THE COCOON® PLATFORM: AN AUTOMATED SYSTEM FOR MANUFACTURING PATIENT-SCALE CELL THERAPIES

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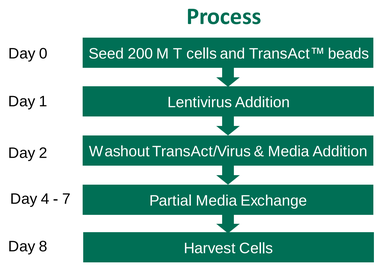
Introduction

Autologous chimeric antigen receptor T-cell (CAR-T) immunotherapies have generated significant enthusiasm due to their robust therapeutic efficacy in hematological malignancies, which has culminated with FDA-approved Kymriah™ and Yescarta™. Although, immunotherapies for blood cancers have dominated research pipelines, treatments for solid tumors are beginning to emerge. However, significant challenges remain including high manufacturing costs due to complex workflows conducted within open, manual cell culture systems, thereby limiting the full utilization of cell therapies. Moreover, as additional cell therapies are approved for indications with larger patient populations, the need for scalable platforms to manufacture patient cell therapies at commercial-scale is essential. Enabling cell therapy clinical and commercial success will entail employing automated platforms to produce cost effective, robust therapies. One solution is the Cocoon® Platform. This study details the steps to translate a CAR-T therapy process from an open, manual method to the fully automated Cocoon® Platform.

Methods

The Cocoon® Platform automates cell seeding, activation, transduction, real time process monitoring, feeding, washing/concentration, and harvesting. Manual research scale processes were optimized, scaled up, and programmed to run without manual intervention in the Cocoon® Platform. In this process, 200 million positively-selected T cells from fresh leukopaks were activated with TransAct™ beads. The following day, cells were transduced with a lentivirus vector that modifies the selected cells to express an engineered TCR. Following transduction, cells were expanded in cytokine and human serum supplemented medium with a pre-defined feeding strategy until they were harvested at Day 8. After harvest, cells were analyzed for cell yield, viability, transduction efficiency, and cell phenotype via flow cytometry.



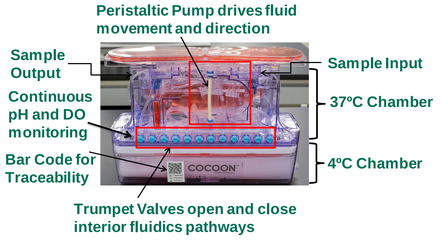
Cocoon® Platform Instrument

An open Cocoon® instrument showing top 37° C warm zone, and bottom 4° C cold zone, peristaltic pump, and computer control center for the protocol design.

The Cocoon® instrument with a sterile and disposable single-use Cocoon® cassette that is used to culture cells.

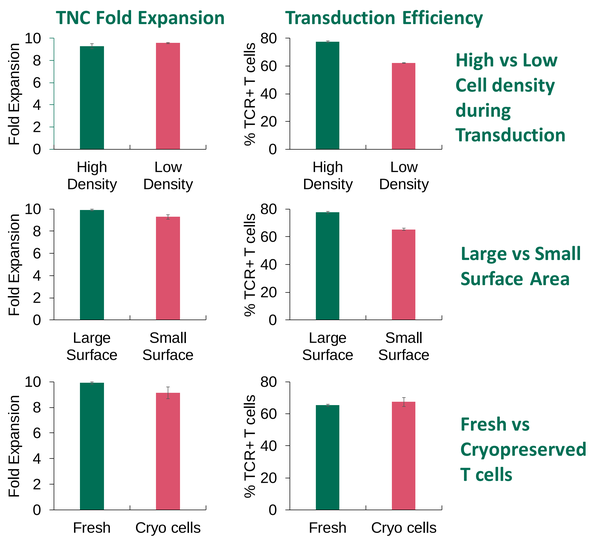
A Cocoon® instrument with closed door ready for cell culture.

