VIRTUAL SCREENING OF HIV PROTEASE AGAINST THE NCI DIVERSITY SET

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Introduction: Virtual screening means use of high-performance computing to analyze large databases of compounds to identify possible drug candidates. When three dimensional structure of the target is known, virtual screening using molecular docking can be used to discover new lead compounds. In this project as model we used x-ray structure of HIV protease as target and part of NCI Diversity set which includes 1990 compounds as our chemical compounds database.

Material and Methods: After downloading NCI diversity set in SDF format, Babel program was used to extract part of NCI Diversity set including 100 compounds for our experiment. After wring different scripts, AutoDock 3 in conjunction with MGLTools (v. 1.4) was used to screen Diversity Set, against HIV protease X-ray structure. Autodock parameters used were 5 million evals per run, 100 runs per compound. The resulting DLG files were analyzed automatically by means of written scripts to extract the best docking energies and binding energies for each ligand. Indinavir which is a known HIV protease inhibitor was used as a positive control. The calculation took 10 days to run on Pentium 2.00GHz processor running Linux.

Results: Docking energy for positive control was -11.18Kcal/mol. We found eleven compounds with lower docking energies than control (-12.91 to -11.18Kcal/mol). These compounds were analyzed by MGLTools to visualize their binding at pocket of the enzyme to ensure they occupy active site.

Conclusion: The eleven hit compounds can be obtained from NCI and may be tested as anti-HIV. They may also be used as lead compounds for further development.

Keywords: Virtual screening, AutoDock, protease