In silico improvement of the cyanobacterial lectin microvirin and Mana(1-2)Man interaction

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Abstract

Given the impact of human immunodeficiency virus (HIV) infection, a portion of the scientific community has been dedicated to the development of drugs capable of preventing the virus from entering the host cell, thus preventing the infection of new individuals. This study aims to perform in vitro microvillin analysis (MVN), a lectin produced by the Microcystis aeruginosa cyanobacterium, aiming at optimizing its binding affinity for the viral gp120 protein, the protein that mediates virus entry into CD4 + T cells. The nucleotide sequence of this work was obtained from a genomic analysis of the Microcystis aeruginosa CACIAM 03, isolated from a surface water sample of the reservoir of the Tucuruí plant. The model was constructed by comparative modeling through the Modeller 9.16 program, having as template the Microcystis aeruginosa MVN of 2YHH PDB code (108 aa). Molecular docking of the MVN with its ligand was performed through Molegro Virtual Docker (version 5.5). The validation of the modeled target was done by analyzing the stereochemical quality, the free energy of the system and the mapping of the molecular electrostatic potential. In addition, three molecular dynamics (DM) of 210 ns were prepared using Amber16 for the refinement of the target. The alanine scanning webserver tool was used to study the importance of protein residues with its ligand. Several information acquired through these computational simulations were used to obtain a mutant. As results, the constructed target of MVN_CACIAM 03 showed 95% sequential identity as compared to the 2YHH template. In the generated MVN_CACIAM 03, 97% of the residues were found in favorable regions, according to the Ramachandran graph. Molecular mooring decreased the energetic state of the complex, which also confirmed the interactions described in the literature. The RMSD values ??of the mannose and the interaction site were very stable during the three trajectories of 210 ns. Calculations of the occupation time of the hydrogen bonds were made for the residues that showed interaction in the MVN_CACIAM03 complex and mannose. And the generated mutant (Thr82Arg), after computational studies, showed to be more efficient during the process of receptor-ligand interaction.

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