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Analysis of Anti-Tuberculosis Immune Response Induced in Lungs by Intranasal Immunization with Mycobacterium indicus pranii

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Abstract : Mycobacterium indicus pranii (MIP) is a saprophytic mycobacterium. It is a predecessor of M. avium complex (MAC). Whole genome analysis and growth kinetics studies have placed MIP in between pathogenic and non-pathogenic species. It shares significant antigenic repertoire with M. tuberculosis and have unique immunomodulatory properties. MIP provides better protection than BCG against pulmonary tuberculosis in animal models. Immunization with MIP by aerosol route provides significantly higher protection as compared to immunization by subcutaneous (s.c.) route. However, mechanism behind differential protection has not been studied. In this study, using mice model we have evaluated and compared the M.tb specific immune response in lung compartments (airway lumen / lung interstitium) as well as spleen following MIP immunization via nasal (i.n.) and s.c. route. MIP i.n. vaccination resulted in increased seeding of memory T cells (CD4+ and CD8+ T-cells) in the airway lumen. Frequency of CD4+ T cells expressing Th1 migratory marker (CXCR3) and activation marker (CD69) were also high in airway lumen of MIP i.n. group. Significantly high ex vivo secretion of cytokines- IFN-□, IL-12, IL-17 and TNF-□ from cells of airway luminal spaces provides evidence of antigen-specific lung immune response, besides generating systemic immunity comparable to MIP s.c. group. Analysis of T cell response on per cell basis revealed that antigen specific T-cells of MIP i.n. group were functionally superior as higher percentage of these cells simultaneously secreted IFN-gamma, IL-2 and TNF-alpha cytokines as compared to MIP s.c. group. T-cells secreting more than one of the cytokines simultaneously are believed to have robust effector response and crucial for protection, compared with single cytokine secreting T-cells. Adoptive transfer of airway luminal T-cells from MIP i.n. group into trachea of naive B6 mice revealed that MIP induced CD8 T-cells play crucial role in providing long term protection. Thus the study demonstrates that MIP intranasal vaccination induces M.tb specific memory T-cells in the airway lumen that results in an early and robust recall response against M.tb infection.

Keywords : airway lumen, Mycobacterium indicus pranii, Th1 migratory markers, vaccination
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