EXPERIMENTAL AND COMPUTATIONAL FLUID DYNAMICS STUDY OF MICROCARRIER SUSPENSION DURING THE CULTIVATION OF MESENCHYMAL STEM CELLS IN AN AMBR250 BIOREACTOR

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The ambr250 unit is a fully automated disposable 100-250 ml bioreactor for R&D that has been developed by TAP Biosystems, now part of Sartorius-Stedim, widely used for scale down and scale up modelling studies. Recently, mesenchymal stem cells (MSCs) have become strong candidates for cell-based therapies based on in vitro growth on microcarriers in stirred bioreactors. However, to fully realize the MSCs potential, a number of key processing issues need to be addressed because of the huge number of cells that are required. Thus, the fluid dynamics characteristics of the stirred ambr250 bioreactor must be sufficiently well understood to enable scale-up to larger bioreactors to be efficiently accomplished particularly because of the special issues arising from the presence of the particulate solid phase.

One of the most critical aspects for MSC cultivation on microcarriers is the minimum agitator speed required to achieve complete microcarriers suspension, NJS. Under these conditions, the surface area of all the attached cells is available for transfer of nutrients (including oxygen) to the cells and metabolites from them, whilst higher speeds hardly increase these transport processes and may lead to damaging fluid dynamic stresses being generated1. This suspension condition can be studied experimentally if equipment is specially modified to make easy visual observation of the two-phase flow in the bioreactor but during actual growth that is very difficult. Therefore, it is extremely beneficial to both measure NJS and compare the measured values with predictions based on computational fluid dynamics (CFD) for validation. Once validated, then CFD is a very useful tool for analyzing flow patterns, mixing time, mean and local specific energy dissipation rates and other parameters important for scale up.

In this work we examined the fluid dynamics of the two-phase particle-liquid system with an experimental analysis and a CFD simulation using a lattice-Boltzmann base software and particle tracking of an ambr250 vessel at different stirring conditions. Cell culture was also performed in parallel to analyse the cell growth at and around NJS and the results were compared to the performance in a spinner flask bioreactor.
The CFD and experimental results will be discussed in detail along with their scale-up implications.

References

1) Nienow, A. W., Coopman, K., Heathman, T. R. J., Rafiq, Q. A. and C. J. Hewitt (2016). "Bioreactor Engineering Fundamentals for Stem Cell Manufacturing". In: "Stem Cell Manufacturing", (Eds. J.M.S. Cabral, C.L. de Silva, L. G. Chase and M. M. Diogo), Elsevier Science, Cambridge, USA; Chapter 3, pp 43 – 76.