Abstract

Over the past several years, there has been a concerted effort to develop a new vaccine against tuberculosis. The existing vaccine, Mycobacterium bovis Bacillus Calmette-Guerin (BCG), has been used for many decades, but meta-analysis of controlled clinical trials has revealed a lack of effectiveness in adults. In order to develop the oral vaccine that is stable during oral administration and is targeted to M cells, we prepared the poly-DL-(lactide-co-glycolide) ? H]PLG ? H^ microspheres containing BCG and LTB by a water-in-oil-in-water emulsion solvent evaporation method. The BCG strain was inoculated in Middlebrook 7H9 broth, and qualified by acid-fast staining, polymerase chain reaction, and Western blotting. The bioadjuvant Escherichia coli heat-labile enterotoxin subunit B (LTB) was expressed from prokaryotic expression system and qualified by GM1-enzyme-linked immunosorbent assay. Two prototypes of oral BCG were constructed in this project. One was the BCG-LTB conjugated vaccine, another was PLG-entrapped BCG-LTB microspheres. The microsphere showed a 41.7% entrapment ratio and a slow release manner. The immunogenicity of these prototype vaccines was further investigated by immunizing young and old mice. Our results showed that LTB indeed enhanced the humoral response of BCG in young and old mice. BCG-LTB conjugated vaccine induced specific IgG and IgA responses by oral route. The specific IgG and IgA were detectable in serum and lung wash. Furthermore, BCG-LTB conjugated vaccine induced the cellular-mediated immunity in young mice and induced the humoral-mediated immunity in old mice. The protective immunity of oral BCG vaccine remained to be proved in animal model. Taken together, our data suggested that oral BCG vaccine could be served as a formulation in the future for protecting human or animal from Mycobacterium infection.

Keywords：Bacillus Calmette-Guerin；Escherichia coli heat-labile enterotoxin；Oral vaccine；Microsphere