Advanced 3D iPSC-derived cardiac model for improved drug-induced cardiotoxicity assessment

S. Dhepe[1], S. Swamy[1], S. Dabbral[1], J. Anjankar[1], S. Shetty[1], K. Rajendran[1], P. Bhanushali[1], A. Khanna[1]*

[1]Yashraj Biotechnology Ltd, Navi Mumbai, India

Contact: marketing@yashraj.com

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3D CELL CULTURE WORKSHOPS & CONFERENCES

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Introduction

- Drug-induced cardiotoxicity remains a major cause of late-stage drug attrition, largely due to the limited physiological relevance and predictive capacity of conventional 2D in vitro cardiac models.
- Advanced 4D tissue engineering platforms enable controlled self-organization, multicellular interactions, and functional maturation, addressing key limitations of static in vitro systems.
- The SmartHeart® Smart Contractility platform (4D Cell) generates self-organized, ring-shaped cardiac tissues with defined geometry, enabling reproducible measurement of synchronized contractile function.
- Hydrogel-based 4D plates provide spatial and mechanical cues that promote tissue alignment, stable force generation, and functional maturation over time.
- In this study, the SmartHeart® platform was evaluated for its compatibility with in-house human iPSC-derived cardiomyocytes (YBLiCardio) co-cultured with human cardiac fibroblasts to establish a physiologically relevant model for improved cardiotoxicity prediction.

Methodology

Human iPSC-derived cardiomyocytes (YBLiCardio) and primary human ventricular cardiac fibroblasts were used to generate 4D cardiac organoid constructs using hydrogel-based SmartHeart® plates. Cells were seeded at a defined cardiomyocyte-to-fibroblast ratio of 3:1 (~85,000 cells per well) using a sequential seeding strategy, enabling guided self-organization into ring-shaped, contractile cardiac organoids. Constructs were maintained for 7 days, and cardiac morphology was assessed using phase-contrast imaging. Functional excitation–contraction coupling was evaluated using calcium flux assays. Cardiac identity, structural organization, and maturation were further characterized by immunocytochemistry and RT-qPCR analysis of key cardiac lineage and maturation markers.

Conclusion

Human iPSC-derived cardiomyocytes (YBLiCardio) were successfully integrated with the SmartHeart® platform, demonstrating platform compatibility. The resulting 4D cardiac rings expressed key markers of cardiomyocyte maturation and exhibited functional activity, as evidenced by calcium flux assay.

Collectively, this technology enables the generation of physiologically relevant 3D cardiac co-culture models, offering a more predictive and translational alternative to conventional 2D assays for early drug safety assessment.

Results

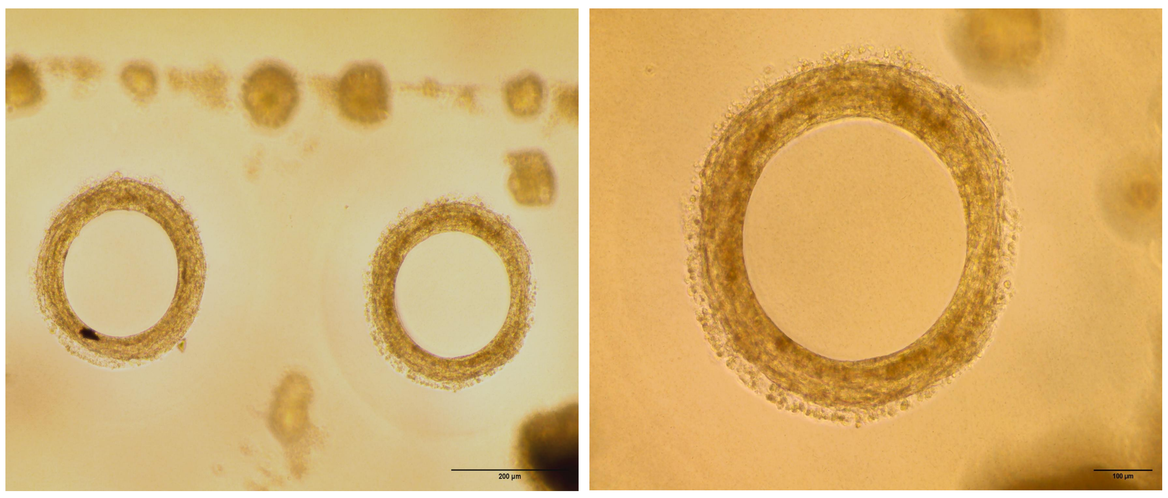

Fig 1: Phase Contrast Images of microwells of SmartHeart® hydrogel-based 4D plate.

