P-1.116

Investigating Gpcr Structure and Dynamics Upon Activation with an Integrating Approach Based on Nmr and Md Simulations.

Fouillen Aurélien [1], Gaibelet Gérald [1], Orcel Hélène [1], Bous Julien [1], Riché Stéphanie [2], Bonnet Dominique [2], Sounier Rémy [1], Granier Sébastien [1], Cong Xiaojing [1], Mouillac Bernard [1], Déméné Hélène [3]

[1] IGF, INSERM, CNRS, Unit Montpellier, France, France

[2] LIT, CNRS-Univ Strasbourg, Strasbourg, France

[3] CBS, CNRS, INSERM, Univ Montpellier, Montpellier, France

The G protein-coupled receptor (GPCR) are membrane proteins which control most of physiological cell responses. The mu-receptor to opioids (MOR) is a key receptor in the management of pain. The vasopressin receptor type 2 type (V2R) governs water reabsorption in renal cells. We have developed specific approaches to understand the relationship between their inherent dynamics and structure and their response to different types of ligands, in particular those that control the selective activation of their cognate G-protein versus the arrestin proteins. Using NMR, we have identified key structural elements of MOR preactive state prior recruiting its intracellular partners [1]. Combining NMR and molecular dynamics simulation allowed us to identify the structural mechanism affecting key transmembrane components involved in the specific recruitment of intracellular partners for MOR and V2R [2, 4]. We have developed a protocol based on specific NMR restraints, ranging from STD to paramagnetic ones, to decipher the pose of its ligands [3,4].

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