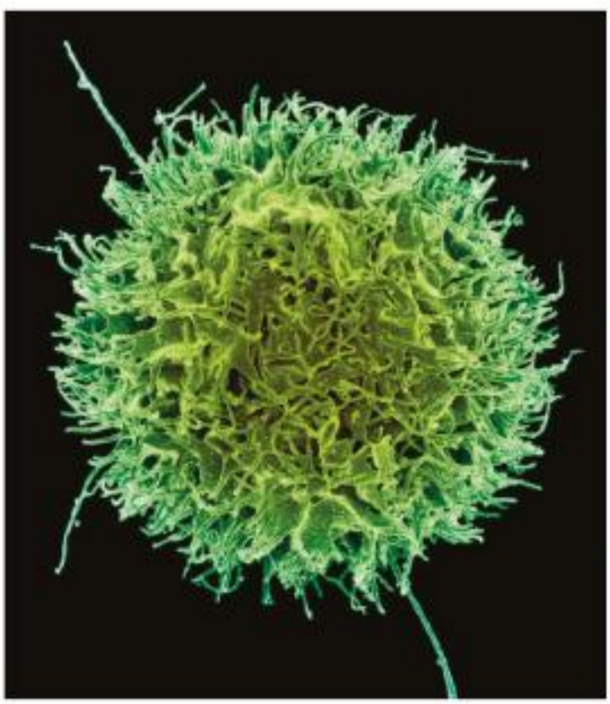
BOOSTED 'KILLER' CELLS SHOW PROMISE FOR AUTOIMMUNE DISEASE

Experimental treatment could offer a safer, cheaper alternative to CAR-T-cell therapies for some disorders.

By Heidi Ledford

Supercharged 'natural killer' cells could become a potent way to reset a disordered immune system — and thus quench some autoimmune disorders.

Results from two small clinical trials suggest that researchers can engineer natural killer cells — immune cells that destroy infected or diseased cells — to assassinate the renegade cells that produce antibodies against the body's own tissues. These 'autoantibodies' can damage tissues, fuelling autoimmune diseases such as lupus and systemic sclerosis.



A natural killer cell (artificially coloured).

"Natural killer cells have evolved to seek and destroy abnormal cells," says Nadir Mahmood, president of Nkarta, a biotechnology company in South San Francisco, California. "And if that's deep enough to drive an immune-system reset, then you can have the reconstitution of a healthy and naive immune system."

Findings from one trial were announced in June at the European Alliance of Associations for Rheumatology (EULAR) meeting in Barcelona, Spain. Results from the other trial were published on 24 June in the journal *Cell* (X. Wang *et al. Cell* https://doi.org/g9spcz; 2025).

Before the killers

This approach has its roots in cancer therapies that rely on another kind of immune cell, called T cells, that can be genetically engineered to recognize and kill tumours. The engineered cells use a protein called a chimeric antigen receptor (CAR) to identify their targets, and are therefore called CAR T cells.

CAR T cells can send some forms of blood cancer into remissions lasting more than a decade, and they have shown early promise against certain autoimmune disorders. But current therapies on the market are expensive and complicated to make: each treatment must be manufactured from the recipient's own T cells.

These factors mean that, at present, only about one-quarter of people in the United States who might benefit from CAR-T-cell cancer therapies can access them, says Katy Rezvani, who studies cell therapy at the University of Texas MD Anderson Cancer Center in Houston. "There are five times as many patients with autoimmunity as there are with cancer," she says. "So how are we ever going to be able to afford these expensive therapies for autoimmune disorders?"

Natural killer cells, however, can be taken from a blood donor and genetically modified to produce 'CAR NK' cells, which can be frozen and used to treat multiple people. Rezvani says that her colleagues at MD Anderson can make hundreds of doses of CAR NK cells from a single donation of umbilical-cord blood.

Perfect fit?

The first trials of CAR NK cells have been in cancer and have had mixed early results, says Mahmood. One possible limitation is that these cells are shorter-lived than are CAR T cells, says Max Qian, chief executive of Rui Therapeutics, a company in Nanjing, China, that is developing CAR-NK-cell therapies. "If the tumour comes back, you need the drug to still be in the body," he says.

But the cells' fleeting presence might not be a problem for treating autoimmune diseases. A brief treatment with CAR NK cells could be enough to wipe out autoantibody production, Qian adds, or a person could receive several doses of the treatment if needed. After that, the immune system could rebuild itself with a fresh population of antibody-producing cells that have not been triggered to make autoantibodies.

