OPTIMIZATION OF A SCALABLE SINGLE-USE MANUFACTURING PLATFORM FOR EXPANSION OF HIGH QUALITY HUMAN MESENCHYMAL STEM CELLS

Dave Splan, Pall Life Sciences 4307 Varsity Drive Suite B. Ann Arbor, Michigan 48108
Dave_Splan@pall.com
Lye-Theng Lock, RoosterBio Inc. 4539 Metropolitan Court Frederick, MD 21704
Jon Rowley, RoosterBio Inc. 4539 Metropolitan Court Frederick, MD 21704
Mark Szczypka, Pall Life Sciences, 4370 Varsity Drive Suit B Ann Arbor, Michigan 48108

Key Words: Scalable, Single-use, human, mesenchymal stem cell, Expansion.

Human mesenchymal stem cells (hMSCs) isolated from various tissues represent the most highly utilized cell type for cell therapy and regenerative medicine applications. Given that large numbers of high quality cells are required for many applications and that large surface area requirement for cell expansion is necessary, a search for a practical manufacturing platform for cell expansion has been ongoing over the last decade. Feasibility studies have demonstrated the utility of using microcarrriers in dynamic cultures for expansion of hMSCs and the results have positioned this technology as the platform of choice for the cost-effective generation of cells. Microcarrier cultures performed in fully closed single-use systems provide a cGMP-compliant platform for cell expansion and are a logical extension of traditional manufacturing technologies. However the use of high quality cell banks and bioprocess medium in these platforms significantly impacts overall performance. In addition, development of methods to reproducibly harvest and concentrate cells expanded on microcarriers in closed systems is critical.

We have developed a rapid and robust manufacturing platform that enables reproducible expansion and harvest of 28 billion hMSCs from a one passage fed-batch microcarrier culture in a single use reactor seed train in only 8 days. Our system reproducibly achieves hMSC media productivity of > 500M cells/L of media consumed. Data will be presented from experiments using sterile microcarriers (Pall SoloHill) in single use bioreactors (Pall Corp) with high volume hMSC seed stock and a fed-batch bioprocess medium (RoosterBio), including quality parameters related to identity flow markers, angiogenic cytokine secretion profile, multi-lineage differentiation, and inducible immunomodulatory functions. This system has the potential to be rapidly implemented at multiple sites enabling product developers to quickly produce tens of billions of high quality hMSCs for Regenerative Medicine product development programs.