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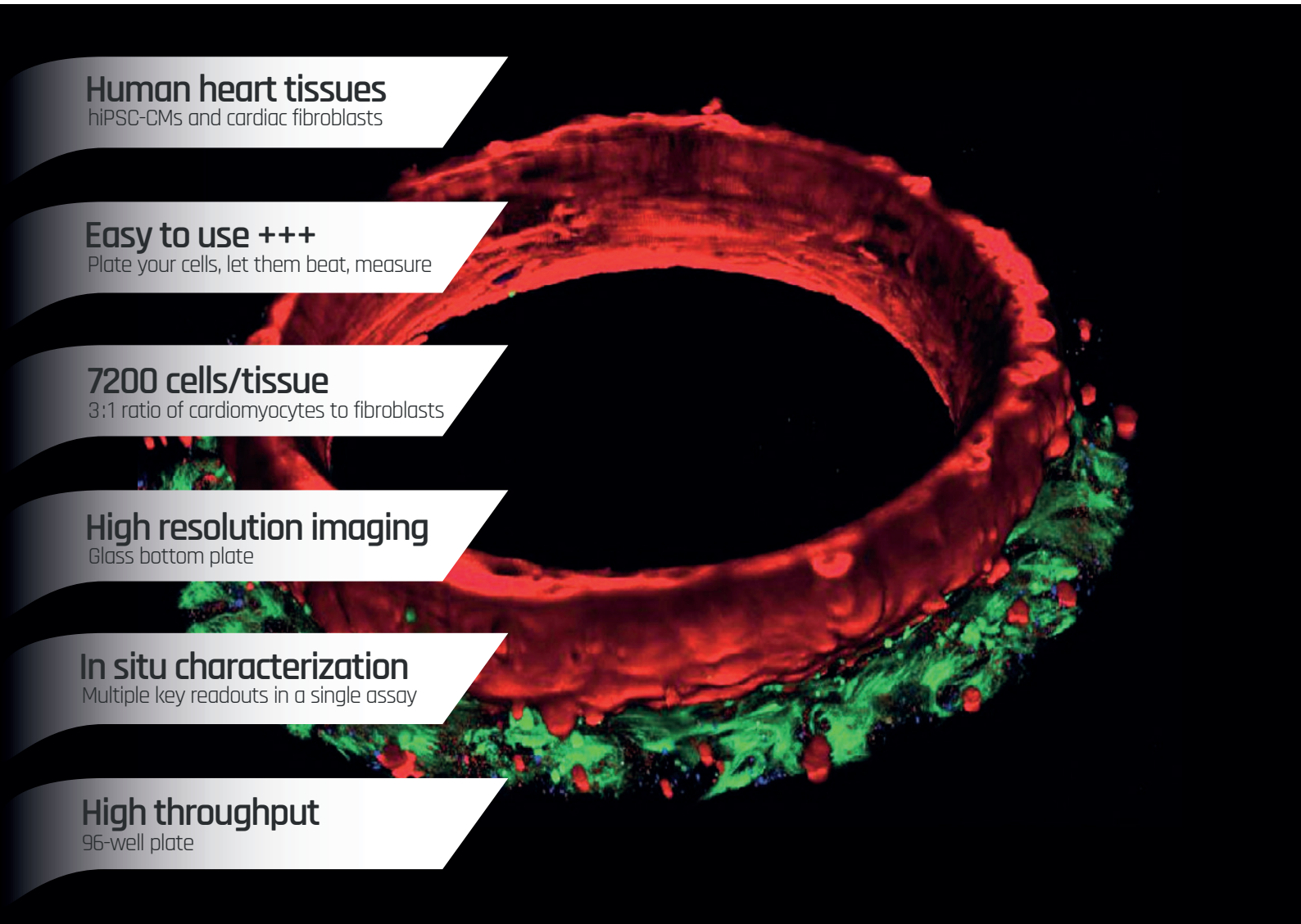
PREDICTIVE CARDIOTOXICITY ASSAY
3D SmartHeart® platform

Reliable, scalable and reproducible 3D assay
to eliminate toxic drugs at the preclinical stage



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Meet the highest cardiotoxicity standards

SmartHeart®, a 3-in-1 3D cardiac assay replicating key in vivo mechanisms

The SmartHeart is an **integrated solution** to measure contractility (1), action potential (2), and calcium handling (3).
This streamlined approach **minimizes variability, delivering unmatched insights into in vivo toxic mechanisms**.

