

4Dcell SmartHeart plates Innovative cardiac organoids

Circular 3D morphology mimicking heart physiology

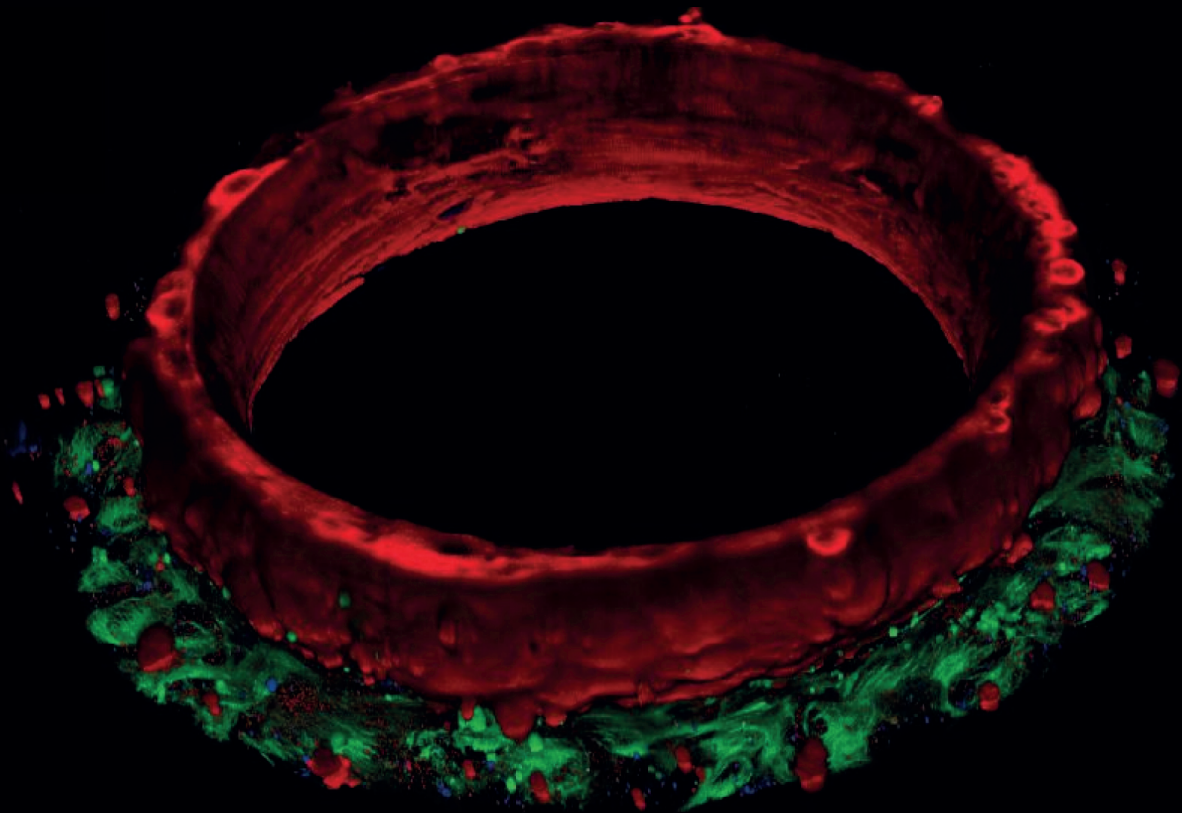
Improved maturation

Reproducible size and shape

Easy to image

High throughput

Multiple key read-outs in a single assay in situ



4Dcell SmartHeart Plates

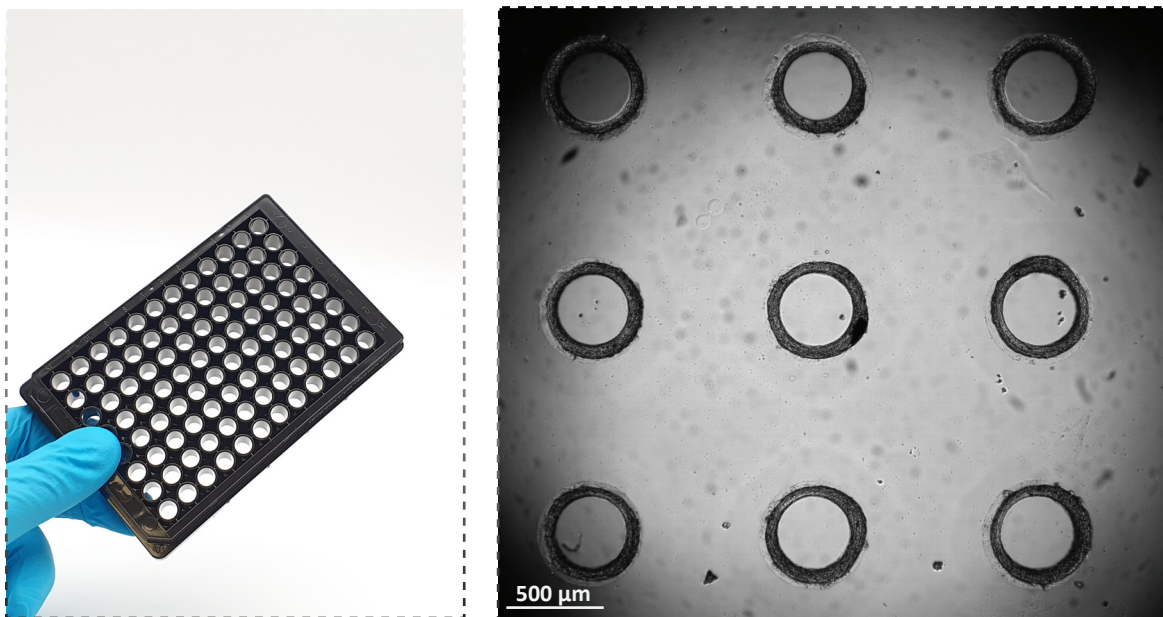
Circular 3D morphology moves towards a better model for heart physiology

The SmartHeart is a 3D cardiac assay, which enables both the self assembly and maturation of functional ring shaped cardiac tissues and the acquisition of the most relevant read outs, all in situ and in a single platform. The tissues are formed by cardiomyocytes (e.g. hiPSC- Cardiomyocytes) and other relevant cells as fibroblasts.

The Polyethylene based hydrogel is optically transparent enabling high resolution imaging of the tissues as well as to observe ionic transients.

The hydrogel shape provides a microenvironment which enables the cells to sediment and self-aggregate into **a beating tissue within hours**.

This versatile solution can be used to test new compounds or assess toxicity of drugs targeting other types of pathologies, as it fits HTS and HCS requirements.



Main read-outs

- ✕ Contractility forces
- ⦿ Beating parameters
- 👁️ Ionic exchange
- 📐 Cell and tissue morphology

Improved maturation

- ⚡ 60 Hz beating frequency
- ⦿ Physiological contractile properties
- 🧬 Cellular organization
- 🌱 Multicellular tissues

4Dcell offers

24 and 96 glass-bottom multiwell plates with microstructured hydrogels.

