ABSTRACT

Adenylate cyclase toxin (CyaA) is a key virulence factor of *Bordetella pertussiss*, the agent of whooping cough (pertussis). CyaA is a secreted bi-functional toxin belonging to the RTX (Repeat in ToXin) family of bacterial cyolysins capable to permeabilize cellular membranes by forming small cation-selective pores. The major activity of CyaA, however, consists in delivery of an adenylate cyclase domain into target cell cytosol, where upon activation by calmodulin it catalyzes uncontrolled conversion of cellular ATP to cAMP, a key signallilng molecule subverting cell functions. Recently, it has been demonstrated that CyaA utilizes the CD11b/CD18 integrin as a specific cellular receptor. The CD11b/CD18 heterodimer is rather promiscuous cell surface molecule, playing an important role in several biological functions of myeloid phagocytic cell, among which are bactericidal functions, such as chemotaxis, phagocytosis, degranulation and superoxide generation. Inhibition of those functions by CyaA action then appears to play an important role in *Bordetella* virulence.

Study of the penetration of CyaA into the cells is important in two reasons. The CyaA toxin is endowed with a unique mechanism of entry into eukaryotic cells that consists in a direct translocation of the catalytic domain across the plasma membrane of the target cells into the cytosol. This ability could be exploited to induce immunity T-cell responses. Various heterologous $CD8^+$, as well as $CD4^+$ T-cell epitopes have been engineered into genetically detoxified CyaA and the resulting toxoids were successfully used as vectors for delivery of inserted epitopes into antigen-presenting cells. Upon processing and presentation, these recombinant CyaAs trigger specific MHC class I and/or class II-restricted T-cell responses both *in vitro* and *in vivo*.

CyaA can also serve as a good model for study of interaction of proteins with the biological membrane, for study of direct translocation of proteins across the plasma membrane or for study of the role posttranslational modification by fatty acid in the protein-protein and protein-membrane interaction. CyaA is an interesting model not only for study of biological features, but also for preparation of novel vaccines.