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How is chimeric antigen receptor T cell therapy applied?

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Chimeric antigen receptor T cell (CAR-T) therapy is a type of immunotherapy that guides T cells to destroy cancer cells. It seeks to expand adaptive immunity by facilitating the transfer of genetically engineered CAR-T cells. The therapy procedure includes leukapheresis, genetic engineering of the cells and infusion. The blood is taken from a patient or a healthy donor by a process similar to donating blood, called leukapheresis where white blood cells are separated from other cells. Following this, the separated T cells are genetically modified in the laboratory. The genetic modification could be done through a viral-based gene transfer by using retroviral vectors. Otherwise, it can be accomplished through non-viral methods, such as DNA-based transposons, clustered regularly interspaced short palindromic repeats (CRISPR-Cas9) technology, electroporation or by direct transfer of in vitro transcribed-mRNA. The genetically modified T cell expresses a special artificial receptor called the chimeric antigen receptor (CAR), which has the ability to bind to specific proteins on the surface of the cancer cell. Thereafter, the modified CAR-T cells are grown and multiplied in the lab, then packed and infused again into the patient. It is important that patients receive rounds of chemotherapy or radiation therapy before the CAR-T cell therapy in order to reduce immunosuppressive cells and aid in the expansion of CAR-T cells. CAR receptor is an engineered receptor that is composed of a single-chain variable fragment (scFv) which identifies antigens on the cell surface of target cells. It binds to antigens on cancer cells through the extracellular domain that is derived from monoclonal antibodies. The receptor-antigen binding induces signalling in the intracellular domain, the cluster of differentiation 3 zeta (CD3ζ) and costimulatory domain. This binding enables T cells to have antitumour activity. The extracellular antigen-binding region, a transmembrane region, and an intracellular signal transduction region impact the efficiency of the recognition and binding on tumour cells. The artificial CAR-T cell receptors have been investigated in preclinical and clinical trials, and have shown significant results in treating haematological malignancies; however, they still pose limitations for treating solid tumours.

Keywords: Cellular therapy, Chimeric antigen receptor T cell, Genetic modification, Immunotherapy, Cancer

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