FLASH TO SEE THE
SMARTHEART BEATING

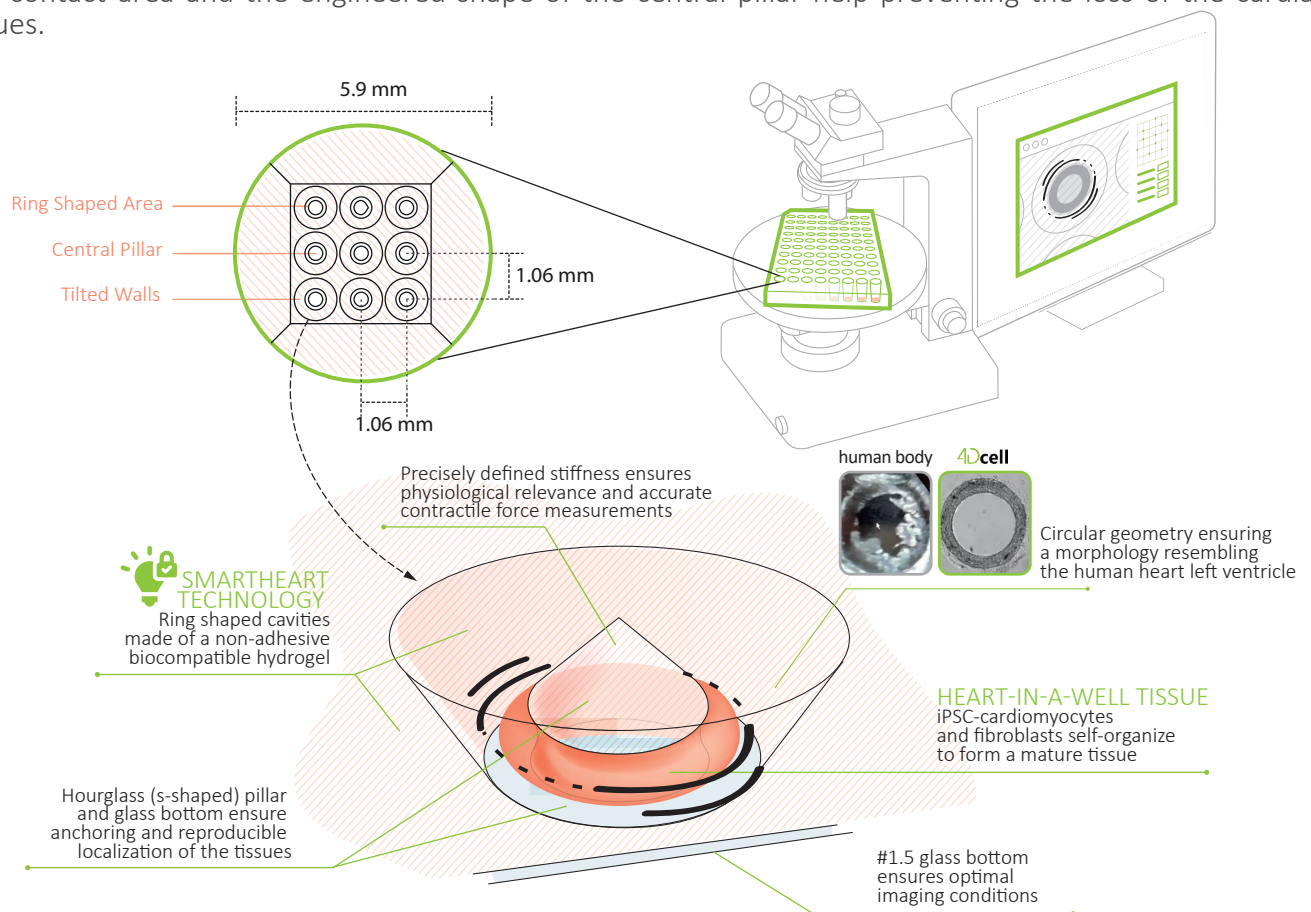


SmartHeart: an innovative micro-engineered hydrogel to mimic the heart morphology

Cell culture substrates, as multiwell plates, are coated with a 3D structured hydrogel, molded into an array of conical-shaped microwells containing a central pillar.

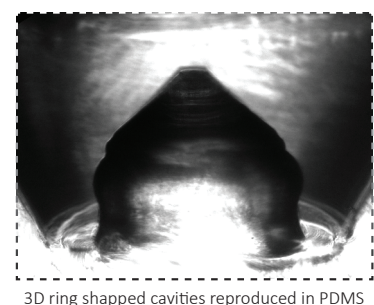
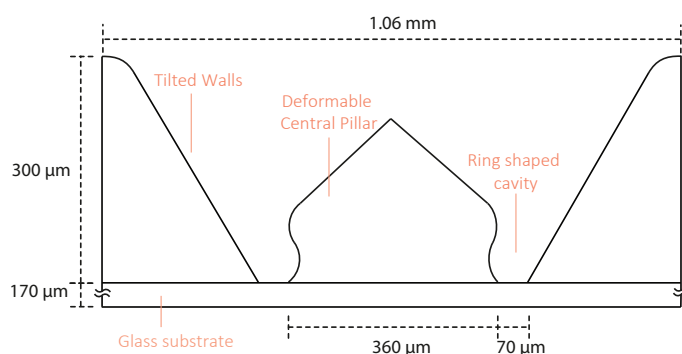
When cells are seeded on top of these microstructures, they are guided towards the ring-shaped cavity, self-assembling into a circular tissue, which surrounds a hydrogel central pillar. The contractility force, beating rate and beating amplitude are assessed through the deformation of the central pillar, as the mechanical properties of the hydrogel are known and can be adjusted to match the cell model.

The contact area and the engineered shape of the central pillar help preventing the loss of the cardiac tissues.



The ring shaped cavities for cell culture are molded on biocompatible hydrogels (polyethylene glycol- PEG), using molds fabricated by high-resolution milling. The hydrogel's stiffness can be adjusted within a range of around 5 kPa to 20 kPa.

