ISOLATION AND EXPANSION OF HUMAN BONE MARROW MESENCHYMAL STEM CELLS DIRECTLY ON MICROCARRIERS IN A STIRRED TANK BIOREACTOR

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Human mesenchymal stem cells (hMSCs) are emerging as a promising treatment for several diseases including diabetes, heart disease and Parkinson's. However, current manufacturing methods are time consuming, expensive and unable to satisfy the increased patient demand. Upscaling the stem cell isolation and expansion process in a cost-effective manner is therefore the key for future affordable therapies. Typically, the isolation of hMSCs from bone marrow would be realised in monolayer in T-flasks followed by scale-out in devices such as Cell Stacks. More recently, following the monolayer stage, further expansion has been successfully achieved at the litre scale in stirred tank bioreactors used in conjunction with microcarriers. Here, to the best of our knowledge, we report for the first time, a bioprocess in a stirred tank bioreactor with microcarriers for the isolation and the subsequent expansion of hMSCs from fresh bone marrow aspirates. The Mobius® 3L single-use stirred tank bioreactor was operated at 1L scale for the isolation from bone marrow and at 2L for the expansion stage. The entire upstream process was performed on the bench with minimal manual handling, thus mimicking an automation-friendly process by making use of peristaltic pumps, aspiration bottles and sterile welders. Cell counts, imaging and metabolite data at different stages of the bioprocess were obtained in order to assess cell growth. Cell quality post-harvesting at the end of the process was assessed by differentiation and CFU-f assays. The hMSCs were successfully isolated on microcarriers from fresh bone marrow and expanded over a 20 day period in the single use stirred tank bioreactor to achieve a total of $760x10^6$ cells with a viability of 95% (*Figure 1*). Additionally, the cells maintained their differentiation potential and showed a CFU-f efficiency of 35%. Nevertheless, we have demonstrated for the first time, proof of concept of a bioprocess that enables the isolation and subsequent expansion of hMSCs on microcarriers directly from bone marrow aspirates.

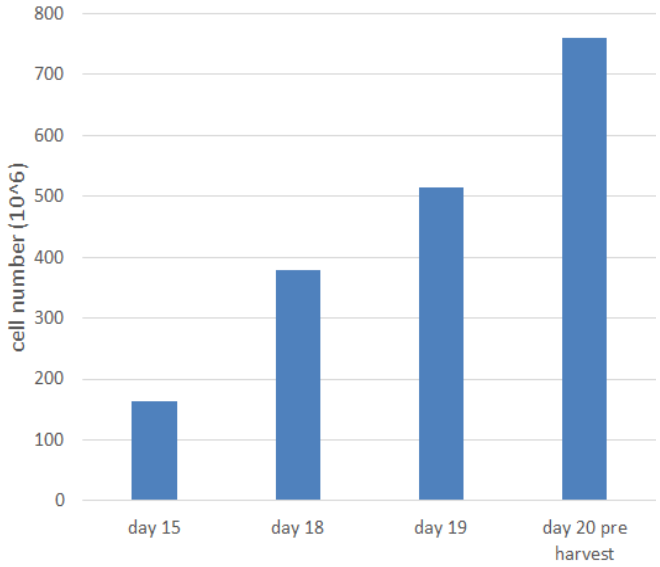

Figure 1 – Cell counts during the 20 day period isolation/expansion culture and post harvesting