



TARP γ -8, γ -2, Cornichon, Auxiliary Binding Proteins and AMPA Receptor Trafficking

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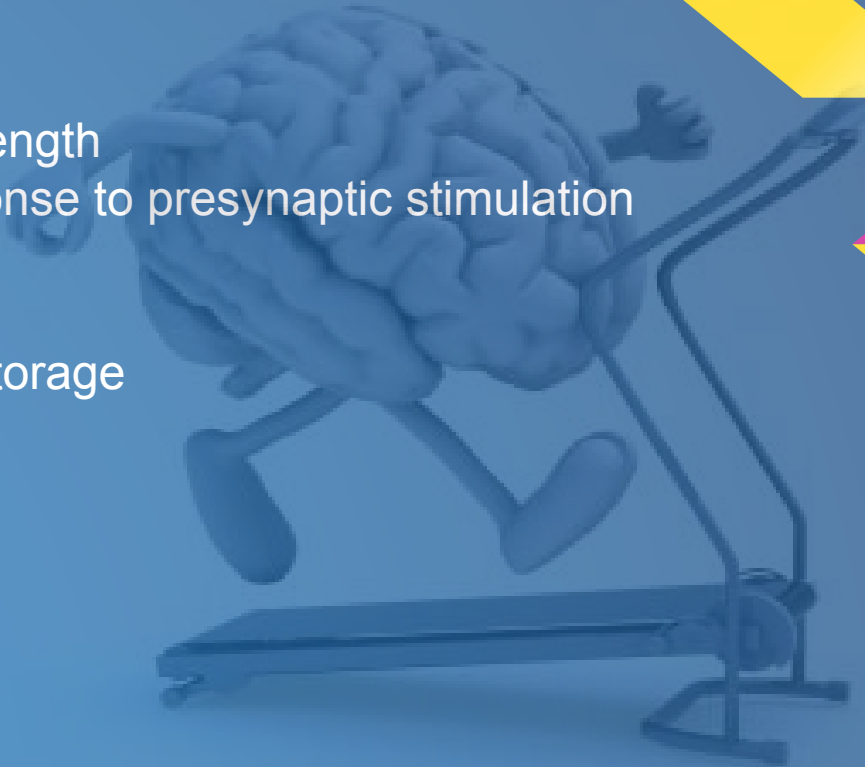
SUH LAB

Seulkee Han

Hyojin Park

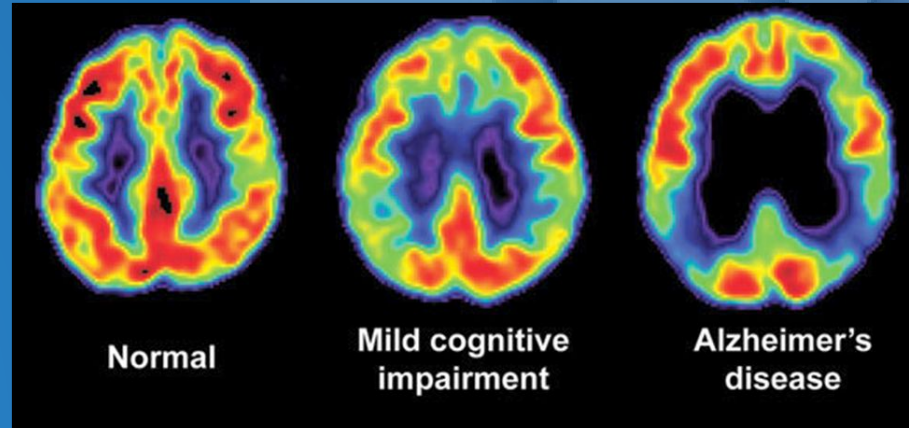
Synaptic Plasticity

- change in pre-/post- synaptic strength
- an increased post-synaptic response to presynaptic stimulation
- Long Term Potentiation (LTP)
- Memory mechanism
- cellular process for information storage
- Clinical Implications
 - Alzheimer's
 - Aging
 - memory loss



