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Preparing for cell culture scale-out: establishing parity of bioreactor- and flask-expanded mesenchymal stromal cell culture

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Abstract:

Background: Cell-based therapies have the potential to become treatment options for many diseases, but efficient scale-out of these therapies has proven to be a major hurdle. Bioreactors can be used to overcome this hurdle, but changing the culture method can introduce unwanted changes to the cell product. Therefore, it is important to establish parity between products generated using traditional methods versus those generated using a bioreactor.
Methods: Mesenchymal stromal cells (MSCs) are cultured in parallel using either traditional culture flasks, spinner vessels or a new bioreactor system. To investigate parity between the cells obtained from different methods, harvested cells are compared in terms of yield, phenotype and functionality.
Results: Bioreactor-based expansion yielded high cell numbers (222 – 510 million cells). Highest cell expansion was observed upon culture in flasks [average 5.9 population doublings (PDL)], followed by bioreactor (4.0 PDL) and spinner flask (3.3 DPL). Flow cytometry confirmed MSC identity ($CD73^+$, $CD90^+$ and $CD105^+$) and lack of contaminating hematopoietic cell populations. Cultured MSCs did not display genetic aberrations and no difference in differentiation and immunomodulatory capacity was observed between culture conditions. The response to IFNγ stimulation was similar for cells obtained from all culture conditions, as was the capacity to inhibit T cell proliferation.
Conclusion: The new bioreactor technology can be used to culture large amounts of cells with characteristics equivalent to those cultured using traditional, flask based, methods.

Keywords: Bioreactor, Mesenchymal stromal cells, Cell Therapy, Cell culture bag