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Comparative molecular modeling study between the pre-fusion and post-fusion conformations of Newcastle disease virus: Homology modeling, and virtual screening

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Paramyxoviridae family is a large family that has many important viruses. The viruses of this family are the main cause of different human diseases such as respiratory tract infections, pneumonia. New castle disease virus causes a severe disease occurs in both domestic, wild animals and may affect human as well. New castle disease virus is a typical paramyxo virus with an enveloped single stranded, negative sense RNA genome. The RNA genome has six genes; nucleocapsid protein, phosphoprotein, matrix protein, polymerase protein, hemagglutinin-neuraminidase protein, and fusion protein. After the binding of virus to the host cell by hemagglutinin-neuraminidase protein, the fusion protein will be involved in a membrane fusion process. This will be followed by an irreversible conformational change from a metastable fusion conformation to a post stable, low energy conformation. This process is very important for the viral virulence. To date there is neither vaccination nor selective antiviral drug for this virus. The design of an inhibitor that can bind to this fusion protein and prevent the conformational change will inhibit the virus. This work aims to design such inhibitor starting by a comparative molecular modeling analysis of the pre and post fusion conformations. Homology modeling study was done to build the pre-fusion conformation. Molecular dynamic simulations were performed to compare between the most stable conformers. Structure-based virtual screening was performed to screen large number of compounds against the built model. Finally, the top-scored hits were selected for biological testing. All the molecular modeling studies were done by MOE 2013.08.

Biography

Mohammed A Khedr is the coordinator of drug design at College of Pharmacy, King Faisal University. He did his PhD in "Computer-aided drug design and synthesis of novel antivirals" in Cardiff University, UK. He was trained in Oxford University, UK on the recent advances in drug design. He discovered novel inhibitors of West Nile Virus by de novo approach and was an oral speaker in "The 2nd International Ligand-based and Fragment-based drug design international conference, Oxford, UK, 2013". He is the PI of two research projects funded by King Faisal University. He has supervised a number of master, PhD, and student projects at different universities.

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