Development of Novel Beta-Adrenergic Receptor Allosteric Modulators

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Technology description

Researchers at UC San Diego have developed a small molecule allosteric modulator that is selective for βARs (AS408). The mode of action for this modulator is to act in a positively cooperative manner with inverse agonists, compounds which stabilize the inactive conformation of the receptor. Thus, the positive allosteric modulatory (PAM) effect on inverse agonist and antagonists has significant clinical potential since beta adrenergic antagonists are used in the clinic to treat cardiovascular diseases.
The G protein-coupled receptors (GPCRs) are a very important family of cell surface receptors that respond to extracellular signals which then transduce those signals into intracellular responses. They are also the largest family of targets of currently available therapeutics. Adrenergic receptors belong to the GPCR superfamily and their natural ligands are the catecholamines, epinephrine and norepinephrine. Adrenergic receptors can be further divided into two receptor subfamilies, α and β that exhibit differences in tissue distribution, ligand specificity and cellular output. The β adrenergic receptors (βARs) are important mediators in diseases like asthma, Parkinson’ s disease, hypertension and heart failure. Therefore, there is a direct need for new modulators for the βARs receptors.

Application area

The current compound would be a potential therapeutic for use as an allosteric modulator which is highly selective the βAR family of adrenergic receptors.

Advantages

This is a novel compound in its class and which is superior to regular antagonist treatment for cardiovascular diseases because it isselective for beta-adrenergic receptors. These new compound(s) will work in conjunction with current beta-adrenergic receptor antagonists and make them more beta-adrenergic receptor-selective.

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