

Oligomerization of GPCR

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Many G protein-coupled receptors (GPCRs) are known to form homo- and hetero-oligomers in the cellular membranes. Because the oligomerization can affect receptor pharmacology, desensitization and trafficking, as well as cellular signaling, it can be a new mechanism to increase the diversity of GPCR functions. Purinergic receptors are classified into two subfamilies, P1 receptors (or adenosine receptors) and P2 receptors (or ATP receptors and further classified into P2Y and P2X receptors) using endogenous metabolites of ATP, *i.e.* adenosine and ADP as ligands to respective receptors. Although physiological interaction between purinergic receptors and other GPCRs are often reported, direct interaction among purinergic receptors has not been well examined. We found that the direct association between G protein-coupled purinergic receptors such as adenosine A₁ receptors and P2Y₁ receptors by immunoprecipitation and BRET technology and it generates pharmacological changes in these purinergic receptors. It was also found that such association between purinergic receptors is not restricted between A₁ and P2Y₁ receptors but also observed between A₁ and P2Y₂ receptors and other combination of purinergic receptors such as A₁/A_{2A}, A_{2A}/P2Y₁ and A_{2A}/P2Y₁₂, and also with other class of GPCRs such as A_{2A}/D₂. These results suggest the novel oligomeric nature of purinergic receptors providing a good experimental system for GPCR oligomerization.