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Title:	Unfolding distinguishes the <i>Vibrio cholerae</i> cytotoxin precursor from the mature form of the toxin
Authors:	Paul, Karan (/jspui/browse?type=author&value=Paul%2C+Karan) Chattopadhyay, K. (/jspui/browse?type=author&value=Chattopadhyay%2C+K.)
Keywords:	Biophysical characterization Chemical denaturants Colloid-osmotic lysis
Issue Date:	2011
Publisher:	American Chemical Society
Citation:	Biochemistry, 50 (19), pp. 3936-3945.
Abstract:	<p><i>Vibrio cholerae</i> cytotoxin (VCC) is a potent cytolytic toxin that induces colloid osmotic lysis of its target eukaryotic cells by forming transmembrane oligomeric β-barrel channels. VCC is secreted by the bacteria as an inactive precursor (Pro-VCC) and is subsequently activated by proteolytic removal of an N-terminal "Pro-domain", thus generating the active form of the toxin (Mature-VCC). Earlier studies have indicated an intramolecular chaperone-like role of the Pro-domain favoring efficient secretion of the toxin from the periplasm into the extracellular space. However, the exact role of the Pro-domain in the VCC structure-function mechanism remains unclear. Here, we have compared the Pro-VCC and Mature-VCC molecules in terms of their structural and conformational properties. We have studied unfolding of the two variants of the VCC molecule in response to an array of denaturing conditions, including low-pH, chemical denaturant and heat-induced unfolding. Pro-VCC shows a more profound tendency to unfold in response to such denaturing conditions compared to Mature-VCC. Biophysical characterization of the isolated Pro-domain further suggests that the increased unfolding propensity of Pro-VCC does not arise because of an increased level of unfolding of the Pro-region itself. Altogether, our results imply that a natively folded architecture of the Pro-VCC molecule with sufficient structural and conformational plasticity presumably allows it to adopt a suitable configuration that is possibly required for its efficient secretion and subsequent proteolytic maturation under physiological conditions.</p>
URI:	http://pubs.acs.org/doi/abs/10.1021/bi200332g (http://pubs.acs.org/doi/abs/10.1021/bi200332g) 10.1021/bi200332g (10.1021/bi200332g)
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