Characterization of the immunoreactive mycobacterial proteins and application for developing the gamechanger tuberculosis vaccine

Hwa-Jung Kim

Department of Microbiology, College of Medicine, Chungnam National University

Tuberculosis (TB) caused more than 1.6 million deaths in 2021 and has remained one of the most severe infectious diseases in Korea. The efficacy of BCG, the only approved vaccine against TB, is variable: although it prevents infants from severe forms of disseminated TB, it does not protect against pulmonary TB in adults. BCG has been used in humans since 1921, but a vaccine with superior efficacy to BCG has not been developed.

The WHO has proposed three strategies for TB vaccine development. (1) Prime vaccine for infants and young children: a BCG replacement vaccine with good safety and effectiveness. (2) BCG booster vaccine for adults: a vaccine that enhances the effect of weakened BCG, usually a protein-based vaccine using a viral vector or adjuvant system. (3) Immunotherapeutic vaccine: a vaccine that uses bacterial extracts or non-tuberculous bacteria (NTM) to shorten the treatment period or inhibit relapse. There are currently about 14 TB vaccines in clinical trials. There are two types of live-attenuated vaccines for BCG replacement in clinical trials. Many researchers have been focused on developing a subunit-based TB vaccine for BCG booster. However, no game-changer vaccines are providing complete prevention.

Different *Mycobacterium tuberculosis* (Mtb) proteins have been combined into a single multiplex chimera to produce vaccines with synergistic characteristics or novel functionality. ESAT-6 and Ag85B, both potent T cell-stimulating antigens, are the most extensively used proteins with a long track record in numerous TB chimeric vaccine candidates: ESAT6-Ag85B and H56 (ESAT6-Ag85B-Rv2660c). We have applied dendritic cells (DCs)- and macrophage-activating proteins with anti-mycobacterial activity to develop novel TB vaccines. Mtb survives within macrophages by arresting phagosomal maturation and impairing the maturation of DCs, preventing them from effectively stimulating T-cell proliferation. Therefore, the appropriate activation of antigen-presenting cells (APCs) and T cells enhancing intracellular bacterial killing is critical to eradicating Mtb.

We have identified and characterized the proteins activating DCs or macrophages, which elicit activation of T cells with anti-mycobactericidal activity, and developed various TB vaccines consisting of these proteins and T cell-stimulating antigens and evaluated their vaccine efficacy. We would like to present the results on the efficacy of the vaccines currently under development.