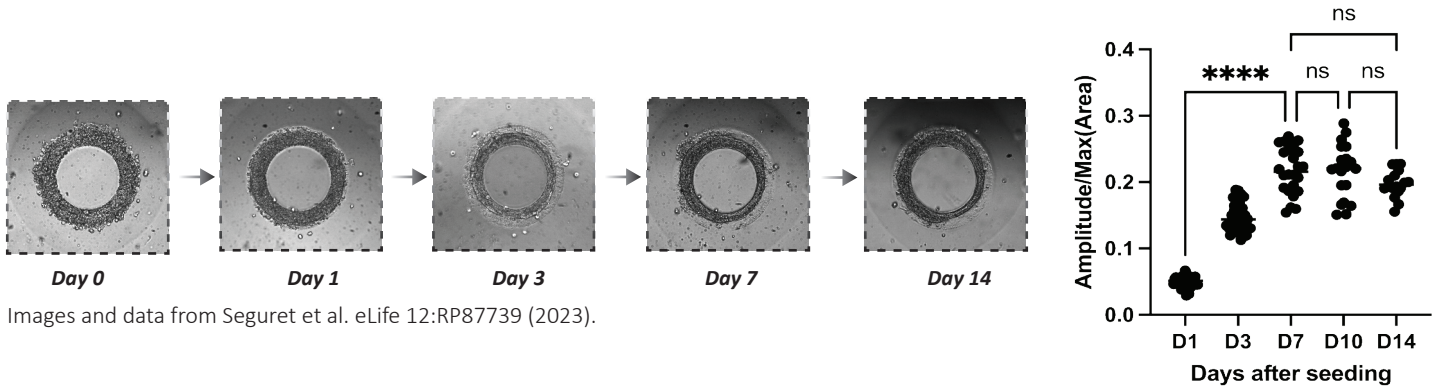
Each well has 21 (for 24 well plate) and 9 (for 96 well plate) individual microwells for tissue formation



3D ring shaped cavities reproduced in PDMS

Assembly and maturation of tissues

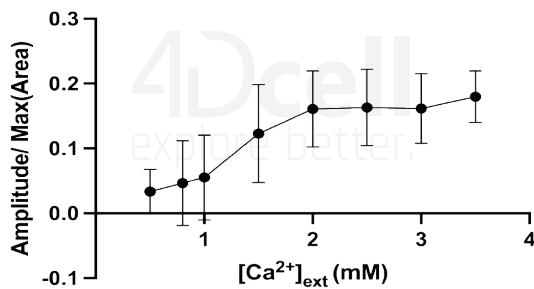
Maturation of the tissues during 14 days. Cells form connections between them and become elongated mimicking the heart tissue. Maximum contraction of the tissues recorded during 14 days, to assess their maturation.



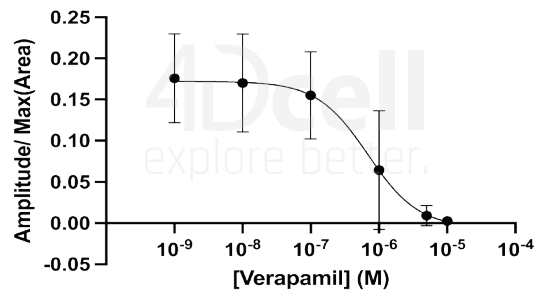
Drug tests

The tissues were subjected to different standard drugs to assess their pharmacological response.

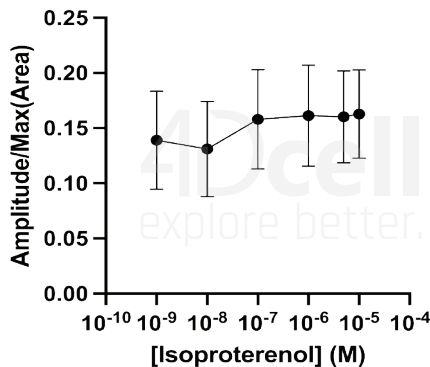
Calcium - induces a larger contraction amplitude of the tissues



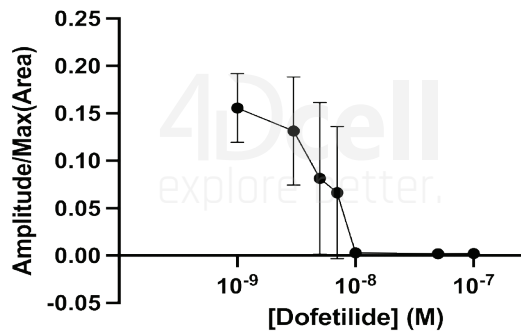
Verapamil - calcium channel blocker



Isoproterenol - adrenergic receptor agonist which results in increased beating frequency and contraction



