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CRISPR-Engineered Universal CAR T-Cells: A Scalable Solution for Rapid Cancer Treatment

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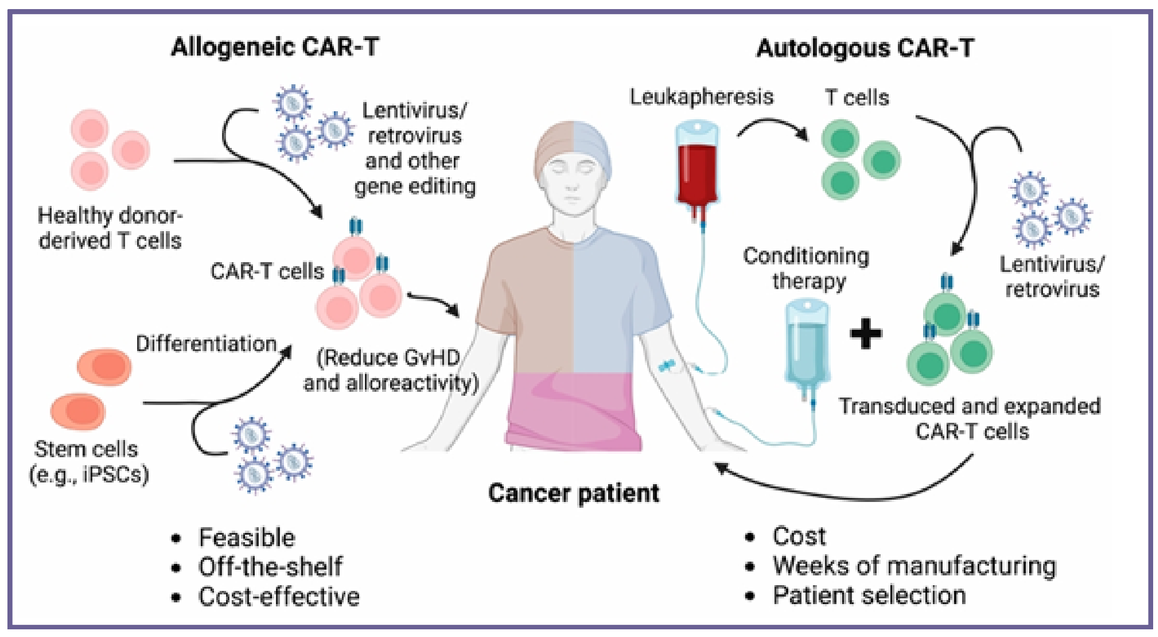
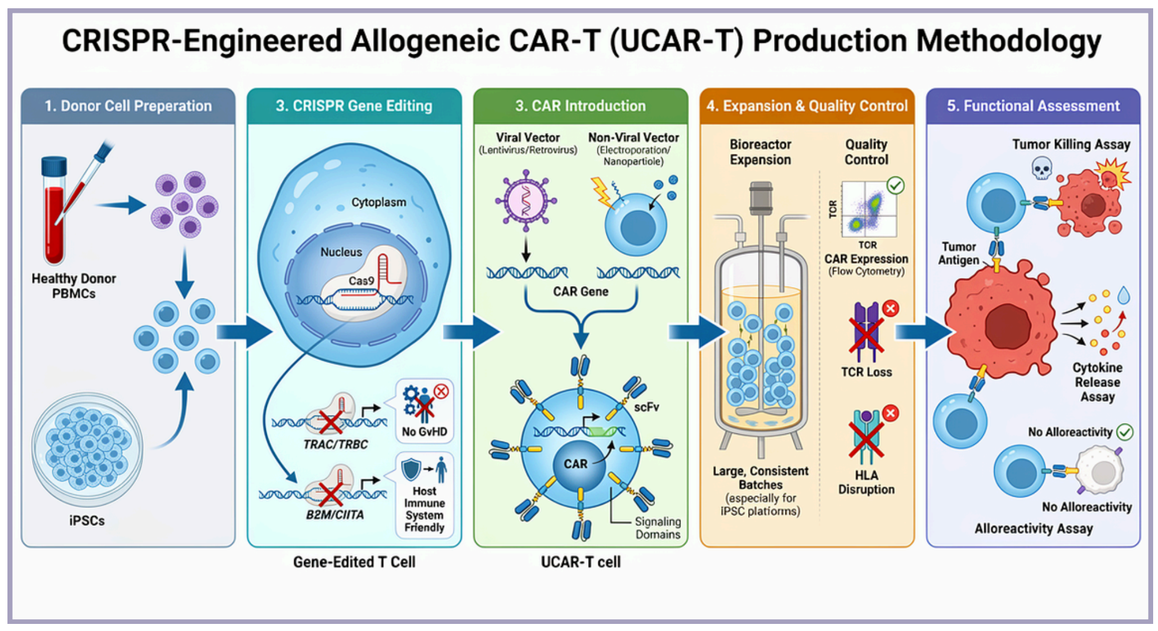
INTRODUCTION & AIM

CAR T treatment is effective but is a lengthy and expensive process as it is a personalized therapy for each patient. The universal CAR-T cells created by CRISPR eliminate TCR and HLA, thus stop the rejection and give the freedom of off-the-shelf utilization. In fact, they can be produced in a much quicker way, less costly and in large quantities. This work demonstrate the role of CRISPR in the creation of a patient-friendly, limitless, and scalable supply of CAR T treatments. [1]



