Study on booster vaccine targeting adult tuberculosis

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Eradication of tuberculosis (TB) is one of the key challenges facing humankind and is included in the SDGs. It is estimated that there will be 10.7 million new cases of TB worldwide in 2024, and that two billion people, or roughly one-quarter of the world's population, are infected with *Mycobacterium tuberculosis* (Mtb). Therefore, TB remains a major global public health problem, and the development of an effective and safe vaccine is indispensable to its resolution. Current BCG vaccine is effective against childhood TB, but its effectiveness is known to fade after approximately 15 years. Currently, the most important issue is the control of pulmonary TB in adults. Therefore, the development of a new TB vaccine for adults is underway worldwide. M72/AS01E vaccine has proceeded to Phase III trial in 2024. However, there is a concern that the amino acid sequence of the PPE18 protein, one of the two Mtb antigens used in the vaccine (PepA and PPE18), is highly diverse between strains, limiting the range of Mtb strains that can be covered by the vaccine. We focused on this point and selected Ag85B as an antigen that meets the following criteria: its sequence is highly conserved among strains, it has been reported to induce Th1 responses in humans, and it has been shown to have protective effects in animal models. DNA vaccines and viral vector vaccines incorporating the Ag85B gene have been shown to induce strong Th1-type immunity in mice and monkeys. Using a mouse Mtb aerosol infection model, we evaluated a vaccine consisting of two antigens including Ag85B, in combination with various adjuvants, and obtained candidate vaccine which have a significant booster effect when administered intranasally or intramuscularly. To develop the candidate vaccine, we have begun producing the recombinant fusion protein of the two antigens in CHO cells by a process compliant with investigational drug GMP.

In this project, we plan to compare booster effect between our candidate fusion protein- and M72-based adjuvanted vaccines in mouse infection model using clinical isolates from various Mtb lineages to demonstrate superiority of our antigen. In addition, we plan formulation study to finalize the pharmaceutical prescription. Finally, we will conduct macaque study to show booster effect in reduction of lung bacterial burden in Mtb-infected animals and obtain preclinical proof-of-concept.