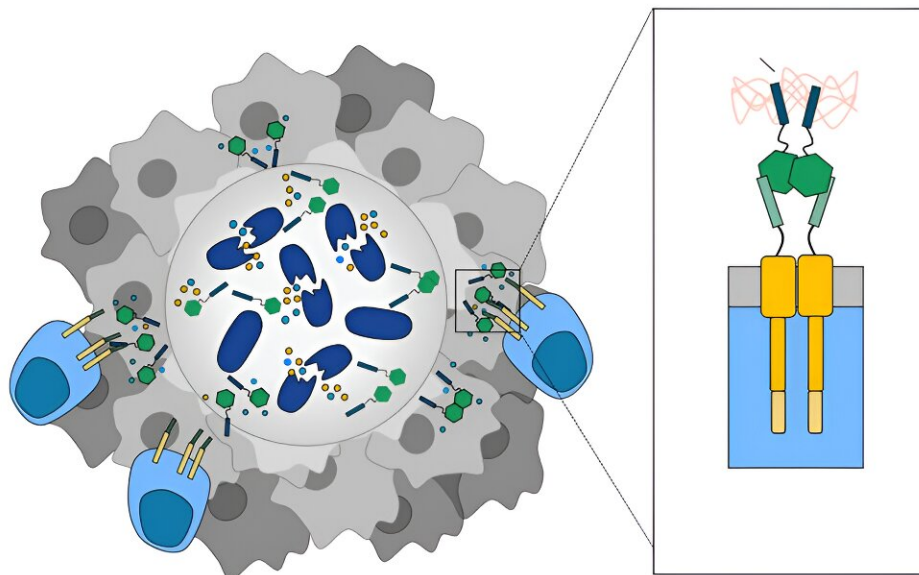


Engineered bacteria paint targets on tumors for cancer-killing T cells to see

October 12 2023, by Holly Evarts



Programmed bacteria acts as beacons that guide engineered T cells to destroy cancer cells in solid tumors. Credit: Synthetic Biological Systems Laboratory/Columbia Engineering

For several years, researchers have been successfully using chimeric antigen receptor (CAR) T cells to target specific antigens found on blood cells as a cure for patients with leukemia and lymphoma. But solid

tumors, like breast and colon cancers, have proven to be more difficult to home in on.

Solid tumors contain a mix of cells that display different antigens on their surface—often shared with [healthy cells](#) in the body. Thus, identifying a consistent and safe target has impeded the success of most CAR-T cell therapy for [solid tumors](#) at the first phase of development.

Breakthrough approach to fighting cancer

Synthetic biologists at Columbia Engineering report today a new approach to attacking tumors. They have engineered tumor-colonizing bacteria (probiotics) to produce synthetic targets in tumors that direct CAR-T cells to destroy the newly highlighted cancer cells.

"Our probiotic platform enables CAR-T cells to attack a broad range of tumor types," said Tal Danino, associate professor of biomedical engineering, who led the [study published today](#) in *Science*. "Traditional CAR-T therapies have relied on targeting natural tumor antigens. This is the first example of pairing engineered T cells with engineered bacteria to deliver synthetic antigens safely, systemically, and effectively to solid tumors. This could have a significant impact on the treatment of many cancers."

Painting targets on solid tumors

Danino's lab has essentially created a universal CAR-T cell that attacks a universal antigen, by programming the tumor-seeking bacteria to paint solid tumors with a synthetic marker that the CAR-T cells can recognize.

