Title:	Tyrosine in the hinge region of the pore-forming motif regulates oligomeric β-barrel pore formation by Vibrio cholerae cytolysin
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Abstract:	β-barrel pore-forming toxins perforate cell membranes by forming oligomeric β-barrel pores. The most crucial step is the membrane-insertion of the pore-forming motifs that create the transmembrane β-barrel scaffold. Molecular mechanism that regulates structural reorganization of these pore-forming motifs during β-barrel pore-formation still remains elusive. Using Vibrio cholerae cytolysin as an archetypical example of the β-barrel pore-forming toxin, we show that a key tyrosine residue (Y321) in the hinge region of the pore-forming motif plays crucial role in this process. Mutation of Y321 abrogates oligomerization of the membrane-bound toxin protomers, and blocks subsequent steps of pore-formation. Our study suggests that the presence of Y321 in the hinge region of the pore-forming motif is crucial for the toxin molecule to sense membrane-binding, and to trigger essential structural rearrangements required for the subsequent oligomerization and pore-formation process. Such a regulatory mechanism of pore-formation by V. cholerae cytolysin has not been documented earlier in the structurally related β-barrel pore-forming toxins.
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