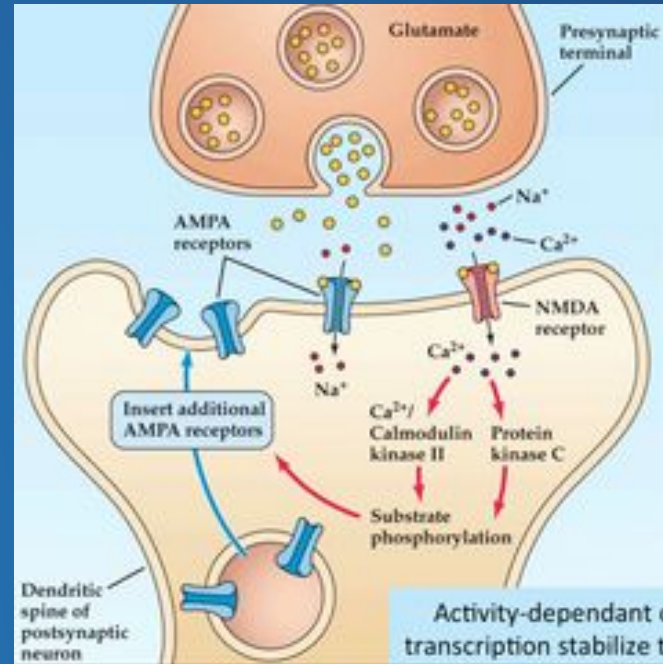
Synaptic Plasticity

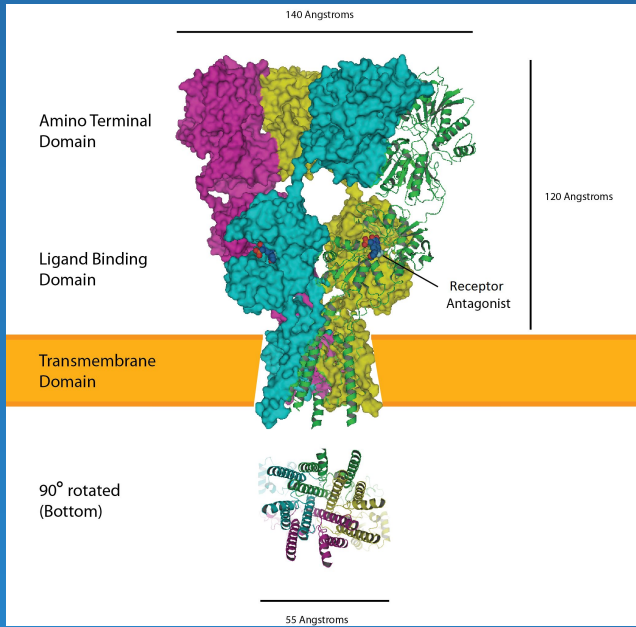
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Ionotropic Glutamate Receptors

- AMPAR
 - GluA1, GluA2, GluA3, GluA4
- NMDAR
 - GluN1, GluN2A, GluN2B, GluN2C, GluN2D, GluN3A, GluN3B





AMPA

- hetero-tetrameric
- critical role LTP LTD
- regulation pathways
- nucleus → ER → Golgi → synaptic membrane → degradation or recycling
- extremely complex synaptic organization

