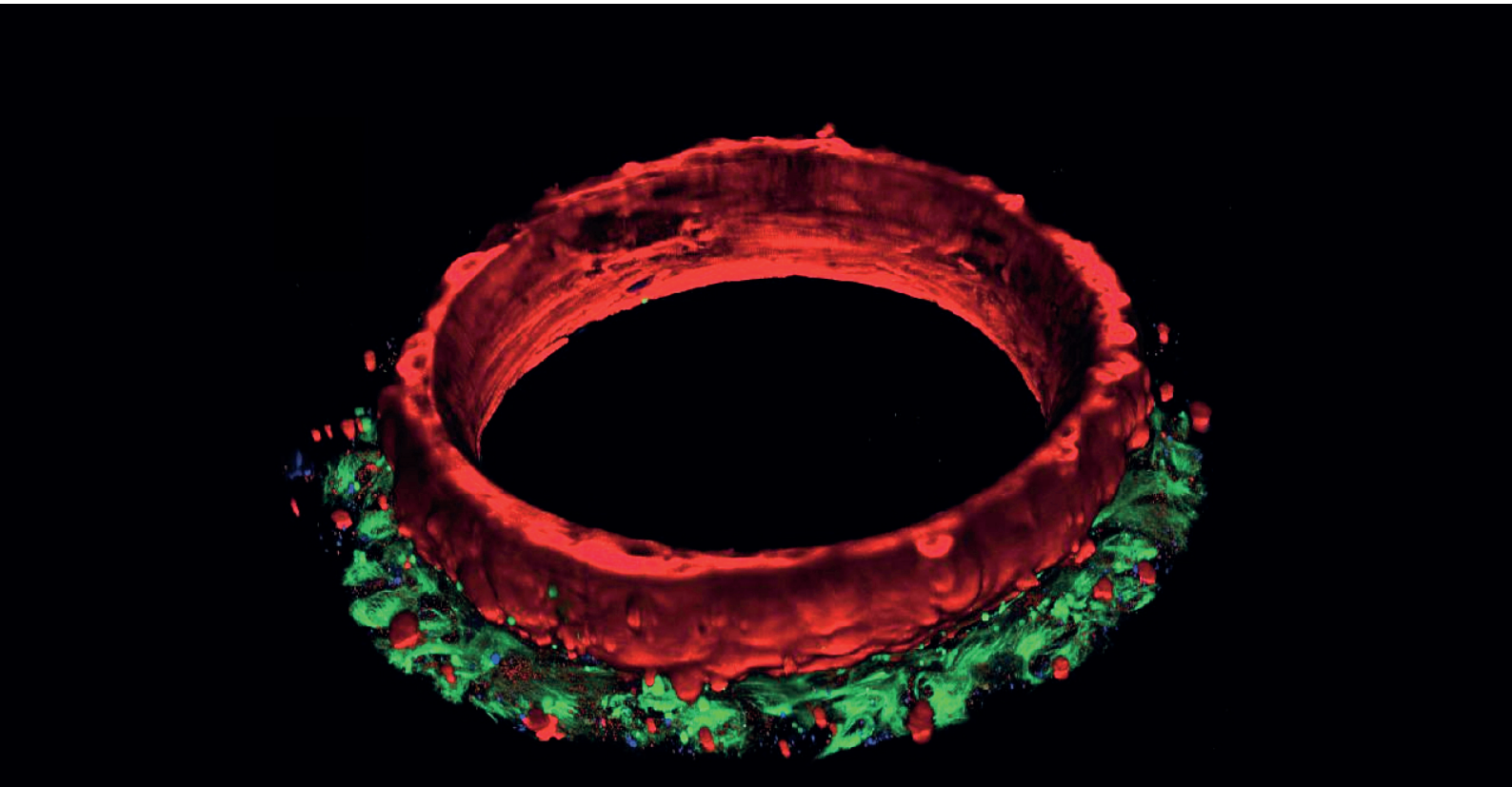
4Dcell
explore better.

SmartHeart® Platform

Self-assembled human cardiac tissues under mechanical load for drug efficacy testing, cardiac safety assessment and disease modeling.

