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Influence of Membrane Composition on the Binding and Folding of a Membrane Lytic Peptide from the Non-Enveloped Flock House Virus

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Abstract

Using a combination of coarse-grained and atomistic molecular dynamics simulations we have investigated the membrane binding and folding properties of the membrane lytic peptide of Flock House virus (FHV). FHV is an animal virus and an excellent model system for studying cell entry mechanisms in non-enveloped viruses. FHV undergoes a maturation event where the 44 C-terminal amino acids are cleaved from the major capsid protein, forming the membrane lytic (γ) peptides. Under acidic conditions, γ is released from the capsid interior allowing the peptides to bind and disrupt membranes. The first 21 N-terminal residues of γ, termed γ_1, have been resolved in the FHV capsid structure and γ_1 has been the subject of *in vitro* studies. γ_1 is structurally dynamic as it adopts helical secondary structure inside the capsid and on membranes, but it is disordered in solution. *In vitro* studies have shown the binding free energies to POPC or POPG membranes are nearly equivalent, but binding to POPC is enthalpically driven, while POPG binding is entropically driven. Through coarse-grained and multiple microsecond all-atom simulations the membrane binding and folding properties of γ_1 are investigated against homogeneous and heterogeneous bilayers to elucidate the dependence of the microenvironment