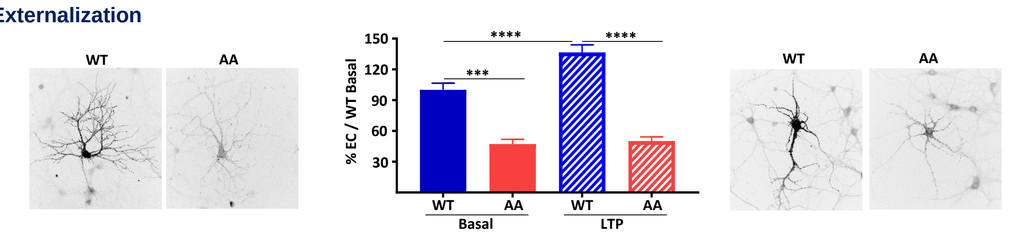


BASAL | **LTP**

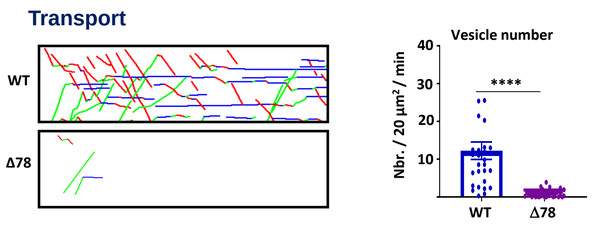
Externalization

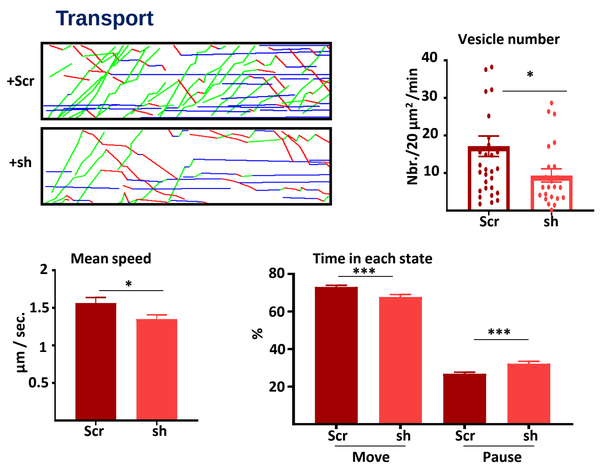


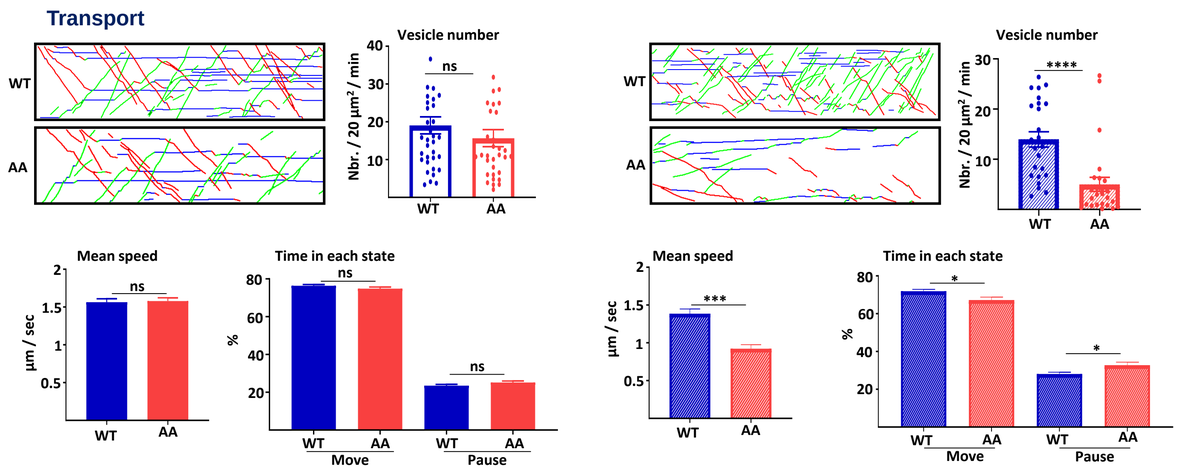




Transport







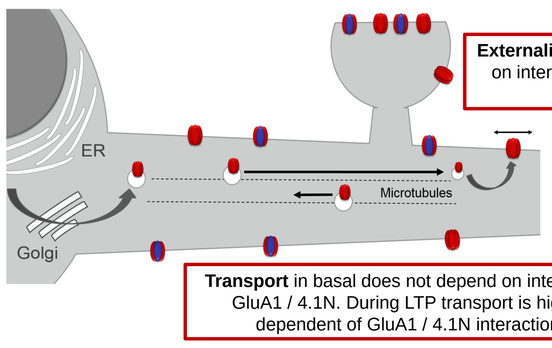
Conclusions

1- Intracellular transport of GluA1 is dependent on its C-term. domain.

2- In basal condition, interaction GluA1 / 4.1N is necessary for the export but NOT for its intracellular transport.

3- During LTP, interaction GluA1 / 4.1N is necessary for the export AND for intracellular transport of GluA1.

