Dissolvable Microcarriers and Capsules by IN-AIR MICROFLUIDICS™ for Scaling 2D & 3D Cell Culture

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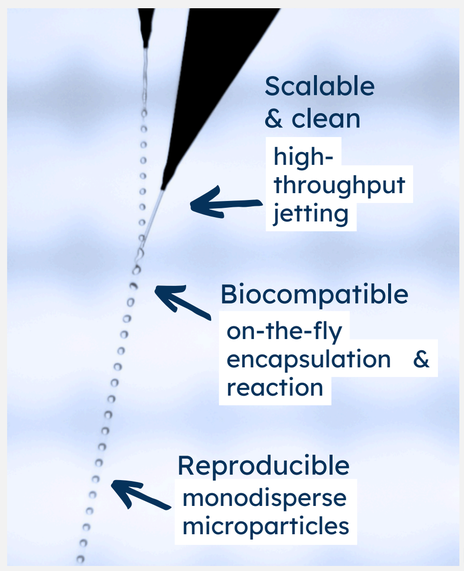
NEED: SCALE CELL CULTURE WITH QUALITY

1. Scaling traditional bioreactor cell cultures is **not reproducible**, because diffusion gradients and shear forces cause uncontrolled cell growth, differentiation, and necrosis.
2. Plate-based microtissue culture is accurate but **not scalable**, for example, hanging drops, microwells, and printed spheroids are typically limited to a few thousand tissues.
3. Current microcarriers suffer from **poor cell harvesting** efficiency (typically 50% loss).
4. Most available cell culture biomaterials are **not xeno-free and/or GMP** compatible.

OUR TECH: IN-AIR MICROFLUIDICS™



compatible with live cells, biologics, and sensitive APIs

low shear stress
no toxic solvents
no pre-treatment

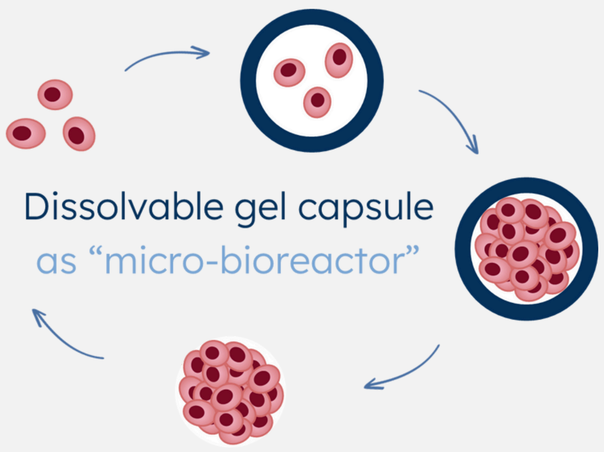
high precision
high throughput
high efficiency

Ref: Visser, C.W. et al. Science Advances, 4(1), 2018

SOLUTION 1: XENO-FREE DISSOLVABLE 3D CELL CAPSULES

HIGH-YIELD ENCAPSULATION, AGGREGATION, AND RELEASE

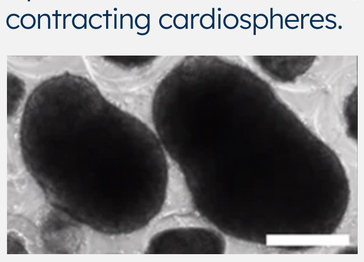
In-air microfluidics enabled high-throughput human embryonic stem cell (hESC) encapsulation into xeno-free calcium-alginate microcapsules at a rate of >1000 cell-laden capsules per second. The semi-permeable microcapsules acted as 'micro-bioreactors' that enabled diffusion of nutrients, waste products, and cytokines. This supported cell proliferation and monodisperse aggregate formation, while preventing uncontrolled cell growth, merging, and hazardous shear stresses. Cell aggregates could be readily released from capsules using mild reagents like phosphate-buffered saline or alginate-lyase.



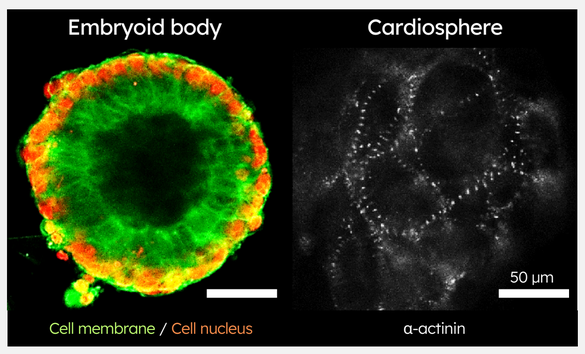
Ref: van Loo, B. et al. Nature Communications,14,2023

IMPROVED PERFORMANCE OF ENCAPSULATED AGGREGATES

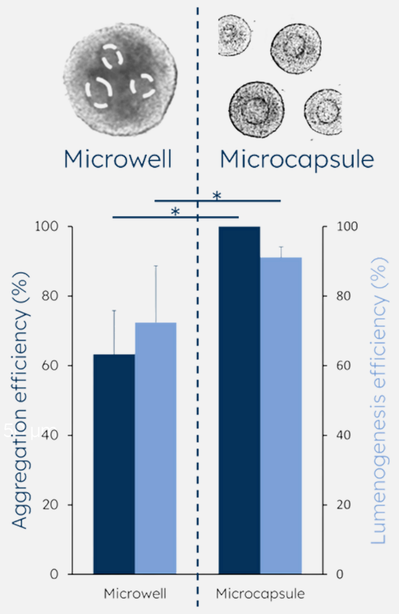
Micro-encapsulated hESCs formed embryoid bodies in a more controlled and efficient manner compared to traditional non-encapsulated suspension or microwell cultures. Furthermore, encapsulated hESCs showed significantly better lumenogenesis (92.4±0.8%) compared to conventional microwell culture (72±16%). Upon chemical stimulation, stem cell aggregates were able to differentiate into contracting cardiospheres.



