MANUFACTURING OF PATIENT SPECIFIC NOVEL T CELL THERAPIES USING THE COCOON® PLATFORM AUTOMATED SYSTEM

Joseph O'Connor, Ph.D., Lonza Walkersville, Inc., USA
joseph.oconnor@lonza.com
Kalyani Daita, Lonza Walkersville, Inc. , USA
Janet Sei, Ph.D., Lonza Walkersville, Inc. , USA
Eytan Abraham, Ph.D., Lonza Walkersville, Inc. , USA
Yaling Shi, Ph.D., Lonza Walkersville, Inc. , USA

Key Words: Cocoon®, automation, manufacturing, autologous, functionally-closed

Engineered T cell therapies, particularly chimeric antigen receptor T cell (CAR-T) immunotherapies, have proved effective against hematologic cancers. However, CAR-T therapies can potentiate immune responses causing cytokine release syndrome (CRS; "cytokine storm") leading to adverse events in patients. Additionally, CAR-T has shown sporadic success in solid tumor indications. Novel therapies which activate T cells via the native T cell receptors (TCR) have shown greater tumor antigen recognition providing an alternative therapy which may prove effective against solid tumors. Utilizing novel cell immunotherapy modalities is only part of the solution as challenges remain to scale manufacturing to meet commercial demand. Scaling out commercial patient-specific cell therapy manufacturing for large populations using current methods will be expensive (cleanrooms and FTEs) and complex (logistics). Innovative manufacturing solutions will be required to manufacture patient-specific therapies in a robust and cost-effective manner. The Cocoon® Platform is one such innovation, a functionally-closed, automated, scalable cell therapy manufacturing platform. This abstract highlights a therapeutic T cell process translated from an open, manual process to the Cocoon® Platform.

During process translation, the functionally-closed Cocoon® Platform was used to automate cell seeding, activation, transduction, feeding, real-time process monitoring, washing, and final product harvest using the single-use Cocoon cassette. During process development and translation, important process parameters were identified, optimized, and programmed enabling multiple process step automation removing the need for manual intervention. For the process, 200 million $CD4^+$ and $CD8^+$ isolated T cells were inoculated with TransAct™ activator. The following day, cells were transduced with HER-2 lentivirus vector at various multiplicities of infection (MOI). Cells were expanded with a predefined feeding strategy in media supplemented with IL-2 until final product harvest. Following harvest, cells were assessed for cell yield, viability, transduction efficiency, and VCN. T cell phenotype and functionality was assessed via flow cytometry.

The Cocoon manufacturing processes yielded 2.7 x 10^9 viable cells on average with viability >85%. The Cocoon processes supported both $CD4^+$ and $CD8^+$ T cell expansion with 68% $CD4^+$ T cells and 31% $CD8^+$ T cells on average. The final product exhibited high T cell purity and viability (i.e. >90% $abTCR^+$ and 89% $abTCR^+$, respectively) with transduction efficiencies varied from ~30% to >65% depending on the process MOI. Vector copy number (VCN) was evaluated after each process and found to be ≤5 copies/transduced T cell.

In summary, a gene-modified T cell process was successfully translated to the Cocoon and the harvested final products met all pre-defined acceptable criteria. The Cocoon represents a tool for manufacturing cell therapies in a robust manner, while maintaining comparability, and lowering manufacturing costs via increased automation. Ultimately the Cocoon will enable and accelerate development of cell therapies to address solid tumor indications and meet a critical patient need.