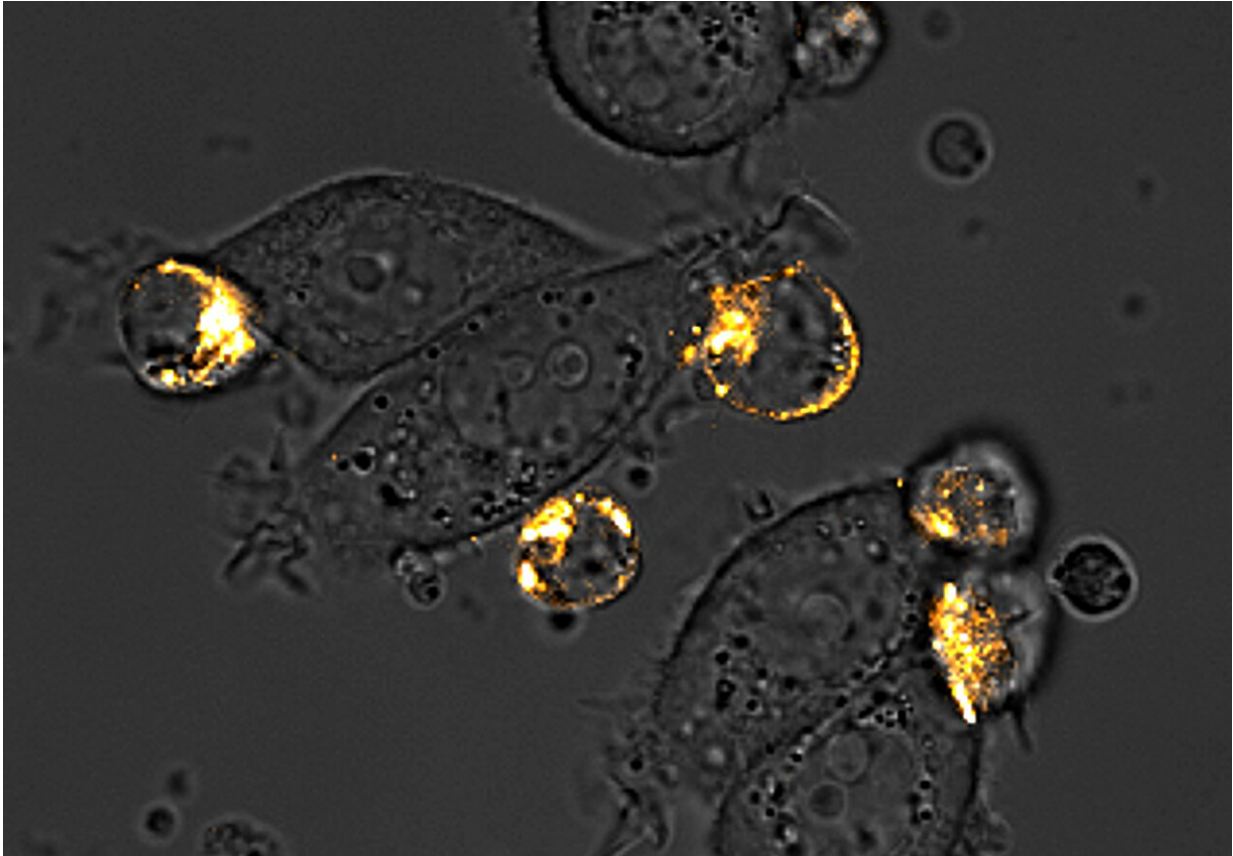
The researchers expect that with further refinements, this platform will enable the treatment of any solid tumor type without the need to identify

a specific tumor antigen—thus bypassing the need to generate a custom CAR-T cell product for each cancer type and each patient.

Engineering 'living medicines'

This probiotic-guided CAR-T cell (ProCAR) platform is the first time that scientists have not only successfully combined engineered probiotics with CAR-T cells, but have also demonstrated the first evidence of CARs responding to synthetic antigens produced directly within the tumor.

"Combining the advantages of tumor-homing bacteria and CAR-T cells provides a new strategy for tumor recognition, and this builds the foundation for engineered communities of living therapies," said the study's co-lead author Rosa Vincent, a Ph.D. student working in Danino's lab. "We chose to bridge the individual limitations of these two cell therapies by combining the best features of each—using bacteria to place the targets, and T cells to destroy the malignant cells."



Microscopy image of CAR-T cells attacking "painted" breast cancer cells.
Credit: Rosa Vincent and Thomas Savage

Safe and effective platform

The platform has proven to be safe and effective across multiple models of human and mouse cancers in both immunocompromised and immune-healthy mice. In fact, the study shows that human T cells in particular benefit so much from the presence of immunostimulatory bacteria within the tumor that their tumor-killing functions are further enhanced.

"Overall, our ProCAR platform represents a new strategy for enhancing the effectiveness of CAR-T cell therapy in solid tumors," said Danino,

who is also affiliated with the Herbert Irving Comprehensive Cancer Center and Data Science Institute. "While we're still in the research phase, it could open up new avenues for cancer therapy."

Next steps in an ongoing collaboration

This work was done as part of an ongoing collaboration with the laboratory of Nicholas Arpaia, assistant professor of microbiology and immunology at Columbia's Vagelos College of Physicians and Surgeons.

The team has [previously developed](#) bacteria that deliver immunotherapy payloads together. The researchers are continuing to refine their work and hope to begin [clinical trials](#) to fully assess the platform's safety and efficacy in human patients.

More information: Rosa L. Vincent et al, Probiotic-guided CAR-T cells for solid tumor targeting, *Science* (2023). [DOI: 10.1126/science.add7034](#).
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www.science.org/doi/10.1126/science.adk6098

Provided by Columbia University School of Engineering and Applied Science

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