Cocoon® Platform Casette (Single-Use)

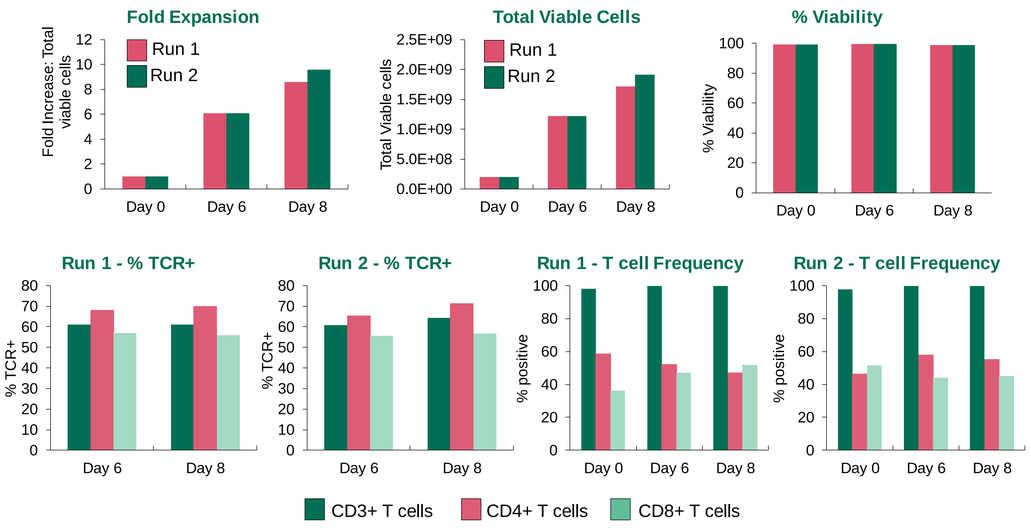


Results

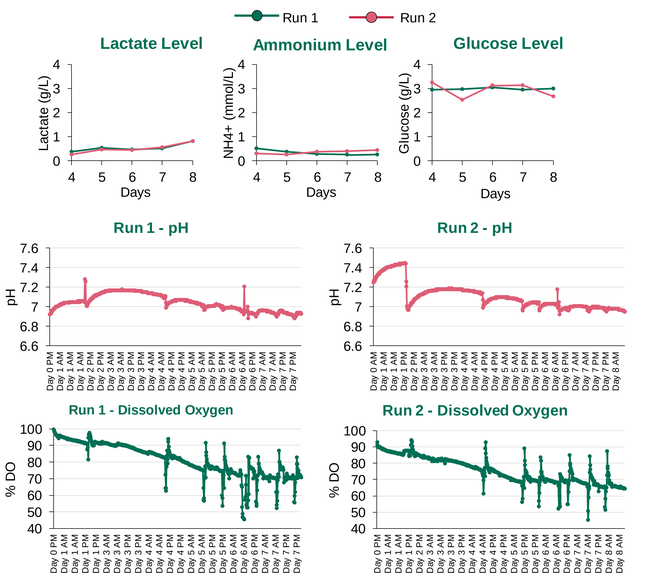
Parameters including cell density during transduction, surface area, and the utilization of cryopreserved or freshly isolated cells were optimized during the 8-day process and applied to generate an optimized manufacturing protocol for the Cocoon® Platform i.e. High cell density, Large surface area, and Freshly isolated T cells.



Two independent Cocoon® Platform runs were conducted using freshly isolated T cells transduced at high cell density with an average cell yield of 1.82 x 10^9 cells and viability of greater than 90%. Fold expansion of total viable cells in the Cocoon® Platform was similar to the manual process. Transduction efficiency averaged 62.5% in the CD3+ TCR+ T cell fraction, with CD4+ and CD8+ T cells at a 1:1 ratio, and transduction efficiencies of 71% TCR+ and 56.5% TCR+, respectively.



By optimizing the feeding strategy and utilizing integrated biofeedback, the nutrients and metabolites were maintained within the desired specifications throughout the 8-day manufacturing process (lactate of < 1 g/L, ammonium of < 0.5 mmol/L, glucose of ~3 g/L, glutamine of < 0.3 mmol/L, and ~7 pH).



Conclusion

The Cocoon® Platform is a viable solution to translate labor-intensive cell therapy processes to an automated system allowing scalability, high yield, reduction of manufacturing cost, minimizing operator error, and improved process control.