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A multi-antigen subunit vaccine improves BCG efficacy in mice and non-human primates

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Introduction: Bacille Calmette-Guerin (BCG) is the only licensed TB vaccine. While BCG provides protection against childhood TB, its effectiveness wanes in adults responsible for most cases. Subunit vaccines, comprising a few mycobacterial antigens delivered with a platform, aim to improve BCG by boosting its immunity. We developed and tested two viral vectors expressing a five-antigen construct (5Ag), based on the Esx-5a secretion system of Mycobacterium tuberculosis (M.tb), to enhance BCG efficacy.

Methods: Mice received intranasal chimpanzee adenovirus (ChAdOx1.5Ag) and a systemic boost of modified vaccinia Ankara virus (MVA.5Ag), expressing PPE15, PE8, esxI, esxJ and Ag85A. Immunogenicity was assessed pre-infection and efficacy was evaluated four weeks post M.tb challenge. Non-human primates (NHP) were vaccinated with BCG in infancy (iBCG) and boosted with ChAdOx1.5Ag and MVA.5Ag (iBCG/ChAdOx1.MVA) after 3 years. A second group of adult NHP, received BCG at 2.5 years (aBCG) and boosted as above 12 weeks post BCG (aBCG/ChAdOx1.MVA). A comparator group of NHP received iBCG and was boosted with aBCG (iBCG/aBCG). All NHP were infected with M.tb to evaluate efficacy.

Results: Vaccination of mice with ChAdOx1.5Ag-MVA.5Ag resulted in the induction of robust lung and spleen immune responses to all five antigens. A significant improvement in BCG-induced protection was observed in the lungs and spleen of vaccinated compared to naïve mice. In NHP, vaccine specific immune responses were detected for all antigens and to PPD-T following all vaccinations. Significantly improved total pathology scores were observed in the iBCG/ChAdOx1.MVA group, with a trend for other efficacy outcomes in this and the aBCG/ChAdOx1.MVA group. No improvement in pathology scores were observed in the iBCG/aBCG group compared to iBCG alone.

Conclusion: The above data show that ChAdOx1.5Ag-MVA.5Ag vaccine combination is immunogenic and can improve the efficacy of BCG administered in infancy.

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Conflicts of Interest
None