Synaptic Organization

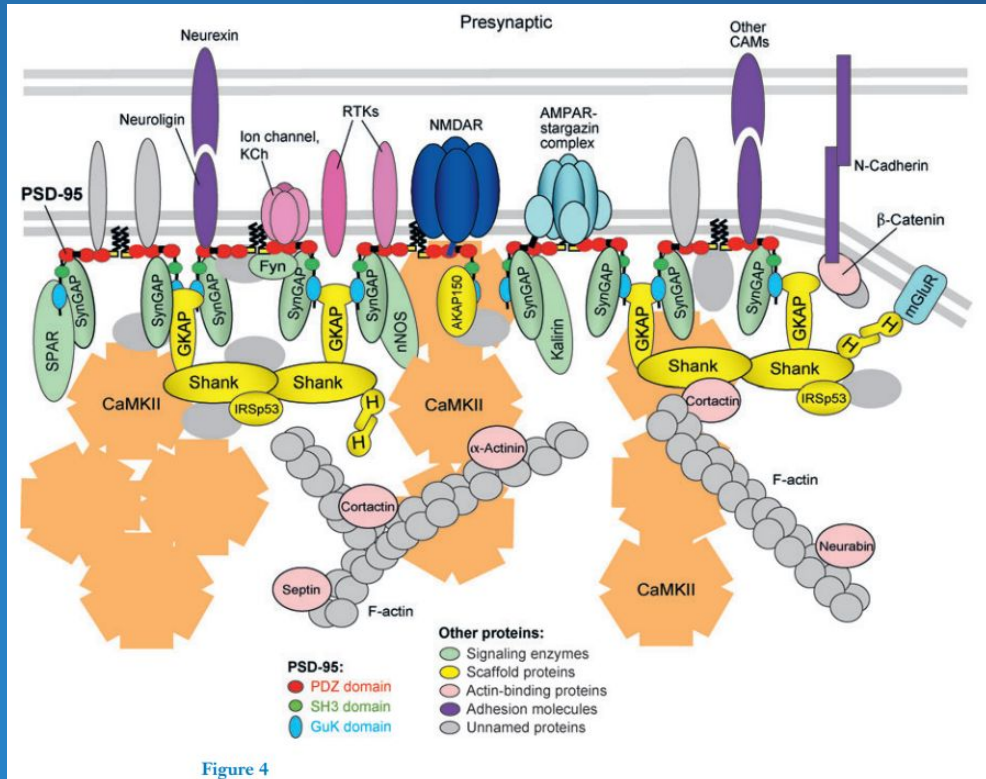


Figure 4

Synaptic Organization

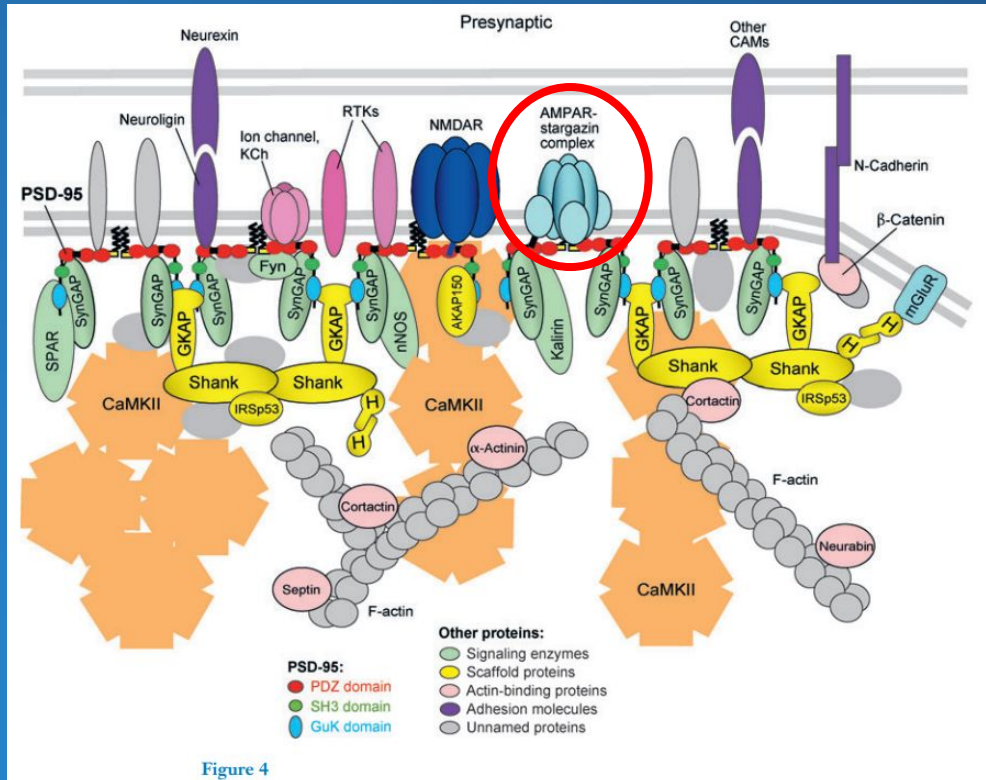
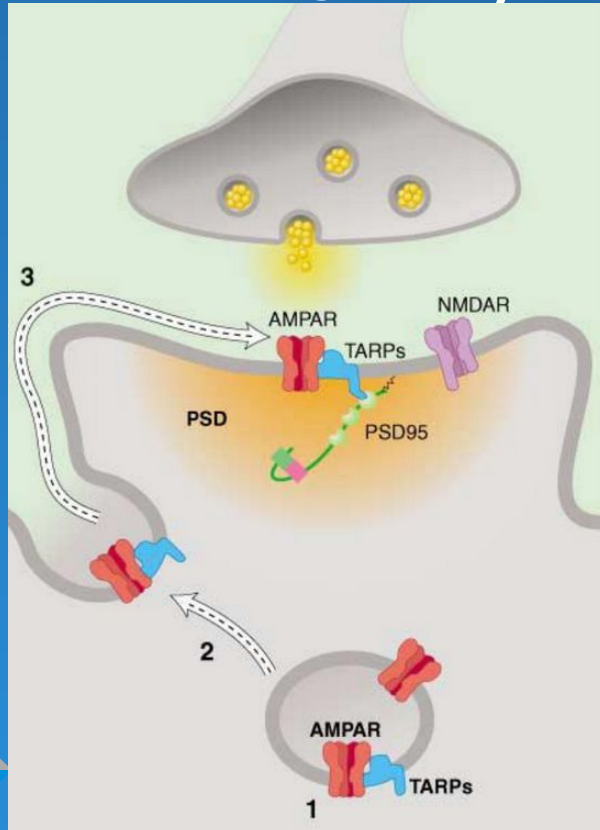