CONTRACTILITY (1)

Contractility Metrics

Frequency
Contraction stress
Contraction speed
Relaxation speed

Drug cardiac tropism

Chronotropic
Inotropic
Chronotropic
Lusitropic

ELECTROPHYSIOLOGY (2)

Action potential Metrics

Frequency
Interpeak duration STD
Rising time, Upstroke velocity
APD10-90
Triangulation, Plateau phase

Electrophysiology features

Rhythm
Regularity
Depolarization

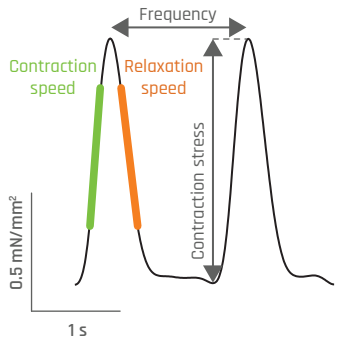
Impacted channels
Proarrhythmia

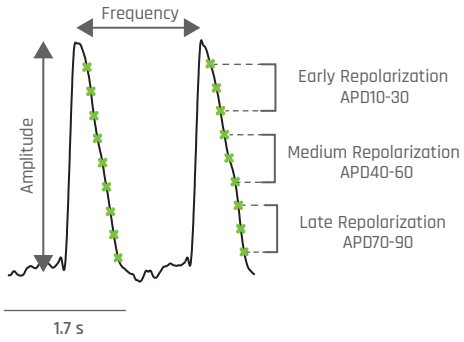
CALCIUM TRANSIENTS (3)

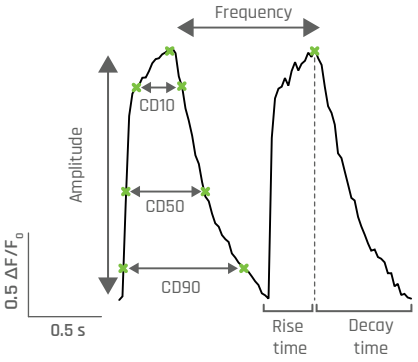
CaT Metrics

Frequency
Interpeak duration STD
Amplitude
Area Under curve
'Rise and decay' duration and speeds
CD10,50,90

Comprehensive understanding of calcium dynamics in tissues





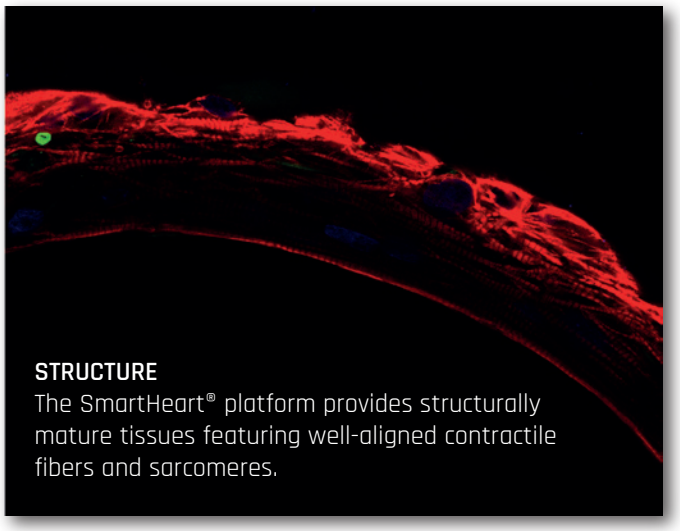


A human-like cardiac model engineered to reach a high level of maturation

SmartHeart® tissues offer enhanced morphological, structural, molecular, and functional **maturity**, increasing the predictability of cardiotoxicity studies and clearly surpassing the limitations of traditional 2D approaches.

MORPHOLOGY

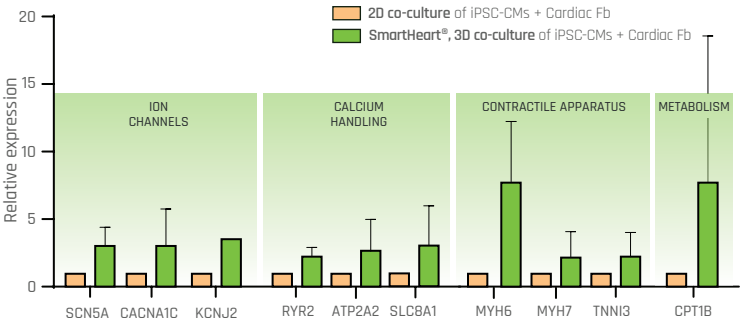
The ring-shaped geometry allows for a more physiologically accurate distribution of forces within the tissue. It facilitates the visualization of re-entrant waves, which are responsible for most clinical arrhythmias.