- **SmartHeart® plate**
- **Biological protocol**
- **SmartX 3.0 analysis software**



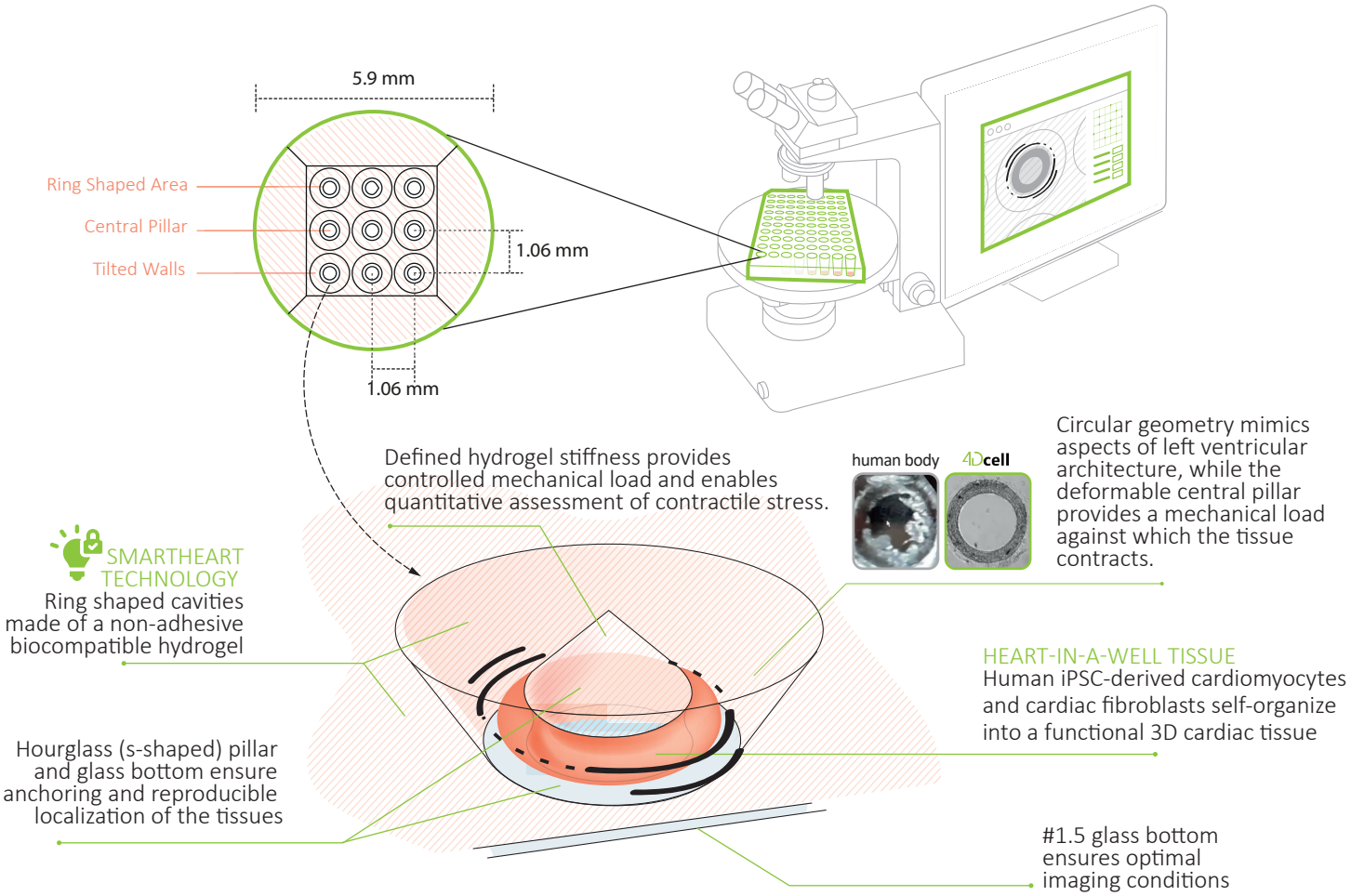
How the geometry guides tissue formation

SmartHeart® plates feature a microstructured hydrogel containing arrays of sloped microwells, each with a deformable central pillar. Biocompatible PEG hydrogel stiffness can be tailored to the cell model (~5–20 kPa).

