

MOLECULAR DOCKING OF ADENOSINE A2A RECEPTOR LIGANDS

Volyntseva A.D., Novoseletsky V.N., Shaitan K.V.

Lomonosov Moscow State University, Faculty of Biology, Department of Bioengineering,
1/12, Leninskiye Gory, Moscow, Russia, 119899 Tel./Fax: (495) 939-57-38 E-mail:
alenskavolynceva@gmail.com

Adenosine A2A receptors, belonging to the family of G-protein coupled receptors (GPCRs), are of particular interest as a drug target for the treatment of Parkinson's disease and Alzheimer's disease, glaucoma, inflammatory diseases. For rational drug design is extremely important to have information about the spatial pattern of the complex of drug prototypes with the target protein. For example, knowledge of the structure of the complex can be used to estimate the binding constant of the potential drugs.

The list of 20 selective adenosine A2A receptor ligands was extracted from scientific literature. The ligands have known binding constants uniformly distributed in the range of 0.3 to 5000 nM. The structure of the receptor was taken from the database PDB (pdb-code 3EML). The structures of ligands were created using molecular editor Maestro. Molecular docking of selected ligands to the binding site of the receptor was performed using DOCK6. Post-docking geometry optimization was performed to improve the precision of the ligand poses. Distance restraints were used between receptor and ligand atoms forming hydrogen bonds. The binding energy calculation was carried out using thermodynamic integration in the force fields gromos53a6 and charmm27. We showed that the value of the binding energy and the corresponding values of the dissociation constants are differ from published data, and the use of force field charmm27 gives more reliable results.

The calculations were performed using the supercomputer complex MSU.

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