Title:	Helicobacter pylori TlyA Forms Amyloid-like Aggregates with Potent Cytotoxic Activit
Authors:	Lata, K. (/jspui/browse?type=author&value=Lata%2C+K.) Chattopadhyay, K. (/jspui/browse?type=author&value=Chattopadhyay%2C+K.)
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Abstract:	Helicobacter pylori is a potent human gastric pathogen. It is known to be associated with several gastroenteric disorders, including gastritis, peptic ulcer, and gastric cancer. The H. pylori genome encodes a gene product TlyA that has been shown to display potent membrane damaging properties and cytotoxic activity. On the basis of such properties, TlyA is considered as a potential virulence factor of H. pylori. In this study, we show that the H. pylori TlyA protein has a strong propensity to convert into the amyloid-like aggregated assemblies, upon exposure to elevated temperatures. Even at the physiological temperature of 37 °C, TlyA shows a strong amyloidogenic property. TlyA aggregates that are generated upon exposure at temperatures of ≥37 °C show prominent binding to dyes like thioflavin T and Nile Red. Transmission electron microscopy also demonstrates the presence of typical amyloid-like fibrils in the TlyA aggregates generated at 37 °C. Conversion of TlyA into the amyloid-like aggregates is found to be associated with major alterations in the secondary and tertiary structural organization of the protein. Finally, our study shows that the preformed amyloid-like aggregates of TlyA are capable of exhibiting potent cytotoxic activities against human gastric adenocarcinoma cells. Altogether, such a propensity of H. pylori TlyA to convert into the amyloid-like aggregated assemblies with cytotoxic activity suggests potential implications for the virulence functionality of the protein
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