Leukaemia: CAR-T Cell Therapy Innovations

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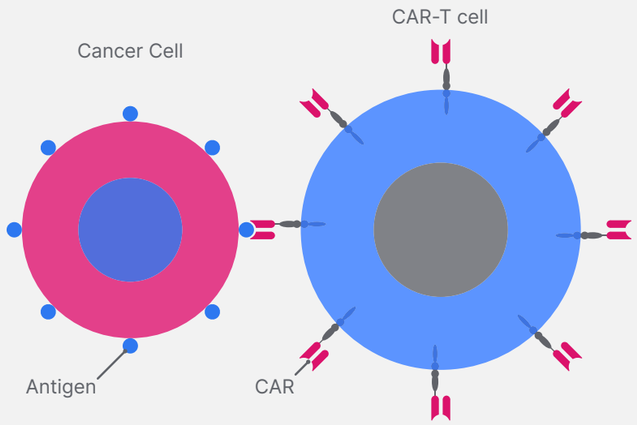
Mechanism of CAR-T Cell Therapy

Introduction:[1]



T cells have protein receptors, that bind to protein fragments, known as **antigens**, on the surface of pathogenic invading cells. If recognised by the T cell as abnormal, the T cell will secrete toxic chemicals that degrade the target cell.

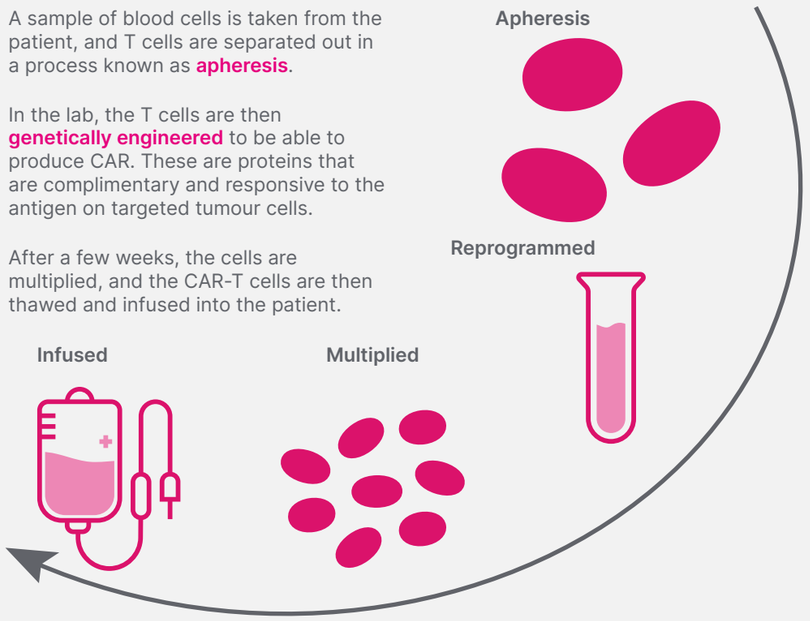
Unfortunately, cancer cells can evade detection, so **CAR-T therapy** has been developed as an immunotherapy approach, boosting the patient's immune system to better kill the cancer cells.

Mechanism of CAR-T:[1]

A sample of blood cells is taken from the patient, and T cells are separated out in a process known as **apheresis**.

In the lab, the T cells are then **genetically engineered** to be able to produce CAR. These are proteins that are complimentary and responsive to the antigen on targeted tumour cells.

After a few weeks, the cells are multiplied, and the CAR-T cells are then thawed and infused into the patient.



Recent Innovations in CAR-T Cell Therapy

Case Study:[2]

In recent years, CAR-T therapy has been promising in treating leukaemia, namely R/R B-ALL.

In **May 2022**, in a collaboration between GOSH for Children and **UCL**, a 13-year-old was the first person in the world to receive base-edited CAR-T cells for the treatment of resistant leukaemia.

She was diagnosed with T-ALL in 2021 and received a bone marrow transplant and chemotherapy, but the disease persisted.

Within 4 weeks of treatment, her leukaemia was undetectable.

