Weill Cornell Medicine

Conditionally Replicating *M. bovis* for Treating Bladder Cancer and Tuberculosis

Lead Inventors:

Dirk Schnappinger, Ph.D.
Professor of Microbiology and Immunology,
Weill Cornell Medical College

Sabine Ehrt, Ph.D.
Professor of Microbiology and Immunology,
Weill Cornell Medical College

Business Development Contact:
Brian Kelly
Director, Technology Licensing

(646) 962-7041
bjk44@cornell.edu

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Background & Unmet Need

- The Bacillus Calmette–Guérin (BCG) vaccine is on of the most effective treatments for preventing tuberculosis (TB) and is formulated with a live attenuated strain of *Mycobacterium bovis*
- BCG administration has also been shown to be an efficacious treatment for bladder cancer, as the *M. bovis* bacteria triggers an immune response which also attacks cancerous cells
- However, live attenuated strains carry risk of infection in immunocompromised patients, and must be administered via the less-effective intramuscular route in TB vaccine patients
- **Unmet Need:** Method for precisely controlling the growth of *M. bovis* strains to avoid infection and enable alternative administration routes

Technology Overview

- **The Technology:** *M. bovis* BCG strains whose replication can be precisely controlled using a TetON/TetOFF system
- The TetON/TetOff system either requires a tetracycline to grow (TetOFF) or are efficiently killed in the presence of tetracyclines (TetON)
- The inventors constructed and validated both TetON and TetOFF *M. bovis* strains
- **PoC Data:** The constructed double lysin TetON *M. bovis* BCG strain provided similar protection to wild-type BCG in a Mtb challenge study in mice but was rapidly eliminated in the presence of doxycycline
- Similarly, the constructed double lysin TetOFF *M. bovis* BCG strain induced faster bacterial death and is rapidly eliminated from immunodeficient mice in the absence of doxycycline

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Dirk Schnappinger
Sabine Ehrt

Patents:
PCT Application Filed

Publications:
N/A

Biz Dev Contact:
Brian Kelly
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Technology Applications

- Development of a BCG vaccine for TB with reduced side effects
- Tunable alternative to *M. bovis* BCG strains currently used in bladder cancer immunotherapy

Technology Advantages

- TetON/TetOFF system allows precise control of conditions under which *M. bovis* bacteria can grow
- Allows to explore intravenous injection of BCG vaccine for TB immunization, which is likely more effective than the intradermal method
- Significantly reduces risk of infection in bladder cancer patients compared to current BCG vaccine

Supporting Data / Figures

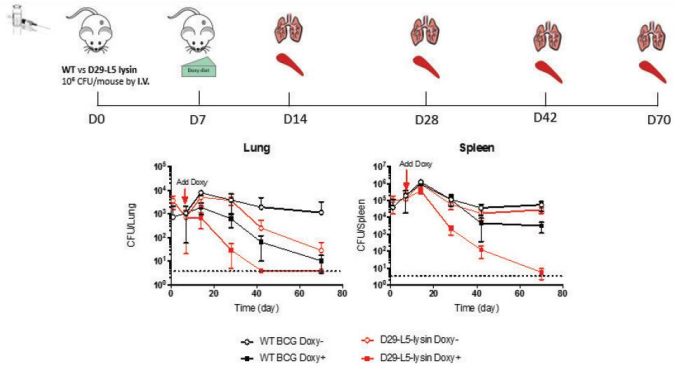

Figure 1: Doxycycline accelerates elimination of a BCG double-lysin TetON strain compared to WT BCG, providing a means of reducing risk of infection in immunocompromised individuals.

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