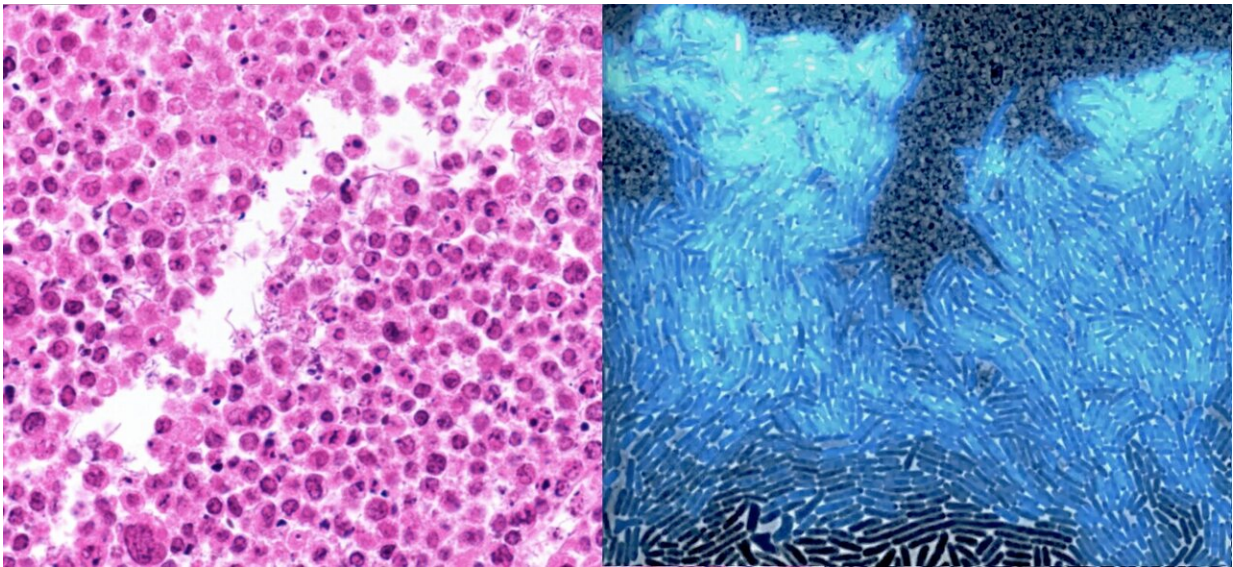


# Bacteria engineered as Trojan horse for cancer immunotherapy

July 3 2019

---



Histology image of bacteria growing within necrotic regions of lymphoma tumors (LEFT). Bacteria are programmed to undergo waves of growth and self-destruction leading to immunotherapeutic release (RIGHT). Credit: Hasty Lab/UCSD

The emerging field of synthetic biology—designing new biological components and systems—is revolutionizing medicine. Through the genetic programming of living cells, researchers are creating engineered systems that intelligently sense and respond to diverse environments, leading to more specific and effective solutions in comparison to current

molecular-based therapeutics.

At the same time, [cancer immunotherapy](#)—using the body's immune defenses to fight cancer—has transformed [cancer treatment](#) over the past decade, but only a handful of [solid tumors](#) have responded, and [systemic therapy](#) often results in significant side effects. Designing therapies that can induce a potent, anti-[tumor](#) immune response within a solid tumor without triggering systemic toxicity has posed a significant challenge.

Researchers at Columbia Engineering and Columbia University Irving Medical Center (CUIMC) announced today that they are addressing this challenge by engineering a strain of non-[pathogenic bacteria](#) that can colonize solid tumors in mice and safely deliver potent immunotherapies, acting as a Trojan Horse that treats tumors from within. The therapy led not only to complete tumor regression in a mouse model of lymphoma, but also significant control of distant, uninjected tumor lesions. Their findings are published today in *Nature Medicine*.

"Seeing untreated tumors respond alongside treatment of primary lesions was an unexpected discovery. It is the first demonstration following a bacterial cancer therapy of what is termed an 'abscopal' effect," says Tal Danino, assistant professor of biomedical engineering. "This means that we'll be able to engineer bacteria to prime tumors locally, and then stimulate the immune system to seek out tumors and metastases that are too small to be detected with imaging or other approaches."

The study was led in collaboration with Nicholas Arpaia, assistant professor of microbiology & immunology at CUIMC, and co-senior author on the publication. The team combined their expertise in synthetic biology and immunology to engineer a strain of bacteria able to grow and multiply in the necrotic core of tumors. When bacteria

numbers reach a critical threshold, the non-pathogenic *E. coli* are then programmed to self-destruct, allowing for effective release of therapeutics and preventing them from wreaking havoc elsewhere in the body. Subsequently, a small fraction of bacteria survive lysis and reseed the population, allowing for repeated rounds of drug delivery inside treated tumors. The [proof of concept](#) in programming the bacteria in this way was originally developed a few years ago (Din & Danino et al. *Nature* 2016). In the current study, the authors chose to release a nanobody that targets a protein called CD47.

CD47, a "don't-eat-me" signal, protects cancer cells from being eaten by innate immune cells such as macrophages and dendritic cells. It is found in abundance on a majority of human solid tumors and has recently become a popular therapeutic target.

"But CD47 is present elsewhere in the body, and systemic targeting of CD47 results in significant toxicity as evidenced by recent clinical trials. To solve this issue, we engineered bacteria to target CD47 exclusively within the tumor and avoid systemic side-effects of treatment," adds Sreyan Chowdhury, the paper's lead author and a Ph.D. student co-mentored by Arpaia and Danino.

The combined effect of bacterially induced local inflammation within the tumor and the blockade of CD47 leads to increased ingestion, or phagocytosis of tumor cells and subsequently to enhanced activation and proliferation of T cells within the treated tumors. The team found that treatment with their engineered bacteria not only cleared the treated tumors but also reduced the incidence of tumor metastasis in multiple models.

"Treatment with engineered bacteria led to priming of tumor-specific T cells in the tumor that then migrated systemically to also treat distant tumors," Arpaia says. "Without both live bugs lysing in the tumor and

the CD47 nanobody payload, we were not able to observe the therapeutic or abscopal effects."

The team is now performing further proof-of-concept tests, as well as safety and toxicology studies, of their engineered immunotherapeutic [bacteria](#) in a range of advanced solid tumor settings in mouse models. Positive results from those tests may lead to a clinical trial in patients. They are also collaborating with Gary Schwartz, CUIMC's chief of hematology/oncology and deputy director of the Herbert Irving Comprehensive Cancer Center, on clinical translation aspects of their work, and have started a company to translate their promising technology to patients.

**More information:** "Programmable bacteria induce durable tumor regression and systemic antitumor immunity." *Nature Medicine* (2019). [DOI: 10.1038/s41591-019-0498-z](https://doi.org/10.1038/s41591-019-0498-z)

Provided by Columbia University School of Engineering and Applied Science

Citation: Bacteria engineered as Trojan horse for cancer immunotherapy (2019, July 3) retrieved 26 April 2024 from <https://medicalxpress.com/news/2019-07-bacteria-trojan-horse-cancer-immunotherapy.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--