Leveraging Bioprocess Platform Technology for the Development of a Robust, Scalable, and Economic Manufacturing Process of Allogeneic CAR-T Cell Therapy Products

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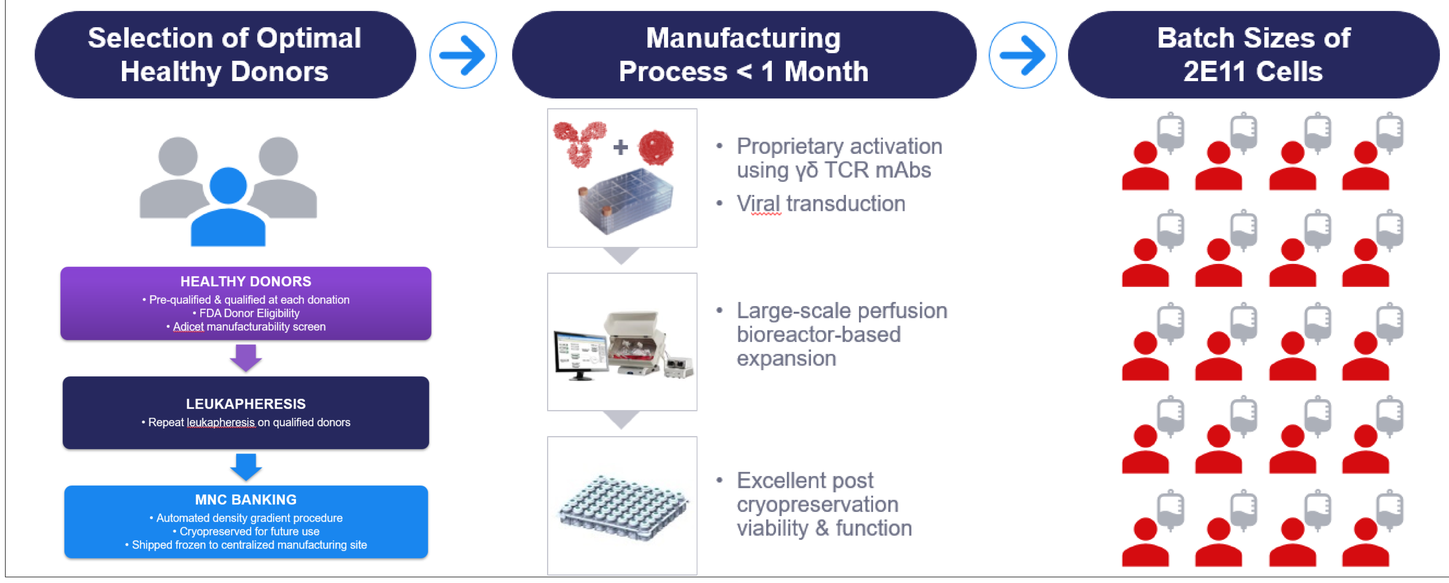
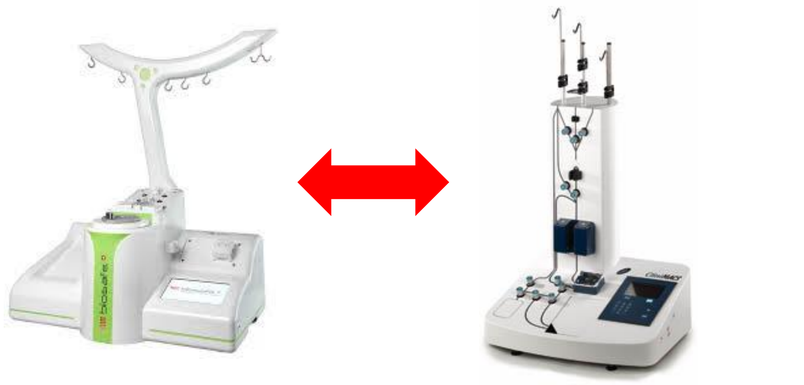
Introduction

Current autologous patient-specific chimeric antigen receptor (CAR)-T cell therapy products, both commercially approved and in clinical development, have been instrumental in providing new treatment options for cancer patients. The therapeutic success of these treatments has, to some extent, been tempered by the challenges of consistently manufacturing patient-specific products and by a manufacturing model that requires scaling-out and subsequently releasing 100-1000s of patient specific lots.

