SCALABLE EXPANSION OF HBM-MSC IN A FED-BATCH MICROCARRIER SUSPENSION BIOREACTOR

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Abstract Text:

Human bone marrow-derived Mesenchymal Stem Cells (hBM-MSCs) have been recognized as potential patient-specific drugstores, and will be a key raw material for future therapeutics, engineered tissues, and medical devices. Production technologies such as suspension bioreactors are robust, scalable platforms for generating hundreds of billions cells per manufacturing run to meet the demand for these applications. Here, we investigate the use of a suspension bioreactor, along with the use of concentrated bioreactor feed to replace nutrients and growth factors depleted from growth medium, for the scalable expansion of hBM-MSCs. The use of a media feed not only minimizes time required for media preparation and exchange, but also minimizes contamination risk associated with process manipulation. With the adaptation of cell culture from a 2D to 3D platform, we confirmed the maintenance of critical hMSC functional properties including angiogenic cytokine (FGF, HGF, IL-8, TIMP-1, TIMP-2, and VEGF) secretion, tri-lineage differentiation, and immunomodulatory potential. hBM-MSCs grown on microcarriers in bioreactors yielded comparable ($4.43x10^5$ vs. $4.25x10^5$ cells/ml) cell growth within 6 days of culture, with either half media exchange or a fed-batch process. Metabolite levels of lactate and ammonia were maintained below growth-suppression concentration of 2g/L and 2.5mM respectively with both feed regimens. In addition, hBM-MSCs in bioreactor cultures maintained their tri-lineage differentiation potential and displayed comparable angiogenic cytokine secretion levels and immunomodulatory activity to 2D cultures. Thus, microcarrier suspension culture of hMSCs, with a bioreactor feed in lieu of full or partial media exchanges, will scale hMSC culture, while streamlining the process, to provide significant time and cost savings for translational researchers in Regenerative Medicine and Tissue Engineering.