Dual Action of Cyclic Antimicrobial Peptides: Fusion and Leakage

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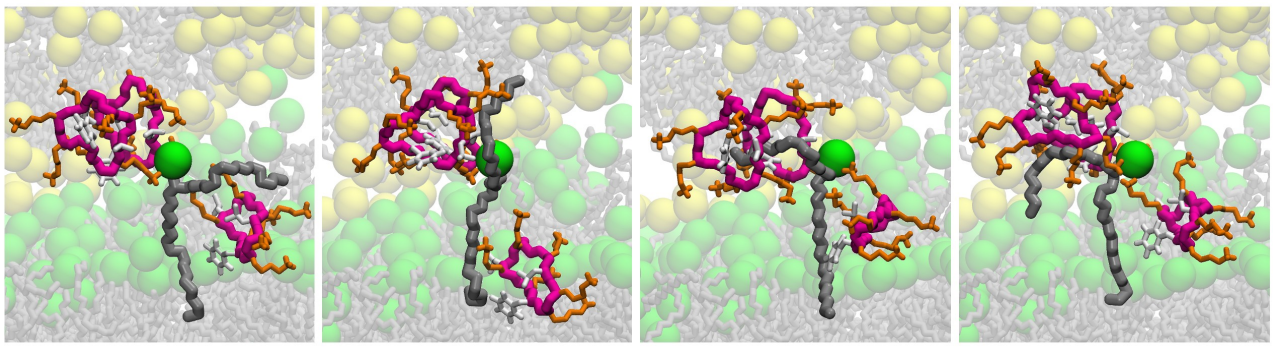
The action of membrane active peptides is an essential process in biology and encompasses fusion, poration and translocation. We show here that two of the processes - fusion and poration are correlated, in the specific case of a cyclic antimicrobial peptide BPC194, and we speculate that it is a more general mechanism of action of membrane active peptides. FRET and cryo-TEM studies show that the peptide is able to cause fusion of vesicles. The fusiogenic action is accompanied by leakage as probed by DCFBA. We also explored how the peptide is able to simultaneously perturb the membrane towards porated and stalk phases by atomistic MD simulations. A pre-stalk intermediate has been identified to be important step towards fusion. Simultaneously, disordered toroidal pores are also formed by the peptides in the vicinity of the pre-stalk. The study provides a detailed analysis of how a simple peptide can effect two seemingly unrelated processes- fusion and pore formation, upon interaction with membranes. For antimicrobial peptides it has been speculated that this “multi-hit” mechanism may even increase their antimicrobial potency.



Molecular details of a lipid splaying by the action of the cyclic antimicrobial peptide BPC194.