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A self-assembling and self-adjuvanting multiepitope peptide nanoparticle vaccine improves the efficacy and immunogenicity of Bacille Calmette-Guérin

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Introduction: After over a century since its initial development, Bacille Calmette-Guérin (BCG) remains the only licensed vaccine against tuberculosis (TB). Subunit boosters are considered a viable strategy to enhance BCG efficacy, which often wanes in adolescence. While many studies on booster subunit vaccines have concentrated on recombinant proteins with adjuvants, we developed a peptide-based, self-assembling and self-adjuvanting nanoparticle vaccine delivery platform.

Methods: In this delivery platform, a Mtb-derived peptide epitope, a HLA-E binding peptide and a 15-leucine moiety were conjugated into a linear peptide construct with the ability to self-assemble into nanoparticle. A total of 6 Mtb epitopes were selected to formulate the BCG booster multiepitope vaccine termed PNx6. The immunogenicity of PNx6 was evaluated in a murine model of TB using ELISA, ELISpot, FACS and multiplex assays, and its protective efficacy was determined in the C57BL/6 mouse model of aerosol Mtb infection.

Results: In vivo experimentation demonstrated that a subcutaneous boost of parenteral BCG vaccinated with PNx6 was safe and induced 350 folds higher production of peptide epitope-specific antibodies in serum and ~10 folds greater numbers of IFNγ producing cells in both spleen and lung compared to BCG only vaccination. PNx6 boost also led to a significant increase in multifunctional T cells in lung and spleen. Furthermore, the protective efficacy of BCG boosted with PNx6 was about 3 folds higher than BCG only.

Discussion and Conclusion: Our results demonstrate that a parenteral PNx6 boost for BCG vaccination enhances anti-TB immunity and leads to significantly improved protective efficacy in murine TB model. The versatility of this multiepitope self-assembling self-adjuvanting nanovaccine delivery platform and the interchangeability of individual vaccine building blocks with different antigens holds promise as a viable solution for mitigating the TB pandemic on a global scale.

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Conflicts of Interest

G.Z. is co-inventor on a patent application entitled “Self-assembling, self-adjuvating system for delivery of vaccines” filed by the University of Queensland (application number: WO/2021/138721, PCT/AU2021/050012). The remaining authors declare no competing interests.