

Exploring Inhalation of Nebulized Bacteriophage D29 to Provide Prophylactic Protection against *Mycobacterium tuberculosis* Aerosol in a Preclinical Mouse Model

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Tuberculosis has led to more deaths worldwide than any other infectious disease for the past four years. The poor protection afforded by the Bacillus Calmette-Guérin vaccine and the emergence of multidrug-resistant and extensively drug-resistant tuberculosis strains warrant the development of alternative interventions. One such alternative is to prophylactically deliver aerosol containing bacteriophage D29, a lytic, parasitic virus receptor-restricted to infecting mycobacteria, including *Mycobacterium tuberculosis*, the causative agent of tuberculosis. In this study, a nose-only inhalation device is adapted for use with a vibrating mesh nebulizer to deliver large amounts of active bacteriophage D29 aerosol, ~1 pfu/alveolus, to the lungs of mice that subsequently receive either a high exposure, 50-100 cfu, or a low exposure, 5-10 cfu, of *M. tuberculosis* H37Rv via a whole-body aerosol exposure system. Bacteriophage D29 remained present and active in the lungs for at least 90 minutes after exposure. Interestingly, pre-treatment with bacteriophage D29 aerosol significantly decreased the burden of *M. tuberculosis* in the lungs of mice ($p < 0.05$) evaluated 24 hours post-challenge. These results suggest that high doses of nebulized bacteriophage D29 aerosol may be worth exploring as a means of providing extra protection to health care professionals regularly exposed to patients with active tuberculosis and to individuals in areas with high rates of tuberculosis transmission.