Advancing high-quality bioreactor-scale cell culture using IN-AIR MICROFLUIDICS™

Maik Schot[1], Vincent Rangel[1], Patrick Blokzijl[1], Vasileios Trikalitis[1,2], Robbert van Dinther[1], Tom Kamperman[1]
[1] IamFluidics BV, High Tech Factory, De Veldmaat 17, 7522NM Enschede, The Netherlands
[2] University of Twente, 7500AE Enschede, the Netherlands

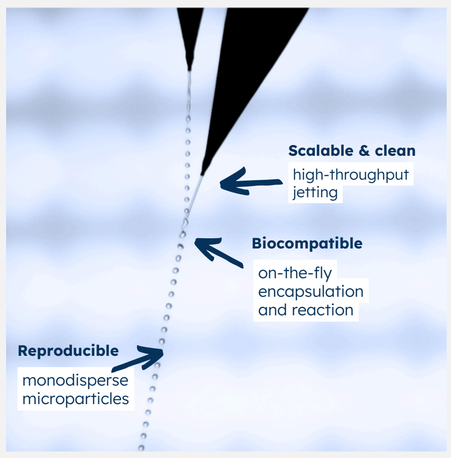
INTRODUCTION

The **fast-growing cell and gene therapy market** demands innovative technologies to facilitate scalable cell expansion and overcome issues related to cell quality and process efficiency. As therapies transition from the experimental phase towards widespread clinical application, traditional cell culture methods fall short, and **scalability becomes a hurdle**.

Common **challenges in upscaling** cell therapy products or producer cultures include **maintaining high cell harvesting efficiencies**, reduced cell quality due to the increase in **shear stress in bioreactors**, and the availability of **xeno-free / GMP-grade** culture components.

IN-AIR MICROFLUIDICS™ is a process based on vibrating jet technology, which enables the production of highly monodisperse microdroplets and encapsulation of sensitive components at ultra-high throughput. Using IN-AIR MICROFLUIDICS™, we developed solutions to tackle the challenges that therapy developers encounter in scale-up. **Our technology enabled the production of well-defined dissolvable microcarriers and protective 3D cell culture microcapsules**. With these developments, we aim to help manufacturers accelerate their development of new life-saving treatments.

IN-AIR MICROFLUIDICS™ ENCAPSULATION TECHNOLOGY



compatible with live cells, biomolecules, and sensitive APIs

low shear stress
no toxic solvents
no pre-treatment

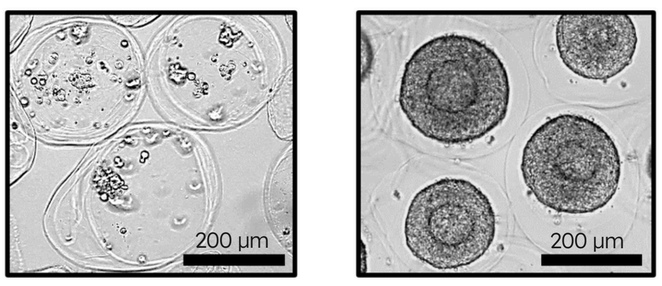
high precision
high throughput
high efficiency

XENO-FREE SUSPENSION CULTURE USING CELL ENCAPSULATION

CONTROLLED AGGREGATE FORMATION & GENTLE RELEASE

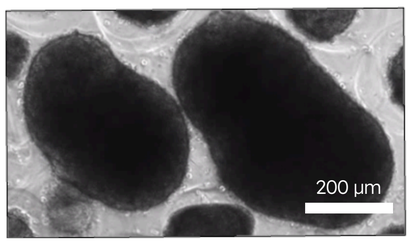
The unique in-air microfluidics process enabled high-throughput cell encapsulation at unprecedented throughputs. Utilizing alginate and calcium chloride, embryonic stem cells were encapsulated in a xeno-free and highly cytocompatible manner using a triple-nozzle jetting approach. The resulting encapsulated embryonic stem cells were transferred to a suspension culture, where they were able to grow in a protected yet size-restricting micro-environment to yield high-quality aggregates. Aggregates could be easily released from capsules using gentle reagentia such as PBS or alginate-lyase.