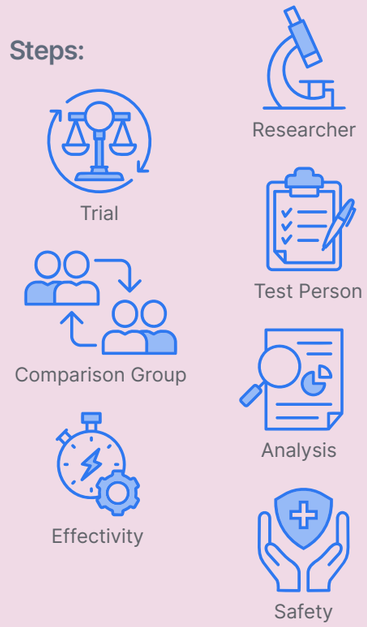
Selected Clinical Trials:

Study at the **Mayo Clinic** to assess the therapeutic efficacy of BAFFR CAR-T cells in BAFFR-expressing B cell haematological malignancies, such as large B cell, mantle cell, and follicular lymphoma CLL and B-ALL.[3]

Phase I clinical trial at **Memorial Sloan Kettering Cancer Center**, New York, USA, led by Jae Park, a haematologist-oncologist, this trial is assessing CAR-T research for the treatment of AML.[4]

Study at **Mayo Clinic** testing IC19/1563, a CD19-targeted CAR-T therapy for R/R B cell malignancies.[5]

Steps:



Benefits and Potential Side Effects[6]

Benefits:

Targeted action: the therapy specifically targets and kills cancerous cells, minimising damage to healthy cells.

Potential for long-term remission: some patients achieve long-term remission, reducing the likelihood of relapse.

Personalised treatment: CAR-T therapy is tailored to the individual, enhancing its effectiveness.

Reduced need for conventional therapies such as chemotherapy and radiotherapy, improving patient's quality of life.

Side Effects:

Patients might experience fever, chills, nausea, and difficulty breathing due to an allergic reaction to CAR-T cells.

CAR T-cells can cause neurotoxicity, leading to headaches, altered consciousness, confusion, speech changes, and seizures.

Symptoms of CRS like fever, low blood pressure, and difficulty breathing can occur as the immune system releases large amounts of cytokines.

Rapid breakdown of cancer cells can elevate uric acid levels in the blood, potentially overloading the kidneys.

Abbreviations:

AML: acute myeloid leukaemia; B-ALL: B-cell acute lymphoblastic leukaemia; BAFFR: B cell activating factor receptor; CAR: chimeric antigen receptors; CLL: chronic lymphocytic leukaemia; CRS: cytokine release syndrome; GOSH: Great Ormond Street Hospital; R/R: relapsed or refractory; T-ALL: T cell acute lymphoblastic leukaemia; UCL: University College London.

References

1. Leukemia & Lymphoma Society. Chimeric antigen receptor (CAR) T cell therapy. Available at: https://www.lls.org/treatment/types-treatment/immunotherapy/chimeric-antigen-receptor-car-t-cell-therapy. Last accessed: 30 May 2024.
2. University College London (UCL). World-first use of base-edited CAR-T cells to treat resistant leukaemia. Available at: https://www.ucl.ac.uk/child-health/news/2022/dec/world-first-use-base-edited-car-t-cells-treat-resistant-leukaemia. Last accessed: 30 May 2024.
3. Mayo Clinic. Exploring the Role of B-cell activating factor receptor (BAFFR)-based chimeric antigen receptor T cell (CAR-T) in BAFFR-expressing B-cell hematologic malignancies and autoimmune rheumatologic disorders. Available at: https://www.mayo.edu/research/clinical-trials/cls-20513089. Last accessed: 30 May 2024.
4. Memorial Sloan Kettering Cancer Center. New CAR-T cell T cell clinical trial for acute myeloid leukemia is first of its kind. Available at: https://www.mskcc.org/news/new-car-cell-clinical-trial-for-acute-myeloid-leukemia-is-first-of-its-kind. Last accessed: 30 May 2024.
5. Mayo Clinic. CD19-Directed CAR-T cell therapy for the treatment of relapsed/refractory b cell malignancies. Available at: https://www.mayo.edu/research/clinical-trials/cls-20512716. Last accessed: 30 May 2024.
6. Blood Cancer UK. What is CAR-T therapy? Available at: https://bloodcancer.org.uk/understanding-blood-cancer/treatment/what-is-car-t-therapy/. Last accessed: 30 May 2024.