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Delta opioid receptor structure and ligand docking analysis

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Delta opioid receptors (DORs) have been considered as a potential target to relieve pain without μ opioid-like side effects as well as treat depression, brain disorders and are known to modulate other physiological responses. Therefore, the DOR is a promising drug target, and study of its structure and activation mechanisms has a great therapeutic significance.

Objectives

In an effort to better understand the structural basis for DOR pharmacology and function we used method of computer molecular modeling. Taking into account the fact that the crystal structure of DOR is chimeric, without N- and C- terminal tails, and III intracellular loop [3], we decided to construct full structure including the missing parts of the molecule, and to verify the structure we make a docking with different ligands.

Methods

For the DOR tertiary structure molecular modeling has been used Rosetta 3.3 software package [6] and for visualization and data analysis - the program VMD 1.9 [5]. Ligand docking was performed using the program swissdock [4]. The binding pocket volume and specific amino acid residues involved in ligand receptor interaction was analyzed using CASTp [7].

Results

Receptor structures were compared with a structure obtained by X-ray analysis, identifying RMSD each of them. Structures alignment shows that the RMSD of the best obtained model is 2.0 Å, which is quite good result for such experiments [1]. CASTp data shows that the localization of the binding pocket and the specific amino acid residues included in the pocket corresponds to the existing data of real experiments [2].

Conclusions

Thus, identifying the tertiary structure of DOR, ligand binding pocket, specific amino acid residues involved in the ligand-receptor interaction may provide a starting point for study of the interaction of different agonists and antagonists with DOR, and for the creation of novel medications.

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