Microencapsulated 3D stem cell aggregates

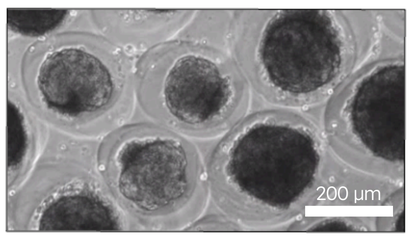


Day 0 Day 6

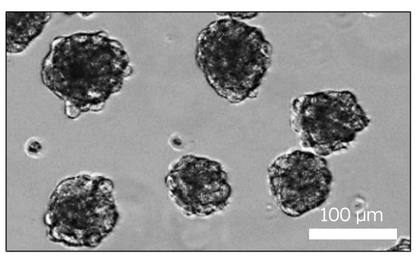
Non-encapsulated aggregates



Encapsulated aggregates

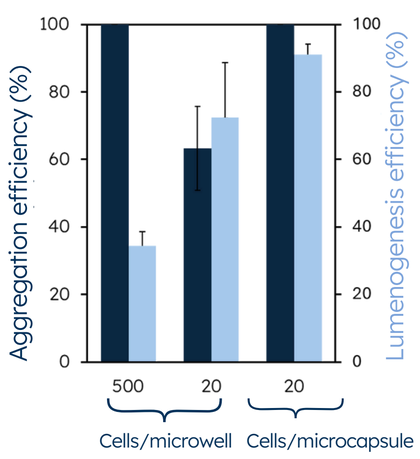


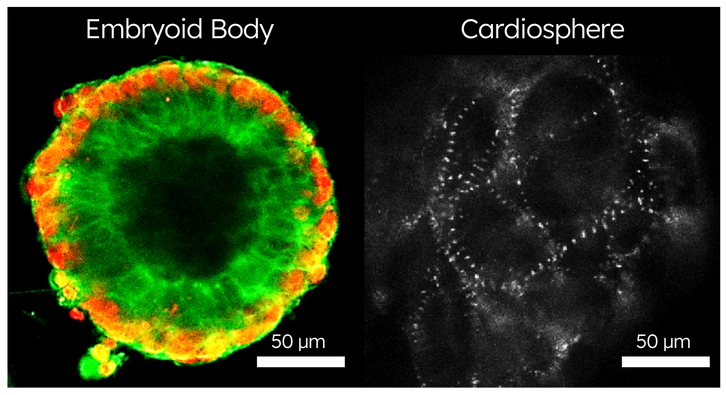
Released aggregates



IMPROVED PERFORMANCE OF ENCAPSULATED AGGREGATES

Encapsulated stem cells were able to form embryoid bodies over time, developing lumens in a significantly more efficient manner (92.4±0.8%) when compared to conventional microwell culture (72±16%). Upon chemical stimulation, stem cell aggregates were able to differentiate into contracting cardiospheres. In summary, stem cell encapsulation within hollow capsules not only protected aggregates from mechanical stress, but led to improved aggregate functionality.
The image in the center below highlights the cell membranes (green) and nuclei (orange) along with lumen formation (black core) in embryoid bodies. The image below on the right shows α-actinin within differentiated cardiospheres.



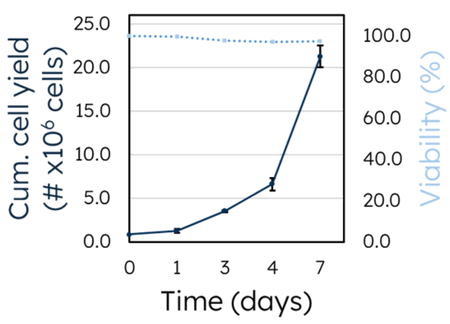


Cell membrane / Cell nucleus α-actinin

ADHERENT CULTURE USING DISSOLVABLE MICROCARRIERS

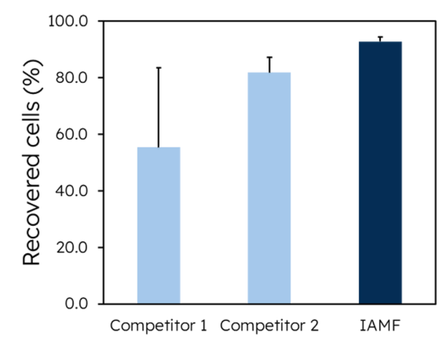
CELL GROWTH ON DISSOLVABLE MICROCARRIERS

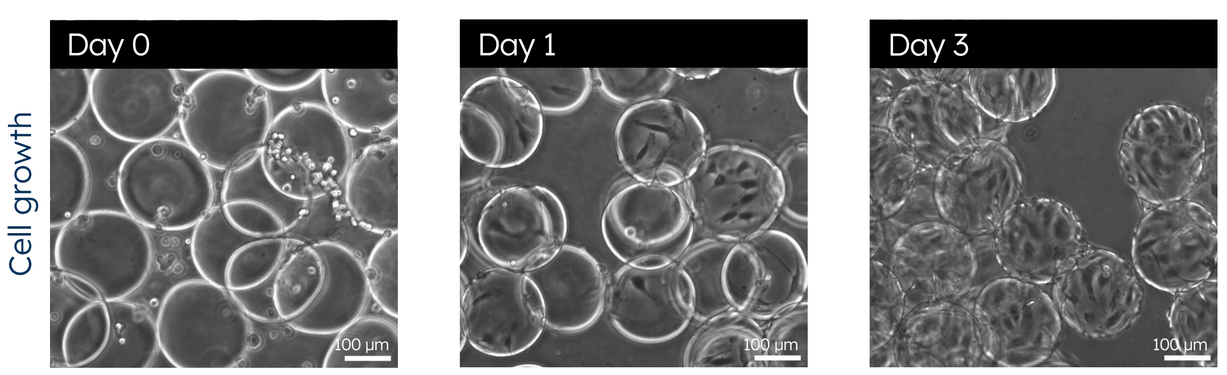
Bone-marrow derived human mesenchymal stem cells (BM-hMSCs) were grown on IamFluidics® dissolvable microcarriers for 7 days in spinner flasks. Exponential cell expansion was observed and cells maintained a high viability throughout the culture period. At day 4, a surface area expansion step was included which enabled bead-to-bead transfer and subsistent cell proliferation.



EFFICIENT HARVESTING

IamFluidics® dissolvable microcarriers were easily dissolved using standard cell culture components, allowing for highly efficient cell harvesting within ~15 minutes of incubation. hMSC recovery percentages of >90% were obtained for cell-covered microcarriers cultured in spinner flasks for at least 7 days.





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[1] Visser, C.W. et al. Science Advances, 4(1), 2018
[2] van Loo, B. et al. Nature Communications,14,2023

IamFluidics

In collaboration with

SCINUS CELL EXPANSION

UNIVERSITY OF TWENTE.

Download our whitepaper

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