Live Recombinant Tuberculosis Vaccine
Tech ID: 23242 / UC Case 2000-377-0

BACKGROUND

Tuberculosis (TB) remains one of the world's most important infectious diseases. The causative agent, Mycobacterium tuberculosis, is the leading cause of death of any infectious agent. Each year, approximately 8 million people develop active pulmonary TB and 2 million die from this disease. The World Health Organization has declared TB a global health emergency, the first disease so designated. Moreover, multi-drug resistant strains of M. tuberculosis have been classified by the Centers for Disease Control and Prevention as potential weapons of bioterrorism. In the United States, the incidence of TB has been falling over the past half-century, but remains high in HIV-infected persons, the elderly, homeless and under-served populations, and immigrants from endemic areas. Moreover, the emergence of multidrug-resistant strains complicates TB control efforts and poses a health threat to the general public, especially immunocompromised individuals. In HIV patients, an infection strain that has developed resistance to available drugs results in a 50% death rate within 60 days. The current TB vaccine, M. bovis BCG, is a live attenuated form of the bovine TB pathogen developed in the 1900s. The vaccine is of modest efficacy but has been used in combination with drug therapy as a means to control the disease.

INNOVATION

UCLA researchers have developed a more effective TB vaccine utilizing a recombinant BCG strain (rBCG30), which over-expresses a 30-kDa protein, the most abundant protein produced by M. tuberculosis. Animal data have exhibited very promising results. rBCG30 vaccinated animals, when challenged by aerosol with a highly virulent strain of M. tuberculosis, exhibit much less lung, spleen and liver pathology, have ~10-fold fewer lesions, and 10-fold fewer M. tuberculosis organisms in their tissues than BCG-immunized animals. In addition, rBCG30 vaccinated animals exposed to TB infection survived significantly longer than BCG vaccinated groups. The possible virulence of rBCG30 has been compared with BCG, which has a well-established safety profile in humans. rBCG30 vaccinated animals displayed no adverse health effects and had the same rate of vaccine clearance as BCG. Additional safety studies investigating the possibility of genetic exchange between rBCG30 and other bacteria concluded that harmful genetic contamination is unlikely. The concept of inducing a strong protective immune response by immunizing with major extracellular proteins of an intracellular pathogen (of which M. tuberculosis is an example) has been demonstrated in the past in the case of Legionella pneumophila, the agent of Legionnaires disease. Immunization with either one of two major extracellular proteins of L. pneumophila was shown to significantly enhance the survival of animals challenged by aerosol with this pathogen. The findings of UCLAs rBCG30 studies lend further support to the extracellular protein hypothesis, which holds that the major secretory proteins of an intracellular pathogen are potentially highly potent immunoprotective molecules.

APPLICATIONS

This invention involves live rBCG30 for vaccination in humans and other mammals. However, this recombinant technology can also be used to produce recombinant vaccines overexpressing proteins of varying mycobacterial species. In addition, this invention offers strategies to create TB vaccines for immunocompromised individuals, such as persons with AIDS. Traditional BCG vaccines can cause disseminated disease in patients with weakened immune systems, which may be fatal. The UCLA Researchers have created strains of the TB vaccine whose growth is regulatable or self-limited. Hence, these strains should be safe in immunocompromised patients.

STATE OF DEVELOPMENT

Rigorous animal testing using guinea pigs, an animal highly susceptible to tuberculosis, has repeatedly demonstrated statistically significant efficacy as well as the safety of the rBCG30 vaccine. The Aeras Global TB Vaccine Foundation, in partnership with the David Geffen School of Medicine at UCLA, began the first clinical trial of the new tuberculosis vaccine in the US in early 2004. Fifteen volunteers have been inoculated with the new vaccine at the Center for Vaccine Development, St. Louis University, Missouri.

RELATED MATERIALS

- Recombinant bacillus calmette-guerin (BCG) vaccines expressing the Mycobacterium tuberculosis 30-kDa major secretory protein induce greater protective immunity against tuberculosis than conventional BCG vaccines in a highly susceptible animal model. Proc Natl Acad Sci U S A. (2000)

PATENT STATUS

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<tr>
<td>China</td>
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United States Of America
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South Africa

United States Of America

Russian Federation
Issued Patent 2266132 04/16/2001 2000-377

Additional Patents Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- New Recombinant Tuberculosis BCG Vaccine for Immunocompromised Patients and Others
- Recombinant Tuberculosis BCG Vaccine Elicits a Highly Protective Host Immune Response
- Method of Producing Novel Unmarked Recombinant Vaccine Vector for Tuberculosis
- Safe and Potent Vaccines against Tularemia
- Novel Vaccines Against Tularemia
- Improved Immunization Strategy Using Recombinant BCG Vaccines
- Novel Live Recombinant Booster Vaccine against Tuberculosis
- Nanoparticles For Specific Detection And Killing of Pathogenic Bacteria

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