Proof of concept in utilizing in-trans surface display system of Lactobacillus plantarum as mucosal tuberculosis vaccine via oral administration in mice

ABSTRACT

Background: Tuberculosis is one of the most common and deadliest infectious diseases worldwide affecting almost a third of the world's population. Although this disease is being prevented and controlled by the Bacille Calmette Guérin (BCG) vaccine, the protective efficacy is highly variable and substandard (0-80%) in adults. Therefore, novel and effective tuberculosis vaccine that can overcome the limitations from BCG vaccine need to be developed. Results: A novel approach of utilizing an in-trans protein surface display system of Lactobacillus plantarum carrying and displaying combination of Mycobacterium tuberculosis subunit epitope antigens (Ag85B, CFP-10, ESAT-6, Rv0475 and Rv2031c) fused with LysM anchor motif designated as ACERL was constructed, cloned and expressed in Esherichia coli Rossetta expression host. Subsequently the binding capability of ACERL to the cell wall of L. plantarum was examined via the immunofluorescence microscopy and whole cell ELISA where successful attachment and consistent stability of cell wall binding up to 4 days was determined. The immunization of the developed vaccine of L. plantarum surface displaying ACERL (Lp ACERL) via the oral route was studied in mice for its immunogenicity effects. Lp ACERL immunization was able to invoke significant immune responses that favor the Th1 type cytokine response of IFN-γ, IL-12 and IL-2 as indicated by the outcome from the cytokine profiling of spleen, lung, gastrointestinal tract (GIT), and the re-stimulation of the splenocytes from the immunized mice. Co-administration of an adjuvant consisting of Lactococcus lactis secreting mouse IL-12 (LcIL-12) with Lp ACERL was also investigated. It was shown that the addition of LcIL-12 was able to further generate significant Th1 type cytokines immune responses, similar or better than that of Lp ACERL alone which can be observed from the cytokine profiling of the immunized mice's spleen, lung and GIT. Conclusions: This study represents a proof of concept in the development of L. plantarum as a carrier for a non-genetically modified organism (GMO) tuberculosis vaccine, which may be the strategy in the future for tuberculosis vaccine development.

Keyword: In-trans approach; L. plantarum; M. tuberculosis vaccine; Surface display vaccine