Implication of lipid monolayer charge characteristics on their selective interactions with a short antimicrobial peptide

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Abstract

Many antibacterial peptides (AMPs) target bacterial membranes and they kill bacteria by causing irreversible structural disruptions[1]. One of the fundamental issues however lies in the selective responses of AMPs to different cell membranes as a lack of selectivity can elicit toxicity and related side effects to mammalian host cells. Following previous reports of the selective killing of bacteria in co-culturing of bacteria and human host cells by a series of designed short peptides[2,3], we report a careful study of the selective binding of one of the representative AMPs, with the general sequence $G(IIKK)_4I$-NH2 (G4), to spread lipid monolayers made of zwitterionic DPPC and anionic DPPG lipids, respectively, using the combined measurements from Langmuir trough, Brewster angle microscopy (BAM) and neutron reflectivity (NR). The difference in pressure rise upon peptide addition into the subphase clearly demonstrated the different interactions between these lipids and the G4 peptide. Whilst the BAM analysis confirmed the association of the peptide into the lipid monolayers, there was little difference in the time dependent morphological changes. NR studies exploiting the new low-Q way to access the interfacial composition revealed that the peptide bound in 4 times greater amounts to DPPG monolayers than to the DPPC monolayers. In addition, whilst the peptide was only associated with the head groups of DPPC it was well penetrated into the entire DPPG monolayer, showing that electrostatic interaction strengthened the molecular interactions involved. The charge interaction could help trigger hydrophobic interaction that may then facilitate the transition of the secondary structures from non-ordered to α-helical conformations so that G4 becomes more powerful at disrupting the charged membranes. The results are discussed in the context of general antibacterial actions as observed from other AMPs and membrane lytic actions.

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