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The study on immunogenicity and protective efficacy of recombinant BCG against tuberculosis

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Introduction: Tuberculosis (TB) is a serious infectious disease caused by M. *tuberculosis*. BCG had been considered to be the only available and effective vaccine in prevention of TB. However, the protective efficacy of BCG on TB was still controversial in different populations and age. Thus, improved TB vaccines are urgently needed to develop as an alternative to BCG which was able to activate immune response and protect against severe forms of TB effectively.

Method: Two BCG strains (Pasteur and Shanghai) were used parental strain and specific antigens of M. *tuberculosis* Ag85A, CFP10, ESAT-6 and immune regulation cytokines GM-CSF, IL-12p70 were integrated into BCGs respectively. BALB/c female mice were immunized subcutaneously with single-gene *rBCGs* and multiple-gene *rBCGs*. The specific antibody levels of lgG, lgG1 and lgG2a in immunized mice were detected by ELISA assay. Detection of proliferation of splenic lymphocytes and splenocytes subsets by flow cytometry were conducted. Nine rBCG strains were chosen for protective efficacy test. After eight weeks of immunization with *rBCGs*, mice were challenged intravenously by M. *tuberculosis* H37Rv. Histopathological examination and bacterial load was performed on the lung, spleen tissues of immune mice.

Results: Both single-gene *rBCGs* and multiple-gene *rBCGs* could induce strong humoral and Th1 cellular immune reaction. Significantly higher levels of Th1 cytokines IFN- γ was revealed in both multiple and single-gene *rBCGs*, while Th2 cytokines IL-4 was not detected in all *rBCGs*. After 18 weeks, the survival rate was 100% in rBCG- Pasteur: A, rBCG- Pasteur: AE and 80% in rBCG-SHanghai: IE, rBCG-Pasteur: GC only 60% in rBCG- Pasteur: GCE.

Conclusion: rBCG had excellent immunogenicity and immune protective efficacy. It could regulate the level of TNF- alpha by p38 MAPK and NF-kB signaling pathway and induce the apoptosis of macrophages. BCG-Pasteur is more suitable for parental BCG than the BCG-SHanghai. These findings can provide ideas and experimental basis for the development of anti-tuberculosis recombinant vaccines.

Biography

Lang Bao is currently working as a Professor in Microbiology and Immunology. He has completed his PhD from West China University of Medical Sciences in 1999 and then moved to WHO Collaborative Research Centre of Infectious Disease, Royal Tropical Institute, Netherlands for his Post-doctoral training. He has published around 100 research papers.