

Molecular Dynamics Study of human beta-defensins 2 and 3 chimeric peptides with the Cell Membrane Model of *Pseudomonas aeruginosa*

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Short title: MD Simulation of chimeric peptides with *P. aeruginosa* Cell Membrane

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Abstract

Pseudomonas aeruginosa has a unique position among the antibiotic-resistant microbial pathogens. Among the various therapeutic approaches, antimicrobial peptides are effective to combat this infection. The chimera C3 is a peptide derived from the human beta-defensins 2 and 3 that previously displayed the antibacterial activity against the Gram-negative and Gram-positive bacteria. In this research, the antibacterial activity and the effect of a new genetically designed chimera C3 (i.e. chimera C3-3) on the bacterial membrane was assessed by molecular dynamics (MD) simulation. To investigate the interactions of the peptide on the lipid bilayer model and their effects on each other, the characterizations such as Area Per Lipid (APL), density, deuterium order parameter, membrane thickness, Mean Square Displacement (MSD), Radial Distribution Function (RDF), hydrogen bonds (H-bond) and root-mean-square-fluctuation (RMSF) were compared between C3 and C3-3 peptides. Furthermore, the MD simulation of the pure membrane was also carried out. Finally, the comparison of the antibacterial effects showed that chimera C3-3 had the less antibacterial effect than the chimera C3 due to the N-terminal deletion of GII residues. Moreover, the results confirmed that the GII residue played the main role of an anchor in binding the membrane and deletion of anchor reduced the antibacterial activity.

Keywords: *Pseudomonas aeruginosa*; Antibacterial activity; Molecular dynamic simulation; human beta-defensins; chimeric peptides