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Protective efficacy of a novel protein adjuvanted formulation PPE15-LMQ: A promising tuberculosis vaccine candidate

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Introduction: Bacillus Calmette–Guérin (BCG), the only licensed tuberculosis (TB) vaccine, is effective in children but its efficacy wanes over time. Mycobacterial antigen PPE15 (Rv1039c), was selected due to its broad and common recognition during human TB infection. When delivered intranasally via a replication-deficient chimpanzee adenovirus vector (ChAdOx1), PPE15 improved BCG-induced protection in mice. This study evaluated efficacy of PPE15 formulated as a protein with emulsion and liposome-based adjuvants.

Methods: C57BL/6 mice received two doses of PPE15 formulated with five different adjuvants (LMQ, LQ, SMQ, SQ, SWE) from Vaccine Formulation Institute. These adjuvants were either squalene or liposome-based, with and without QS21 and/or a synthetic TLR4 ligand. Vaccine efficacy was evaluated alone and as a prime-boost to BCG, following aerosol challenge with M.tb Erdman (Fig. 1a). Immunogenicity was assessed in the spleen and lungs using PPE15-tetramers and in vivo staining.

Results: PPE15 induced cellular and antibody responses with all adjuvants tested, with stronger responses detected with PPE15 formulated in LMQ adjuvant. This formulation resulted in the generation of polyfunctional CD4+ T cells and high levels of PPE15-specific IgG. Mycobacterial growth inhibition assays demonstrated superior control by splenocytes from the PPE15-LMQ vaccinated group compared to other adjuvants and unvaccinated mice. In vivo challenge showed a significant reduction in the lung and spleen bacterial load of PPE15-LMQ vaccinated compared to unvaccinated animals and improved BCG protection when used as a boost to BCG (Fig. 1b,c). Protection was associated with enhanced PPE15-specific CD4+ and CD8+ responses in the lung and spleen, with a notable increase in protective lung parenchymal CD4+ CXCR3+ KLRG1- T cells.

Conclusion: PPE15-LMQ showed promise when used alone and as a booster to BCG. These findings support advancing this vaccine to next stages of development.

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Conflicts of Interest
None

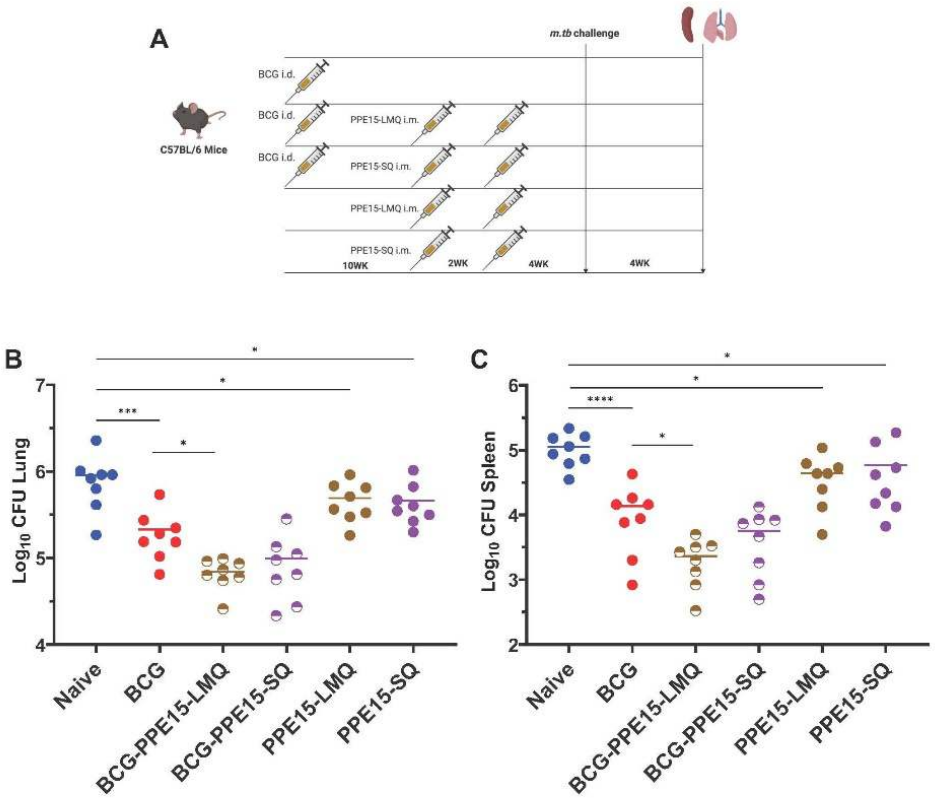

Figure 1: Evaluating the Protective Efficacy of PPE15 Protein-Adjuvanted Vaccines. (A) C57BL/6 mice were initially primed via intradermal (i.d.) injection with BCG and later boosted with two doses of either PPE15-SQ or LMQ, administered intramuscularly (i.m.) 10 weeks after the prime and spaced 2 weeks apart. Control groups consisted of unvaccinated mice (Naïve) and those vaccinated with only BCG. Four weeks after the final vaccination, mice were challenged with an aerosolized *M.tb*. (B) Lungs and (C) spleens were harvested for colony-forming unit (CFU) enumeration four weeks post-challenge. Each dot in the figures represents an individual animal, and the lines indicate the mean CFU count for each group. Statistical significance was assessed using One-Way ANOVA followed by Dunnett's multi-comparison test, with significance levels indicated as follows: *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001. CFU = colony forming units, i.d. = intradermal, i.m. = intramuscular.