STRUCTURE
The SmartHeart® platform provides structurally mature tissues featuring well-aligned contractile fibers and sarcomeres.

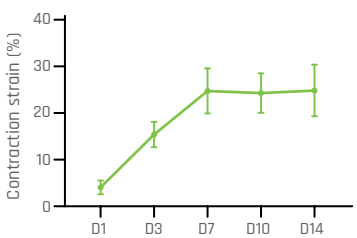
MOLECULAR EXPRESSION

RT-qPCR data highlight the upregulation of key genes for cardiac function compared to 2D models.



IN VIVO FUNCTION RECAPITULATED IN VITRO

SmartHeart® tissues exhibit human-like contractility, with an **ejection fraction** of 30%, as evidenced by a progressive increase in contraction strain that reaches 25% after 7 days in culture.

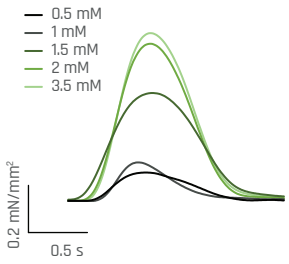


Commercial and patient derived iPSC lines **VALIDATED**

SmartHeart® quantifies drug-induced contractile changes

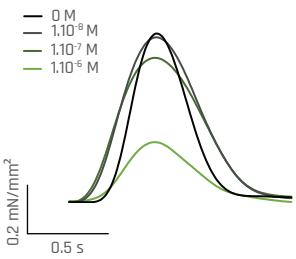
SmartHeart® tissues reproduce the physiological responses to classic cardiotropic agents targeting various mechanisms, enabling both acute and chronic experiments. The tissues exhibit a positive force-frequency relationship under isoproterenol stimulation, a definitive indicator of tissue maturity.

Extracellular Calcium



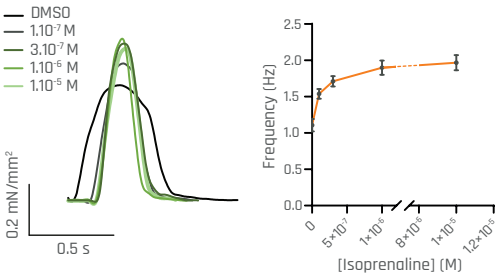
Positive inotropic response

Verapamil
calcium channel blocker



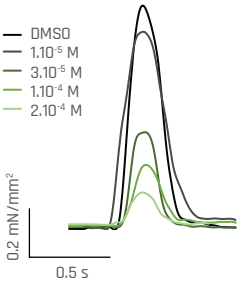
Negative inotropic response

Isoprenaline
agonist of the α-adrenergic receptors



Positive inotropic response + **Positive** chronotropic response
Positive force-frequency relationship not observed in 2D

Metoprolol
selective β1 receptor blocker

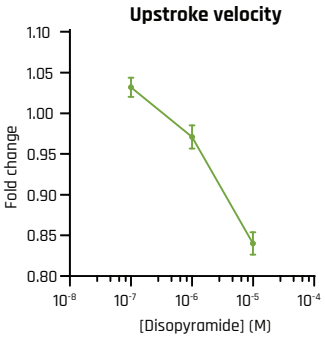


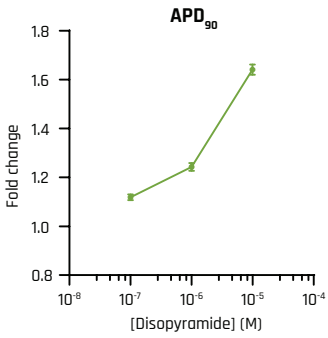
Negative inotropic response

SmartHeart® recapitulates electrophysiological drug response

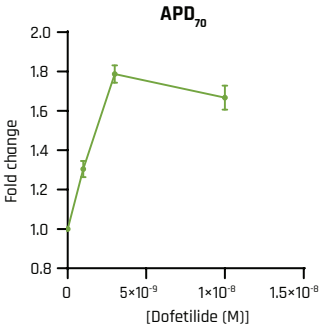
SmartHeart® reliably replicates the electrophysiological (via optical mapping assessment) responses to CiPA panel drugs, ensuring high-fidelity cardiac safety assessments.

