Type 1 metabotropic glutamate receptor 1 and GABA B receptor form complexes at cell membrane and mutually modulate their function

Hakushun Sakairi[1], Yuji Kamikubo[2], Toshihide Tabata[3], Takashi Sakurai[1]

[1]Department of Pharmacology, Juntendo University Graduate School of Medicine, Japan, [2]Department of Pharmacology, Juntendo University School of Medicine, Japan, [3]Laboratory for Biological Information Processing, Graduate School of Science and Engineering, University of Toyama, Japan

G-protein coupled receptors (GPCRs) are one of the largest membrane protein families in eukaryotes and mediates various important function of the cells. Recently, there is increasing evidence that several GPCRs may form complexes, and complexed GPCRs may mutually regulate their function. Previous reports including ours unveiled the interaction between two GPCRs expressed in neurons, type 1 metabotropic glutamate receptor (mGluR1) and gamma-aminobutyric acid B receptor ($GABA_BR$). mGluR1 is expressed particularly in cerebellum and known to play crucial roles in synaptic plasticity and motor learning. $GABA_BR$ is widely expressed in central nervous system and regulates neuronal excitability. Our previous study suggested that $GABA_BR$ modulates mGluR1-mediated synaptic plasticity in cerebellar Purkinje cell. In this study, we showed the mechanism underlying modulation between mGluR1 and $GABA_BR$. Biochemical analysis and molecular imaging assay showed that mGluR1 form complexes with $GABA_BR$ at the cell membrane. Moreover, an assay monitored intracellular signaling transduction revealed functional interaction between these GPCRs. Our findings provide a novel insight into the regulatory mechanism of synaptic plasticity and motor learning, and indicate that complex formation and functional interaction between distinct GPCRs might have significant roles under physiological and pathophysiological conditions.