Figure 4

Auxiliary Binding Proteins

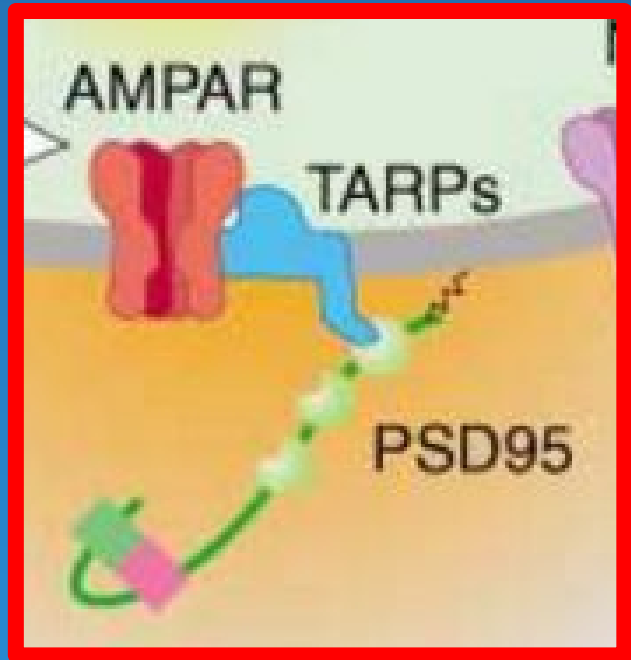
- PSD-MAGUK family scaffolding proteins
 - PSD-95/SAP90, PSD-93/chapsyn-110, SAP102, SAP97
- Stargazer mice (1980)
 - lack synaptic AMPAR currents
- TARP: The Missing Link!
 - Transmembrane **AMPA**R **R**egulatory **P**rotein

TARP family



- Differential distribution
- Type 1 TARP
 - γ -2, γ -3, γ -4, γ -8
- intermediate auxiliary subunit
- Trafficking
- Channel Kinetics

