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Commentary

Role of Chimeric Antigen Receptor T-Cell in Immunotherapy

Angelico Roberta*

Department of Surgical Sciences, University of Rome, Tor Vergata, Rome, Italy

DESCRIPTION

Chimeric antigen receptor T cells also known as CAR T cells are T cells that have been genetically engineered to produce an artificial T-cell receptor for use in immunotherapy.

Antigen receptors with chimeric antigens CARs are receptor proteins that have been created to provide T cells the ability to target a specific protein. They are also known as chimeric immune receptors, chimeric T cell receptors, or artificial T cell receptors. Because they integrate antigen-binding and T-cell activation activities into a single receptor, the receptors are chimeric.

T cells modified with CARs are used in CAR-T cell therapy to treat cancer. The idea behind CAR-T immunotherapy is to alter T cells so that they can recognize cancer cells and target and destroy them more effectively. Scientists take T cells from humans, change them genetically, and then inject the resulting CAR-T cells into patients to target tumors. CAR T-cells can be CD4+ or CD8+, with a 1-to-1 ratio of the two cell types having synergistic antitumor effects.

CAR-T cells can be produced from a patient's own T cells (autologous) or from T cells from another healthy donor (allogeneic) (allogeneic). These T cells are genetically modified to express a specific CAR, which directs them to target an antigen found on the surface of tumors, after being extracted from a person. CAR-T cells are developed to be selective to an antigen expressed on a tumour but not on healthy cells for safety.

CAR-T cells work as a "living medicine" against cancer cells after being administered into a patient. CAR-T cells connect to and activate their targeted antigen on a cell when they come into contact with it, then proliferate and become cytotoxic. CAR-T cells kill cells by a variety of ways, including widespread accelerated cell proliferation, increased cytotoxicity (toxicity to other live cells), and increased release of substances that impact other cells, such as cytokines, interleukins, and growth factors. The FDA authorised the first CAR-T cell therapy in 2017, and there are now five approved CAR-T cell therapies.

Clinical applications in cancer

CD19 is still the most widely targeted antigen, followed by BCMA (commonly expressed in multiple myeloma). In 2016, research on the viability of other antigens, such as CD20, began. Trials for solid tumors are less dominated by CAR-T, with about half of cell therapy-based trials involving other platforms such as NK cells. As of March 2019, there were over 364 ongoing clinical trials employing CAR-T cells around the world. The vast majority of these studies are focused on blood malignancies. More than half of the trials for haematological malignancies are using CAR-T treatments.

T cells are genetically modified to express chimeric antigen receptors that are specific for antigens found on a patient's tumor cells, and then infused into the patient, where they assault and kill the cancer cells. Adoptive transfer of T cells expressing CARs is a promising anti-cancer therapeutic, as CAR-modified T cells can be engineered to target virtually any tumor associated antigen.

Blood malignancies were the focus of early CAR-T cell research. CARs that target the antigen CD19, which is found in B-cell-derived malignancies such acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphoma, are the first authorised therapy (DLBCL).

Many other blood cancer antigens are being worked on as well, such as CD30 in refractory Hodgkin's lymphoma, CD33, CD123, and FLT3 in acute myeloid leukemia (AML), and BCMA in multiple myeloma.

Solid tumors have proven to be more difficult to eliminate. It's been difficult to find excellent antigens because they have to be strongly expressed on the majority of cancer cells yet largely missing in normal tissues. CAR-T cells are also not efficiently transported into the center of solid tumor masses, and T cell function is suppressed by the hostile tumor microenvironment.

Correspondence to: Roberta A, Department of Surgical Sciences, University of Rome, Tor Vergata, Rome, Italy, E-mail: roberta.angelico@uniroma2.it

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