

## 7<sup>th</sup> Middle East - Global Summit and Expo on **Vaccines & Vaccination**

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### **Why whooping cough is back and what vaccines need to be developed to counter it: Next generation pertussis vaccines and relevance of adenylate cyclase toxin-hemolysin**

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The adenylate cyclase toxin-hemolysin (ACT, AC-Hly or CyaA) is a key virulence factor of *Bordetella pertussis*. It targets bactericidal activities of phagocytes such as oxidative burst and complement or antibody-mediated opsonophagocytic killing of bacteria. Through cAMP signaling, CyaA skews also TLR-triggered maturation of dendritic cells inhibiting pro-inflammatory IL-12 and TNF- $\alpha$  secretion and enhancing IL-10 production and Treg expansion likely hampering also induction of adaptive immune responses to *Bordetella* infections. Non-enzymatic CyaA toxoid is a potent protective antigen and adjuvant that boosts immunogenicity of co-administered *B. pertussis* antigens and improves potency of acellular pertussis (aP) vaccines in mice. This makes CyaA to a prime antigen candidate for inclusion into a next generation of aP vaccines. Moreover, recombinant CyaA toxoids were recently shown to be safe in humans in frame of phase-I clinical evaluation of a CyaA-based immunotherapeutic vaccine that induces Th1-polarized CD8<sup>+</sup> cytotoxic T-lymphocyte response targeting cervical tumors. In the last part of the lecture, the need for and ways of making a safer next generation whole cell pertussis vaccine (wP) for most developed countries will be outlined.

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