METHOD

CRISPR was applied to develop CAR T cells that are universal by sequentially editing donor-obtained T cells to remove alloreactivity and increase therapeutic potential. Some of the important engineering procedures involved TRAC knockout to avoid TCR-mediated GvHD, β2M and HLA class I interference to mitigate host-versus-graft rejection, and deletion of the CD52 to allow survival in lymphodepleting regimens. Further additions to PD-1 knockout, cytokine receptor engineering (IL-15/IL-21), and tumor-microenvironment resistance edits (A2AR, TGF-β pathway) were added to enhance persistence, cytotoxicity, and tumor infiltration. The cells were then edited and transduced with tumor specific CAR constructs and scaled to produce a uniform and scalable UCAR-T product. [2]



RESULTS & DISCUSSION

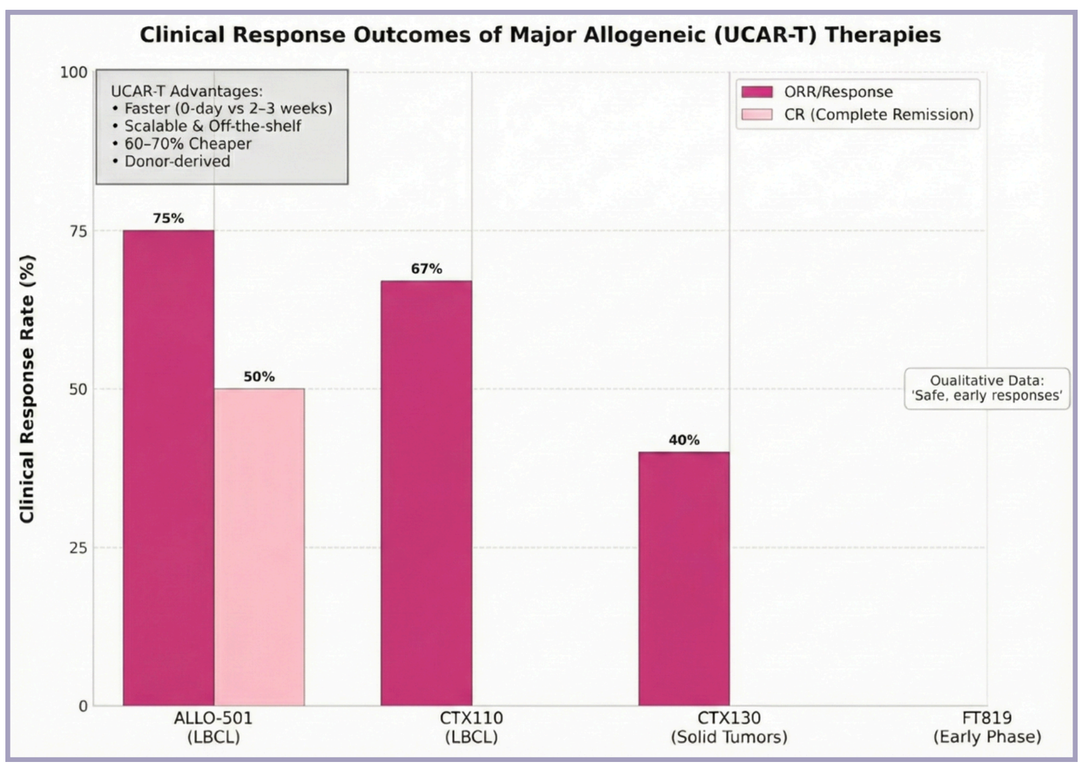
CRISPR-engineered Universal CAR-T (UCAR-T) is more effective than autologous CAR-T for scalable, rapid cancer therapy. The gene-edited allogeneic T-cells (TRAC/B2M/HLA knockouts) allow immediate off-the-shelf availability vs. 2-3 week waiting time, with 60-70% cost reduction and high proliferation from healthy donors.

Breakthroughs in clinics are the main points of the following:

- ·ALLO-501: 75% ORR, 50% CR (32 rr-B lymphoma patients)
- ·CTX110: 67% response in LBCL
- ·FT819 (iPSC-derived): Safe, first B-cell malignancy reactions

Despite TME challenges, solid tumors have the potential (CTX130: 40% ORR) with PD-1 knockouts improving persistence. UCAR-T changes access - no patient cell failures, a perfect case for rapid progression.

Future: multi-antigen + automation for worldwide scale. [3]



CONCLUSION

By using CRISPR to modify Universal CAR T-cells, the major issues with autologous therapy can be resolved as this technology allows cancer treatment that is safe, scalable, and ready-to-use. The TCR and HLA knockouts performed at high efficiency lower the chances of immune rejection, and the two platforms, iPSC and donor, ensure a stable, strong, and quickly consumable CAR T product. So, in a way, these innovations make UCAR-T cells be the future of cancer immunotherapy which is not only fast and efficient but also revolutionary, and broadly available

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3. Mishra, H.K.; Kalyuzhny, A. Revolutionizing Cancer Treatments through Stem Cell-Derived CAR T Cells for Immunotherapy. Cells 2024, 13, 1516.