DIFFERENTIATING DROPLET-ENCAPSULATED STEM CELLS INTO CARDIAC ORGANOIDS FOR A HIGH-THROUGHPUT MODEL OF THE HUMAN HEART

Iris Teunissen van Manen (TNW-AST), Johanna Husch (TNW-DBE), Isa Porsul (TNW-DBE), Carla Cofiño-Fabres (TNW-AST), Jeroen Leijten (TNW-DBE), Robert Passier (TNW-AST)

Introduction

Lab-grown self-organised heart tissues (cardiac organoids) are a valuable tool to study the human heart in health and disease. However, current models are typically low-throughput and suffer from high variability between and within batches.

Objectives

We aimed to develop a robust, high-throughput cardiac organoid model using microfluidic encapsulation of stem cells into microgel droplets. This approach enables the production of smaller, more consistent organoids optimised for large-scale studies.

Methods

Using an established microfluidic strategy (1,2), we encapsulated human stem cells into hollow hydrogel droplets and compared various encapsulation parameters, including droplet size and cell density. After aggregation, encapsulated stem cells were guided through a three-step culture protocol (3) to mimic early human heart development and promote differentiation and self-organisation of multiple cardiac cell types. These encapsulated organoids were compared to control organoids grown in traditional culture dishes. We assessed differentiation efficiency by evaluating beating capacity and stained for various cardiac proteins using fluorescent microscopy.

Results

Control organoids successfully developed into beating structures containing diverse cardiac cell populations. For the encapsulation approach, differentiation efficiency was highly dependent on the initial aggregate size. The optimised condition reproducibly resulted in beating encapsulated organoids that were similar in cellular diversity as control organoids, but more consistent and easier to produce in large numbers.

Conclusion

Microfluidic encapsulation provides a scalable, reproducible method for generating cardiac organoids. This high-throughput platform has potential for applications such as cardiac toxicity testing and disease modelling. Future research will further compare their molecular and electrophysiological properties to traditional models.

References

1. Araújo-Gomes N, Zoetebier-Liszka B, van Loo B, Becker M, Nijhuis S, Smink AM, et al. Microfluidic Generation of Thin-Shelled Polyethylene Glycol-Tyramine Microgels for Non-Invasive Delivery of Immunoprotected β-Cells. Adv Healthc Mater [Internet]. 2024 Oct 1 [cited 2025 Mar 10];13(25):2301552. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/adhm.202301552
2. Husch JFA, Araújo-Gomes N, Willemen NGA, Cofiño-Fabrés C, van Creij N, Passier R, et al. Upscaling Osteoclast Generation by Enhancing Macrophage Aggregation Using Hollow Microgels. Small [Internet]. 2024 Nov 1 [cited 2025 Mar 10];20(46):2403272. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/smll.202403272
3. Lewis-Israeli YR, Wasserman AH, Gabalski MA, Volmert BD, Ming Y, Ball KA, et al. Self-assembling human heart organoids for the modeling of cardiac development and congenital heart disease. Nat Commun [Internet]. 2021 Dec 1 [cited 2023 Nov 6];12(1). Available from: /pmc/articles/PMC8390749/