Non-encapsulated cell aggregates spontaneously and uncontrollably merge in culture.



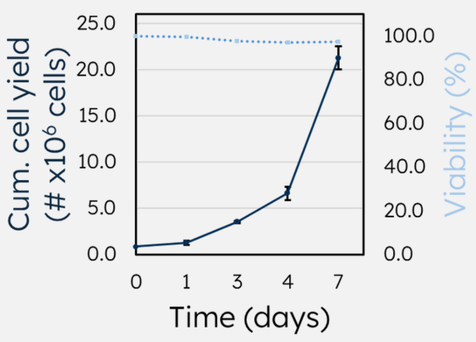
Micro-encapsulated

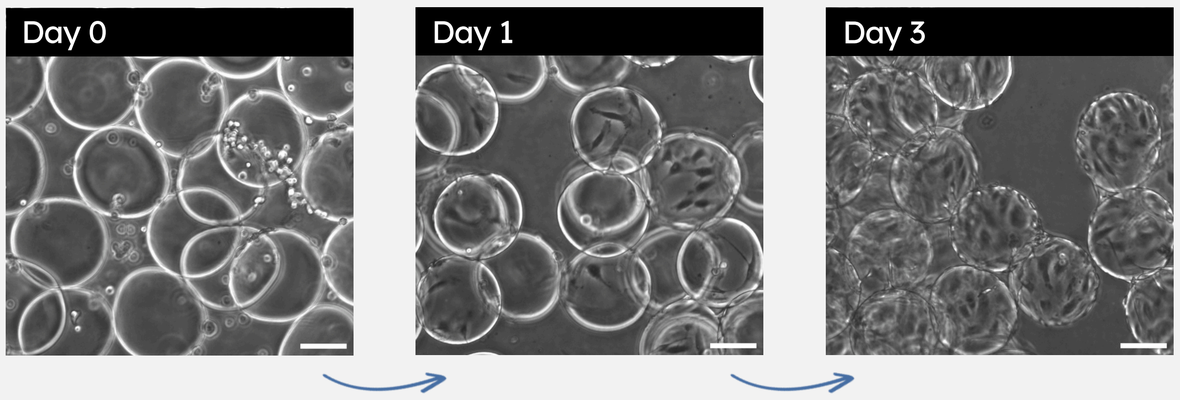


SOLUTION 2: GELATIN-COATED DISSOLVABLE MICROCARRIERS

HIGH VIABILITY AND EXPONENTIAL PROLIFERATION

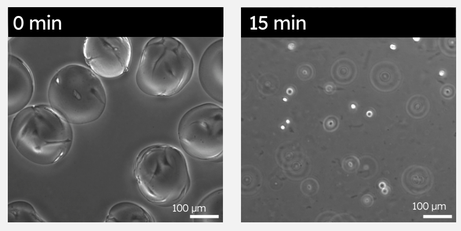
Bone marrow-derived human mesenchymal stem cells (BM-hMSCs) were grown on dissolvable microcarriers for 7 days in spinner flasks. Exponential cell expansion was observed and cells maintained a high viability throughout the culture period. At day 4, a surface area expansion step was included which successfully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

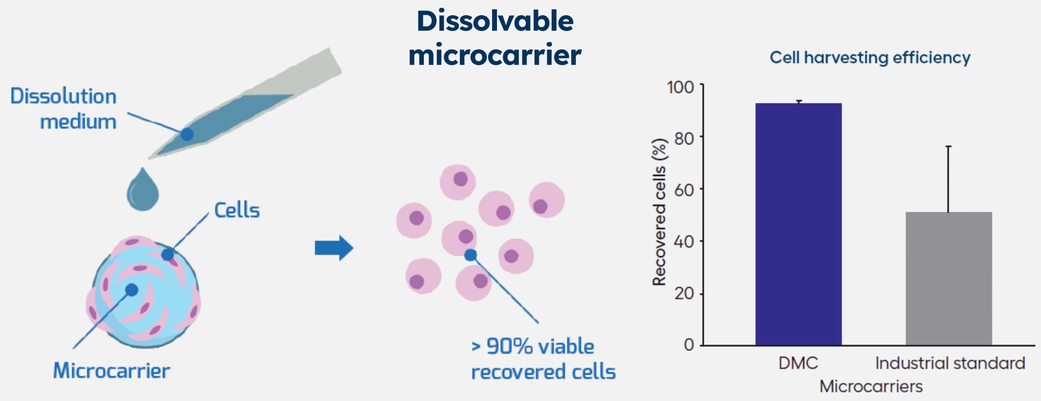




EFFICIENT HARVESTING WITH TRADITIONAL REAGENTS

The microcarriers could be dissolved within 15 minutes using standard cell culture components like EDTA/Trypsin or TrypLE™. This resulted in >90% harvesting efficiency as compared to only ~50% with traditional non-dissolvable microcarriers.





PARTNERSHIP & ACKNOWLEDGEMENT

Cell culture work has been partly performed at University of Twente: Leijten Laboratory, Developmental BioEngineering department, and Applied Stem Cell Technologies group as, amongst others, published in Nature Communications (2023) 14:6685. Gelatin-coated dissolvable microcarriers have been developed in partnership with Rousselot Biomedical and commercialized, as published on microparticles.shop. Microcarriers have been successfully tested by myriad academic and industrial beta testers. Special thanks to early adopters Dr. Rouwkema's Vascularization lab (UTwente), Dr. Farrell's lab (Erasmus MC / TKI ADDBONE), and Scinus Cell Expansion.

Dissolvable microcarriers

Available at microparticles.shop

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