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Homology-based modeling of the C-terminal inner region of pandemic H1N1 Influenza virus hemagglutinin

Content

Influenza virus hemagglutinin cytoplasmic (intraviral) domain plays crucial role in membrane fusion promotion during virus entry and participates in progeny virions assembly. The structure of this C-terminal region located inside the virion under the viral membrane has not been determined by crystallographic methods yet. The ab-initio PepFOLD 3.5 method of 3D-modeling predicts that the NH2-FWMCSNGSLQCRICI-COOH fragment of hemagglutinin from pandemic H1N1 influenza virus (residues 552 – 566) forms a beta hairpin. In nature, three fatty acid residues are linked to side chains of three cysteine residues within this fragment, and the only relatively hydrophilic region is obviously a loop having sequence SNGSLQ. The aim of this study is to model 3D structure of the hemagglutinin inner region with the help of homology-based methods. Using the MOTIF search server (https://www.genome.jp/tools/motif/MOTIF2.html) that utilizes an algorithm developed for Kyoto Encyclopedia of Genes and Genomes (KEGG) we found a protein (human m-calpain form II; PDB ID: 1kfu) possessing the same sequence motif SNGSLQ. The motif is situated between two beta strands and has a beta-turn formed by amino acid residues NG. Using the calpain-2 3D-structure as a template we further built a 3D model for the hemagglutinin inner region FWMCSNGSLQCRICI via SWISS-MODEL server (https://swissmodel.expasy.org/). According to our modeling predictions, the region forms a beta-hairpin with a beta-turn around the glycine. The loop SNGSLQ is stabilized by five hydrogen bonds between following amino acid residues: S1 and G3; S1 and S4; S4 and Q6 (including three hydrogen bonds found by Protein Interactions Calculator (http://pic.mbu.iisc.ernet.in/) between hydroxyl and amide groups from side chains of the respective residues). The obtained model could be used in future for in silico experiments to search for short peptide blockers of virus pathogenesis. The work was supported by Russian Foundation for Basic Research grant 18-54-00019 (to L.V.Kordyukova) and Belarusian Republican Foundation for Fundamental Research grant B18R-113 (to V.V.Khrustalev).

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