Each plate has 96 wells and each well has 9 hydrogel- based microwells

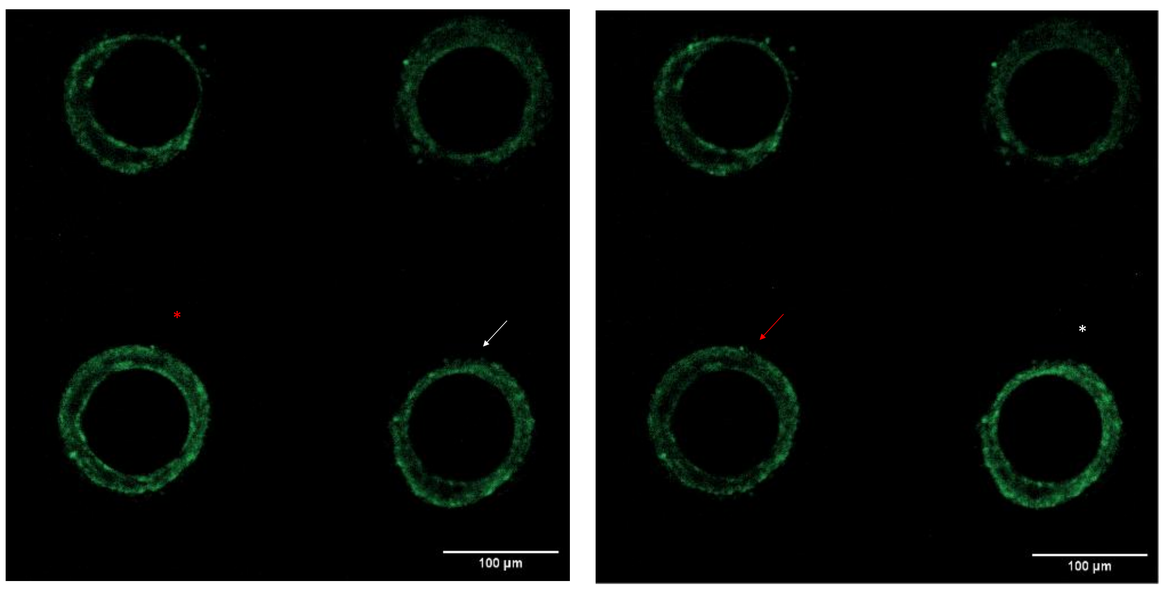

Fig 2: Calcium Flux Assay using Fluo-4 AM.

(A) And (B) demonstrate calcium influx and efflux activity.

*: Contraction phase associated with calcium influx and increased fluorescence.

: Relaxation phase associated with calcium efflux and decreased fluorescence.

