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PII: S0005-2736(17)30319-X
DOI: doi:10.1016/j.bbamem.2017.10.009
Reference: BBAMEM 82609

To appear in:

Received date: 5 June 2017
Revised date: 5 October 2017
Accepted date: 6 October 2017

Please cite this article as: Nasim Cheraghi, Mahdieh Hosseini, Sarah Mohammadinejad , Pore formation and the key factors in antibacterial activity of Aurein 1.2 and LLAA inside lipid bilayers, a molecular dynamics study. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bbamem(2017), doi:10.1016/j.bbamem.2017.10.009

Pore Formation and the Key Factors in Antibacterial Activity of Aurein 1.2 and LLAA inside Lipid Bilayers, a Molecular Dynamics Study

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Aurein 1.2 and LLAA are two antimicrobial peptides with different antibacterial activities (LLAA > Aurein 1.2), though their amino acid sequences are similar. In this manuscript, we study the key features for the different antibacterial activities of these peptides using molecular dynamics simulation. We find that in water, both peptides become disordered and LLAA is observed to have higher water-solubility, a feature which may contribute to enhancing its propensity to disrupt the bilayer and thus higher activity. Both peptides are also investigated while they are initially located inside lipid bilayer as a pre-formed vertical channel composed of five parallel copies of each peptide. LLAA demonstrates larger structural deviation from the initial helical structure and also more structural flexibility which is concluded to be a key feature in its stronger activity. In the presence of LLAA, the bilayer order is perturbed more pronouncedly and the number of water molecules penetrating into bilayer is higher. It is shown that stronger electrostatic interactions, more hydrophobic contacts and more hydrogen bonds between lipid and LLAA also lead to stronger activity of LLAA. The simulation results show instability of the barrel-stave pores for our peptides inside lipid bilayers.

Keyword: Antimicrobial peptide, Lipid bilayer, Pore formation, Aurein 1.2, LLAA, Molecular dynamics simulation.

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Abbreviations: AMPs, antimicrobial peptides; DPPC, dipalmitoyl phosphatidylcholine; RMSD, Root Mean Square Deviation ;RMSF, Root Mean Square Fluctuation ; MD, molecular dynamics; SAS, solvent accessible surface; DSSP, define secondary structure of proteins; 5PM, 5-peptide in membrane simulation; 5PW, 5-peptide in water simulation.

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