

Development of Recombinant BCG Based Epitope Vaccine Candidate for Tuberculosis

Aparna Christy, Karthika K.D, P. Kannan and Sujatha Narayanan

Department of Immunology, Tuberculosis Research Centre, Chennai -31

Introduction

Tuberculosis (TB) remains a global health challenge. BCG, the only available vaccine for TB provides variable efficacy in protection against adult pulmonary TB. Developing better vaccines using novel approaches is a major goal for the TB research community. Epitope-based vaccines designed to induce T cell responses specific for *M.tb* antigens are being developed as one of the means of improving vaccine potential. The aim of our study was to construct a recombinant BCG (rBCG) based epitope vaccine for TB and prove its immunogenicity in a mouse model.

Materials and Methods

Epitope grafting was done by Splicing by Overlap Extension (SOE) PCR. Expression of the chimeric antigens in BCG was proved by Western blotting. For the immunogenicity experiments, Balb/c mice were immunized subcutaneously with BCG or individual rBCGs. Cell - mediated immune response to specific mycobacterial antigens was studied by evaluation of in vitro splenocyte proliferation (MTT assay) and cytokine estimation (ELISA). Humoral

immune response was studied by measure of serum antibody titre.

Results

Immunodominant epitopes were chosen from three well defined *M.tb* antigens (CFP-10, FBP and INV2). rBCGs (BCG::Cfp, BCG::Fbp and BCG::Inv) expressing the above epitopes on the *M.tb* Chaperonin 10 back ground of the epitope delivery system was constructed. Expression of chimeric antigens in BCG was verified. Immunogenicity studies show that, compared to BCG vaccinated group the splenocytes derived from rBCG vaccinated groups showed greater antigen specific proliferation, characterized with higher IFN-gamma response and reduced IL-4 secretion. Also rBCG vaccination was able to induce specific humoral immune response with an enhanced IgG2a/IgG1 ratio.

Conclusion

Our results indicate that the rBCGs favour a Th1 type response, which is known to be important for mycobacterial immunity and are thus promising TB vaccine candidates.