Understanding CAR-T cell therapy for cancer: Researcher explains how it works

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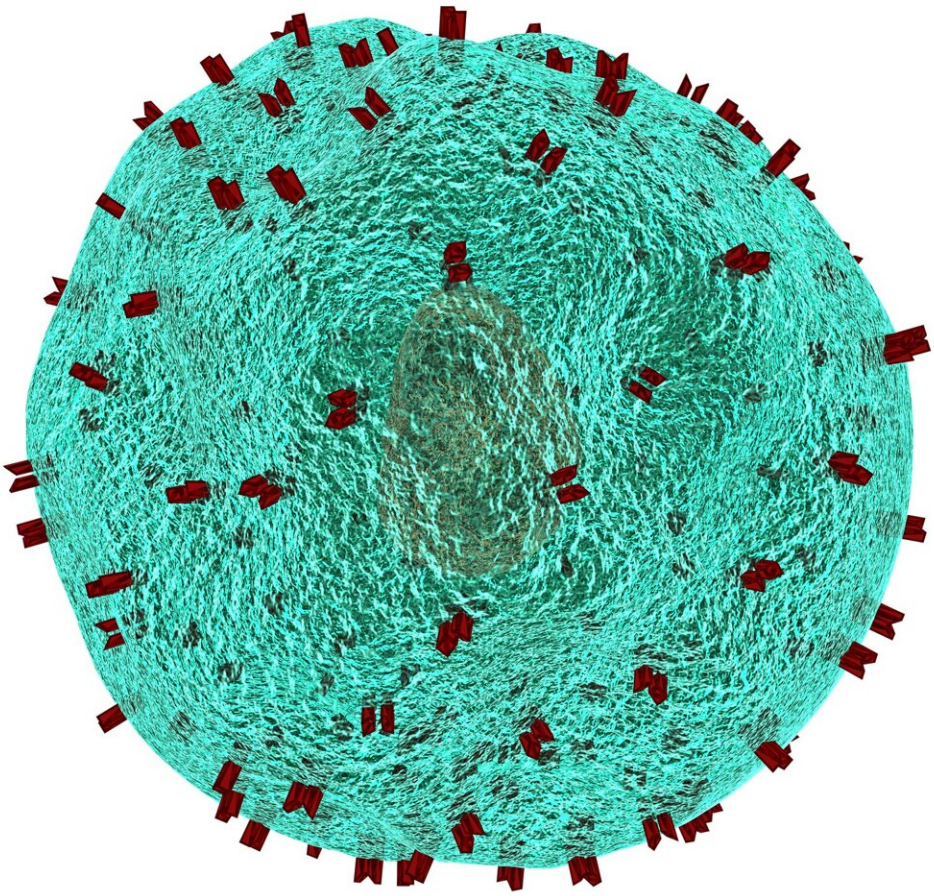

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For many doctors and researchers, immunotherapy that uses someone's own immune system to target and attack cancer cells is the next and best frontier of cancer treatment. Chimeric antigen receptor T-cell therapy, or CAR-T cell therapy, is one type of immunotherapy. Sometimes likened to a "smart drug" or "living drug," CAR-T cell therapy relies on genetically modified immune cells to recognize and destroy cancer cells. In this expert alert, Richard Vile, Ph.D., an immunologist and cancer researcher at Mayo Clinic in Rochester, Minnesota, explains how CAR-T cell therapy works, including the benefits, risks and realities of treatment.

Over the last decade, immunotherapy-focused research has expanded, and results point toward promising, less arduous cancer treatments. Some immune system-focused drugs, for example, have shrunk or eliminated tumors—even in people with advanced cancers.

"The holy grail of all cancer therapies throughout the years has been to develop a treatment that targets only cancerous cells and not normal or healthy cells," Dr. Vile says. "One of the reasons chemotherapy can be so toxic and unpleasant is that it is very rarely highly selective for the cancer cells, and as a result it can harm other cells. CAR-T cell therapy, in theory, only kills cancer cells, which makes the treatment much gentler on the body."

The U.S. Food and Drug Administration has approved CAR-T cell therapy for several conditions, including different types of B-cell lymphoma, some forms of leukemia and myeloma. Research is underway at Mayo Clinic to explore CAR-T's potential to treat diseases beyond cancer.

Like all immunotherapy, CAR-T cell therapy harnesses the power of the immune system—in this case, by using and modifying the body's T cells. As an important part of the immune system, T cells are a type of white blood cell that helps defend the body from infection and are thought to fight cancer.

To prepare these cells for targeted cancer treatment, T cells are collected from the body—typically through blood work—and are genetically treated in a lab. During this process, the T cells are modified to produce special receptors called chimeric antigen receptors (CARs). These CARs change the T cells in two important ways. First, the T cells can "see" certain antigens, called markers, on cancer cells they were previously blind to. Second, the CARs activate the T cell's ability to kill the cancer cells. In short, Dr. Vile says that CAR-T cell therapy offers the immune system a sort of honing ability on cancer cells that it otherwise wouldn't have.

From there, millions of these modified T cells are infused back into the bloodstream. In some cases, other cancer treatments, such as low-dose chemotherapy, are used in tandem with CAR-T cell therapy. The process overall is complex and time-intensive. The lab process alone can take several weeks to prepare the CAR-T cells, although people don't need to be in the hospital during this process. It's also possible that people receiving CAR-T therapy may experience a reaction when the CAR-T cells are reinfused back into the bloodstream. A reaction, if it occurs, may require treatment in a hospital.

CAR-T cell therapy is not yet effective for all types of cancer. Dr. Vile says this type of therapy is most effective for blood cancers, called hematological cancers, where tumors tend to be diffuse in the blood.

"In people, CAR-T cell therapy has been extremely successful for blood cancers, likely because the T cells are circulating in the blood, just like

the cancer cells are," says Dr. Vile. "Challenges remain for treating solid tumors, which grow in a localized place, such as in an organ. These tumor sites have evolved to become extremely hostile to immune cells."

CAR-T cell therapy has been an effective treatment for some forms of cancer—particularly for hard-to-treat or recurrent cancers. In fact, one study found that 18% of people with relapsing, treatment-unresponsive chronic lymphocytic leukemia (CLL) experienced full remission after a single CAR-T cell therapy treatment. Additionally, CAR-T cell therapy has the potential to keep cancer in remission for many years.

Like most cancer therapies, CAR-T cell therapy comes with side effects, Dr. Vile says. Side effects may include:

- Cytokine release syndrome (CRS), a severe immune system reaction that can lead to death.
- Noticeable but often temporary neurological side effects such as confusion, seizures, and difficulty speaking or walking.
- Temporary blood conditions like anemia and low platelet count.
- An increased risk of infection, particularly after the first few weeks of treatment.

Scientists are working to develop next-generation methods that will reduce side effects, lower or even eliminate cancer recurrence, and better target treatment-resistant B-cell cancers. Critically, researchers also are focusing on expanding the scope of cancer targets to include a wider number of blood cancers, as well as solid tumors.

"Immunotherapy has really advanced hugely in recent years," says Dr. Vile. "I believe future CAR-T cell treatment will involve targeting more than a single antigen in cancer cells so that the cancers can't escape the therapy. Another major advancement would be understanding how we can put CAR-T cells into people so that the cells persist and keep people

in remission for long periods of time, potentially for someone's entire lifetime."

There may be uses for CAR-T cell therapy aside from cancer treatment. Mayo Clinic researchers are studying whether CAR-T cell therapy may improve treatments for autoimmune diseases as well as reduce the risks of organ rejection in those who receive organ transplants.

Provided by Mayo Clinic

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