After seeding, the microwell geometry guides cells into an annular cavity, where they self-assemble into a ring-shaped tissue around the pillar.

During contraction, the tissue deforms the pillar. Tracking this deformation enables quantitative analysis of contraction strain, beating frequency, and contraction and relaxation kinetics. Contractile stress is calculated using the hydrogel's characterized mechanical properties.

The pillar's engineered shape helps anchor the tissue, maintaining its position during culture and in situ imaging.



96
wells

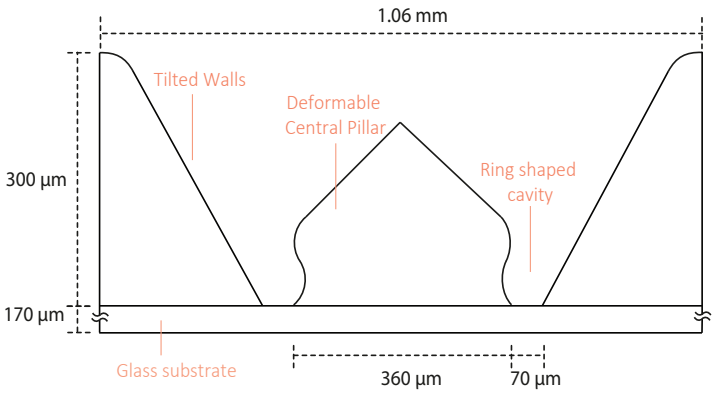
9
tissues/well

7200
cells/tissue

FLASH TO SEE THE SMARTHEART BEATING

SmartHeart microwell anatomy & dimensions

SmartHeart® provides a defined microenvironment that guides cardiac tissue formation and enables functional measurements in situ. Ring-shaped cavities promote self-assembly around deformable hydrogel pillars, which anchor the tissues and provide mechanical resistance during contraction. The optically transparent hydrogel supports brightfield and fluorescence imaging to assess contractility, electrical activity and calcium dynamics. Together, these complementary readouts help characterize how compounds affect excitation–contraction coupling in human 3D cardiac tissues.



The industry-standard 96-well format is compatible with automated liquid-handling and imaging platforms, enabling integration into high-throughput screening (HTS) and high-content screening (HCS) workflows for drug efficacy testing, cardiac safety assessment and disease modeling.

Defined cellular composition

SmartHeart® tissues combine human iPSC-derived cardiomyocytes and primary human ventricular cardiac fibroblasts at a 3:1 ratio. Cardiomyocytes provide the contractile component, while fibroblasts support tissue organization and structural stability.

- 75% cardiomyocytes / 25% cardiac fibroblasts
- Approximately 7,200 cells per microtissue, corresponding to 65,000 cells per well across nine tissue-forming cavities
- Culture at 37°C and 5% CO_2

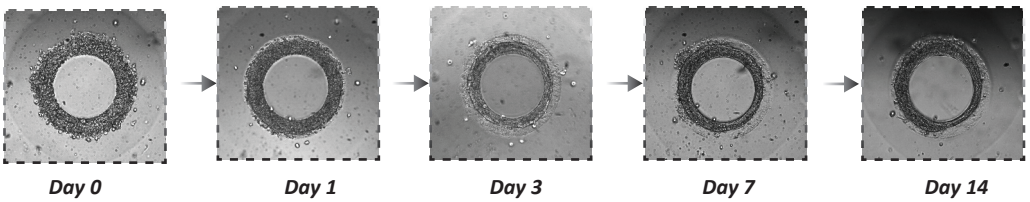
Reference composition used in the SmartHeart® contractility qualification study.

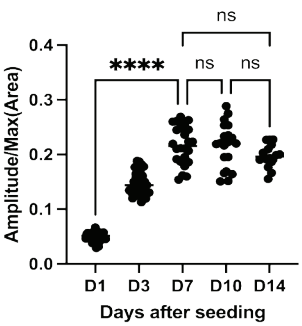
Self-assembly & functional development in culture

Over 14 days of culture, cells formed connections and became elongated as the cardiac tissues organized and developed contractile function.

Contraction amplitude:
- Increased during the first week.
- Remained broadly stable through D14.

