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Microbiology Congress 2018: Evaluation of immune response against live recombinant Mycobacterium smegmatis expressing Mycobacterium tuberculosis proteins in mice - Hanady Amoudy - Kuwait University, Kuwait

Hanady Amoudy
Kuwait University, Kuwait

Tuberculosis remains a major health problem responsible for 8-10 million new cases and 1.3 million deaths annually. Until today, the only approved vaccine is BCG which has been used since 1921 and provides variable efficacy in adults around the world probably because it is void of some immunodominant key antigens of Mycobacterium tuberculosis. Development of non-pathogenic recombinant constructs delivering Mycobacterium tuberculosis-specific proteins antigens provides the chance to evaluate candidates to be included in diagnostic tools and preventive vaccines. PE35, esxA, esxB and Rv3619 are among the major antigenic proteins of Mycobacterium tuberculosis with vaccine potentials. For this reason, we are introducing these Mycobacterium tuberculosis genes in Mycobacterium smegmatis and evaluating the immune response against these recombinant constructs in mice.

Cellular mediated immune response of Th1 type, characterized by production of INF-γ cytokine, is associated with protection against the infection. On the other hand, Th2 type of immune response characterized by production of IL-5, Th17 characterized by production of IL-17 and Treg characterized by production of IL-10 are associated with progressive pathological tuberculosis infection. For this, mice were immunized with Mycobacterium smegmatis recombinant constructs and their splenocytes were cultured and assayed for various cytokines to analyze the type of immune response provoked against the introduced antigens. Results from our experiments showed an elevated ratio of Th1:Th2 response in the case of Rv3619 only and not the others.

Mycobacterium bovis Bacille Calmette-Guerin (BCG), a live, attenuated mycobacterial strain first utilized in humans in 1921 remains currently the sole vaccine available against tuberculosis (TB) but its protection is extremely variable. While effective against the severe sorts of the disease in children, BCG displays limited effects on adult pulmonary TB and transmission of the causative agent, tubercle bacillus (MTB).Hence, and improved vaccines against TB are desperately needed. Mycobacterium smegmatis may be a rapidly growing saprophyte, ready to propagate one generation every 1–3 h. It is non-pathogenic and commensal in humans and can act as a powerful cellular immune adjuvant. M. smegmatis also has a number of properties that renders it an effective vaccine vector. This fast-growing Mycobacterium is helpless to capture phagolysosome maturation and cannot evade intracellular killing. Moreover, its rapid clearance by the host differs from that of M.

tuberculosis or even the vaccine strain BCG M. smegmatis can activate dendritic cells and induce CD8-mediated immune responses, and immunization with recombinant M. Smegmatis has been shown to get more durable memory T cells as compared to intramuscular DNA vaccination . These observations encourage further development of mycobacteria as efficient recombinant vaccine delivery vectors. Aside from having an efficient delivery vector, the choice of an immunogenic target antigen is also important for developing a successful vaccine. The heparin-binding hemagglutinin (HBHA) may be a mycobacterial cell surface protein that mediates adhesion to epithelial cells which has been implicated within the dissemination of M. tuberculosis from the site of primary infection.

The lymphocytes from healthy human individuals infected with M. tuberculosis produce high levels of HBHA-specific interferon-γ (IFN-γ). Protective immunity convinced by methylated HBHA is like that afforded by vaccination with BCG, and DNA vaccination with the HBHA gene has resulted in both HBHA-specific antibodies and IFN-γ production. Recombinant HBHA which has no methylation produced in Escherichia coli isn't immunogenic. Methylation of HBHA is required for the complete immunological properties of the protein. It has been proved that HBHA produced in recombinant M. smegmatis (rMS) can express the immunogenic methylated sort of HBHA.

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