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Overview of recent GPCR research

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G protein-coupled receptors (GPCRs) receive a wide range of extracellular stimuli, and transduce their information into the cells. As the first step, GPCR bind agonist. Then, GPCRs change their conformation to transduce information of agonists through transmembrane. However, GPCRs do not directly activate intracellular signaling molecules. GPCR-mediated signaling always requires G proteins to generate second messengers. GPCR research starts from analysis of the tissue responses by agonist stimulation. Then, GPCRs are labeled and quantified by radioactive ligands. It revealed heterogeneity of GPCRs that we have imaged before. Nucleotide sequences of GPCRs are subsequently determined and function of GPCRs are analyzed by gene mutation, overexpression and knockout. Application of imaging techniques to GPCR research reveals interaction with accessary proteins, dimerization, and so on. Structures of GPCRs are finally determined by X-ray analysis. Although crystallization of GPCR has resolved many important issues of GPCRs, there are many unresolved issues such as structural basis of G protein selectivity and drug design based on structural information. I will overview history and progress of GPCR research.