Tissue formation is illustrated through D14; pharmacological qualification was performed at D21.

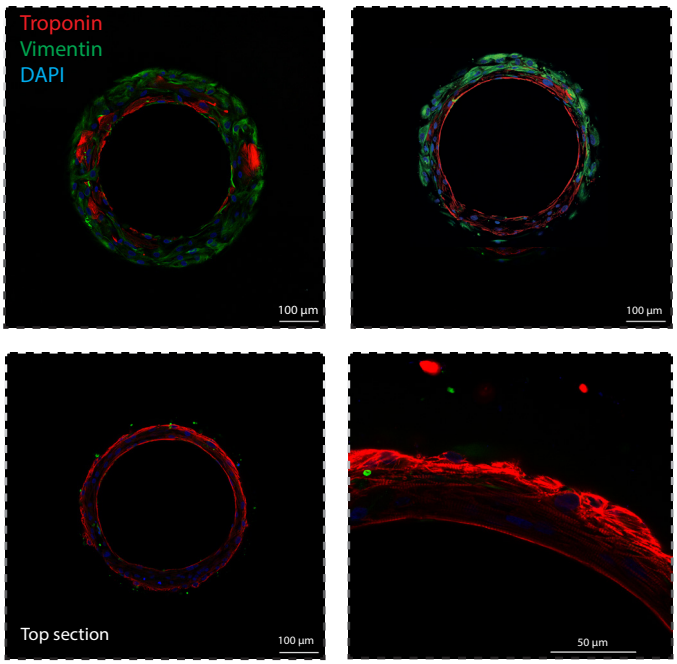




Images and data from Seguret et al. eLife 12:RP87739 (2023).

Tissue morphology & Structural organization

Confocal immunofluorescence imaging after 14 days of culture reveals organized troponin-positive contractile fibers above a fibroblast-rich basal layer that provides structural support. These structural observations complement contractility, electrophysiology and calcium-handling measurements when assessing tissue maturation.



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

Excitation–contraction coupling: why an integrated system matters

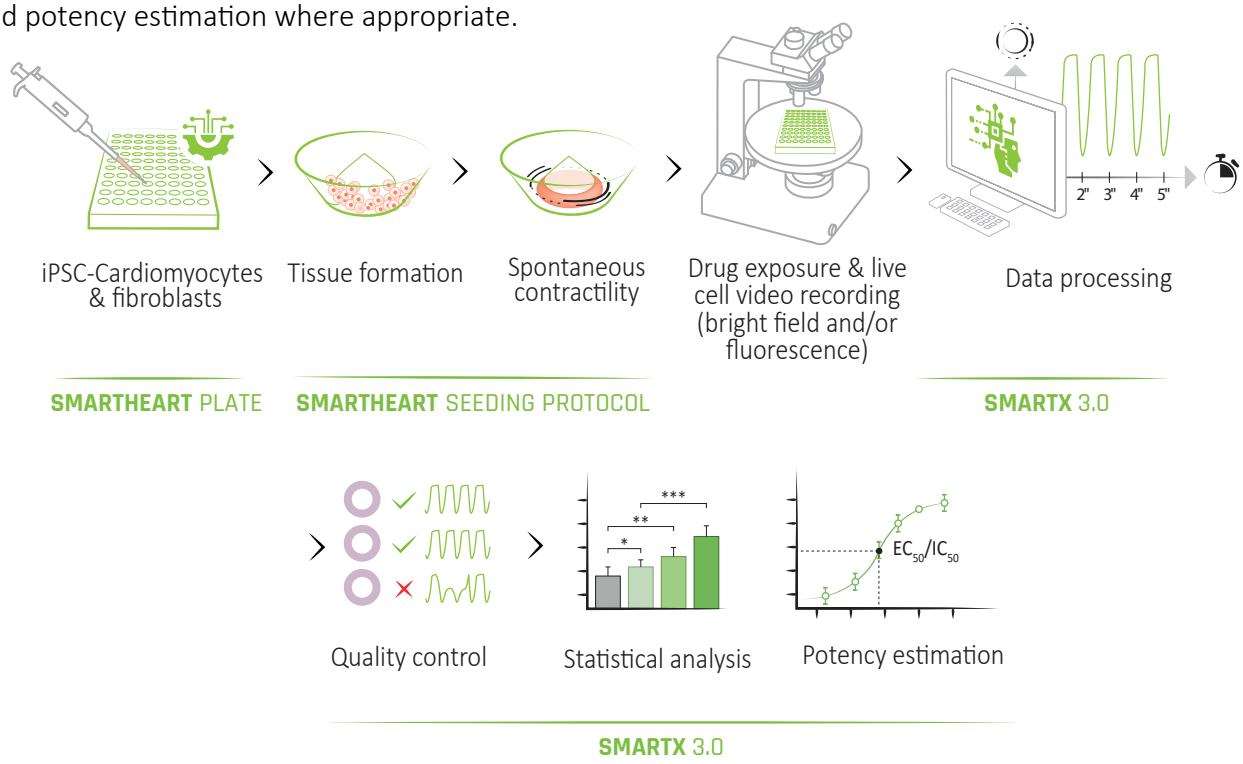
Cardiac contraction emerges from interacting ion channels, intracellular calcium cycling and the contractile machinery within a loaded tissue. Calcium entry can trigger sarcoplasmic-reticulum calcium release. Calcium binding to troponin enables contraction. Calcium removal supports relaxation.

