A Single-Use Novel Bioreactor System For Expansion of Human Mesenchymal Stem/Stromal Cells

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ABSTRACT

There is a significant need identified for a robust, scalable, single-use bioreactor system that can be used to efficiently expand primary cells and stem cells. This would expedite process development studies and pre-clinical testing through commercial manufacturing.

There are several bioreactors available from Pall Biotech:
- Pall SoloHill Collagen microcarriers
- AMDS microcarriers
- Cell factories
- AMDS microcarriers

Pall Biotech has previously demonstrated efficient expansion of human mesenchymal stem/stromal (hMSC) in the PadReactor® single-use bioreactor system at the 40 L scale.

Pall’s Allegro™ STR 50 bioreactor is a stirred tank bioreactor platform which is scalable, ergonomic and designed to maximize usability and process assurance.

MATERIALS

Commercially-available bone marrow-derived human mesenchymal cells and medium

The process used in the Allegro STR 50 bioreactor was the same process used in the PadReactor bioreactor runs.

Cell factories

Multi-plate cell culture vessel used in seed train for bioreactor experiments.

AMDS microcarriers

Pall SoloHill Collagen microcarriers

Microcarriers allow for direct transfer out of fluidware culture and into space-efficient 3D cultures with minimal development time.

Excellent attachment and growth across multiple cell types.

Solid core design able to withstand mechanical harvest methods.

Offered in a pre-sterilized, ready-to-use format: The Allegro Microcarrier Delivery System (AMDS).

No hydration needed, simply connect and use.

PERFORMANCE

Figure 1
Expansion of hMSC in Pall’s Allegro STR 50 L single-use bioreactor

Cryopreserved cells

Multi-plate cell culture vessel

Expansion process for hMSC and on Pall’s SoloHill microcarriers using the Allegro STR 50 L single-use bioreactor. Cells thawed from liquid nitrogen were seeded onto multi-plate cell culture vessels and expanded for 3 days. Cells were harvested and seeded onto microcarriers in the Allegro STR 50 L single-use bioreactor at 30 L volume and cultured for 6 days.

Figure 2
Pall’s Allegro STR 50 L single-use bioreactor culture

Process Parameters
- Seeding density: 3000 cells/cm²
- Microcarrier: AMDS, collagen
- Microcarrier concentration: 10 cm²/mL
- pH: 7.35
- Dissolved Oxygen (DO): 50%
- Agitation: 30-40 rpm

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(A) hMSC cell yield from the Allegro STR 50 bioreactor at day 5 is comparable to the PadReactor bioreactor results.
(B) Viability of harvested cells from both bioreactors was also comparable. The same donor and medium used in the PadReactor bioreactor runs was used in the Allegro STR 50 L bioreactor.

Figure 3
Cell yield and viability obtained in the Allegro STR 50 bioreactor is comparable to PadReactor bioreactor results

Figure 4
Allegro STR 50 L bioreactor – expanded hMSC retain critical quality attributes

Cell characteristics are retained when hMSCs are expanded on SoloHill microcarriers in the Allegro STR 50 bioreactor.

The cells maintained differentiation potential, demonstrating adipogenic and osteogenic differentiation capacity.

CONCLUSIONS

The Allegro STR 50 bioreactor supports expansion of human mesenchymal stem/stromal cells on microcarriers delivered into the bioreactor via the Allegro Microcarrier Delivery System (AMDS).

This microcarrier culture enabled cell numbers to reach 0.79 B cells/L in 6 days, with a total of 22 B cells being obtained after harvest.

Cell yield and viability obtained in Pall’s Allegro STR 50 bioreactor was comparable to Pall’s PadReactor bioreactor results.

Expanded hMSC maintained critical quality attributes, including multi-lineage differentiation capacity.

The results obtained in this study lay the groundwork for a complete system for efficient generation of high quality cells.

Together, Pall’s Allegro STR 50 bioreactor and the SoloHill microcarriers in AMDS provide a practical manufacturing platform for dynamic culture and expansion of adherent cells.

hMSC were cultured at 30 L scale in microcarrier-based cultures in the Allegro STR bioreactor for 6 days.

Cells harvested from microcarriers retained critical quality attributes when examined in standard cell characterization assays and bioreactor performance was comparable to the PadReactor bioreactor.

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