Modified bladder cancer treatment shows promise in animal studies

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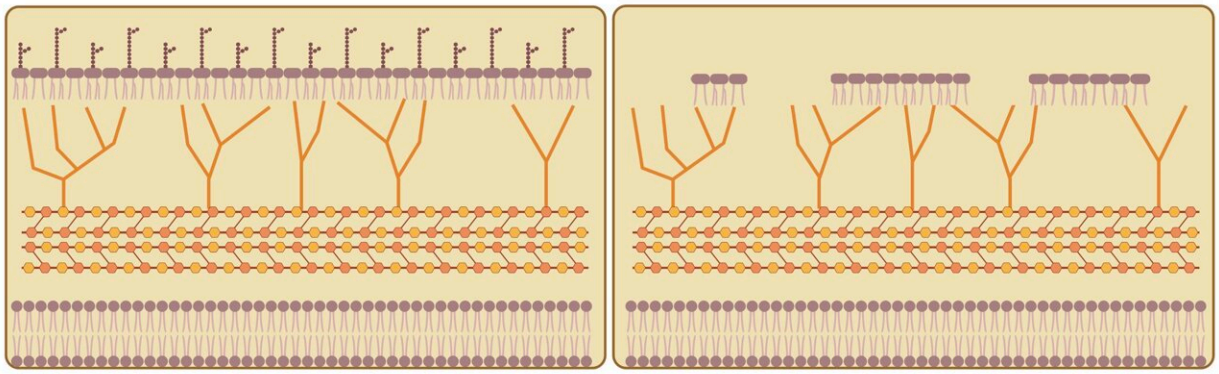

BCG is a live attenuated vaccine used to protect against the development of tuberculosis disease, and is also used as the gold standard treatment for bladder cancer. BCG contains an array of surface lipids that are highly inflammatory (top row). The Texas Biomed team “delipidated” the BCG vaccine by removing some, but not all, of these lipids from the outer layer (right panel). This approach enables the delipidated BCG vaccine to still function and elicit an immune response, but minimizes severe inflammation and tissue damage. Credit: Texas Biomed

A modified tuberculosis (TB) vaccine developed at Texas Biomed could help treat a form of bladder cancer, called non-muscle invasive bladder cancer, without strong side effects. Results in mouse models and human cells show promising results and pave the way for human clinical trials. The research, conducted in close collaboration with UT Health San

Antonio, was published online in June in the journal *Cancer Immunology, Immunotherapy*.

"I'm hopeful that with grant or industry support, we can move this right along to clinical trials and explore this treatment for patients who don't have options other than bladder removal," says Robert S. Svatek, MD, a urologic oncologist who treats bladder cancer patients at the Mays Cancer Center at UT Health San Antonio and is co-senior author of the research paper.

Each year in the United States, about 61,700 men and 19,480 women get bladder cancer, and about 17,100 deaths due to the disease occur (12,120 men and 4,980 women), according to the American Cancer Society. Bladder cancer is the fourth most common type of cancer in men. About 75% of bladder cancer cases are classified as non-muscle invasive, which means the cancer affects the tissue lining the inner surface of the bladder, but not the bladder muscle.

The Mycobacterium bovis bacille Calmette-Guérin (BCG) vaccine was developed for tuberculosis in the 1920s, and has also been used to treat non-muscle invasive bladder cancer since the late 1970s by stimulating an immune response at the cancer site. It was one of the first cancer immunotherapies and is more effective than chemotherapy for this type of cancer—but up to 84% of patients cannot tolerate the strong side effects and don't complete the three years of BCG treatment. When treatments fail, the last option is to remove the bladder, which leads to reduced quality of life.

"Imagine that there's this great drug that works really well, but you're not able to tolerate it," Dr. Svatek says. "We're talking about a very select group of patients, but for whom this really, really matters."

Texas Biomed Professor Jordi B. Torrelles, Ph.D. specializes in

tuberculosis, and has been working on a modified BCG vaccine for the past six years to improve TB treatment in the lungs. Specifically, Dr. Torrelles and his team remove certain lipids from the cell envelopes of the bacteria in the BCG vaccine. This "delipidated" vaccine still triggers the body to produce well-regulated immune responses, but reduces overzealous inflammation that causes severe tissue damage.

"It is more targeted and allows for a longer, slower response, which makes it more effective," Dr. Torrelles says.

Dr. Torrelles was able to team up with Dr. Svatek and Hong Dixon, Ph.D., a research scientist specializing in drug development at Southwest Research Institute (SwRI), to test the modified vaccine for bladder cancer as well.

Dr. Torrelles and his lab made two versions of the delipidated vaccine based on different TB bacteria strains: one known as sub-strain TICE, which is developed in the U.S., and one known as sub-strain Tokyo, which is developed in Japan.

Dr. Svatek's lab conducted the tests in a mouse model of bladder cancer and in cells collected from human cancer patients. They tested both delipidated BCG versions, and found that both were equally effective compared with the original BCG vaccine at killing the cancer, but that the modified Tokyo version performed better than the TICE version, with far less inflammation and minimal side effects.

"We were not expecting such a clear difference between the strains," says Dr. Torrelles, who has patented the modified vaccine for bladder cancer. Now, the collaborators plan to seek funding for a phase 1 clinical trial in human patients. SwRI is assessing manufacturing the modified vaccine for the clinical trial.

"We are excited to see this move forward and since it is based on an already U.S. FDA-approved treatment, we are hopeful it can proceed in a timely way," Dr. Torrelles says.

More information: Niannian Ji et al, Selective delipidation of Mycobacterium bovis BCG retains antitumor efficacy against non-muscle invasive bladder cancer, *Cancer Immunology, Immunotherapy* (2022). DOI: 10.1007/s00262-022-03236-y

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