Detecting Asymmetry and Lateral Heterogeneity Caused by Antimicrobial Peptides in Fluid Lipid Bilayer Membranes

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Antimicrobial peptides (AMPs) are a class of promising broad-spectrum antibiotics against drug-resistant bacteria. Many of them are found to bind bacterial membranes spontaneously, and cause disruption to membrane integrity. The understanding of the interaction is critical to decipher their mode of action and to design more potent antimicrobial agent. Many AMPs have been found to form membrane pores to lyse cell[1,2], but more details are needed to understand the delicate interaction under conditions that no pore is present in membrane. The contrast variation technique in neutron scattering affords us to probe the interaction in multi-component fluid lipid membranes. By taking advantage of the contrast between protiated and deuterated lipids, we have found some AMPs induce a more asymmetric and lateral segregated lipid bilayers with redistribution of charged lipid within intact membranes. For example, Aurein 1.2, a 13-amino acid AMP discovered in Australia frog *Litoria genus*, drives anionic lipid from the inner leaflet of a bilayer to the outer leaflet. It leads to lateral segregation that is similar to the domain formed below the lipid order−disorder phase-transition temperature. To our knowledge, this is the first direct observation of lateral segregation caused by a peptide. With quasi-elastic neutron scattering, we found that the lipid lateral motion in the fluid phase was reduced by Aurein 1.2. With this[3,4] and our other study on AMPs such as Alamethicin[5] and melittin[6], the results point to an alternate mechanism of AMPs on disrupting membrane without disintegrating it. I will discuss how we used neutron scattering to approach this problem and the implication for AMPs research.

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