OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Vaccines & Vaccination

22-24 Nov 2011 Philadelphia Airport Marriott, USA

Increased efficacy of BCG vaccines against experimental tuberculosis through genetic engineering of Th1 driving and immune-modulatory peptide epitopes

Chinnaswamy Jagannath

Dept. of Pathology, University of Texas Health Sciences Center, USA

Tuberculosis is the leading cause of death due to bacterial infections and BCG vaccine is effective only against childhood TB. BCG also sequesters within phagosomes of macrophages and DCs (APCs) with minimal contact with the antigen processing machinery involving lysosomes and cathepsins. We therefore attempted to improve immunogenicity of BCG through two novel strategies. First, antigen-85B was hyper-expressed in BCG vaccine (BCG85B) which enhanced the secretion of this protein into the cytosol of APCs. This led to autophagic localization of BCG into lysosomes and an enhanced presentation of peptides through MHC-II pathway to the T cells in vitro and in vivo. Second, we identified peptide and protein motifs from *Mycobacterium tuberculosis* that triggered Toll-like receptors on APCs (TLR-priming peptides; TPPs) enhancing their ability to prime T cells. TPPs were then cloned into BCG vaccine along with Ag85B yielding BCG85B-TPP.Wild type BCG,BCG85B and BCG85B-TPP were then used as vaccines in mice and protection against tuberculosis was measured using an aerosol challenge model. In vitro studies with antigen presenting cells and T cells established that the BCG85BTPP was more effective in priming Th1 cytokine release and priming of T cells. Consistent with this in vitro finding, the latter vaccine was more powerful in protecting mice against aerosol induced infection. In mice wt-BCG induced a 1-log10 protection, BCG85, 2-log10 protection and BCG85TPP produced 2.5 log10 protection ($p < 0.009$ vs BCG85) against tuberculosis. The latter vaccine was also a strong inducer of Th1 immunity and CD4 T cells secreting IFNγ and IL-2. *Supported by* NIH AI49534 &AI78420.

Biography

Dr. Jagannath received his Ph.D degree from Jawaharlal Institute of Postgraduate Medical Education and Research, University of Madras, India in 1987, pursued his doctoral career in UIC and Emory University School of Medicine and currently is a Professor in the department of Pathology and Laboratory Medicine, UT-Houston, Texas. He has published more than 50 papers in tuberculosis research. His expertise is in developing novel vaccines, vaccine adjuvants and investigating antigen processing.