

Structure based virtual screening on DrugBank database to find ligands interfering arginine transportation through the cationic amino acid transporter

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ABSTRACT

The cationic amino acid transporter 1 (CAT-1) is a membrane protein that mediated arginine uptake into the cells in mammals; it has been shown that arginine is an essential amino acid for the proliferation of various types of cancerous cells such as acute lymphoblastic leukemia (ALL). Hence, deprivation the cancerous cells from arginine by blocking the CAT-1 can be considered as an appropriate approach to suppress the uncontrolled proliferating cells. In this study, we used an innovative computational approach to find chemical ligands targeting the arginine transporter. Firstly, the three-dimensional (3D) structure of the CAT-1 was generated using homology modeling by MODELLER software based on its prokaryotic homologue (GkApcT) structure (PDB ID: 6F34). Subsequently, a library containing 13125 chemical candidates was downloaded from the DrugBank database. The ADMET properties were applied to the library using FAF-DRUG4 webserver. The chemical compounds that did not acquire the physicochemical criteria were filtered out from the library. Afterwards, the passed compounds were docked on the predicted pockets of the CAT-1 using AutoDock VINA. Finally, hit compounds docking firmly within the pocket of the transporter with reasonable binding energies, were selected. The introduced ligands in this study are the promising novel hit molecules, blocking the cationic amino acid transporter. However, more experiments need to be performed for recognition of the discovered ligands as lead compounds.

Keywords: cationic amino acid transporter; DrugBank; virtual screening; arginine