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Analysis of binding properties of influenza hemagglutinins and human receptor analog

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Motivation and Aim: The surface protein of the influenza virus, hemagglutinin, plays a key role in the virus entry into the cell. When infecting a cell, the virus first binds to a receptor on the cell membrane surface, followed by the capture of the virus inside the cell. The influenza virus infectivity is defined by the duration of binding persistence, which is related to energy characteristics of the bonds.

The new group of A(H3N2) influenza virus serotype, the Bangladesh group, has spread in recent years in Russia, replacing other groups of this serotype. The aim of this work was to compare the binding properties of Bangladesh group representatives with the international reference strain of A(H3N2) subtype in the complex with the human receptor analog 6'-sialyl-N-acetyllactosamine.

Methods and Algorithms: The initial structures of hemagglutinins under study were modelled with MODELLER with the template of the known structure H3N2 from the Protein Data Bank (sequence identity 95 %, code PDB 6bkt). The molecular dynamics simulations were performed using NAMD during 4 nanoseconds to determine more precisely the orientation of the model side chains and receptor position. The structures of the time interval from 3 to 4 nanoseconds with the time step of 1 picosecond were sampled for the subsequent docking analysis using the AutoDock Vina program.

Results: During the molecular dynamics simulations, the receptor analog was in the correct stable binding conformation. However, the root-mean-square deviation of heavy atoms was greater for the international reference strain. Docking analysis allowed a numerical estimation of the free energy of protein binding to the receptor analog. A histogram was built for the data obtained (Fig. 1).

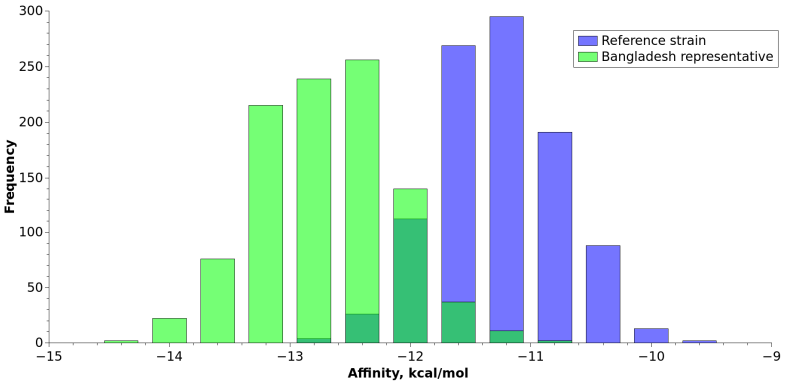

Fig. 1. Distributions of AutoDock Vina energy for the strains studied

For a protein and the receptor analog prepared as rigid structures, the free energy estimate is 11.27 kcal/mol for the reference system and 12.7 kcal/mol for the Bangladesh group representative, with the standard deviation being 0.5 and 0.56 kcal/mol respectively.

Conclusion: The results demonstrate Bangladesh group influenza virus to have a higher affinity for the human receptor analog. The T-statistic being equal to 60 confirms the statistical validity of the results, suggesting the possibility of higher virulence of Bangladesh group viruses compared to other groups. The energy assessment and structural reasons for the higher affinity are likely to be important for the development of drugs against this group of the influenza virus.