Conclusion
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Tuberculosis (TB), consumption or phthisis is the most dreaded scourge of mankind from the antiquity. It has been for many centuries, the most important of human infections in its global prevalence with devastating morbidity and massive mortality. Rising incidence of tuberculosis due to resurgence of AIDS and emergence of multi-drug resistant strains of *M. tuberculosis* have assumed frightening catastrophic dimension (Styblo, 1991). The existing vaccine against tuberculosis namely BCG (Bacillus Calmette and Guérin) has not been able to control TB. Keeping this controversial status in mind, we used *Mycobacterium habana* (*M. simiae* serovar I), as a vaccine strain for protection in mouse against experimental *M. tuberculosis* challenge.

We have chosen murine model, intravenous infection for the purpose of evaluation of protective efficacy of the immunogenic agent. A number of parameters have to be tested and verified to detect immunogenicity; a direct and indirect one through which the immunogenic agent must pass. One of the direct tests of measure the potency of strain is the protectivity test; other indirect tests are the ability of the immunogenic strain to generate the cell-mediated immune response. We have used eight parameters to evaluate our results. All the parameters of study have indicated that live *M. habana* is also offering protection against *M. tuberculosis*. 
The protective effectiveness of live *M. habana* has been the major finding by us for the murine model of tuberculosis. Using intravenous immunization protocols, we have identified that *M. habana* elicit substantial resistance when evaluated 30 days after a moderate dose (1 x 10^6 /mouse) of intravenous challenge. Intravenous exposure to *M. tuberculosis* (1 x 10^6) showed distinct organotropism as the bacilli got settled only in lung tissue. Liver and spleen showed changes that are seen in conditions of general stress and debility. Histologically, the protective effects of *M. habana* (10^6) in AKR mice became obvious after two months of challenge with *M. tuberculosis* (1 x 10^6). The density of AFB was much less along with a greater clearance of the acute inflammatory reaction, showing more prominent air spaces, suggesting restoration for alveolar septa in lungs of mice immunized with live *M. habana*. Examination of the lungs of unimmunized mice showed a marked acute inflammatory reaction (bronchopneumonia) with a large number of tubercle bacilli in groups in each oil immersion field. Macrophages fully packed with AFB were also seen in the lungs of control mice.

Cell mediated immune responses in tuberculosis are orchestrated to involve several phenotypic subsets, multiple mechanisms of antigen recognition and distinct effector functions. Phenotypically T cells contribution to protective immunity in TB includes CD4^+, CD8^+ and DN (double negative) cells and expresses either α/β or γ/δ TCRs. Both peptide and non-peptide antigens can be recognized by T cells, in the context of polymorphic and non-polymorphic antigen presenting molecules. Finally, depending on the functional subset, T cells can contribute to protective immunity by distinct mechanisms. The traditional concept that T cells confer immunity solely by secreting Th1 cytokines that activate the infected host cell to kill the pathogen has been extended by recent studies demonstrating that lysis of the infected targets as well as the direct killing of intracellular bacteria by CTLs are also involved in the T cell response to mycobacterial infection. In conclusion, this study confirms that CD8^+ as well as CD4^+ T cells are involved in host immune responses to *M. habana*. Both T cell subsets displayed protective effects in the spleens. These results cannot be extrapolated to the role of CD8^+ T cells in *M. tuberculosis* infection.

Our evaluation of the immune response elicited by vaccination with the live *M. habana* suggests that the superior protection afforded by *M. habana* in the mice model
may be due to its capacity to induce a substantial cell-mediated response with a predominant Th1 phenotype in the spleens of the vaccinated animals. The cytokine based ELISA data clearly shows that *M. habana* elicits a Th1-biased immune response, because an elevated IFN-γ and IL-2 response and a relatively low IL-4 and IL-10 response were detected in the spleen of *M. habana* vaccinated mice. Live *M. habana* induced more or less similar levels of IFN-γ as compared to BCG as reported by other workers.

There is an increasing interest in obtaining an attenuated *M. habana* strain to be used as a live vaccine in immunocompromised hosts. One approach to this problem would be to create *M. habana* auxotrophs. An ideal vaccine might be a double mutant in which the probability of reversion to a fully viable organism is remote and which is attenuated in the host as was reported in the case of BCG (Bloom and Fine, 1994).

These real possibilities for improving and refining live vaccination against this important human pathogen strongly suggest that this approach could eventually contribute to the global control of pulmonary tuberculosis. Further study is needed to modify live *M. habana* so that it reduces the extent of lesions completely but also prevents infection and/or enhances elimination of the organism and eventually contribute to the global control of pulmonary tuberculosis.