VIRTUAL SCREENING OF LIBRARIES KNOWN INHIBITOR MDM2

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The purpose of research. One of the up-to-date drug targets- protein MDM2 (HDM2), is involved in the process of apoptosis. The inhibition of this protein leads to rapid apoptosis and can be used for the treatment of some cancers. However, the found experimental data [1] shows that lead inhibitors of protein MDM2 (HDM2) series of Nutlin also interact with anti-apoptotic protein Bcl-xl. We suppose that other, currently known inhibitors, that cause cell apoptosis and have a very low affinity according to the computer simulation to MDM2, can have a high affinity for Bcl-xl; interaction with this protein causes the induction of apoptotic processes. According to modern standards, the molecular target of the drug should be rigorously defined, that's why it is important to define accurately the target-specificity of other suggested MDM2-active molecules.

Research methods. Using the software package CCDC GOLD, MolTech LeadFinder and MolSoft ICM-pro database of known compounds virtual screening using MDM2 (PDB ID 1Z1M) and Bcl-xl (PDB ID 2O2N) targets was performed. The database was formed from the literature sources about the inhibition of the MDM2 activity.

Conclusions. During the screening of a database of known MDM2 small molecule inhibitors were identified compounds that have high affinity for the protein Bcl-xl. The results indicate that the target of these inhibitors is not so much MDM2, but rather - Bcl-xl, and the suppression of its activity is triggered apoptosis in cells, which refers to a different mechanism of action of the active molecules.

This work was done with support of the grant of the Government of the Russian Federation for state support of scientific research under the guidance of leading scientists at Russian institutions of higher education № 11.G34.31.0069.

References

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