OMICS Group Conferences
Accelerating Scientific Discovery
4th International Conference on
Vaccines & Vaccination
September 24-26, 2014 Valencia Convention Centre, Spain

Highly immunogenic C-terminal binding domain of *Clostridium difficile* toxin A stimulates dendritic cell maturation

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Clostridium difficile (Cd) is implicated as opportunistically nosocomial infection in hospitalized patients due to disrupt the antagonistic balance in the intestinal micro-flora by prior antibiotic therapies. The major pathogenicity of CDI is correlated with clostridial toxins, toxin A and toxin B, secreted into the host gastrointestinal environment to disrupt barriers of epithelial cell in small intestine. Non-toxic domain on C-terminal regions of toxin A (tcdA) and toxin B (tcdB), responsible for cell binding and pathogenesis, are emerging targets for Cd vaccine development. In this study, we designed and expressed a recombinant C-terminal receptor binding domain of toxins rRBD). rRBD has been characterized and found to have cell binding and hemagglutination activity *in vitro* and rapidly internalized into cytosol and then be degraded quickly. Mouse immunogenicity studies indicated that rRBD can specifically elicit strong IgG antibody without any adjuvant at 10-30 ug dose in the BALB/c mice. Moreover, protection of rRBD immunization at 30 ug achieved 70% survival rate after lethal challenge of C. difficile toxin A. Indeed, this C-terminal binding domain is found to be capable of stimulating different immune cells to enhance immune responses. In addition, the results supported rRBD could directly upregulate surface markers of DC maturation and trigger cytokines secretion of IL6, IL12, and TNF-alpha. Thus, the activity of triggering DC maturation becomes one route which contributes to highly immunogenic property and could be a potent Cd vaccine component.

Biography

Pele Choi-Sing Chong obtained his BSc and PhD from the Department of Biochemistry in the University of Alberta, Edmonton, Canada. He was trained as a protein chemist and specialized in peptide synthesis for protein structure and function studies. He had spent 15 years at Connaught Laboratory Limited (now called Sanofi Pasteur) in human vaccine research and development. During his tenure there, he had developed two human vaccines, ProHibit against H. influenzae type b (Hib) and the component pertussis vaccine. In June/2003, he was recruited and joined NHRI to develop and establish the Vaccine Research and Development Center (VRDC). He has authored over 150 original research articles and has over 80 patents filed and/or granted.

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