BIOPROCESSING AND ENGINEERING CHARACTERISATION OF T-CELL THERAPY MANUFACTURE IN AN AMBR® 250 BIOREACTOR

Elena Costariol, Biochemical Engineering Department, University College London, Bernard Katz Building, Gower Street, Londn WC1E 6BT, United Kingdom
elena.costariol.16@ucl.ac.uk
Marco Rotondi, Aston Medical Research Institute, School of Life and Health Sciences, Aston University, UK
Qasim Rafiq, Biochemical Engineering Department, University College London, Bernard Katz Building, Gower Street, Londn WC1E 6BT, United Kingdom

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The use of engineered CAR-T cells in clinical trials has been growing over the last years. The recent approval of Kymriah® (Novartis) and Yescarta® (KitePharma) made CAR-T cell treatments available to a broader public. However, despite the recent successes and significant improvements, there are different aspects that need to be further assessed in order to develop a reproducible, cost-effective manufacturing process for the production of personalized T-cell therapies. This requires an approach, which generates sufficient quantities of patient-specific cells at the appropriate quality required for clinical application, overcoming the challenge imposed by significantly different starting material.

The work carried out is focused on the growth of T-cells in stirred tank bioreactors. In order to do so, experiments were carried out in an ambr® 250 (Sartorius) single use bioreactor. The ambr® 250 has already demonstrated significant success for suspension-based mammalian cell culture applications, both as a product development and scale-up tool. Both commercially available vessels were characterised in terms of cell yield, viability, metabolites profile and T-cell subpopulations after expansion. The comparison between the two vessels was performed based on stirring speed and power per unit volume.

T-Flask expansion of primary T-cells was carried out as a static control and results were compared with the dynamic culture conditions. Results revealed a higher final cell density in the ambr® 250 bioreactor compared to the static platform (Figure 1). Moreover, the final product composition was not significantly affected by the stirring regime.

Small scales bioreactors, as the ambr® 250, are a big resource for autologous therapies, where a volume of 250ml is enough for a single dose. A 24 way ambr® 250 system has the potential to produce 24 patient-specific treatments in parallel. On the other hand, this results can be used for scaling-up the manufacturing process to 1-5l stirred tank bioreactors. This will be of uttermost importance for allogeneic therapies, where single donor material is expanded in larger volumes in order to reach the number of cells needed multiple doses. Investigating and optimising the manufacturing process will improve the consistency, yield and quality of T-cells and facilitate more cost effective production for both autologous and allogeneic CAR-T cell therapies.

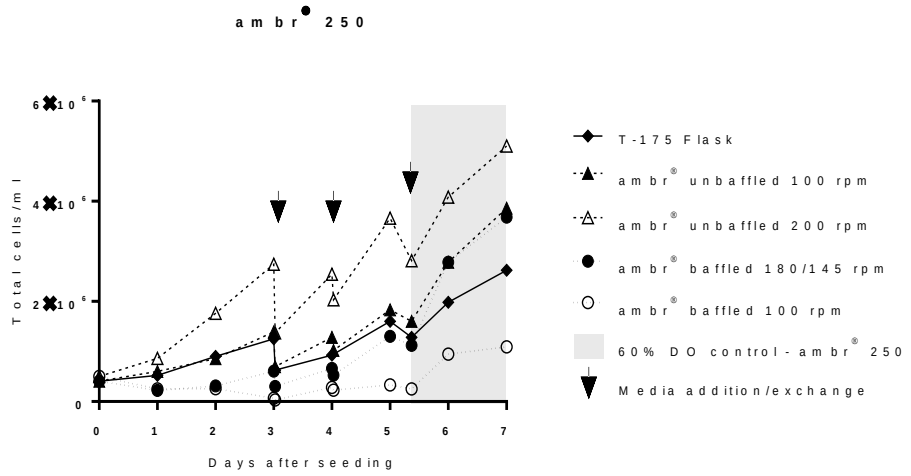

Figure 1 – Growth curve (Total cells/ml) for primary T-cells isolated form healthy donors. The growth in T-175 Flasks was compared to ambr® 250 vessels (baffled and unbaffled) at different speeds. It can be seen how the baffled vessels performed better that the T-Flask in all tested conditions, while the baffled vessel at 100 rpm was the only one to have a lower yield when compared to the static control.