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Driving innovation from discovery to access

Prior BCG vaccination protects against subsequent aerosol BCG challenge in UK adults

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The absence of validated immune markers for protection, combined with an incomplete understanding of immune responses triggered by Mycobacterium tuberculosis (M.tb) infection, presents significant hurdles in TB vaccine development. Using a controlled human infection model could aid early vaccine development and identification of potential immune protection markers.

In our research, we employed live attenuated Mycobacterium bovis (M.bovis) Bacille Calmette-Guérin (BCG) as a surrogate for M.tb. Our studies have shown that prior BCG vaccination alters mycobacterial recovery following a subsequent intradermal BCG challenge. Subsequently, we utilised the aerosol route to deliver BCG to the lungs of healthy BCG-naïve adults to better simulate the natural route of M.tb infection. This aerosolised BCG was well tolerated and induced an immune response. We were able to recover BCG from the bronchoalveolar lavage fluid collected two weeks post-infection.

This research was expanded to investigate immune responses and BCG recovery from the lung mucosa following aerosol BCG infection in BCG-vaccinated healthy UK adult volunteers. The UK population is one where the protective efficacy of BCG is well-established.

Volunteers were challenged with an aerosol containing 1x10e7 CFU of BCG Danish 1331. Bronchoalveolar lavage (BAL) samples were collected on Day 14 post-challenge, and peripheral blood mononuclear cells (PBMCs) were collected at various time points following BCG infection.

BCG was quantified by MGIA in BAL samples. Both systemic and mucosal cellular and humoral immune responses in blood and lung mucosa were assessed using flow cytometry, ELISpot, and ELISA.

The aerosolised BCG infection of BCG-vaccinated healthy adults was well tolerated. Data on BAL BCG recovery, systemic, and mucosal cellular and humoral immune responses will be presented.

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Conflicts of Interest

None