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Strategically targeting mucosal immunity increases the effectiveness of tuberculosis vaccines

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Background: Research comparing intradermal (ID) and oral BCG in humans showed that ID-BCG had a strong systemic effect but had no effect on mucosal respiratory immunity. In contrast, oral BCG increased inflammasome activation, Mycobacterium tuberculosis (Mtb)-specific secretory IgA, and antigen-specific T lymphocytes in the bronchoalveolar lavage fluid. An alternative to an oral vaccine that can be readily delivered to the respiratory mucosa is an intranasal vaccine. Intranasal and aerosolized vaccines have been researched to target respiratory mucosal immunity as prime vaccines, but few have examined mucosal boosting after ID-BCG. We present here significant anti-Mtb protective capacity after mucosal immunization, as a boosting mechanism to ID-BCG.

Methods: To generate a safe and antigenic nasal vaccine H37Rv was inactivated using the SolaVAX technology which utilizes riboflavin, UVA & UVA light to modify the pathogen's nucleic acid structure. The specificity of this chemistry for nucleic acid modification prevents pathogen replication but preserves antigen integrity. SolaVAX-TB was administered with a liposomal immune stimulant containing TLR 3 and 9 agonists (MucV) designed to activate mucosal immunity. At 3 weeks old, C57BL/6 mice were intradermally vaccinated with BCG Pasteur. 45 days later, they got the first IN SolaVAX+MucV booster, and 45 days later, another dose. After 7 weeks animals were aerosolized with Mtb Beijing HN878; bacterial burden and pathology was evaluated 30- & 90-days post infection.

Results: Bacterial burden control of one log10, 30 days after infection was evidenced in the control group ID-BCG and ID-BCG+2xIN SolaVAX-MucV. ID-BCG alone lost all its protective ability 90 days postinfection, however ID-BCG+2xIN SolaVAX-MucV mice had 2 log10 fewer Mtb in the lungs.

Discussion: Despite their complexity, mucosal vaccinations have the potential to reduce Mtb transmission and offer protection against infection; therefore, we should invest in them.

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Conflicts of Interest
None