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Study of V2 vasopressin receptor hormone binding site using in silico methods

S. Sardari[1], Y. Sebti[2,*], H. Mir Mohammad Sadeghi[2]

[1]Medical Biotechnology Department, Pasteur Institute of Iran, Tehran, Iran
[2]Department of Pharmaceutical Biotechnology and Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Background and Aims: The docking study of ligand arginine vasopressin (AVP) to its receptor V2 Vasopressin Receptor (V2R) helps in identifying important amino acid residues that might be involved in AVP binding for predicting the lowest free energy state of the protein complex. Whereas the previous researchers weren't able to detect the exact site of the ligand –receptor binding, we have decided to do that by using bioinformatic methods.

Methods: With in silico studies on ligand and receptor, we determined the optimize conditions for ligand_receptor binding using receptor binding domain. The tertiary structure would be determined using 3D structure of the ligand, available from the Protein Data Bank. No suitable template resembling V2 Receptor was found. Therefore, an ab initio approach was chosen to model the protein receptor. Using protein docking methods for example Hex protein-protein docking software 5.1 and its server, the model of V2R was docked to the peptide ligand AVP to identify possible binding sites then predicting the lowest free energy state of the protein complex followed by mutated receptor. The amount of gained energies permits us to compare the mutant forms. Assessment of the critical positive and critical negative mutations then will be followed by ranking.

Results: Based on the mutation/docking predictions, we determined some mutants, such as W293D and A300E possess positively inducing effect in ligand binding and some of them such as A300R possess negatively inducing effect in ligand binding.

Conclusions: Regarding to the above information, we hopefully can make our significant steps regarding to the synthesis of effective therapeutic compounds.

Keywords: V2 vasopressin receptor; Binding site; Energy minimization