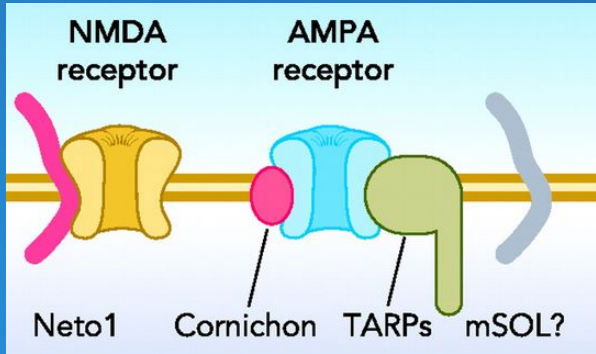
TARP family



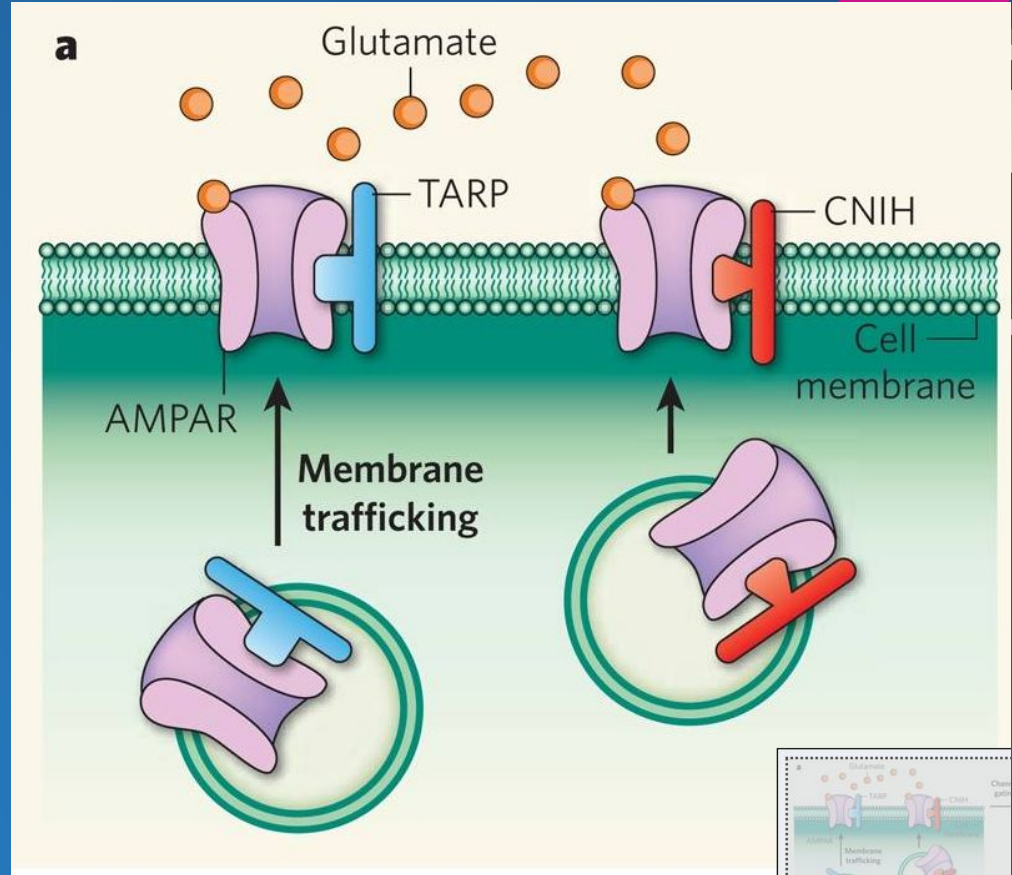
- Differential distribution
- Type 1 TARP
 - γ -2, γ -3, γ -4, γ -8
- intermediate auxiliary subunit
- Trafficking
- Channel Kinetics

