Researchers load CAR T cells with oncolytic virus to treat solid cancer tumors

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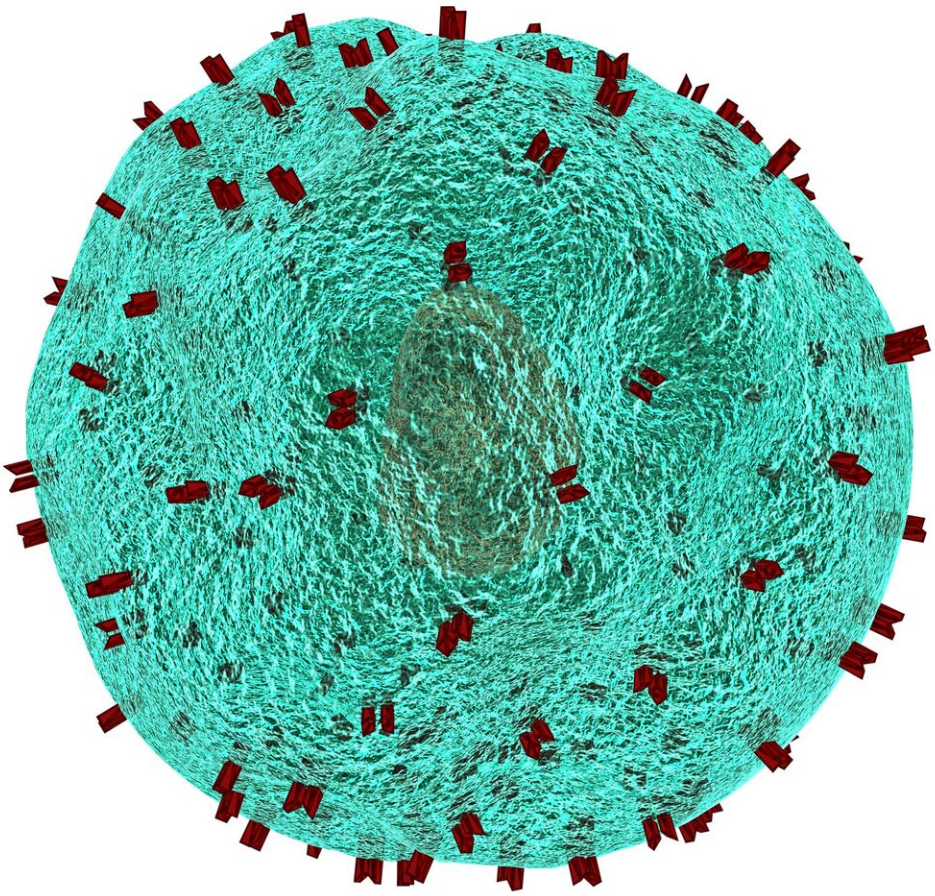

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Researchers at Mayo Clinic's Center for Individualized Medicine have devised an immunotherapy technique that combines chimeric antigen receptor-T cell therapy, or CAR-T cell therapy, with a cancer-killing virus to more effectively target and treat solid cancer tumors.

The combination approach, published in *Science Translational Medicine,* involves loading CAR-T cells, which are engineered to look for antigens on cancer cells, with an oncolytic virus. Oncolytic viruses are naturally occurring viruses that can infect and break down cancer cells. They either naturally replicate well in cancer cells or can be engineered to selectively target cancer cells.

The study suggests CAR-T cells can deliver the oncolytic virus to the tumor. Then the virus can infiltrate tumor cells, replicate to bust the cells open, and stimulate a potent immune response.

"This approach allows the tumor to be killed by the virus as well as by the CAR-T cells," explains Richard Vile, Ph.D., co-leader of the Gene and Virus Therapy Program within Mayo Clinic Cancer Center. "In addition, when the virus is delivered, it turns the tumor into a very inflammatory environment, which the patient's own immune system then sees and starts to attack."

The therapeutic strategy addresses two major challenges that make solid tumors difficult to treat with CAR-T cell therapy alone. First, the oncolytic virus can break down the molecular shield that some solid tumors use to avoid an immune system attack. Second, the virus can invade into the core of the cancer cells—a near-impossible feat for immune cells alone, which often lose their power in the attempt.

The researchers also found that the combination approach provided an immune memory phenotype against the tumor.

"By putting the virus onto the CAR-T, we activate them against both the virus and the tumor, and they acquire immunological memory," Dr. Vile says. "This allows us to give a boost with the virus at a later time point, which in turn makes the CAR-T cells wake up again and undergo additional rounds of killing the tumor."

Using mouse models, Dr. Vile and his team delivered the dual therapy intravenously to treat pediatric and adult high-grade glioma, as well as melanoma in the skin. They found that the combination therapy led to high cure rates in tumors in multiple sites without causing significant toxicity. They also found it resulted in apparent protection in the cured mice against tumor recurrence.

"Clinically, delivering the therapy systemically is a potential advantage because you could possibly treat patients with metastatic disease without having to inject each tumor," Dr. Vile explains.

Next, Dr. Vile emphasizes it will be important to be cautious about how well studies in animal models of cancer will translate into patient care.

"Nonetheless, we are hopeful that we will be able to take this strategy into clinical trials within a year or two," Dr. Vile says. "By doing such trials at Mayo Clinic, it will be possible to see if we can add a further level of efficacy of CAR-T cell therapy to the treatment of solid tumors of different types."

More information: Oncolytic virus–mediated expansion of dual specific CAR T cells improves efficacy against solid tumors in mice, *Science Translational Medicine* (2022). dx.doi.org/10.1126/scitranslmed.abn2231

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