FUNCTIONAL OLIGOMERS OF RHODOPSIN - A G PROTEIN-COUPLED RECEPTOR TEMPLATE

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Recent biochemical and biophysical studies have challenged traditional view of GPCR as monomeric protein, and indicated that many of these receptors exist as homo- and hetero-dimers. Furthermore, their higher oligomeric assemblies may also have specific functional roles [reviews 1-3]. Cooperative interactions within such an oligomeric array may be critical for the propagation of an external signal across the cell membrane and to the G protein, and may therefore underlie the basis of signaling. Several studies have shown that dimerization occurs early after biosynthesis. It may help in receptor maturation. Other processes such as G-protein binding, downstream signaling and internalization have also been shown to be influenced by the dimeric/oligomeric nature of these receptors.

In addition to revealing key mechanisms of GPCR action, the concept of dimerization could be important in the development and screening of drugs that target GPCRs. The changes in ligand-binding, cross-talking and signaling properties that accompany oligomerization could potentially lead to new pharmacological classes of drugs.

Rhodopsin is still the only GPCR with three-dimensional structure known. To investigate mechanisms of activation, passing the signal and deactivation of rhodopsin, complexes of activated rhodopsin with its G-protein (transducin), rhodopsin kinase and arrestin were built. All complexes were generated based on oligomeric state of rhodopsin [4, 5]. Modeling revealed that both G-protein and arrestin bind to rhodopsin dimer, a basic unit of rhodopsin in paracrystal. In case of transducin adjacent dimer gives an additional surface to stabilize the complex. After unbinding of transducin beta-gamma subunit, remaining alpha part can bind to the second molecule of transducin and facilitate docking to rhodopsin [6]. The similar positive cooperativity effect was observed in arrestin-rhodopsin complex.

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