LTP requires postsynaptic PDZ-domain interactions with glutamate receptor/auxiliary protein complexes

Nengyin Sheng¹,²,³*, Michael A. Bemben³, Javier Díaz-Alonso³, Wucheng Tao³, Yun Stone Shi³,⁵, and Roger A. Nicoll³,⁴*

¹State Key Laboratory of Genetic Resources and Evolution, Kunming Institute of Zoology
²Center for Excellence in Animal Evolution and Genetics, Chinese Academy of Sciences, Kunming, Yunnan 650223, China
³Department of Cellular and Molecular Pharmacology
⁴Department of Physiology, University of California, San Francisco, CA 94143,
⁵The Model Animal Research Center, Key Laboratory of Model Animal for Disease Study of Ministry of Education, Nanjing University, Nanjing 210061, China

*Address correspondence to:
Roger A. Nicoll, M.D.
Department of Cellular and Molecular Pharmacology, University of California, San Francisco, CA 94143
Email: roger.nicoll@ucsf.edu; Phone: (415) 476-2018

Nengyin Sheng, Ph.D.
State Key Laboratory of Genetic Resources and Evolution, Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, Yunnan 650223, China
Email: shengnengyin@mail.kiz.ac.cn; Phone: 86-871-65198969
Abstract

Long-term potentiation (LTP) is a persistent strengthening of synaptic transmission in the brain and is arguably the most compelling cellular and molecular model for learning and memory. Previous work found that both AMPA receptors and exogenously expressed kainate receptors are equally capable of expressing LTP, despite their limited homology and their association with distinct auxiliary subunits, indicating that LTP is far more promiscuous than previously thought. What might these two subtypes of glutamate receptor have in common? Using a single-cell molecular replacement strategy, we demonstrate that the AMPA receptor auxiliary subunit TARP γ-8, via its PDZ binding motif, is indispensable for both basal synaptic transmission and LTP. Remarkably, kainate receptors and their auxiliary subunits Neto share the same requirement of PDZ binding domains for synaptic trafficking and LTP. Together, these results suggest that a minimal postsynaptic requirement for LTP is the PDZ binding of glutamate receptors/auxiliary subunits to PSD scaffolding proteins.

Key words: long-term potentiation, glutamate receptor, auxiliary protein, PDZ binding domain