Harnessing a Patient’s Immune Cells to Fight Cancer

Over the past several years, CAR T-cell immunotherapy has emerged as a promising new approach to cancer treatment. 

History of CAR-T: Sixty Years in Development

Sixty years ago, in 1956, E. Donnall Thomas, MD, performed the first successful bone marrow transplant to treat a child patient with leukemia. This groundbreaking procedure laid the groundwork for developing this therapy. This was the first concept of infusing cells from a healthy patient into a patient who had a disease, a dream of the medical community. Today, that dream is a reality.

Antibodies Discovered

In 1975, Georges Köhler, PhD, and César Milstein, PhD, from The Weizmann Institute of Science, Israel, invented a technique to create “monoclonal antibodies,” which guide the immune system to identify and attack harmful substances in the body, such as tumors, viruses, or bacteria. That guide is an “antibody.” Antibodies are a protein that serves as a natural homing device for the immune system. They can recognize specific substances on the surface of a cell and bind to them, akin to a key opening a lock. This allows the immune system to recognize and destroy the cell.

Genetically Engineering T Cells

While antibodies are effective at identifying and engaging with targets, they cannot divide or multiply outside the body. T cells, a component of the immune system, can do this. Anas Younes, MD, PhD, of Memorial Sloan Kettering Cancer Center, and his colleague, Dr. Zelig Eshhar, had an idea: to package a cancer-fighting antibody into T cells in the lab, then return them to the patient's body. This would allow the T cells to multiply and fight cancer, and if the T cells became harmful, then they could be removed from the body. This is CAR T-cell therapy.

A New Day in Cancer Treatment: CAR T-Cell Immunotherapy

In 2011, Steven Rosenberg, MD, PhD, of the National Cancer Institute (NCI), and his colleagues, David Porter, M.D., and Anas Younes, M.D., at The University of Pennsylvania, announced the first successful cancer treatment with CAR-T. The therapy was for an advanced form of follicular lymphoma, a cancer of the lymph nodes, which had spread to the bone marrow. The patient was a 56-year-old woman named Ingrid.

The Therapy Works

T cells were collected from Ingrid’s blood, then genetically modified to express antibodies that would recognize the cancer cells. These T cells were grown in the lab and then returned to Ingrid’s blood. The therapy worked: the patient’s lymphoma cleared up and she remained healthy.

Cancer-Free After 10 Years

In 2017, Ingrid was still cancer-free, 10 years after her CAR T-cell treatment. This was a major breakthrough, and it encouraged the scientific community to continue researching CAR T-cell therapy.

Combinations with Other Therapies

The therapy is not limited to blood cancers. CAR T cells have also been used to treat a variety of solid tumors, including glioblastoma, liver, lung, colon, esophageal, pancreatic, prostate, and gastric cancers. CAR T cells work with other immunotherapeutic approaches, such as checkpoint inhibitors and vaccines.

Mobilizing T Cells

Over the past several years, CAR T cells have become more effective at mobilizing T cells to fight cancer. Early developers include University of California San Diego, The Ohio State University, University of Pennsylvania, and Memorial Sloan Kettering Cancer Center. The goal of their research is to develop even better CAR T cells that can target more types of cancers, including adult ALL, mantle cell lymphoma (MCL), myeloma, and acute myeloid leukemia (AML). Based on the success of CAR T in blood cancers, some CAR T cells are moving into solid tumors.

Memorial Sloan Kettering Cancer Center. The Leukemia & Lymphoma Society (LLS) is supporting much of this work. LLS has funded $40 million in CAR T-cell immunotherapy research since 1998, and has invested approximately $20 million over two decades. Novartis licensed that therapy in 2012 and replicated these dramatic results.

Kymriah

In 2017, Novartis received approval from the U.S. Food and Drug Administration (FDA) for Kymriah (tisagenlecleucel), the first CAR T-cell immunotherapy approved by the FDA. It was approved for children and young adults aged 25 and under with certain types of lymphoma, including a subtype of acute lymphocytic leukemia (ALL) and a subtype of Burkitt lymphoma.

The therapy was tested on 72 children and adolescents with a type of blood cancer called acute lymphocytic leukemia (ALL). The response rate was 80% in children and adolescents who failed standard chemotherapy, and 93% in children and adolescents with ALL who had failed prior therapy. 

For the treatment, LLS provided $2.5 million in support for the Kymriah clinical trial. Today, Kymriah is the only FDA-approved CAR T-cell immunotherapy.

Grupp and Porter were both funded by LLS in the 1990s through LLS’s Career Development Program. Designed to help promising scientists launch independent careers, LLS’s Career Development Program has funded research that led to FDA approval of Kymriah. LLS has provided $2.25 billion in research support since its founding in 1956. LLS has supported the breakthrough by funding early research...-

The Ultimate Breakthrough: Genetically Engineering T Cells

The future of CAR T-cell immunotherapy includes developing treatments for childhood cancers. A 7-year-old named Kaitlyn has been cancer-free for more than three years after receiving CAR T-cell treatment for childhood ALL. LLS has provided $2.5 million in support for Kaitlyn’s CAR T-cell treatment.

Kymriah was approved for the treatment of certain types of lymphoma. The antibody binds to surface molecules on the cancer cells and activates T cells to fight the cancer cells. This therapy is an example of CAR T-cell immunotherapy.

CAR T-Cell Therapy

CAR T-cell therapy harnessing a patient’s immune system laid the groundwork for developing this therapy. This was the first concept of infusing cells from a healthy patient into a patient who had a disease, a dream of the medical community. Today, that dream is a reality.

Immunotherapy – harnessing a patient's immune system laid the groundwork for developing this therapy. The therapy is a revolutionary, lifesaving therapy that is changing the way cancer is treated. CAR T-cell therapy is a type of immunotherapy that can be used to treat cancer. CAR T cells are genetically modified to recognize and fight cancer.