

Listeria-based booster improves vaccine's protection against recurring colon cancer

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Colorectal, pancreatic, esophageal and stomach cancers—some of the deadliest kinds of cancer—have high recurrence rates where the cancer comes back even after successful surgery or radiation treatment.

To combat these treatment-resistant cancers, Thomas University Jefferson researchers led by Adam Snook, Ph.D., an associate professor of pharmacology and experimental therapeutics, instead use what are, in essence, vaccines to train patients' immune systems to keep the [cancer](#) from coming back. Typically, the vaccines use either modified viruses or modified bacteria.

Now new research from Dr. Snook's lab shows in an [animal model](#) that using viral and bacterial vaccine approaches together is safe and far more effective at fighting the cancer than either approach by itself.

"The vaccine platforms are not unique," says Dr. Snook who is also a researcher at the Sidney Kimmel Cancer Center—Jefferson Health. "But nobody's put them together into a [combination vaccine](#), yet that's when we saw the immune response really take off."

In previous work, Dr. Snook and his team used a modified form of a common virus known as adenovirus as the backbone of a cancer vaccine that trains patients' immune systems to identify and attack a unique colorectal cancer molecule called GUCY2C (pronounced goosey-toosey). This vaccine treatment, dubbed Ad5.F35-GUCY2C, is [currently in Phase II clinical trials](#).

Although the adenovirus-based vaccine approach stimulates a highly effective immune response in patients, the effect doesn't last. To create the best possible immune response, vaccines often require additional doses. However, once introduced, the body becomes familiar with the adenovirus and as a result does not produce the same kind of immune response with additional doses. To keep the primed immune system pumping out cancer-fighting immunity, the body needed a different kind of booster.

Dr. Snook and his team turned to a bacteria-based vaccine approach using a modified form of *Listeria monocytogenes* that is unable to cause illness in mice or people. Unlike the adenovirus platform, the *Listeria* approach is not great at creating an immune response, but excels at boosting a response, even with additional doses.

Plus, "it's really good at infecting a particular kind of immune cell called antigen presenting cells that's critical to generating an effective immune response against the cancer," says Dr. Snook.

That's when they had the idea to combine the two platforms. When the researchers used the adenovirus-based vaccine to first prime the animals' immune systems and then later boosted it with the *Listeria*-based vaccine, [immune cells](#) that attack [cancer cells](#) shot up more than 15-fold in the mice.

In a model of recurrent colorectal cancer that has spread to parts of the body beyond the colon, the

combination vaccine approach reduced metastases and increased survival in the animals, the researchers reported June 23rd in the journal *npj Vaccines*.

"Combining these two platforms together actually worked way, way better than either platform alone for creating an [immune response](#) targeting the cancer," Dr. Snook says.

The vaccine strategy also did not produce toxicity or inflammation in the animals indicating that the treatment was well-tolerated without unintended effects.

The findings have laid the groundwork to examine for the first time whether this combination could prevent cancers from coming back in patients. The Department of Defense recently awarded Dr. Snook, and colleague Babar Bashir, MD, an assistant professor of medical oncology at Jefferson, a "Team Science" grant to take the combination vaccine approach into a Phase I clinical trial. The researchers are working to manufacture the vaccine now and expect to begin enrolling patients next year.

The one-two hit of the combo vaccine platform also has implications for other cancers and even diseases such as HIV and malaria, where effective [vaccine](#) strategies have been difficult to produce.

"A platform like this could work really well for those diseases also," says Dr. Snook.

More information: Prime-Boost Immunization with Chimeric Adenoviral (Ad5.F35) and Listeria Vectors is a Safe and Effective Strategy for Cancer Immunotherapy., *npj Vaccines* (2022). DOI: [10.1038/s41541-022-00483-z](https://doi.org/10.1038/s41541-022-00483-z)

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