Increased B and T Cell Responses in M. bovis Bacille Calmette-Guérin Vaccinated Pigs Co-Immunized with Plasmid DNA Encoding a Prototype Tuberculosis Antigen

The only tuberculosis vaccine currently available, bacille Calmette-Guérin (BCG) is a poor inducer of CD8+ T cells, which are particularly important for the control of latent tuberculosis and protection against reactivation. As the induction of strong CD8+ T cell responses is a hallmark of DNA vaccines, a combination of BCG with plasmid DNA encoding a prototype TB antigen (Ag85A) was tested. As an alternative animal model, pigs were primed with BCG mixed with empty vector or codon-optimized pAg85A by the intradermal route and boosted with plasmid delivered by intramuscular electroporation. Control pigs received unformulated BCG. The BCG-pAg85A combination stimulated robust and sustained Ag85A specific antibody, lymphoproliferative, IL-6, IL-10 and IFN-γ responses. IgG1/IgG2 antibody isotype ratio reflected the Th1 helper type biased response. T lymphocyte responses against purified protein derivative of tuberculin (PPD) were induced in all (BCG) vaccinated animals, but responses were much stronger in BCG-pAg85A vaccinated pigs. Finally, Ag85A-specific IFN-γ producing CD8+ T cells were detected by intracellular cytokine staining and a synthetic peptide, spanning Ag85A131-150 and encompassing two regions with strong predicted SLA-1*0401/SLA-1*0801 binding affinity, was promiscuously recognized by 6/6 animals vaccinated with the BCG-pAg85A combination. Our study provides a proof of concept in a large mammalian species, for a new Th1 and CD8+ targeting tuberculosis vaccine, based on BCG-plasmid DNA co-administration.
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