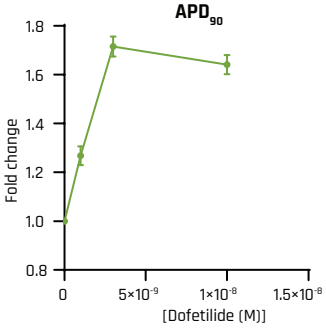
Disopyramide High TdP risk
Sodium channel blocker & moderate blockade of potassium channels
Decrease in upstroke velocity
Prolongation in late APDs



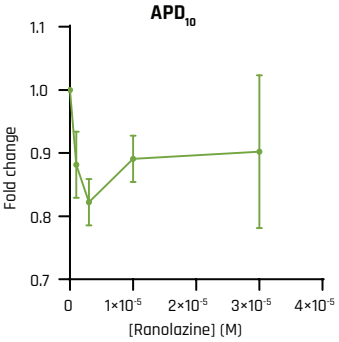


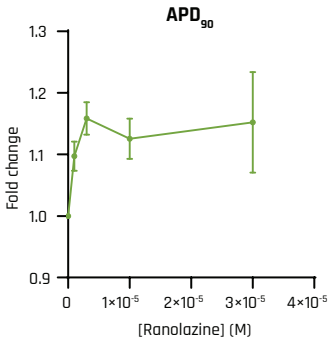
Dofetilide High TdP risk
hERG channel blocker
Prolongation in late repolarization phases (APD_{70} and APD_{90})



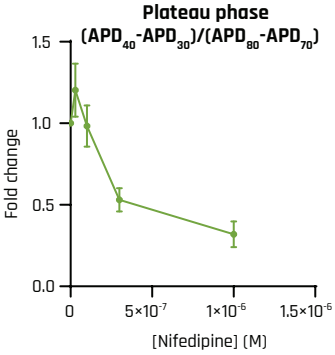


Ranolazine Low TdP risk
Inhibits late sodium current
Minimal shortening of APD_{10}
Slight prolongation of ADP_{90}

