CAR-T and the Dawn of Immunotherapy

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Immunotherapy has become one of the most popular topics of research in the biomedical sciences and shown promise in treating cancer due to its high target specificity and remission rates in clinical trials. Current cancer treatments involve transplantation of donor organs, which relies on limited amounts of donors and may result in immune rejection, and drugs, which are highly toxic to the body. However, the potential of the current methods pale in comparison to the prospect of immunotherapy.

One treatment in particular, called CAR-T therapy, has gained significant attention both in the clinic and at the bench. CAR-T stands for chimeric antigen receptor T-cells, and uses specially human-engineered T-cells to attack cancer cells. The basic function of a T-cell in the body is to bind to pathogens with one-to-one specificity and destroy its target using cytotoxic vesicles. In CAR-T therapy, the human-engineered T-cells are harvested from the patient’s own population of native T-cells, genetically modified to become capable of attacking and targeting specific pathogens or cancers, then transplanted or reintroduced into the body to fight the disease.

This immunological approach to cancer may be novel in its clinical application, but immunology has had an extensive history in the past century and beyond.

The first instance of manipulating the immune system to ward off disease dates back to 1796 when Edward Jenner successfully inoculated 23 individuals against cowpox. Almost two centuries later in 1967, after many keystone developments in biosciences and technology, Jacques Miller published a paper characterizing the T-cell’s role in adaptive immunity. His discovery prompted further research in immunology. Within a decade of Miller’s breakthrough, scientists were able to characterize dendritic cells, MHC restriction, and NK cells, all three of which were critical in the development of immunotherapy. The first clinical trial of CAR-T cell therapy was conducted in 1993 but failed. Shortly after, Dr. Carl June and his team were able to fully cure a young patient diagnosed with chronic lymphocytic leukemia with an autologous T-cell transplant.

The golden age of immunotherapy is only just beginning. This August, the FDA approved the first CAR-T cell therapy for ALL (acute lymphoblastic leukemia), called Kymriah. The therapy was developed by Novartis, which reported remission in 83% of 63 juvenile patients. After the stunning success in its effectiveness against blood cancer, scientists are now attempting to apply the method to solid tumors of different areas of the body. City of Hope’s recently established partnership with Mustang Bio to work on a newly funded Phase 1 clinical trial of CAR-T therapy for malignant glioma, is one of many endeavors to explore the new treatment. However, like most treatments, CAR-T therapy is not without side effects. Notable side effects include B-cell aplasia (killing of tumorous AND normal B-cells during therapy), and TLC (tumor lysis syndrome, the results of rapid breakdown of tumor cells).

The process of developing such treatments also pose challenges—like creating and engineering the antigen receptors on the surface of the T-cells to allow them to target only cancerous cells. However, this is difficult as the receptors still need to be recognized as “self” by the body and not be destroyed as foreign material. Finding solutions to these clinical challenges could prove to be just as difficult as developing the therapy itself. Success in overcoming these challenges will not only make the therapy more effective, but also more accessible to patients.

The popularity of immunotherapy comes from its potency and practicality; the body’s native immune system is specifically designed to detect, target, destroy, and heal—immunotherapy is simply strengthening such forces and arming them to do its natural job more efficiently. Immunotherapy is now known as the “fifth pillar” of cancer treatment, aside from surgery, chemotherapy, radiation therapy, and targeted checkpoint-inhibitor drugs. As science pushes further, immunotherapy could potentially become the most efficient, most specific and patient-personalized treatment for a variety of tumor-related diseases.

REFERENCES


