

Latest paper from the father of CAR-T: CAR-T really completely cured cancer

Latest paper from the father of CAR-T: CAR-T really completely cured cancer, the effect of more than ten years.

More than a decade later, when doctors announced that his cancer was cured, Doug Olson recalled the fall of 2010 when he participated in a clinical trial of CAR-T cell therapy, and he still remembers that he was full of excitement and hope for the scientific experiment.

He said that when he was doing scientific research, like many young scientists, he dreamed of making a discovery that would have an impact on human beings, but he never thought that it would end up in this way—as a patient participating in a CAR that changes the way of cancer treatment- T clinical trials.

The rise of cancer immunotherapy has brought new hope to the majority of cancer patients.

Among them, CAR-T cell therapy has proven to be a powerful weapon against blood cancers.

However, little is known about the long-term potential and clonal stability of these genetically engineered CAR-T cells reinfused into cancer patients.

Doug Olson , an unfortunate patient with chronic lymphocytic leukemia (CLL) , was diagnosed in 1996 with CLL, a slow-growing but incurable leukemia.

After years of chemotherapy, his condition continued to progress, at which point he began to consider a bone marrow transplant. David Porter , his attending doctor at the time, told him that the University of Pennsylvania was about to start a clinical trial of CAR-T cell therapy.

After reading the trial protocol, he felt promising in the medical industry and decided to participate in the clinical trial.

On September 13, 2010, he became the second leukemia patient in the world to receive CAR-T cell therapy.

The doctors who formulated the treatment plan for him included Carl June and David Porter, but no one knew what CAR-T cell therapy was at the time.

What kind of effect can be achieved, they hoped that these genetically engineered CAR-T cells could survive in the body for a month, and even dared not expect to cure leukemia.

After a few weeks of CAR-T cell therapy, Doug Olson had no cancer cells in his body. After doctors told him the news, he was very optimistic that he had gotten rid of the cancer, but his doctors were not so sure.

The time has come to 2022, more than a decade has passed, Doug Olson. The CAR-T cells in the body are still working normally, and he is still in remission. During this period, Carl June was also known as the father of CAR-T for his contributions to CAR-T .

Now, he says, it's now conceivable that CAR- T cures Doug Olson, CAR-T can really cure leukemia.

On February 2, 2022, [Carl June](#) et al. published a paper titled: Decade-long leukaemia remissions with persistence of CD4+ CAR T cells in Nature , detailing Bill Ludwig and the first patient in the world to receive CAR-T therapy .

The treatment results of two CAR-T-treated Doug Olsons , who have not detected any signs of leukemia for more than ten years after treatment , but unfortunately, Bill Ludwig died of COVID-19 pneumonia in January 2021.

This study provides a proof-of-concept for the long-term therapeutic efficacy and safety of integration into the body of CAR-T cell therapy .

CAR-T cells are the natural anti-infection and anti-cancer immune cells T cells from the blood of cancer patients are genetically reprogrammed in vitro to express receptor proteins that can recognize specific antigens on cancer cells in the patient, which is the so-called chimeric antigen receptor (CAR) .

These genetically engineered CAR-T cells are then expanded using cell culture techniques and reinjected into patients to attack cancer cells.

Since 2017, the US FDA has successively approved five CAR-T cell therapies for the treatment of leukemia, lymphoma and myeloma.

Carl June estimates that tens of thousands of people around the world have now received CAR-T cell therapy.

Although CAR-T has brought great hope to cancer patients, especially blood cancer patients, the therapy also has many limitations – very expensive, high risk of treatment, and high technical difficulty .

Therefore, at present, CAR-T is still used as the last resort after other conventional treatment methods are ineffective.

In addition, although some patients have achieved long-term remission after receiving CAR-T therapy, not every patient is so lucky, in the beginning, only about 25%-35% of chronic lymphocytic leukemia (CLL) are receiving CAR-T therapy after complete remission.

Since then, with the improvement of technology, this proportion has increased year by year, but some patients who were in complete remission have still relapsed.

Therefore, long-term follow-up studies of cancer patients receiving CAR-T therapy can reveal which factors contribute to durable remission, which is particularly important for improving CAR-T therapy and improving cancer cure rates.

For more than a decade, Carl June et al. analyzed and studied the incidence of CD19 - targeted CAR-T therapy in 2010. Doug Olson and Bill Ludwig , tracking their CAR-T cells and looking for any possible safety issues.

More than a decade later, they can still detect the presence of the CAR-T cells infused that year, and the two patients still have no signs of leukemia.

It is unclear whether the CAR-T cells killed all the leukemia cells shortly after infusion, or whether the CAR-T cells, while circulating in the body, were able to eliminate the leukemia cells before they reached detectable levels.

Notably, both patients developed highly activated CD4+ T cell populations that dominated the late CAR-T cell population (over 95%) .

This transition is reflected in the stabilization of the CAR-T cell clonal composition, dominated by a small number of clones. Single-cell analysis showed that these long-lived CD4+ CAR-T cells exhibited cytotoxicity characteristics and sustained functional activation and proliferation.

In addition, the initial response phase of one of the patients showed a $\gamma\delta$ CAR-T cell population accompanied by a significant expansion of CD8+ CAR-T cells.

The identification and characterization of these unexpected CAR-T cell populations provides new insights into CAR-T cell signatures associated with anticancer response and long-term remission, the research team said.

Doug Olson , a healthcare worker, returned to medical diagnostics after a few years of CAR-T therapy, while he started exercising and running a half-marathon.

He joked that he was cured of cancer, but did not want to end up dying of a heart attack. In order to help more cancer patients, he chose to publish his story of cancer treatment and recovery, so that more cancer patients can see hope.

He said: "It may not be possible to cure their cancer today, but it is possible that something good is about to happen.

Reference :

<https://www.nature.com/articles/s41586-021-04390-6>

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