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Self-adjuvanting promiscuous peptide of *Mycobacterium tuberculosis* augments polyfunctional Th1 and Th17 cells and evokes better protection and endurance of memory T cell response than BCG

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In tuberculosis-endemic population, the main reason for the failure of BCG vaccine is the obstacle caused by non-tuberculous mycobacteria and helminths in its processing and presentation. Usually, peptides do not require extensive antigen processing since they can bind to major histocompatibility complex molecules and therefore can be directly presented to T cells. As a result, peptide vaccines can surmount the problems associated with BCG failure. It is well-established fact that not only adaptive but also innate immunity plays a crucial role in protection against tuberculosis. Hence we have constructed a novel lipopeptide vaccine by linking promiscuous CD4 and CD8 epitopes of Mycobacterium tuberculosis to Pam2Cys, a Toll like Receptor-2 agonist. This lipopeptide has unique property of self-adjuvanting and concurrently activating both innate and adaptive immunity. The vaccine binds directly to MHC I and MHC II molecules and TLR-2. It stimulates dendritic cells to secrete cytokines, upregulates the expression of costimulatory molecules and significantly augments their ability to present antigen to T cells. Further, the vaccinated animals impart robust and enduring memory Th1 and Th17 response. The protection observed is significantly better than BCG. This lipidated-peptide vaccine is unique since it overcomes MHC barriers and evokes immune response irrespective of HLA polymorphism in human. This vaccine has enough potential to induce long-lasting protection against Mycobacterium tuberculosis. Therefore it can be a potent future vaccine candidate for controlling tuberculosis.

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