Advancing cardiovascular drug discovery with iPSC-Derived 3D cardiac microtissues in High-Throughput Screening

Benoit Samson-Couterie [1], Benjamin B Johnson [2,3], Katerina Pitsa[1], Tessa de Korte[2], Mariana Argenziano[1], Christine L Mummery[2,3], Richard P Davis[2,3], Shushant Jain[1]
[1] Ncardia Services BV, Leiden, The Netherlands, support@ncardia.com, www.ncardia.com
[2] Dept. of Anatomy and Embryology, Leiden University Medical Center, Leiden, The Netherlands
[3] The Novo Nordisk Foundation Center for Stem Cell Medicine (reNEW)

Background

Induced pluripotent stem cell (iPSC)-derived models are revolutionizing drug discovery by providing human-relevant cell types for more accurate preclinical evaluations, especially for cardiovascular diseases and drug-induced cardiotoxicity. 3D cardiac microtissues, which replicate the architecture and function of the human heart, offer improved drug screening for both efficacy and safety compared to traditional models. These models, developed from patient-derived iPSCs, increase the relevance and predictability of cardiovascular drug testing, allowing for more reliable preclinical data. We have developed a wide range of assays suing 3D cardiac microtissues including imaging, calcium imaging, biomarker detection and ischemia reperfusion model

1. Ncardia's approach for HTS with Cardiac Microtissue:

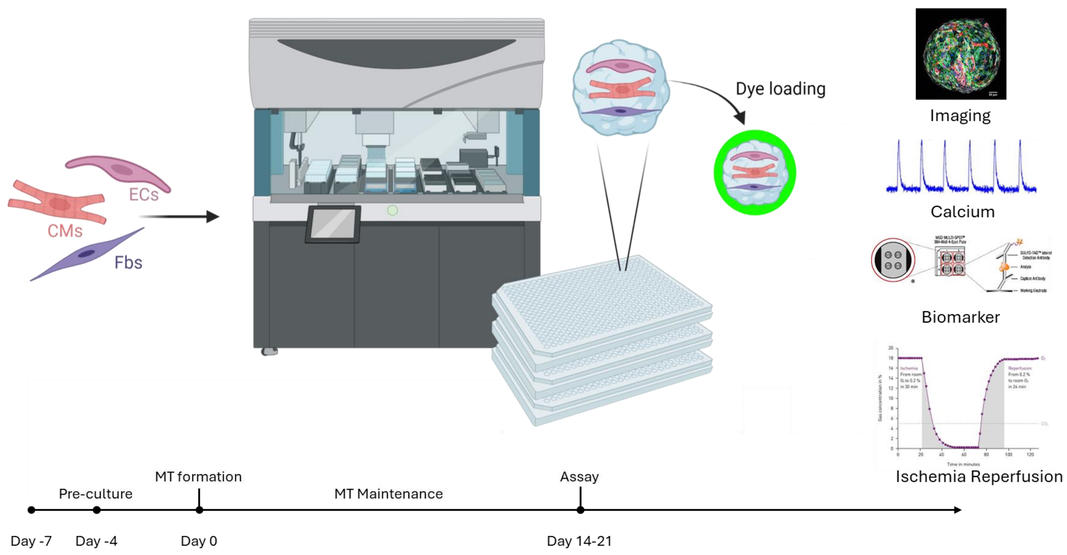

Figure 1. Workflow illustrating the preparation and use of 3D cardiac microtissues from Ncyte® iPSC-derived cardiomyocytes, endothelial cells, and cardiac fibroblasts for high throughput screening (Modified from https://doi.org/10.1016/j.tibtech.2025.11.016.)

