^{19}F-NMR studies to understand pH induced structural changes in protective antigen anthrax toxin

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Anthrax bacteria (*Bacillus anthracis*) produces Protective antigen toxin (PA), Lethal factor (LF) and Edema factor (EF) protein components into the host cells. Protective antigen toxin (PA83 – 83kDa polypeptide) binds to cell surface receptors. PA is cleaved into a 20kDa fragment PA_{20} and 63kDa fragment PA_{63} by Furin like protease. The PA_{20} is released, resulting in spontaneous oligomerization into heptamer $(PA63)_7$ that facilitates EF and LF to bind. The complex is endocytosed and acidic conditions in endosome triggers conformational changes in prepore complex and leading to a membrane spanning pore formation. Formation of pore allows translocation of LF and EF components into the cell.

In pore structure "O"-ring shaped narrow 6 Å diameter ring Φ-clamp is formed by seven phenylalanine residues (Phe427). The Φ-clamp is not wide enough to allow protein secondary structure elements, it may allow only fully unfolded polypeptides to pass through PA pore. To use ^{19}F NMR as a tool, PA83 is labelled site specifically with *p*-Fluoro-Phenyalalanine at Phe427 residue. Site specifically introduced ^{19}F probe helps to follow conformational changes and dynamic behavior of the Φ-clamp in prepore, LF_N bound prepore and pore state.

Our results indicate that *p*F-Phe427 is dynamic in the prepore state and then becomes more dynamic in the transition to the pore state. Further increase in dynamic behavior at the Φ-clamp in pore state may provide the necessary room for movement needed in translocating EF and LF into the cell cytosol.