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The pharmacodynamic study and safety evaluation on tuberculosis DNA vaccines

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Abstract

The situation of TB and MDR-TB was severe, especially in developing countries. It is mainly due to lacking of effective vaccine and the funding to support the treatment of MDR-TB with second line anti-TB drugs. It was proved that DNA vaccine could be a novel and potentially powerful agent to prevent and treat disease. We have constructed various TB DNA vaccines used plasmid pVAX1 as vector, for example, DNA vaccines expressing proliferating antigens, latency antigens, cytokines, chimeric DNA vaccine (Ag85A/ESAT6, Ag85A/Ag85B) and mixed DNA vaccines. ESAT6, Ag85A, Ag85B DNA mainly elicit Th1 type immune responses, and MPT64 DNA elicit both humoral and cellular immune responses. ESAT6, Ag85A and Ag85B DNAs had better protective efficacy than MPT64 DNA. IFN-γ and IL-12 DNAs can enhance the protective efficacy of MPT64 DNA. Ag85A or Ag85A/Ag85B DNA alone or combined with RFP or PZA had better immunotherapeutic effects on drug-sensitive or MDR-TB mouse model, but Ag85A/ESAT6 DNA may cause the death of mice, which is mainly caused by hypersensitivity. The immune responses were enhanced in mice after vaccination intramuscularly with electroporation using Ag85A DNA. Electroporation improved the efficiency of gene expression and the immunogenicity of DNA, and can reduce10 times amount of DNA. 1mg TB DNA vaccines can elicit effectively immune responses in the primate animals. The cynomolgus monkey immunized by 0.2, 1, 5mg Ag85A DNA did not found any adverse reaction. The therapeutic Ag85A DNA vaccine and the combination with anti-TB drugs are the promising and affordable strategies for the treatment of MDR-TB disease in developing countries.

Biography

Xueqiong Wu, MD, Ph.D, The director of Army Tuberculosis Prevention and Control Key Laboratory, the vice head of Institute of Tuberculosis Research, the 309th Hospital of Chinese PLA, Beijing 100091, China. She does research on tuberculosis (TB) in the following directions: (1) New TB vaccines; (2) the new, rapid diagnostic techniques of TB, for example, mycobacterial species identification, rapid detection of *M. tuberculosis* and its drug resistance, risk prediction of anti-TB drug-induced hepatotoxicity, rapid diagnosis of bacterium-negative TB, etc.; (3) New Chinese herbal medicine.