INTELLIGENT PHARMA

Designing your drugs for a decade!

DEVELOPING SOLUTIONS. DISCOVERING DRUGS.

GPCR conformations: Eurostars project

GPCRs (seven-transmembrane domain receptors), of high interest for the pharmaceutical industry, remain very challenging targets. GPCR have multiple conformations, which in turn promote opposite effects on diverse intracellular signaling pathways. Candidate drugs should activate or inhibit certain signaling pathways with high efficacy without unleashing undersired side effects.

eurostars™

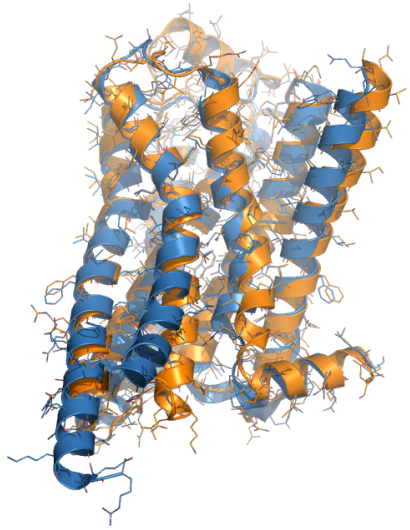

Figure 1: Comparison of β2-adrenergic receptor in its active (blue) and inactive (orange) conformation. As other proteins in the GPCR class A, main differences are observed in TM3, TM6 and TM7.

The aim of the Eurostars project ***Pathway Disco*** is to find conformation-stabilized GPCRs for pathway specific drug discovery. It is known that a chemical compound that binds to a GPCR is able to trigger multiple responses in the downstream cascade of the signaling process, activating (agonist) or inhibiting (antagonist) different processes. These responses are also regulated by protein-protein interactions (PPI) between the GPCR and the G-protein or the arrestin protein. The use of synergistic physical and computational methods will permit to define and lock-in GPCR conformational states for further studies. Intelligent Pharma is the partner responsible for performing the computational studies in this three party consortium (www.eurostars-eureka.eu/project/id/10575).

Intelligent Pharma's milestones in the ***Pathway Disco*** project are:

- Construction of a database of different conformational states of GPCRs, taking into account the active and inactive states
- Development of phamacophore models for all conformations
- Analysis of pharmacophore models in combination with docking studies using Mobius technology (a multi-parametric software based on genetic algorithms)
- Construction of a platform enabling the generation of GPCR models for related GPCRs
- Screening of new compounds for GPCRs without known ligands

Visit us!

www.intelligentpharma.com