Late last year, Nkarta announced that it would end its efforts to make CAR-NK-cell cancer therapies and would instead focus on autoimmune disorders. "It seemed like CAR-NK-cell therapy was tailor-made for autoimmune disease," says Mahmood.

At the EULAR conference last month, Rui Therapeutics and its collaborators presented data from 27 people who had received CAR NK cells as treatment for the autoimmune disorder systemic lupus erythematosus, which can cause inflammation in the joints, kidneys, brain and other organs. All of the participants saw some improvement after treatment. Some participants have been followed for nearly two years after treatment and are still in remission.

Multi-target assassins

The CAR NK cells that these participants received targeted a single protein called CD19, which is made by many cells that produce antibodies. But in some autoimmune conditions, it might be necessary to also target a group of long-lived, antibody-producing cells that don't make CD19, says Anca Askanase, a rheumatologist at Columbia University in New York City.

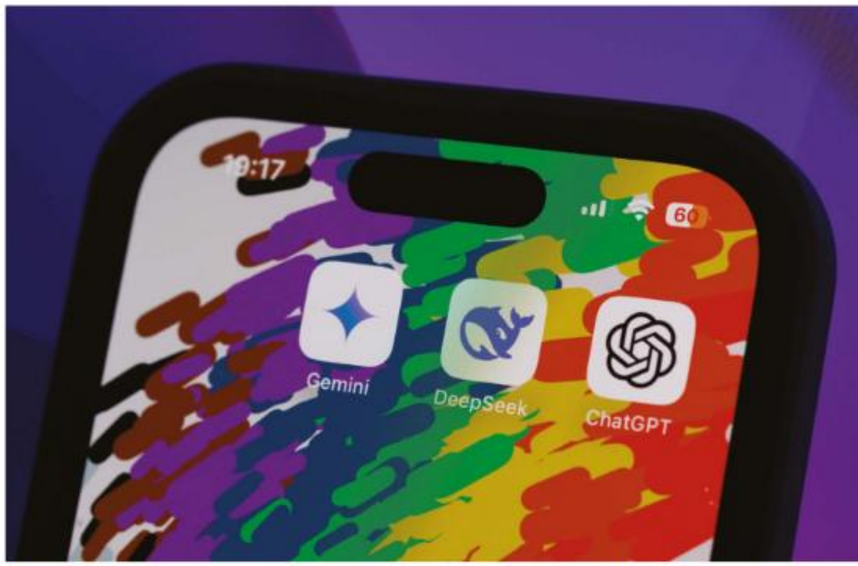
Researchers led by rheumatologist Huji Xu at the Naval Medical University in Shanghai, China, took that approach to treat a person with the autoimmune disease systemic sclerosis, which can cause the production of excessive amounts of scar tissue. This hardens the skin, blood vessels and other tissues.

The team engineered CAR NK cells that target both CD19 and a protein called BCMA, which is produced by the long-lived antibody-producing cells. After the treatment, the person's autoantibody levels dropped, the researchers reported in the *Cell* paper.

The CAR NK cells also seemed to reverse the hardening of the person's tissues, restoring normal skin and blood-vessel structure.

That finding was particularly remarkable, says Rezvani, because it raises hope that some damage caused by autoimmune disorders can be not only prevented, but also reversed. "The promise is there," she says. "Now we need more data."

ANDREY RUDAKOV/BLOOMBERG VIA GETTY



The AI tools Gemini and DeepSeek came behind OpenAI's o3 model in the league table.

OPENAI MODEL TOPS NEW AI LEAGUE TABLE FOR SCIENCE QUERIES

SciArena uses votes by researchers to evaluate large language models' responses on technical topics.

By Rachel Fieldhouse

An artificial intelligence (AI) model called o3, developed by the creators of ChatGPT, has been ranked the best AI tool for answering scientific questions in multiple fields, according to a benchmarking platform launched on 30 June.

SciArena, developed by the Allen Institute for Artificial Intelligence (Ai2) in Seattle, Washington, ranked 23 large language models (LLMs) according to their answers to scientific questions. The quality of the answers was voted on by 102 researchers. o3, created by OpenAI in San Francisco, California, was ranked the best at answering questions on natural sciences, health care, engineering and humanities and social science, after more than 13,000 votes.

DeepSeek-R1, built by DeepSeek in Hangzhou, China, came second on natural-sciences questions and fourth on engineering. Google's Gemini-2.5-Pro ranked third in natural sciences and fifth in engineering and health care.

Users' preference for o3 might stem from the model's tendency to give a lot of detail on the literature it cites and to produce technically nuanced responses, says Arman Cohan, a research scientist at Ai2. But explaining why