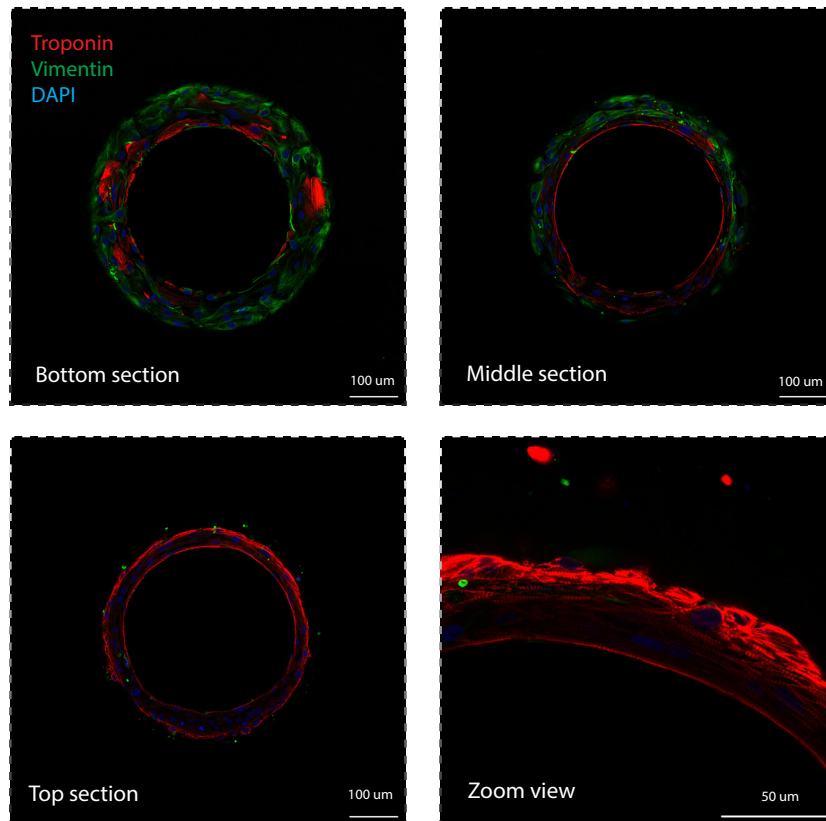
Dofetilide - antiarrhythmic agent, can have toxic effects when overdosed



Data from Seguret et al. eLife 12:RP87739 (2023).

High-resolution imaging: tissue morphology and intracellular imaging

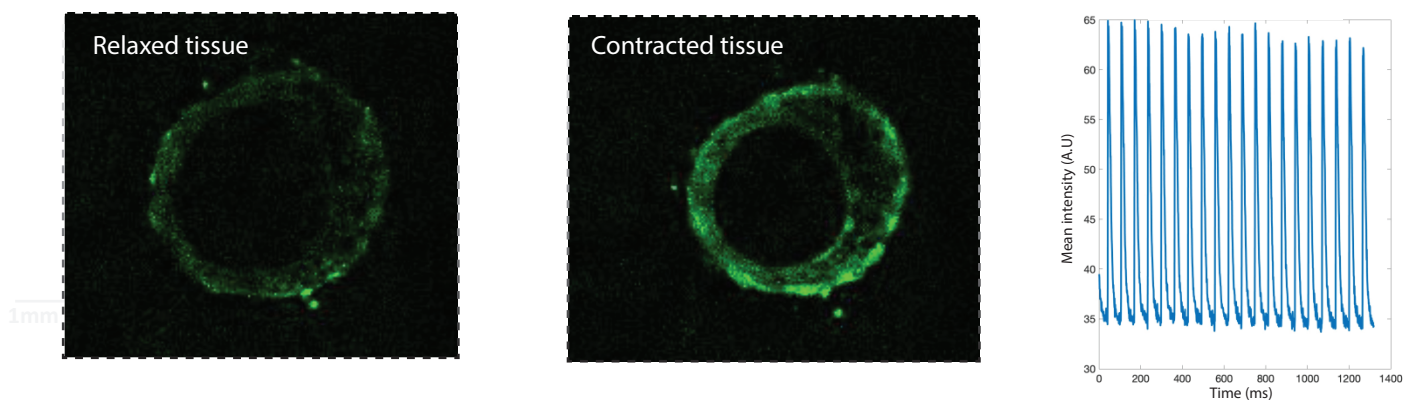
Immunofluorescence imaging of the tissues after 14 days. Z-scan using confocal microscopy. Fibroblasts are added to provide stability to the tissues, by forming a structural layer below the iPSC-CMs.



Images from Seguret et al. eLife 12:RP87739 (2023).

Calcium imaging

Preliminary data of tissues stained with a calcium fluorescent dye.



Stability and storage

The plates can be stored at room temperature for up to 3 months from the date of delivery.

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