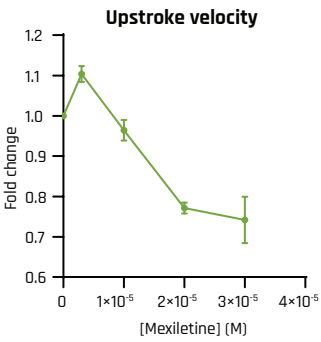




Nifedipine Low TdP risk
Calcium channel blocker
Shortened plateau phase

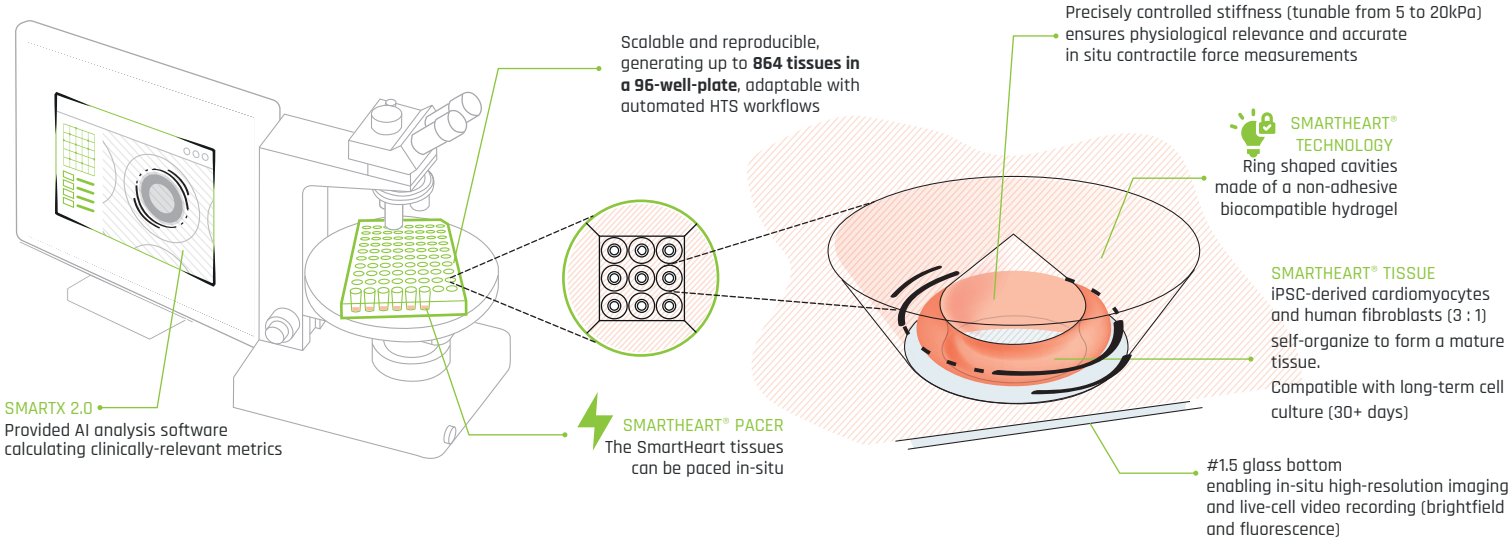


Mexiletine Low TdP risk
Sodium channel blocker
Decrease in upstroke velocity

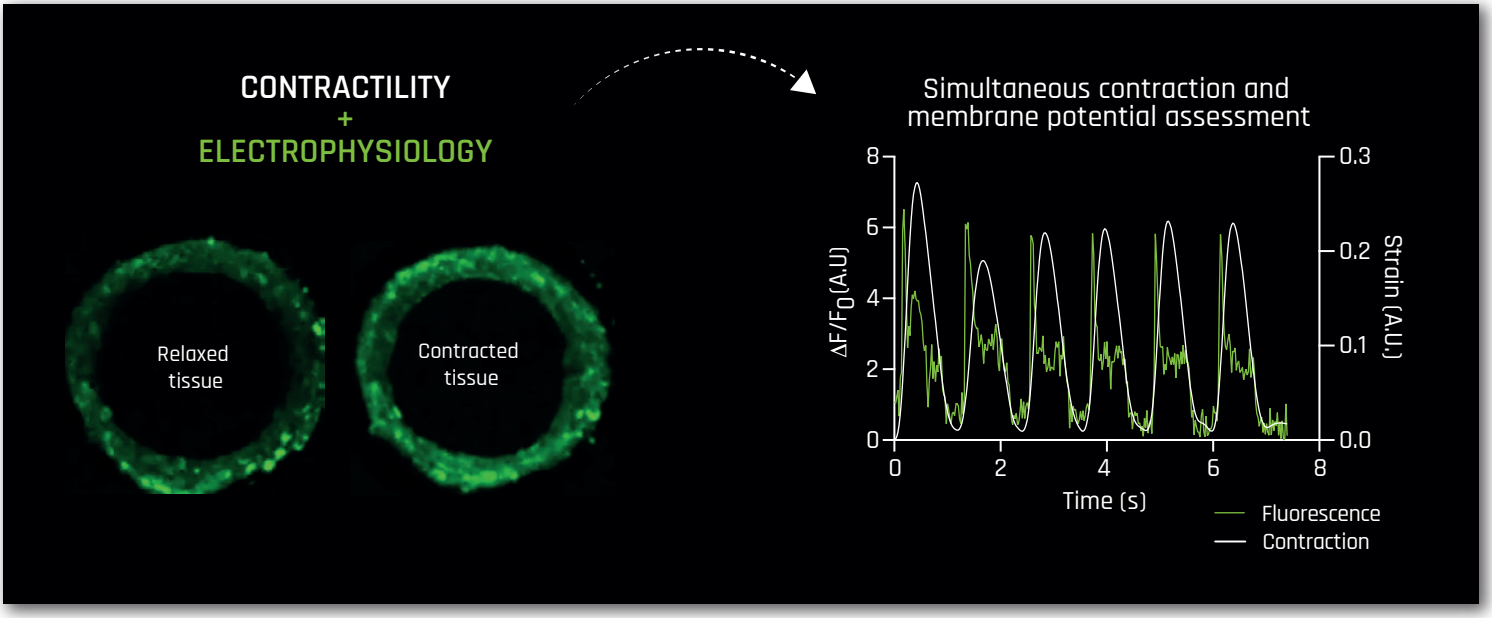


SmartHeart® Key features

The SmartHeart® platform is a 3D cardiac assay that enables both the self-assembly and maturation of functional, ring-shaped cardiac tissues, as well as the acquisition of key readouts, all in situ on a single platform (as illustrated in the scheme below). Contractility parameters are measured by tracking the deformation of the central pillar over time. The system supports high-resolution imaging of live or fixed tissues, allowing for easy assessment of action potentials, calcium transients, and morphology. The SmartHeart® Pacer allows to pace the tissues at a specific frequency defined by the user.



SmartHeart®'s design is compatible with in situ fluorescence imaging, allowing precise assessment of fixed tissue structures as well as live fluorescence imaging and optical mapping. Contractility and electrophysiology can be measured from the same videos, enabling the evaluation of excitation-contraction efficiency in the tissues.



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**