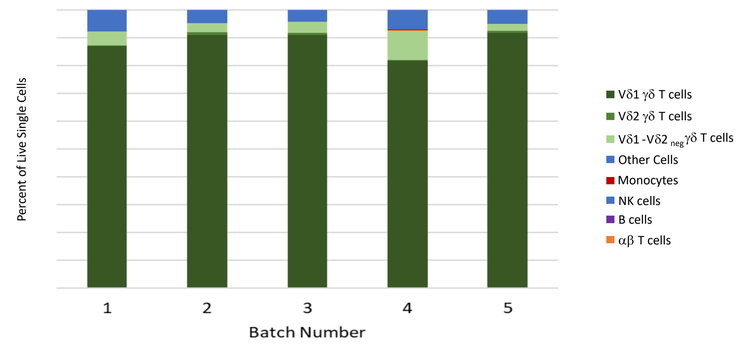
Adicet Bio is overcoming the challenges of patient-specific CAR-T cell therapies by employing healthy donor-derived gamma delta (γδ) T cells and engineered T-cell receptor like tumor recognition to improve the safety and efficacy of CAR-T cell therapies against both liquid and solid tumors. Additionally, we have optimized the manufacturing process of allogeneic CAR γδ-T cells to facilitate the off-the-shelf treatment of nominally hundreds, potentially thousands, of patients per manufacturing run. This approach greatly simplifies the complexity of manufacturing associated with autologous model through minimizing the variation of processing patient material and efficiently utilizing support product release testing infrastructure. By leveraging established bioprocess platform technologies, we can efficiently engineer, expand, harvest, and cryopreserve up to $2x10^{11}$ CAR-T cells from a single healthy donor in a cGMP-compliant manner. This approach is scalable to both support the needs of internal product development as well as clinical trials, achieving substantial economies of scale while maintaining product quality and consistency.

Proprietary Large-Scale Manufacturing Process





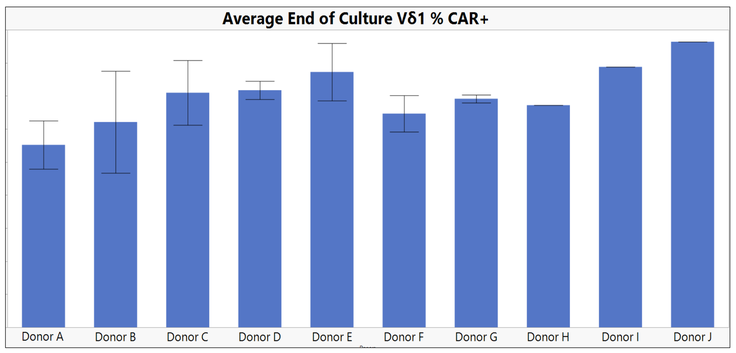
Incorporating GE Sefia Cell Processing System and Miltenyi CliniMACS for functionally closed and automated downstream cell processing

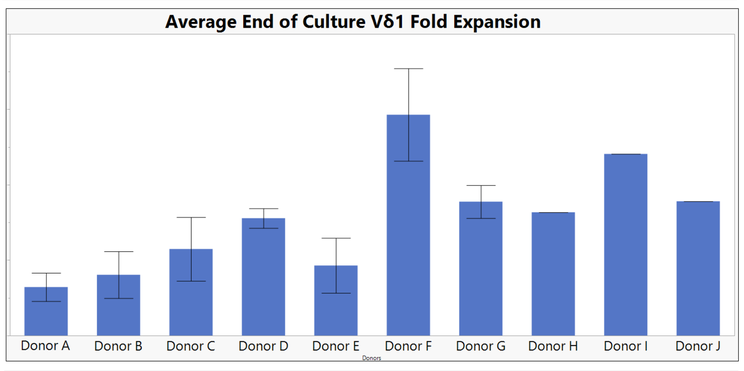


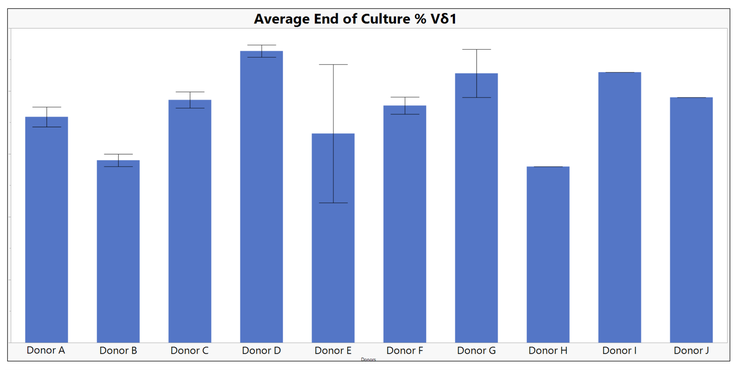
Efficient depletion of αβ-T cells to minimize risk of GVHD

