Title:	Understanding the role of post-synaptic density proteins in the trafficking of group I mGluRs
Authors:	Pal, Subhajit.
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Abstract:	Glutamate is the major excitatory neurotransmitter in the central nervous system (CNS). There are two types of glutamate receptors; ionotropic glutamate receptors (iGluRs) and metabotropic glutamate receptors (mGluRs). mGluRs are divided into three subclasses depending on their sequence similarity, agonist preference and coupled G-proteins. Group I mGluRs are crucial for neuroprotection, neurodevelopment and various kind of synaptic plasticity including learning and memory formation. Aberrations in the glutamate signalling pathway are basis for various neurological and neurodevelopmental disorders like Fragile X syndrome, ischemia, ALS, multiple sclerosis, diabetes, Huntington's disease and Parkinson's disease (Bear MF, Huber KM, Warren ST, 2004). Exact spatio-temporal localization of these receptors at the cell surface is necessary for the normal signalling and functionality of the receptors. Intracellular trafficking of these receptors play critical role in regulating the spatio-temporal localization of these receptors. Although, the agonist-mediated trafficking of group I mGluRs have been studied in some detail,. role of the post-synaptic density proteins in the trafficking of these receptors, if any, have not been investigated. Group I mGluRs also undergo internalization through agonist-independent mechanisms. Other than agonists, antagonists are another type of ligand of mGluRs. These molecules bind to the receptor and block their normal activity. There have been few reports where people have shown that antagonist also induces internalization of few GPCRs (B. F. Roettger et al, 1997). But no studies have been done till date to check the role of antagonists in the trafficking of group I mGluRs. The antagonists of these receptors have various therapeutic benefits for various pain states, neuropsychiatric disorders like anxiety and depression, drug addiction and drug withdrawal. The aim of this study was to understand the role of antagonists in the trafficking of group I mGluRs and also to investigate the role of various post-synaptic density proteins in the antagonist-mediated trafficking of group I mGluRs. I also studied role of the post-synaptic density protein, Norbin in the agonist-mediated trafficking of mGluR5.
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