Development of a Semi-automated Closed CAR-T Manufacturing Process

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Introduction
Immunotherapy has generated excitement as what many are calling the “fifth pillar” of cancer treatment. Among the several types of therapies, CAR-T cells have shown impressive therapeutic efficacy, especially in advanced blood cancers. With the recent approval of Ykymriah™ and Yescarta™, CAR-T cells continue to be the focus of a growing clinical trial pipeline. However, there are remain challenges associated with routinely offering these products as treatment alternatives, including a costly manufacturing process that relies on a lengthy and complex open workflow with manual manipulations that lead to product variability. To address these challenges, we have investigated individual CAR-T unit operations to identify commercially available reagents and modular equipment to drive process closure and automation that will improve workflow efficiency and product consistency.

Objectives
Systematically build a robust semi-automated closed CAR-T manufacturing process that can be widely adopted by the T-cell immunotherapy industry:
- Identify and apply commercially available reagents that enhance process efficiency
- Integrate automation strategies to reduce manual and open operations
- Maintain flexibility to concurrently manufacture CAR-T products

Methods

Results

T-cell Selection and Enrichment

T-cell Modification

Identification of an Early Closed Culture Alternative

Evaluation of an Automated Closed Transduction (ACTd) Method

Simulated CAR-T Manufacturing Runs

Conclusions

Developed a semi-automated closed CAR-T manufacturing process that can be widely adopted by the T-cell immunotherapy industry:
- 1E10 GFP transduced T-cells in an 8 day process, n=2 donors
- Identified EasySep™ as a commercially available reagent to enhance process efficiency
- Integrated the the Smart-Max, Sepax™ C-Pro, Xuri™ W25 bioreactor, Sefia™ and VIA Freeze™as automation strategies to reduce manual and open operations

Future Work
- Development of an isolation process with closed an EasySep™ platform
- CAR-T manufacturing runs with transduction, expansion and harvest
- CAR-T manufacturing runs with patient material
- Further optimization of T-cell bioreactor expansion
- Integration of GMP-grade reagents currently in development

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