Molecular docking of small molecules that inhibit vimentin-plectin interaction

P-06.5-31

A. Vakhrusheva[I], A. Kudriavtsev[I], O. Sokolova[I]

[I]Lomonosov Moscow State University, Moscow, Russia

Vimentin forms a major type of cytoskeleton intermediate filaments that participate in many cell processes including cell migration. Particularly, it was shown that vimentin determines migration directionality both in filament form and in the form of ULF (unit-length filament), possibly due to its interaction with adaptor protein - plectin. Therefore, potentially, vimentin-plectin interaction is a new target for searching and testing small molecules inhibiting this interaction in order to lower the migration capacity of the cells.

According to literature, the interaction sites of vimentin and plectin were both identified: the fifth plakin repeat domain (PRD) and a plectin linker from the plectin side and a 1B segment (PDB ID 3UF1) from the vimentin side. Here, the homology model of the fifth PRD and the linker of plectin were constructed based on structures PDB ID 5DZZ and PDB ID 4Q28. The protein-protein docking was performed and the amino acids that participate in the interaction of vimentin and plectin were identified. Based on the determined binding site, a library of small molecules (around 1 million compounds) was docked to vimentin and the substances were ranked according to the docking score and MM-GBSA parameters. Additionally, the docking scoring function was calculated for evaluation and verification of substances. Finally, two molecules, Amikacin and Paromomycin, were chosen for further *in vitro* experiments to verify their influence on cell stiffness and cell migration.

The research was carried out using the equipment of the shared research facilities of HPC computing resources at Lomonosov Moscow State University. The reported study was funded by RFBR, project number 19-34-90178.