Translocation from ER to Golgi to vesicles depends on 4.1N and SAP-97 (data not shown)



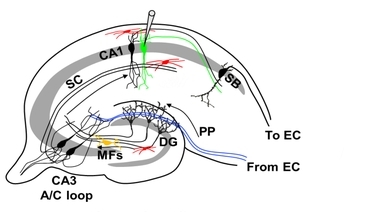
Externalization depends on interaction GluA1 / 4.1N

Transport in basal does not depend on interaction GluA1 / 4.1N. During LTP transport is highly dependent of GluA1 / 4.1N interaction

- **Exocytosis is dependent of the interaction GluA1 / 4,1N both in basal transmission and during LTP.**
- **Intracellular transport depends on interaction GluA1 / 4.1N only during LTP**

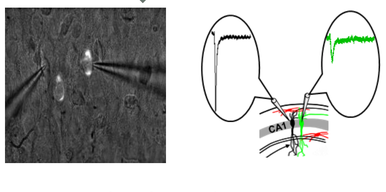
Role of neo-synthetized GluA1 in the induction and maintenance of LTP in hippocampal slices

Method



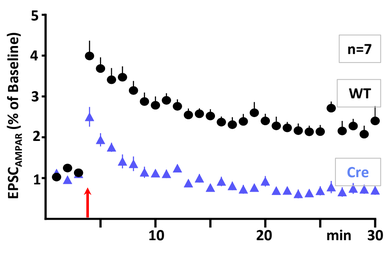
Expression 7 days

Incubation during different time with Ariad ligand

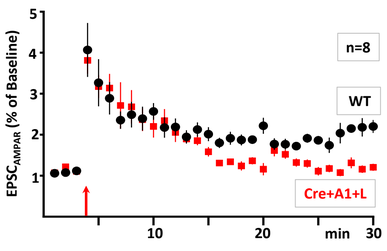


Dual Patch-Recording, LTP

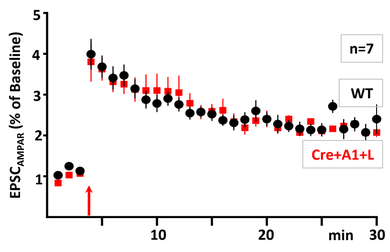
No Ligand



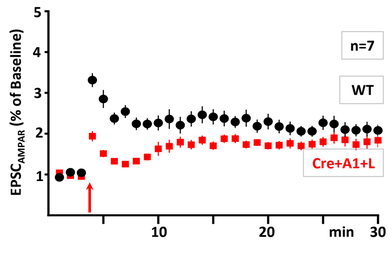
30 min Ligand



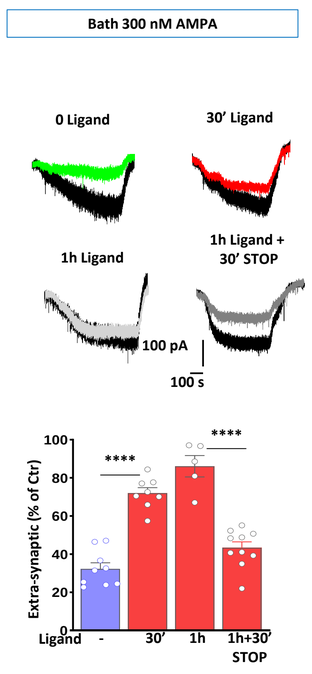
1 hour Ligand



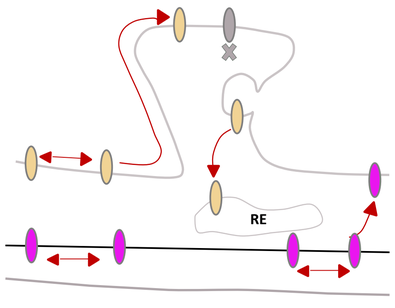
1 hour Ligand then 30 min stop



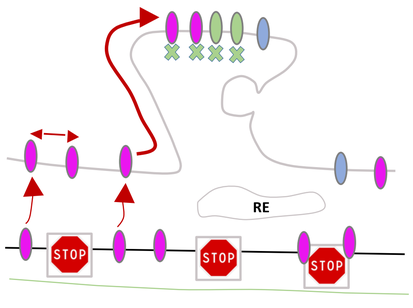
Extrasynaptic receptors



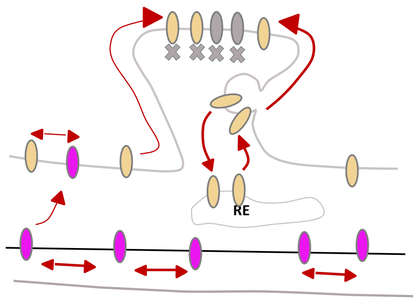
Basal



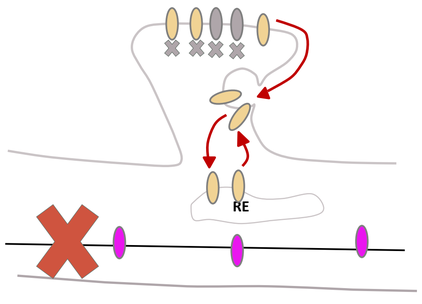
LTP, first phase



LTP, sustained phase



LTP without new AMPAR



- «Old» mobile receptor
- «Old» trap receptor
- Neo-synthetized receptor

RE: recycling endosomes