A COST/QUALITY ANALYSIS OF PRIMARY HUMAN T-CELLS IN DIFFERENT EXPANSION SYSTEMS

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Recent developments in cell and gene therapy, in particular the emergence of Chimeric Antigen Receptor (CAR) T-cell immunotherapies, have demonstrated a new therapeutic modality to combat life-threatening diseases. Kymriah® (Novartis) and Yescarta® (Gilead) are the first CAR-T therapies that have been approved by both FDA and EMA. They are autologous therapies, where T-cells are isolated from the patient and engineered in order to express a specific CAR which recognizes and targets cancer cells.

The clinical success of these products is driving the need for a consistent and cost effective manufacturing process to meet the lot-sizes required for commercial production. Current T-cell manufacturing and production capabilities are greatly lagging and will not be able to meet the predicted surge in demand (£6.8 bn by 2028, CAGR of 46%) unless new technologies and processes are developed. These technologies need to be highly regulated and consistently achieve high yield, without compromising the quality of the cells, irrespective of donor.

A number of systems have been used for CAR-T cell expansion, namely flasks, bags (static or dynamic), G-Rex® (WolfonWilson) and CliniMACS Prodigy® (Miltenyi Biotec). All these technologies have many advantages, but they generally lack in scalability, suffer from manufacturing bottlenecks or incur in high suppliers costs and manual intervention.

The aim of this work is to understand the relation between reduction of production costs and cell growth quality. We compared the growth of human primary T-cells from multiple healthy donors in the aforementioned culture platforms, characterizing cell growth and phenotype. Cells were expanded for 7 days in each of the platforms with the aim of comparing the different systems with respect to scalability, productivity and efficiency. The phenotype composition of the final product was determined by flow cytometry.

A cost analysis for the different platforms related to the final product, as well as the cost related to the media and supplements consumption, has been performed. The different platforms have been compared with automated systems on the market or those in final development stage. Additional work includes bioprocess development for T-cell production with batch, fed-batch, and continuous systems to improve consistency and to provide a greater understanding of how selected process parameters influence T-cells critical-to-quality attributes.

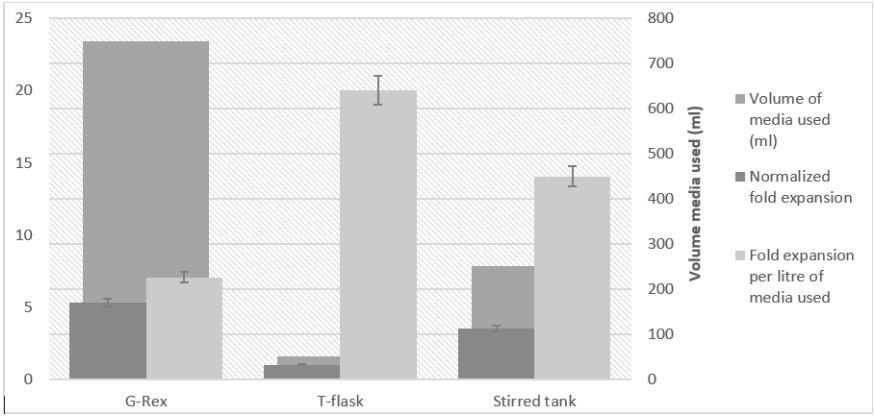

Figure 1 – Preliminary results on fold expansion and volume used to grow T-Cells in cRPMI with IL-2 addition in different expansion platform.