ABSTRACT

The cholera toxin (CT) from *Vibrio cholerae* is associated with the clinical symptoms of cholera. The toxin is a hetero-hexamer (AB_5) complex consisting of a subunit A (CTA) with a pentamer (B_5) of subunits B (CTB). The importance of the AB_5 complex for pathogenesis is established in the wild type O1 serotype using known structural and functional data. However, its role is not yet documented in other known serotypes harboring sequence level residue mutations. The sequences for the toxin from different other serotypes are available in GenBank. These sequences show mutations to the wild type O1 strain. Therefore, it is of interest to locate the position of these mutations in AB_5 structure to infer complex assembly for functional role. We show that mutations in CTA are at the solvent exposed regions of the AB_5 complex, while those in CTB are at the CTB/CTB interface of the homo pentamer complex. Thus, the role of mutations at the CTB/CTB interface for B_5 complex assembly is implied. It is observed that these mutations are also often non-synonymous (i.e. polar to non-polar or vice versa) in chemical property. The formation of the AB_5 complex involves intersubunit residue-residue interactions at the protein-protein interfaces and thus, these structurally relevant mutations are of importance for the understanding of pathogenesis among serotypes. This is also of significance in the improvement of recombinant CT protein complex analogs for vaccine design and their use against multiple serotypes.