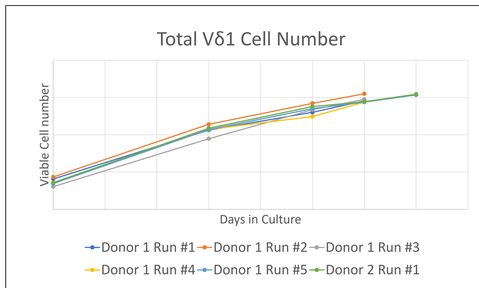
Manufacturing Considerations for Engineered γδ T Cells

- Low starting γδ T cell percentage (<1-5%) in donor PBMC compared to αβ T cells
- Variability of donor starting material
- Specific activation of different γδ T cell subsets (Vδ1, Vδ2, etc.)
- Engineering of TCRs/CARs onto γδ T cells
- Scalability of expansion to reach clinically meaningful cell bank size
- Efficient depletion of TCRαβ to minimize risk of GVHD
- Robust cryopreservation of cell product to preserve cell viability, health, and function





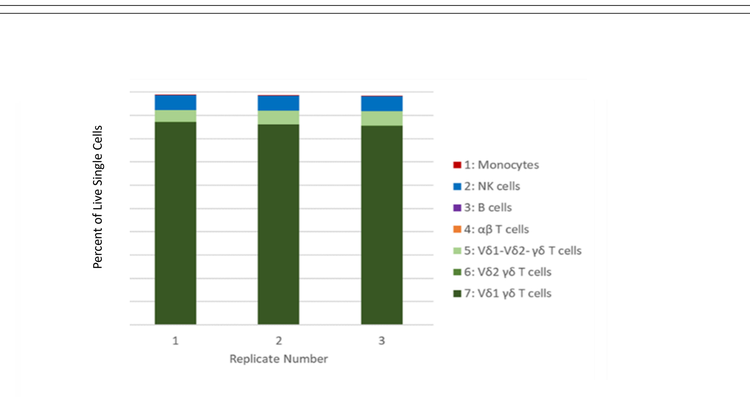




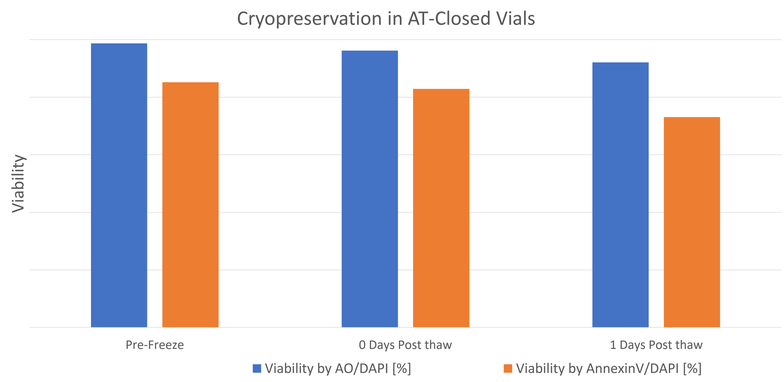
Consistent cell expansions profiles from multiple donor staring material at pilot scale using GE Xuri Cell Expansion System

Summary

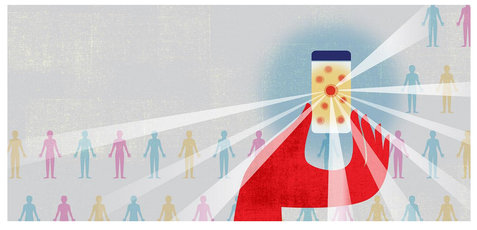
- Successfully demonstrated activation, transduction, and expansion using a variety of starting donor material
- Consistently deplete TCRαβ less than 0.04%
- Implemented of automated downstream cell wash and concentration with robust cell product recovery
- Demonstrated reliable cryopreservation, preserving post-thaw cell viability and health
- All processed compatible with cGMP-compliant clinical-scale manufacturing



High degree of analytical replicate reproducibility



Preservation of cell viability (AO/DAPI) and cell health (AnnexinV/DAPI) after cryopreservation



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