

Engineering Immune Cells Within the Body

New approach could make CAR T-cell therapies more accessible for treating cancer and autoimmune diseases.

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Chimeric antigen receptor (CAR) T cell therapies involve taking immune cells, called T cells, from a patient and engineering them to make a protein that lets them recognize and attack the patient's cancer cells. CAR T cells have proven effective at treating cancers that arise from a different type of immune cell, called B cells. Since B cells are also involved in various autoimmune diseases, CAR T cell therapies may be able to treat these diseases, too.

But access to CAR T cell therapies is limited by several factors. Making CAR T cells is complex and costly, and can't currently be done on a large scale. Also, patients being treated with CAR T cells must first undergo chemotherapy to deplete their existing T cells.

One way to make CAR T cell therapy simpler and more accessible would be to make the CAR T cells within the patient's body. Researchers, led by Dr. Haig Aghajanian at Capstan Therapeutics and Dr. Carl June at the University of Pennsylvania Perelman School of Medicine, developed a way to do this using targeted lipid nanoparticles (LNPs). The results of their work, which was supported in part by NIH, appeared in [Science](#) on June 19, 2025.

LNPs are tiny spheres made of molecules like those that make up cell membranes. They can be used to carry a molecular cargo into cells. The research team wanted to create LNPs that targeted a specific type of T cell. To do so, they designed LNPs with an antibody that bound to a protein found on the surface of these cells. Then they loaded the nanoparticles with the genetic instructions needed to make the T cells recognize and attack B cells.

In laboratory studies, the targeted LNPs effectively reprogrammed T cells from both healthy donors and autoimmune patients into CAR T cells. CAR T cells from all donor types, as intended, killed B cells from the same donor.

The researchers then tested the LNPs in mice engrafted with human leukemia cells. The mice received five total doses of LNPs over a period of two weeks. Those who received low LNP doses had much slower tumor growth than untreated mice. In mice that received higher doses, tumors were almost completely cleared within a few days of the second dose.

The team next tested the LNPs in monkeys. Each monkey received three doses of LNPs, three days apart. The monkeys' B cell levels dropped within hours of the first dose and were close to undetectable after 24 hours. B cells levels began to recover after about three weeks and returned to normal levels within seven weeks. Most of the B cells that returned after the treatment were immunologically naïve, meaning that they didn't have a memory of prior infection. This suggests that the immune system had been "reset." Resetting the immune system could help prevent future autoimmune reactions.

The findings suggest that targeted LNPs might be a viable approach to creating CAR T cells in patients. Because the changes in the T cells are temporary, they avoid potential long-term risks that more permanent gene-editing methods may pose. This approach could lead to safer and more accessible CAR T therapies for treating a wider range of conditions.

"This approach offers a way to quickly and deeply deplete B cells using a transient, tunable, and fully off-the-shelf in vivo CAR-T technology. Eventually, we hope it could be used to treat autoimmune diseases and B cell cancers," Aghajanian says.

Capstan Therapeutics is now testing targeted LNPs in a phase 1 trial to evaluate safety, dosing, and other questions. More study will be needed before the treatment could be available in the clinic.

This [research summary](#) was published by the National Institutes of Health on July 15, 2025.