CNIH family

- CNIH 1,2,3,4
- AMPAR co-assembly

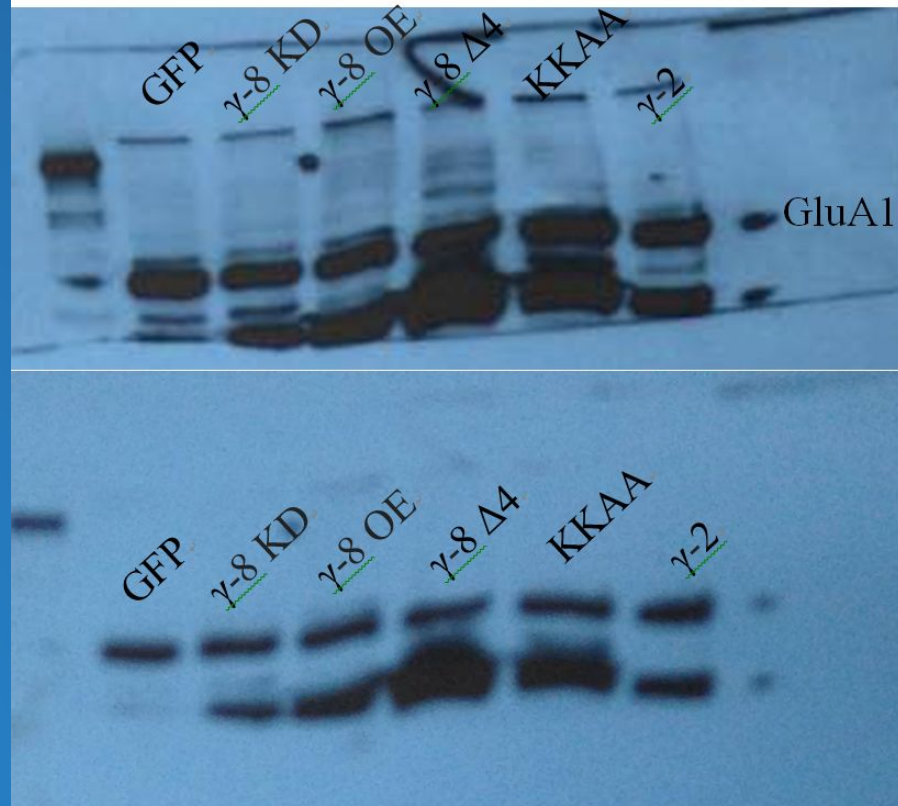


Tomita, American Physiology Society 2010

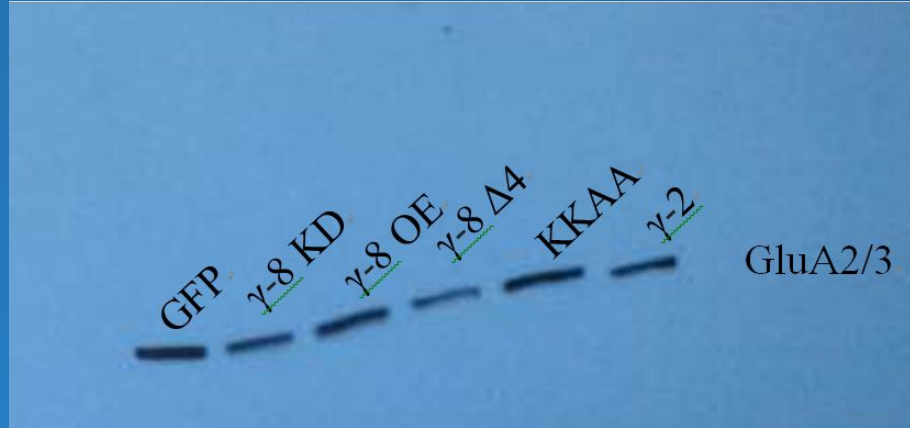


Nicoll RA et al., Science 2006

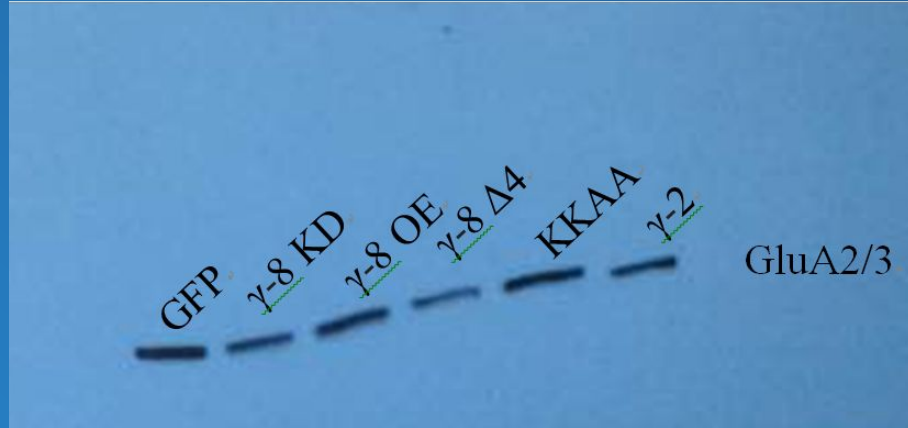
Results



Results

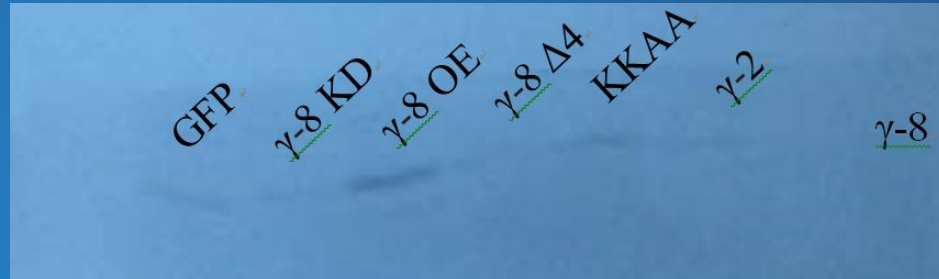


Results

