Bugs as Drugs: Engineered Gut Bacteria Show Promise Against Pancreatic Cancer

Researchers used an engineered strain of *Bifidobacterium longum* to deliver an immune-stimulating therapy directly inside tumors.

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Cancer immunotherapies have transformed treatment for many cancers, but pancreatic cancer remains especially difficult to treat. One major reason is that pancreatic tumors often create a "cold" tumor microenvironment, where the tumor prevents immune cells from mounting a strong attack.

In a new study published in Science Advances, researchers at the University of Chicago report a promising new strategy to overcome this barrier using BifidoSumIL-2, an engineered bacterial strain of Bifidobacterium longum, a probiotic bacterium naturally found in the gut, to deliver an immune-stimulating therapy directly inside tumors.

The treatment suppressed pancreatic tumor growth by selectively activating cancer-fighting T cells. The effects were further enhanced when combined with chemotherapy, radiotherapy or immunotherapy. The study highlights BifidoSumIL-2 as a potentially powerful approach for improving treatment response in pancreatic cancer.

A novel bacterial delivery strategy

"A big unmet medical need has been pancreatic cancer, and so that was going to be our mountain to climb," said Ralph Weichselbaum, MD, the Daniel K. Ludwig Distinguished Service Professor and Chair of Radiation and Cellular Oncology at the University of Chicago.

The new therapy, called BifidoSumIL-2, is designed to release a modified form of interleukin-2 (IL-2) inside tumors. IL-2 is a powerful immune molecule that activates T cells, which help the body fight cancer. However, traditional IL-2 therapy can cause harmful side effects and may also activate immune cells that suppress the antitumor response.

To address this, the team used SumIL-2, an engineered version of IL-2 designed to more selectively stimulate cancer-fighting T cells while limiting activation of regulatory T cells. By

placing SumIL-2 inside Bifidobacterium longum, the researchers aimed to concentrate the treatment directly within tumors.

The work required expertise across multiple fields, from microbiology and synthetic biology to oncology and immunology.

“This was a highly interdisciplinary effort,” said Mark Mimee, PhD, Assistant Professor of Microbiology at the University of Chicago. “We had to bring together people who understand bacteria, people who understand tumors, and people who understand the immune system to make something like this possible.”

Engineering the bacteria

Bifidobacterium was an attractive delivery vehicle because it thrives in anaerobic environments, meaning low-oxygen environments, a common feature of many solid tumors, including pancreatic tumors. Healthy tissues generally have higher oxygen levels, making them less favorable for bacterial growth.

“Bifidobacterium is an obligate anaerobe, so it doesn’t grow in the presence of oxygen,” Mimee said. After systemic injection, the bacteria are cleared from oxygen-rich healthy tissues but can become active in the low-oxygen regions of tumors.

This tumor-seeking behavior allows the bacteria to act like microscopic drug factories. Essentially, these little factories produce the SumIL-2 only on the tumor site where the drug is needed. The researchers noted that Bifidobacterium has a favorable safety profile in preclinical models and is already widely recognized as a probiotic organism. It is commonly found in yogurt, so it is generally recognized as a safe, off-the-shelf probiotic.

“Bifidobacterium is not the easiest organism to work with,” Mimee said. “It’s anaerobic, it grows slowly, and the genetic tools for manipulating it are much more limited compared to model bacteria like E. coli. A lot of the work was just figuring out how to reliably engineer it.”

Enhanced effects with combination therapy

In animal models, BifidoSumIL-2 selectively accumulated in tumors, activated immune responses, and slowed pancreatic tumor growth. The treatment also helped reshape the tumor microenvironment by increasing the activity of cancer-fighting CD8+ T cells.

The therapy became even more effective when combined with standard cancer treatments. Pairing BifidoSumIL-2 with chemotherapy, radiation therapy, or anti-PD-L1 immunotherapy further improved tumor control and survival compared with single treatments alone.

“This combination potential is one of the study’s most important findings; BifidoSumIL-2 not only works by itself — it works with radiotherapy, chemotherapy, and immunotherapy," Weichselbaum said.

Although the results are promising, BifidoSumIL-2 has not yet been tested in people. Future studies will need to evaluate long-term safety, possible off-target effects, durability of the immune response, and whether the bacteria can be delivered orally rather than by injection. Researchers are also interested in combining this approach with newer pancreatic cancer therapies, including KRAS inhibitors.

The study highlights a growing “bugs as drugs” strategy, in which engineered probiotic bacteria could provide a new way to deliver immune therapies directly into hard-to-treat tumors while limiting side effects elsewhere in the body.

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UChicago Medicine and the Biological Sciences Division continue to be at the forefront of cancer care and research. In April 2027, UChicago Medicine will open the AbbVie Foundation Cancer Pavilion, Chicago’s first freestanding cancer pavilion, to bring advanced diagnostics, innovative treatments, translational discoveries, and comprehensive support to patients and the community.

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