



## Technical Note:

# Microcarrier Selection for Use in Spinner Flask Based Cell Cultures with Mesenchymal Stem Cells.

### Introduction

Large scale manufacturing of adherent-dependent cell types for regenerative medicine applications will require transitioning away from planar type cell culture towards stirred tank bioreactors using microcarriers. Microcarriers are available in a range of formats that includes dextran, glass and polystyrene that have been derivatized or coated to carry a charge, peptides or extra cellular matric proteins such as collagen. Microcarriers B and C were animal origin free.

### Methods

In this technical note, the results of experiments to evaluate 6 different microcarriers as a base matrix for scaling up from planer cultures (Petrie dishes) to stirred tank culture (125mL spinner flasks) are detailed.

All experiments were performed using human adipose derived mesenchymal stem cells (aMSCs) grown on a panel of microcarriers in DMEM (Dulbecco's Modified Eagle Medium) supplemented with 10% FBS (Fetal Bovine Serum) and 8ng/mL bFGF (basic Fibroblast Growth Factor).

Cells were detached from the microcarriers using TrypLE to allow assessment of cell recovery. TrypLE is a series of highly purified, animal origin free cell dissociation enzymes that are used for dissociating a wide range of adherent mammalian cells.

### Results.

Microcarrier Type	Fold Increase in Cell Density @ Day 7		Cell Recovery %		Cell Viability %		Cell Yield (E+04 cells/mL)	
	Petrie	Spinner	Petrie	Spinner	Petrie	Spinner	Petrie	Spinner
A	24	24	35	52	98	95	4.5	10.3
B	28	15	46	58	92	91	9.2	8.3
C	21	16	52	86	98	93	11.6	18.8
D	28	12	28	84	97	95	2.9	13.5
E	29	16	27	46	96	97	3.3	5.3
F	24	17	22	30	91	90	1.9	2.4
<b>Averages</b>	<b>25.67</b>	16.67	35.00	<b>59.33</b>	<b>95.33</b>	93.50	5.57	<b>9.77</b>

- The results show that microcarriers that demonstrated robust growth in static culture did not always translate to robust growth in stirred tank cultures, with all microcarriers in planar culture showing an equal or higher growth over the same microcarriers in a spinner flask.
- Microcarriers B, D and E supported robust growth in planar culture (28, 28 and 29 fold increases by day 7), but all performed poorly in agitated suspension culture (15-, 12- and 16-fold increases by day 7).

- Cell recovery was significantly higher for all microcarriers used in suspension culture with increases in recovery ranging from 26% higher with microcarrier B, to 200% higher with microcarrier D.
- Recovered cell viability was very similar in all experiments, although recovery for planer cultures was higher in 5 of the 6 experiments. The maximum difference observed was 5% with microcarrier C, with only a 6% range covering all microcarriers tested.
- 5 of the 6 microcarriers tested exhibited higher cell yields in suspension culture than in planar culture. Microcarrier B was the exception showing a 9.78% lower yield in suspension culture than in planar culture.
- Microcarriers A and D both exhibited over 100% difference (124% and 365%) in cell yield in suspension culture than in planar culture.

## Conclusions

Microcarriers that support robust growth in planar (static) culture do not always translate to robust growth in microcarrier based suspension cultures. The results shown highlight the complex interactions that occur between microcarrier surfaces and the hydrodynamic forces that occur in agitated suspension cell culture systems.

It is critical to screen different microcarriers in both static and suspension cultures to understand which is the best for scaling up and achieving a higher level of cell density, growth and recovery.

Small scale platforms, such as Petrie dishes and small volume spinner flasks allow for rapid, economical, initial comparisons between culture conditions, microcarrier types, seeding densities and media selection (the last two variables are not considered here), without requiring commitments to production of large volumes of media or cells.

## References

- Schnitzler, A. et. al. (2015). Media and microcarrier surface must be optimized when transitioning MSC cell expansion to stirred tank bioreactors. *BMC Proceedings*, **9**(Suppl 9): p57.
- Simaria, A.S. et.al. (2104). Allogeneic cell therapy bioprocess economics and optimization: single-use cell expansion technologies. *Biotechnol Bioeng.* **111**. 69-83.

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