Can a modified poliovirus fight advanced prostate cancer too?

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Smita Nair (left) and Daniel George (right) are investigating the use of a modified polio virus to treat incurable prostate cancer.

Duke researchers made a big splash in the news last spring when 60

Minutes featured the success of early clinical trials using a modified poliovirus in the fight against a deadly form of brain cancer. Now, with funding from the Duke CTSA through the Duke Translational Research Institute (DTRI) Collaborative Pilot Award, an interdisciplinary team of researchers is on the path to apply this promising new therapy, known as PVSRIPO, in patients with incurable metastatic prostate cancer.

"The idea is that we have some success in brain tumor—now how do you move it into a non-central nervous system indication?" asked Smita Nair (link is external), a principal investigator of the new effort and a cancer immunotherapy researcher at Duke in the Dept of Surgery and director of the Immunotherapy Sciences Focus Group at the Duke Cancer Institute.

Survival rates for people with prostate cancer are excellent if doctors find the tumor early, before the cancer has spread or when it has spread only to nearby areas of the body. Once prostate cancer reaches distant locations, including lymph nodes, bones, or other organs, the outlook is grim. According to the American Cancer Society, the five-year survival in the case of advanced, metastatic diseases is just 28 percent.

With no hope for a cure, doctors attempt to manage the cancer and delay patients' deterioration with a long line of hormonal therapies, chemotherapies, and radiation, explains Dan George (link is external), a medical oncologist at Duke specializing in urologic cancers and a co-investigator on the new CTSA-supported poliovirus work.

"We desperately need new therapies to alter the course," he said.

More Than a Cancer Killer

George and Nair, along with colleagues including cancer biologist and virologist and inventor of the oncolytic poliovirus, PVSRIPO, Matthias

Gromeier (link is external) and urologist Brant Inman (link is external), think that one of those new therapies might just be poliovirus. PVSRIPO has been modified and tamed with the addition of a rhinovirus, the virus responsible for the common cold. The engineered virus specifically targets and destroys tumor cells while leaving healthy cells unscathed.

But the virus's destruction of cancer cells alone doesn't explain the long-term response they've seen in some patients with brain tumors.

"At first the thinking was that the virus is killing tumor cells," Nair said. "[But] there may be more happening."

Investigating that question about what else is happening is how Nair got involved in the poliovirus work in the first place. She is an expert in the field of cancer vaccines and immunotherapies, treatments designed to enlist the immune system in the fight against the disease. The Duke researchers now suspect tumors infected with poliovirus spew out proteins and other bits as they die, revving up the immune system and training it to fight the cancer in the event that it recurs locally or spreads.

Finding a treatment that combines destruction of tumors and immunotherapy for prostate cancer would be an exciting advance in medicine. In fact, prostate cancer is the only tumor type for which there is an FDA-approved tumor vaccine. The vaccine, called Provenge, doesn't cure prostate cancer, but it does train the immune system to help control it in some patients who have stopped responding to hormonal therapy.

Nair and George have been interested in immunotherapies for prostate cancer for many years. This current research aims to discover whether PVSRIPO might offer a new form of immunotherapeutic cancer treatment for previously incurable prostate cancer.

The first step for Nair, George and their colleagues is to test their hunch about PVSRIPO and its effects on the immune system in laboratory mice. Those studies involve mice with a fully functioning immune system that have been modified to express the poliovirus receptor. (Poliovirus normally isn't capable of infecting mouse cells). They'll be looking for signs that the PVSRIPO not only kills cancer cells, but that it also initiates immune events in the process that are capable of eliminating recurrent and metastatic disease.

Looking Ahead

Meanwhile, the team is preparing for a future clinical trial of the poliovirus treatment in patients with prostate cancer so that they can move quickly when the DTRI-funded results from the mouse studies and the needed funding for a new trial come in. They say that the ongoing studies in animals and future trials in prostate cancer will also help researchers to understand how the treatment works in patients with brain tumors. Those insights may help to improve the treatment and to explain why some patients respond to the poliovirus so well and others don't.

"This is why we're at Duke," George said. "This is the kind of work that can change a field and move a field in a direction it wasn't previously going in, and that's incredibly exciting for us as investigators. We've seen those long-term remissions in patients with brain cancer. In our prostate cancer patients, we'll be looking and hoping for that same kind of response."

Provided by Duke University