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Designing an inhibitor for a novel target site identified in beta arrestins for initiating apoptosis.

Abstract

Beta arrestins are cytoplasmic proteins that bind specifically to active (phosphorylated) G- protein coupled receptors (GPCRs) and arrest or reduce signaling by these receptors. Consequently, it plays a crucial role in cell signaling and various physiological responses. Beta arrestins suppress the GPCR mediated apoptosis. The availability of crystal structure of Beta arrestin-2 with IP6 has offered a great opportunity for homology modeling of Beta arrestins and rationale design of specific Beta arrestins inhibitors. Thus selective Beta arrestins inhibition could be potential therapeutic target for the treatment of cancer and autoimmune diseases. This study is aimed to generate 3-D structures of Beta arrestins and find out the potent and specific Beta arrestins inhibitor by different approaches including homology modeling, molecular docking, virtual screening of ligand databases (drug like) and de novo drug designing. New classes of putative ligands i.e. N- (cyclohexylmethyl) cyclohexanecarbohydrazide were found. After further optimization process these probable drug like molecules can generate a potent inhibitor for the Beta arrestins leading to activation of apoptosis through mitochondrial route.