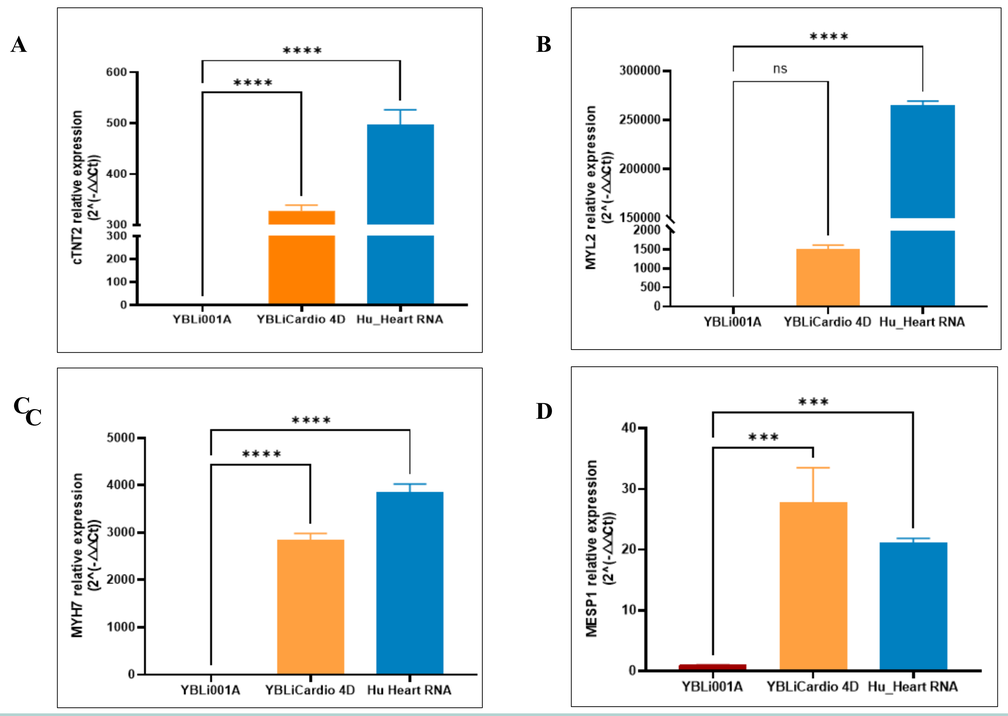

Fig 3: Gene expression of Cardiomyocytes genes. Graph showing the expression of cardiac related genes A) CTNT2, B) MYL2, C) MYH7, D) MESP1. *p**** : <0.0001, p*** : 0.0001, ns – non significant*

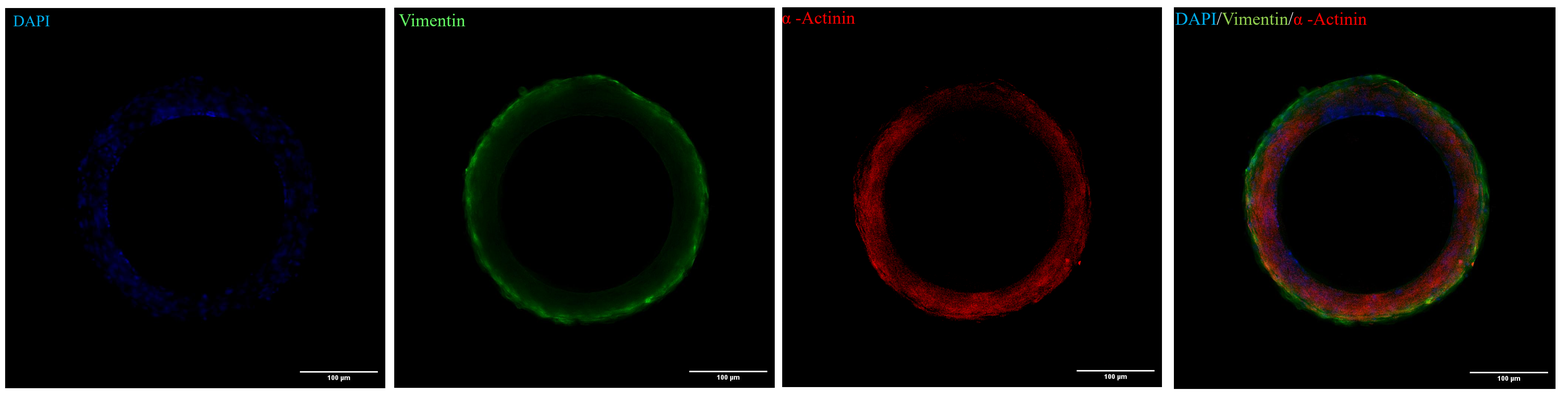

Fig. 4: Immunocytochemistry for cardiac and fibroblast markers demonstrates the expression of (A) DAPI (750nM), (B) Vimentin (1:2000 dilution), (C) α –Actinin (1:1500 dilution), (D) Merged image of (A), (B), (C).

CONTACT
Ms. Shreya Dhepe
Yashraj Biotechnology Ltd.
Email: shreya.dhepe@yashraj.com
Website: www.yashraj.com

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