Electrical excitation	→	***Calcium dynamics***	→	***Mechanical response***
Membrane potential and ion-channel activity		Ca^{2+} release, transient and removal		Myofilament activation, contraction and relaxation
Optical action potential		***Calcium transient***		***Tissue strain & kinetics***

Integrated component	Why it matters for interpreting the response
Geometry and load	Contraction develops against a defined deformable pillar
Tissue organization	Cell arrangement and contractile fibers shape tissue mechanics
Maturation context	Channel activity and calcium cycling shape functional maturity
Functional response	Complementary endpoints show how electrical changes relate to mechanics

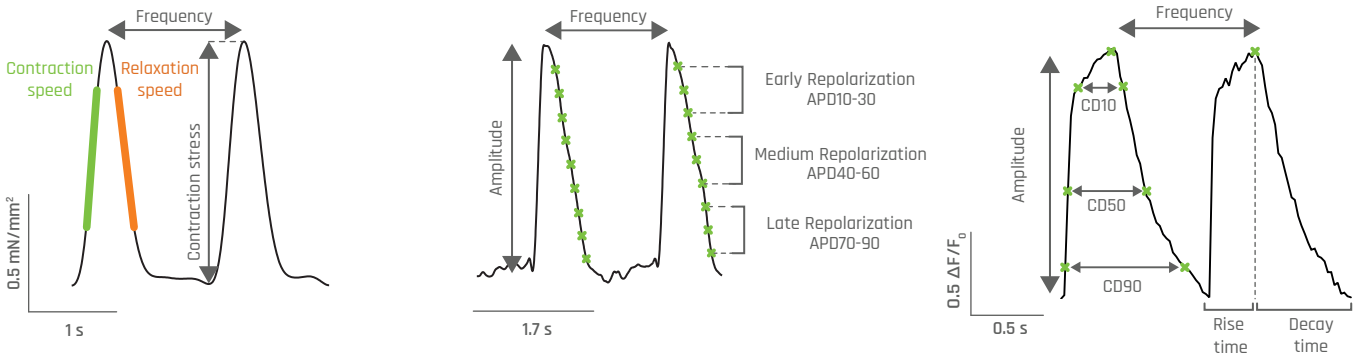
SmartHeart® workflow

SmartHeart® provides an integrated workflow to characterize how compounds affect human 3D cardiac contractility. Tissue self-assembly, in situ imaging and SmartX 3.0 analysis connect biological responses with quantitative measurements. Quality control and statistical evaluation support concentration–response profiling and potency estimation where appropriate.



3-in-1 cardiac platform

SmartHeart® measures three interconnected components of cardiac function: electrical excitation, intracellular calcium dynamics and mechanical contraction. Together, these readouts help characterize how compounds affect excitation–contraction coupling in human 3D cardiac microtissues.



