Bacteria Programmed to Kill Cancer Cells in Mice

The innovative approach, which eliminated tumors, may lead to more effective therapies for people with cancer.

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Nicholas Arpaia, PhD (Damon Runyon Fellow ’13–’16), and Tal Danino, PhD, at Columbia University have genetically programmed E. coli bacteria to uncloak tumor cells and activate the immune system to attack them. The innovative approach eliminated tumors and distant metastases in mice and may lead to more effective therapies for cancer patients.

The researchers developed a strain of non-pathogenic bacteria that are designed to enter tumors, multiply until they reach a critical threshold and then self-destruct, releasing a potent immunotherapy. Subsequently, a few surviving bacteria reseed the population, allowing for repeated rounds of drug delivery inside treated tumors.

The tumors completely regressed in a mouse model of lymphoma and distant tumor lesions shrunk. This suggests that the treatment has the potential to stimulate the immune system to seek out metastases far from the treatment site.

The engineered bacteria that are injected into a tumor release a “nanobody,” a small form of an antibody, that targets a protein called CD47. Mutations in cancer cells can cause the CD47 gene to switch on, releasing a “don’t-eat-me” signal that helps them avoid elimination by the immune system. The cancer cells are then free to grow into malignant tumors. The nanobody binds to CD47, unmasking the cancer cells.

To avoid affecting normal cells with CD47 elsewhere in the body, the bacteria target CD47 exclusively within the tumor and avoid systemic side-effects of treatment.

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 tumors in mouse models. Positive results from those tests may lead to a clinical trial in patients.

Read more in the New York Times.

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