IN SILICO STUDY OF NLRP3 INHIBITORS AND MODULATORS

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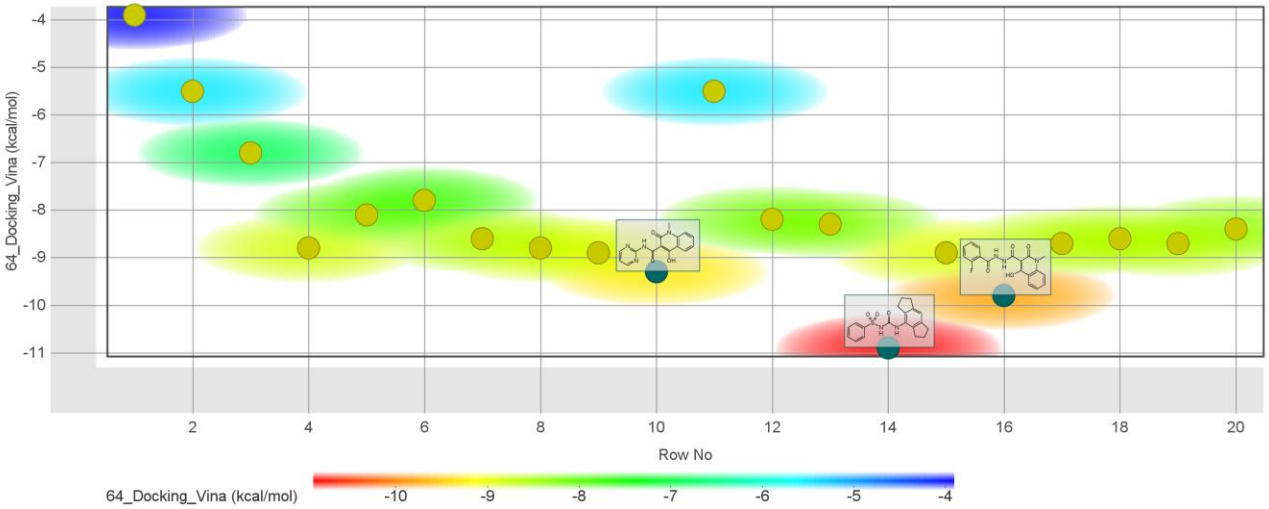
Introduction. The term "inflammaging" was introduced in 2000 by Italian scientist Claudio Franceschi, who along with his colleagues investigated the link between aging and chronic inflammation. NLRP3 inflammasome (or NOD-like receptor with pyrin domain 3 inflammasome) is a complex of proteins that plays an important role in the regulation of the body's immune and inflammatory responses. There are numerous studies that show a link between NLRP3 inflammasome activation and aging.

Aim. Analysis of ChemBL database of existing compounds affecting NACHT, LRR and PYD domains containing protein 3. Performing SAR analysis based on the results.

Materials and methods. To obtain and visualize the data, we used a package of chemoinformatic programs running under the Linux operating system - DataWarrior, QVina2.0, Obabel, RDKit, PyMol. The NACHT, LRR and PYD domains containing protein 3 (PDB: 7ALV) were chosen as the target. The structures of the tested compounds were obtained from the ChemBL 32.

Results and discussion Currently, there are 20 inhibitors NLRRP3in the ChemBl 32 database, which belong to different classes of compounds. We performed two types of docking, this so-called "blind docking" and targeted docking at the binding sites of the known inhibitors of the 7ALV protein.



Pic.1. 2D visualization of compound distribution based on docking results

Conclusions. The research and development of NLRP3 inhibitors presents great potential for the development of new therapeutic approaches in the treatment of various inflammatory and immune diseases. However, the mechanisms of NLRP3 activation and regulation of the inflammasome are not fully understood, and further research is needed to better understand and develop effective and safe inhibitors