Armored CAR T Cells Deliver Cancer-Killing Molecules to Brain Tumors

"We have reason to hope that the basic principle could help glioblastoma patients. The next step is to work on a clinical trial to test this."

August 2, 2019 By Damon Runyon Cancer Research Foundation

CAR (chimeric antigen receptor) T cell immunotherapy has generated much excitement in the last two years, saving the lives of some blood cancer patients when other treatments have failed. Developing CAR T therapies for solid tumors has been far more challenging. That could be changing. Marcela V. Maus, MD, PhD (Damon Runyon-Rachleff Innovator '17-'20), and colleagues at Massachusetts General Hospital have turned CAR T cells into virtual armored vehicles, capable of launching deadly strikes against glioblastoma brain tumors.

More than 80% of mice with human glioblastomas grafted into their brains showed a complete response three weeks after treatment, meaning no evidence of tumors remained.

Maus designed a CAR T that homes in on an antigen called EGFRvIII only found on the surface of glioblastoma cells. The scientists then introduced a second gene into the CAR T cells, which produces a molecule called a BiTE (Bispecific T cell Engager) that is normally too large to cross the blood-brain barrier. This creative engineering takes advantage of CAR T's ability to cross the blood-brain barrier and deliver BiTEs directly to the tumor. The CAR T continues producing the short-lived molecules until the tumor is destroyed. "To our knowledge, this is the first time that BiTE-secreting CAR T cells have been described," said Maus.

The "bi" in bispecific refers to the two arms, each a fragment of an antibody, on these small molecules. Acting like a matchmaker, one arm grabs an antigen target on a tumor cell, and the other reaches out to a receptor on a T cell — a crucial player in the body's immune response. Once the two adversaries are in close proximity, the T cell is able to destroy the cancer cell. Without the help of the BiTEs, the T cells might have wandered through the bloodstream without ever being activated into tumor-killing mode. By forcing tumor cells and T cells together, bispecifics can provoke an immune attack on cancer even when the T cells don't recognize tumor antigens.

Previously, Maus tested the CAR T immunotherapy without the BiTE component in a clinical trial of 10 glioblastoma patients. T cells were collected from each patient, engineered to recognize and kill glioblastoma cells, and then the engineered CAR T cells were infused back into the patient. Though the CAR T cells were detectable in the brain tumor of patients, their tumors did not shrink

significantly. The cancer cells shed the “target” antigen, so the CAR T cells could no longer recognize them. “The clinical trial showed that there was a need to target additional antigens in glioblastoma, as well as overcome the defenses cancer cells put up in response to CAR T cells,” said Maus. “The mouse study addresses the shortcomings of the first CAR T design. We have reason to hope that the basic principle of combining the CAR T technology with the BiTE approach could help glioblastoma patients. The next step is to work on a clinical trial to test this.”

Published in Nature, July 22, 2019. Read More.

This post was originally published by Damon Runyon Cancer Research Foundation. It is republished with permission.

© 2026 Smart + Strong All Rights Reserved.
http://beta.docker.cancerhealth.com/blog/armored-car-t-cells-deliver-cancerkilling-molecules-brain-tumors