GROWTH BEHAVIOR OF HUMAN ADIPOSE TISSUE-DERIVED STROMAL/STEM CELLS IN SINGLE-USE SPINNER FLASKS: NUMERICAL AND EXPERIMENTAL INVESTIGATIONS

Valentin Jossen, Zurich University of Applied Sciences (ZHAW), Wädenswil, Switzerland
valentin.jossen@zhaw.ch
Regine Eibl, Zurich University of Applied Sciences (ZHAW), Wädenswil, Switzerland
Matthias Kraume, Technical University of Berlin, Berlin, Germany
Dieter Eibl, Zurich University of Applied Sciences (ZHAW), Wädenswil, Switzerland

Key Words: Single-use spinner flasks, Computational Fluid Dynamics (CFD), Euler-Euler and Euler-Lagrange model, human adipose tissue-derived stromal/stem cells, MC-associated growth model

Human adipose tissue-derived stromal/stem cells (hASC) represent a valuable source of cells for clinical applications, especially in the field of regenerative medicine. Therefore, it comes as no surprise that interest in hASCs has increased greatly over the last decade. However, in order to use hASCs successfully in clinical applications, *in vitro* expansion is required. Single-use bioreactors in combination with microcarriers (MC) have been shown to be suitable systems for this task (1-3). However, hASCs are prone to higher shear sensitivity than conventional cell lines (e.g. CHO, BHK) that are normally expanded in these systems. Hence, the goal of this study was to investigate the influence of different shear stress levels on the growth of hASCs in small scale single-use spinner flasks. For this purpose, *Computational Fluid Dynamics* simulations based on a *Euler-Euler* and *Euler-Lagrange* approach were performed to predict the hydrodynamic stresses (0.06 – 0.87 Pa), the residence times (0.4 – 7.3 s) and the circulation times (1.6 - 16.6 s) of the MCs in various high shear zones. The numerical findings were combined with experimental data from cultivation studies (0.29 – $1.1 \cdot 10^6$ hASC/mL) in order to develop a segregated mathematical growth model for the prediction of MC-associated hASC growth in small scale single-use spinner flasks.

1. V., Jossen, R., Pörtner, S.C., Kaiser, M., Kraume, D., Eibl, R., Eibl. Mass Production of Mesenchymal Stem Cells – Impact of Bioreactor Design and Flow Conditions on Proliferation and Differentiation. In: *Cells and Biomaterials in Regenerative Medicine*, D. Eberli (ed.), 119-174, InTech 2014.
2. C., Schirmaier, V., Jossen, S.C., Kaiser, F., Jüngerkes, S., Brill, A., Safavi-Nab, A., Siehoff, C., van den Bos, D. Eibl, R., Eibl. Scale-up of adipose tissue-derived mesenchymal stem cell production in stirred single-use bioreactors under low-serum conditions. *Eng. Life Sci*. 2014, 14: 292-303
3. T., Lawson, D.E., Kehoe, A.C., Schnitzler, P.J., Rapiejko, K.A., Der, K., Philbrick, S., Punreddy, S., Rigby, R., Smith, Q., Feng. *Biochem Eng J*. 2017, 120: 49-62