Self Assembly and Pore Formation at the Membrane Interface with Pore Forming Toxins

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Pore forming toxins are protein molecules that have specifically evolved to form unregulated pores on the cell membrane leading to osmotic stress and lysis. These water soluble proteins bind to lipid membranes and following a process of self assembly at the membrane interface form nanometer sized pores. Although pore forming toxins have been extensively studied, the molecular mechanisms of the oligomerization pathways and the fate of lipids during the final stages of pore formation are incompletely understood. Using a combination of experimental and molecular dynamics simulations we study the pore forming mechanism for the Cytolysin-A pore forming toxin. Using supported lipid bilayer platforms and atomic force microscopy, several intermediate states of pore formation are captured. Using molecular dynamics simulations we comment on the stability of these partially formed intermediates as well the manner in which lipids reorganize during the pore formation process.