

## **Bacterial biosurgery shows promise for reducing the size of inoperable tumors**

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Kansas City, MO. — Deep within most tumors lie areas that remain untouched by chemotherapy and radiation. These troublesome spots lack the blood and oxygen needed for traditional therapies to work, but provide the perfect target for a new cancer treatment using bacteria that thrive in oxygen-poor conditions. Now, researchers have shown that injections of a weakened version of one such anaerobic bacteria — the microbe *Clostridium novyi* — can shrink tumors in rats, pet dogs, and a human patient.

The findings from BioMed Valley Discoveries and a nationwide team of collaborators demonstrate that *C. novyi*-NT, a version without the ability to make certain toxins, can act as a new type of “biosurgery” to eat away tumors in hard to reach places. The bacteria excise tumor tissue in a precise, localized way that spares surrounding normal tissue. The study — which represents a new take on an approach first attempted a century ago — indicates that further testing of this agent in selected patients is warranted.

“We have encouraging signs that this bacteria could be used to treat certain inoperable tumors, and that could give hope to some patients who don’t have any other options,” said Saurabh Saha, M.D., Ph.D., a longtime cancer researcher at BioMed Valley Discoveries and senior author of the study. “But we are still in the early stages, and need to further assess the safety and efficacy of the treatment, as well as explore how well it works in combination with other cancer therapies.”

The study was published August 13, 2014, in *Science Translational Medicine*.

The idea of using bacteria to combat cancer dates back to the 1890’s, when cancer researcher William Coley noticed that some patients who developed postsurgical infections went into remission or were even cured of their disease. Despite the approach’s initial promise, progress was slow for the next century.

Over a decade ago Bert Vogelstein, M.D., a cancer researcher at the Johns Hopkins School of Medicine and one of the study co-authors, tested a number of microbes before identifying a particularly promising one called *Clostridium novyi*. Because *C. novyi* is exquisitely sensitive to oxygen, it would grow inside the oxygen-poor core of tumors but stop once it reached healthy tissue. In previous studies, Vogelstein and his colleagues tamed the bacteria further by removing its ability to make toxins and then injected it intravenously into laboratory animals. Though the bacterial treatment had dramatic effects in a third of the mice and rabbits, no complete responses were seen in dogs with naturally occurring cancers.

Dr. Saha and his colleagues at BioMed Valley Discoveries wondered if this failure was due more to the route of administration than to the therapy itself. One issue with intravenous delivery is the small proportion of spores that actually make it to the tumors. The researchers hypothesized that injecting the spores directly into tumors would not only overcome this problem, but might also trigger localized inflammatory and immune responses against tumor cells.

The researchers tested *C. novyi*-NT via directly injecting the bacteria into tumors in pet dogs with naturally occurring cancers and whose owners volunteered them for the trial. Each dog received between one and four cycles of the new treatment, consisting of a single injection of 100 million spores directly into the target tumor. Of sixteen dogs evaluated after treatment, three had significant shrinkage of their tumors and three had tumors that were completely destroyed.

The next step was to attempt the treatment in humans. The first patient to enroll in this Phase I investigational study was a 53-year old woman with retroperitoneal leiomyosarcoma whose disease, despite eight rounds of chemotherapy and radiation, had spread to her liver, lungs, abdomen, upper arm, and shoulder. The researchers injected 10,000 spores into the patient's metastatic right shoulder tumor. Within days, CT scans and biopsies demonstrated that the bacteria had infiltrated the tumor and had begun destroying tumor cells. Weeks later, a follow-up MRI showed that a significant amount of tumor had been destroyed. As a result of treatment, the patient's shoulder pain subsided and she was able to move her arm again.

Studies in other patients are currently underway at multiple sites to test the safety and efficacy of this new approach. Though these results are preliminary, the researchers believe that *C. novyi*-NT could potentially become part of a new arsenal of immunotherapies that prime a patient's immune system to fight off cancer.

"Earlier pre-clinical studies showed that in the process of destroying cancer tissue, *C. novyi*-NT generates a potent innate immune response which also contributes to the localized tumor destruction," said Dr. Saha. "The hope is that *C. novyi*-NT will be a useful adjuvant to the new immune checkpoint inhibitors that can block the ability of tumors to evade a host mediated immune response. It will be interesting to see if a combination of the two approaches could destroy tumors not just at the injection site, but also at any other sites where the cancer may have spread to throughout the body."

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### **About BioMed Valley Discoveries**

BioMed Valley Discoveries, Inc. is a for-profit, disease-related research and development organization, whose mission is to address unmet medical needs in areas that are considered too early, too unconventional or too unprofitable for traditional biotech and pharmaceutical companies. Operating since 2007, BVD advances its mission with commercial capabilities and resources typically unavailable to academic institutions. As a member of the Stowers Group of Companies, BVD receives its funding principally from an endowment supporting the Stowers Institute for Medical Research, a non-profit 550-person basic biomedical research organization. One hundred percent of the profits from BVD will also accrue to the benefit of the Stowers Institute. James Stowers, Jr., founder of American Century Investments, and his wife Virginia established BioMed Valley Discoveries and the Stowers Institute for Medical Research. Together, Jim and Virginia Stowers have endowed the Institute with over \$2 billion in donations, including a controlling interest in American Century Investments. Since it began operations in 2000, the Institute has received and spent over \$1 billion in dividends from its ownership stake in American Century Investments.