

## Abstract

Adenylate cyclase toxin (CyaA) produced by the causative agent of whooping cough *Bordetella pertussis*, is a key virulence factor important for colonization of the host. CyaA targets preferentially myeloid phagocytes expressing CD11b/CD18 integrin. By elevating cytosolic cAMP in the host cells, CyaA interferes with their phagocytic, chemotactic and oxidative burst capacities. Furthermore, CyaA modulates the secretion of cytokines and the maturation state in LPS-stimulated dendritic cells (DC) by affecting the expression of costimulatory molecules. In this study, we investigated the effects of CyaA on the capacity of murine bone-marrow DC to prime CD4<sup>+</sup> and CD8<sup>+</sup> T cells in response to ovalbumin epitopes delivered by the CyaA-AC- toxoid, as a model antigen. Further, we examined the possible impact of CyaA on the antigen uptake and processing for MHC class I and II-restricted presentation by DC, as we previously observed a decreased T cell stimulatory capacity of CyaA-treated DC in response to soluble ovalbumin.

We found out that the high levels of cAMP generated by CyaA in LPS-stimulated DC account for the decreased presentation of ovalbumin epitopes carried by CyaA-AC- toxoid on MHC class I and II molecules, thereby impairing the CD8<sup>+</sup> and CD4<sup>+</sup> T cell responses. Whereas CyaA did not influence the antigen uptake via receptor-mediated endocytosis, it notably decreased the macropinocytosis in DC. However, CyaA did not affect antigen processing neither for MHC class I nor for MHC class II presentation in DC. Therefore it seems possible, that in our model system the ability of CyaA to decrease T cell-stimulatory capacity of DC is mainly due to the inhibition of the expression of co-stimulatory molecules and the production of immunomodulatory cytokines like IL-10.