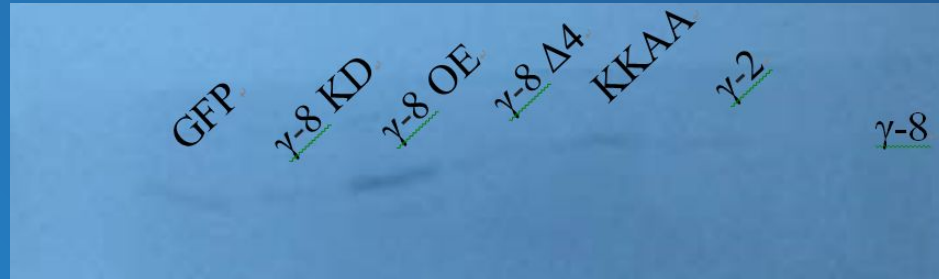


GluA1, GluA2/3 expression was reduced in γ -8 -2 KD

Results γ -8

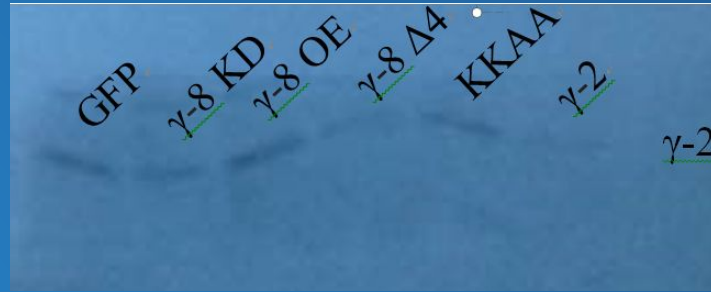


Results γ -8



- decreased γ -8 KD expression
- increased γ -8 OE expression
- decreased γ -2 KD expression

Results γ -2

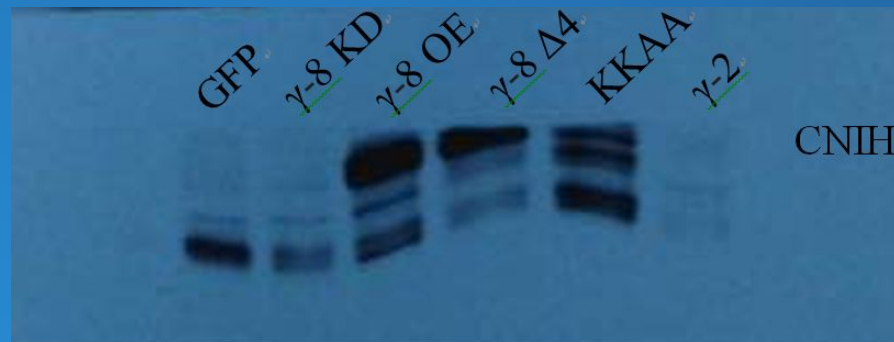
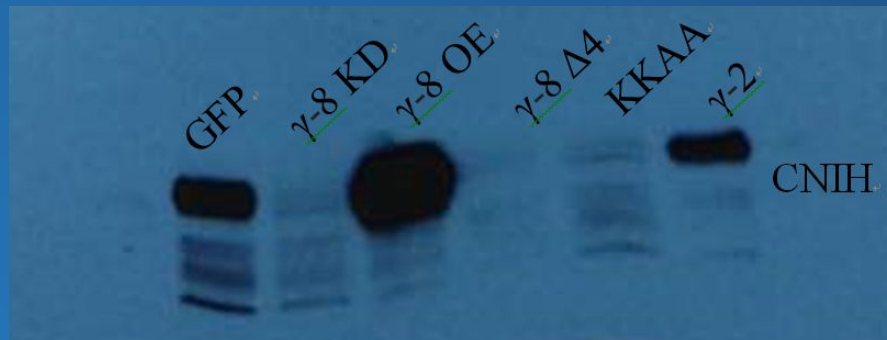


