AI-Guided Design and Preliminary Validation of Anti-Tuberculosis Subunit Vaccine

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To use AI technology to evaluate the structural proteins of the ESX-1 secretion system of Mycobacterium tuberculosis and experimentally assess the potential of EccA1 as a preventive DNA vaccine against tuberculosis. Methods: The immunogenicity of ESX-1 secretion system proteins was predicted using AI online software programs. The structural component antigen EccA1 protein, which showed excellent prediction results, was further evaluated for its biological characteristics. The EccA1 recombinant plasmid was transfected into the HEK293T cell line, and the expression of the EccA1 protein was verified by Western-blotting experiments and its cytotoxicity was assessed. The plasmid was injected intramuscularly to immunize zebrafish larvae, and the safety at the animal level of the recombinant plasmid was evaluated by observing the survival of zebrafish. The larvae were infected with Mycobacterium marinum 24 hours after immunization, and the change in the weight of the larvae was used as an evaluation index; adult fish were infected with Mycobacterium marinum 3 weeks after immunization, and the change in the bacterial load in the adult fish was used as an index to evaluate the preventive protective ability of pcDNA::Rv3868 against tuberculosis. Results: The EccA1 protein is predicted to be a secreted antigen. The antigen contains both strong B cell and T cell epitopes. pcDNA::Rv3868 can be highly expressed in eukaryotic cells and is safe for cell lines and zebrafish larvae. The weight of zebrafish infected with Mycobacterium tuberculosis after immunization with pcDNA::Rv3868 was higher than that of the negative control group, and the bacterial load in the body significantly decreased. Conclusion: EccA1 is a very promising target for an anti-tuberculosis vaccine candidate.

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