生命科学セミナー

ABHD6 negatively regulates the trafficking and function of AMPA receptors

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Regulation of AMPA receptor (AMPAR)-mediated synaptic transmission is a key mechanism for synaptic plasticity. High-resolution proteomics analysis revealed that native AMPARs were macromolecular complex including a number of auxiliary subunits, including TARPs, CNIHs, GSG1L and CKAMP44, which are important for AMPARs forward trafficking to synapses. Our studies shows that ABHD6 negatively regulates AMPAR-mediated synaptic transmission. Overexpression of ABHD6 in neurons drastically reduced, and ABHD6 knockout (KO) enhances, excitatory neurotransmission mediated by AMPARs and surface expression levels of AMPARs. Interestingly, overexpression of ABHD6 reduced glutamate-induced currents and the surface expression of GluA1 in HEK293T cells expressing GluA1 and stargazin, suggesting a direct functional interaction between ABHD6 and GluA1.The C-terminal tail of GluA1 was required for the binding between of ABHD6 and GluA1, suggested by pull down assay. Future analysis showed that overexpression of ABHD6 led to the retention of AMPARs in the endoplasmic reticulum and thus inhibited the surface delivery of AMPARs and AMPAR-mediated responses. Futuremore, overexpression of ABHD6 decreased the tau of desesitization. Finally, ABHD6 KO mice exhibited decreased LTP and incresed LTD. Thus, our findings reveal a novel and unexpected mechanism governing AMPAR trafficking at synapses through ABHD6.

Keywords: AMPA receptor, ABHD6, trafficking, synaptic plasticity

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