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WHAT CAN YOU DO WITH A α -HELICAL STRUCTURE ?

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Autotransporter (AT) proteins are important virulence factors and constitute the largest family of secreted and outer membrane proteins in Gram-negative bacteria. Despite their importance in bacterial pathogenesis there are only 12 structures of AT α -domains in the PDB and their mechanisms of action are poorly understood. Most structurally determined AT α -domains were found to be built upon right-handed α -helical structures. Our crystal structure of Antigen 43a from uropathogenic *Escherichia coli* (UPEC) showed that two self-associating interfaces along with bending of the α -helical structure were critical for dimerization, which in turn promotes UPEC aggregation and biofilm formation. Using the MX beamlines at the Australian Synchrotron along with some assistance from an Australian Synchrotron fellowship we have determined the structures of two new AT α -domains; UpaB and TibA from UPEC and enterotoxigenic *E. coli* (ETEC) respectively. These new structures demonstrate the large plasticity in their α -helical scaffolds that along with further modifications, allow these proteins with the same basic architecture to promote different functions in pathogenesis. The UpaB structure revealed unique extensions of the α -strands at the centre of the α -helix that gives rise to a 'belly' domain. In contrast, TibA forms a long narrow twisted α -helix that allows for extensive interactions to occur between neighbouring monomers. Unusually TibA is also glycosylated by an associated glycosyltransferase TibC. I will discuss how these different structures and modifications facilitate interactions with their newly identified protein binding targets and how this affects their role in bacterial pathogenesis.

Keywords

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