CONTRACTILITY METRICS

Contraction stress
Contraction strain
Beating frequency
Contraction & relaxation speed

ELECTROPHYSIOLOGY METRICS

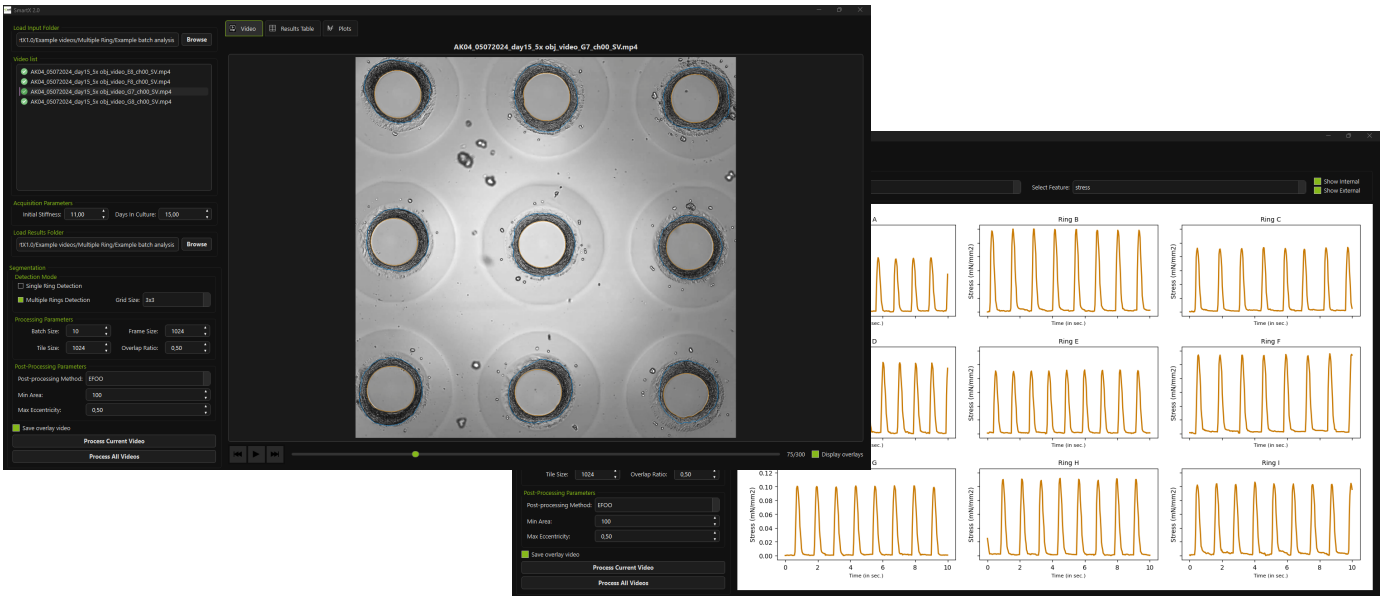
Frequency
Interpeak duration STD
Rise time, upstroke velocity
Triangulation & plateau duration
APD10-90

CALCIUM METRICS

Frequency
Area under curve
Rise & decay duration & velocity
CD10, 50, 90

SmartX 3.0 - Deep-learning contractility analysis

SmartX 3.0 analyzes brightfield videos to quantify cardiac tissue contraction. Its deep-learning algorithm detects individual ring contours and tracks their deformation over time.



Quantifying contractile function

SmartX extracts 22 metrics describing tissue morphology and contractile activity, including contraction strain, beating frequency, rhythm regularity, and contraction and relaxation speeds.

Contraction strain measures the relative change in tissue radius:
$\varepsilon(t) = [R_{max} - R(t)] / R_{max}$

Post-processing and pharmacological analysis

SmartX 3.0 supports systematic, controlled data curation, baseline normalization, concentration–response plotting and statistical analysis.

Automated criteria and visual review assess segmentation, tissue morphology and baseline activity. Each evaluable ring is normalized to its own vehicle baseline to quantify compound-induced changes.

Drug-induced loss of beating or irregularity is retained as a biological response when recordings remain technically evaluable.

How to work with 4Dcell?

To integrate our platform into your lab or have our expert manage your project in our facilities, feel free to contact us at: contact@4dcell.com

Explore SmartHeart for your cardiac research