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Title: The pH-induced Structural Changes in Helicobacter Pylori TlyA

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Abstract:

Helicobacter pylori TlyA is a novel pore-forming toxin which is amyloidogenic in nature. Mode of action and virulence mechanism of this toxin remain obscure. However, cytotoxicity of its amyloid fibrils over a range of temperature has given new insights toward this. Our understanding of protein behavior in other physiologically relevant environment would take us rather close to its virulence mechanism. We know that Helicobacter pylori (HP) survive in extremely low pH for being a gastric pathogen. Furthermore, it has been shown that HP inflammation causes acid production in stomach. Hence we studied the structural changes in H. Pylori TlyA brought about by low pH environment. In this study, we observed that even at the pH of 3 the protein retains its secondary structure intact and shows only sparse amyloid fibril formation. The protein shows tremendous ANS binding upon low pH incubation suggesting a prominent conformational change, exposing its hydrophobic patches on the surface. The protein in reinstated neutral pH showed significantly low ANS binding presumably due to the refolding of the protein. The functionality of the native and refolded protein has been studied via hemolytic assay. In this assay we show that the refolded protein achieves a higher activity than the native protein. Finally, our data suggest pH as one of the major physico-chemical constraint for the virulence activity of the protein. Altogether we report that H. Pylori TlyA has a propensity to reversibly unfold over a range of acidic pH while retaining the structural integrity and functionality to a great extent.

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