Results γ -2

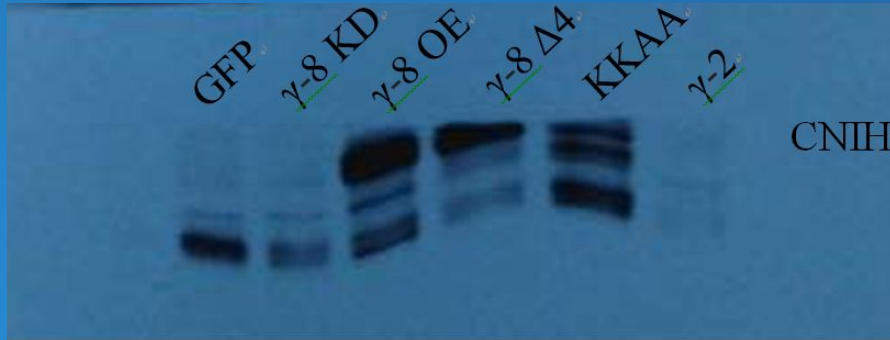
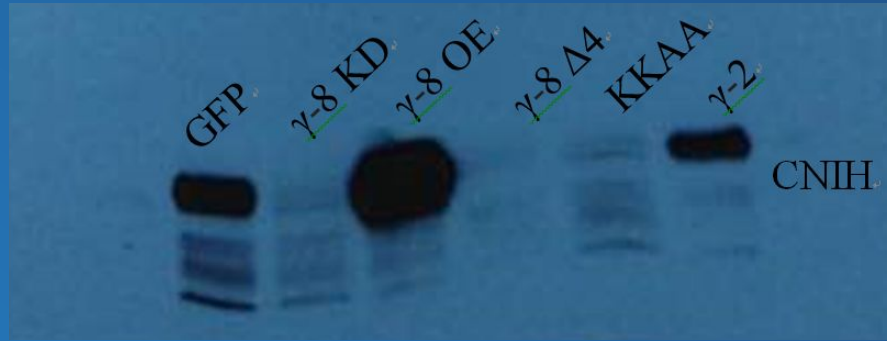


- decreased γ -8 KD expression
- increased γ -8 OE expression
- decreased γ -2 KD expression

Results CNIH-2



Results CNIH-2



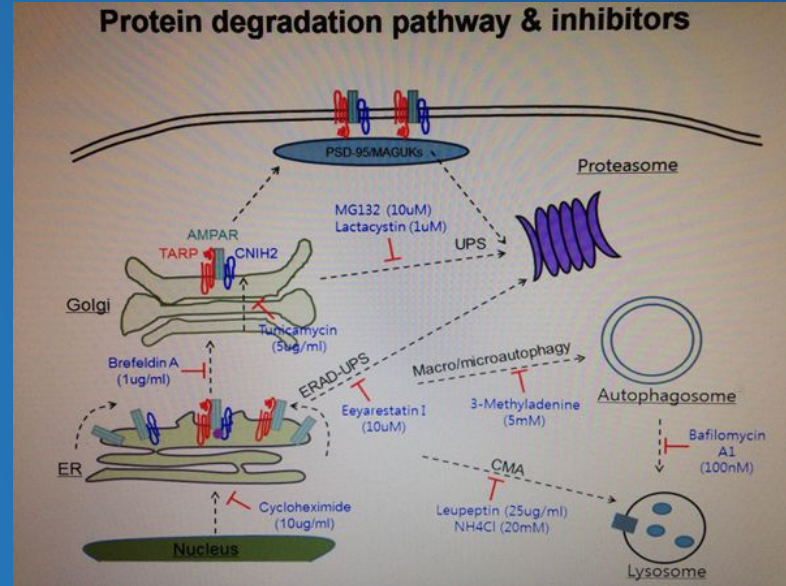
γ -8 -2 KD caused low expression of CNIH-2

Conclusion

This study sheds light on a complicated relationship between TARP, cornichon, GluA1 and GluA2/3 subunits. It is apparent that γ -2 and γ -8 expression are interdependent and vary together. Our data also indicate that TARP γ -8 and γ -2 increase expression of the GluA2 and 3 AMPAR subunits. To further understand the relationship between auxiliary binding proteins and synaptic transmission, we need to explore the mechanisms that regulate the AMPARs expression. An experiment currently in the works is the investigation of expression pathway blockers and their effects on AMPAR expression. This includes an investigation of AMPAR levels in MG132 and leupeptin treated rat hippocampal neuron. By studying these inhibitors we can further understand the nature of AMPAR expression and the various mechanisms underlying its trafficking at the synapse.

Further Investigation

- AMPAR Regulatory pathways
 - inhibitors



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Thank You!



- ★ Professor Suh
- ★ Hyojin & Seulkee
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- ★ Internship Program
- ★ Princeton University
- ★ Roche Lab



QUESTIONS

