Summary

- A significant challenge for the Regenerative Medicine (RM) industry is to develop cell culture processes that are affordable, well characterised and can be scaled up for production to ensure clinical and commercial success.

- ambr® 15 is an automated micro-scale bioreactor system that mimics the features and process control (pH, DO, temperature, stirring rate) provided by much larger scale bioreactors, but in a volume of 10 - 15 mL. Parallel processing capability and excellent consistency enable rapid, high throughput process optimisation and improvement, including DoE studies.

- ambr® 15 is widely used in the bio-process industry for process development, cell line selection and effective media optimisation in less time with reduced reagent use and labour saving (1, 2). It can also be used as a novel small scale continuous culture perfusion mimic.

- ambr® 15 has been successfully used in RM applications; including processing microcarriers, cell aggregates e.g. embryoid bodies and HSCs (3, 4).

- High throughput tools with parallel processing, such as ambr® 15, help address a major biomanufacturing bottleneck and improve economic models by reducing the resources and timescale needed to develop robust and cost-effective manufacturing processes, so bringing novel therapies to patients sooner.

Optimizing culture conditions for NK92 cells

The ambr® 15 system can be used for automated optimisation of critical process parameters, with automatic feeding, control and sampling.

- Optimum stirrer speed for NK92 culture found to be 450 RPM.

- No strong correlation between inoculum density and viability.

- NK92 cells in ambr® 15 are as uniform, well mixed cell suspension.

Embryoid bodies successfully cultured in ambr® 15

Cellular aggregates such as embryoid bodies (EB) can be successfully cultured in ambr® 15.

- EBs show good survival, and proliferate

- The optimisation speed influences cell yield, with a speed of 300 RPM (4 and 5) giving larger EB size than 400 RPM (6 and 7) and the orbital shaker speed at 50 rpm.

Reliable automation of microcarrier studies

ambr® 15 can be effectively used as a high throughput scale-down model for microcarrier work.

- Tarifold liquid handling offers consistent microcarrier loading (A).

- Settling method (B) enables challenging media exchange operations.

- Cell growth on microcarriers is comparable to standard culture.

Proven high throughput tool for scale Up

Industrial users have demonstrated that the ambr® 15 system matches the data produced in much larger, for example 5 L, bench scale systems.

hESC expansion and differentiation in ambr® 15

Embryonic stem cell derived from hES and hESC cell lines can be successfully expanded and differentiated in ambr® 15.

- ambr® 15 significantly improved aggregate expansion (A) and cardiomyocyte differentiation (B) compared to orbital shaker control.

DoE process and media optimisation

The ambr® 15 platform has been successfully implemented by a number of industrial companies for media development and feed strategy optimisation.

- The ability to compare multiple variables simultaneously in one run provides:

- A many-fold data production increase in less time and a smaller footprint

- Higher comparability for DoE runs in one experiment

- Greater process understanding for manufacturing and FDA filing.