3. Application of Ncyte® Heart in a Box™

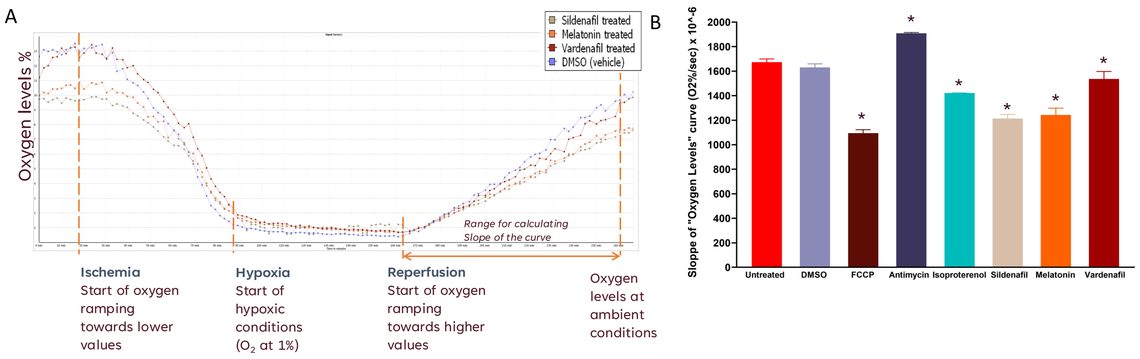

Figure 3.The Ncyte® Heart in a boxTM is model effectively models cellular oxygen consumption during ischemia-reperfusion.
A. Real-time changes in oxygen percentage over time for cells treated with DMSO (control), FCCP (uncoupler, increasing oxygen consumption), and Antimycin (complex III inhibitor, decreasing oxygen consumption). Phases of ischemia (oxygen depletion), hypoxia (sustained low oxygen), and reperfusion (oxygen reintroduction) are indicated, highlighting the period used for oxygen consumption rate calculations. B. Bar graph showing the slope of oxygen consumption (O_2%/sec × 10^{-6}) in cells treated with the indicated compounds. Data represent mean ± SEM; *p < 0.05 versus untreated.

2. Heart in a box: identity, morphology and functionality

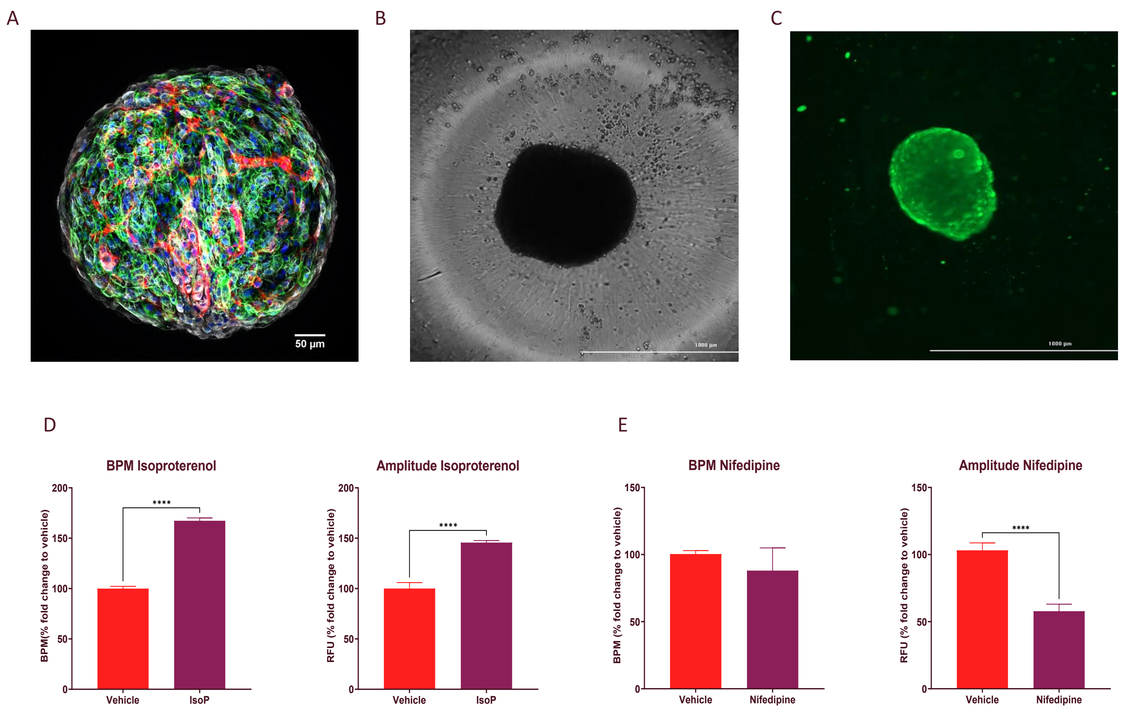

Figure 2. Identity and morphology of Heart in Box™ Microtissue.
A. Immunostaining of Ncyte® Heart in a Box. Nucleus (blue), Cardiac troponin T (green), CD31 (red), α SMA (white). 20X Image.
B. Brightfield image showing the morphology and structure of a 3D cardiac microtissue
C. 3D cardiac microtissues stained using FLIPR6 for calcium imaging.
D. Isoproterenol, a β-adrenergic agonist, significantly increases the beating rate (BPM) and amplitude of 3D cardiac microtissues, indicating a positive chronotropic effect.
E. Nifedipine, a calcium channel blocker, shows no effect on the beating rate (BPM) of 3D cardiac microtissues while significantly decreases the amplitude of contraction in CMs, demonstrating a negative inotropic effect

4. Partnership with LUMC – Disease modeling and Drug screening

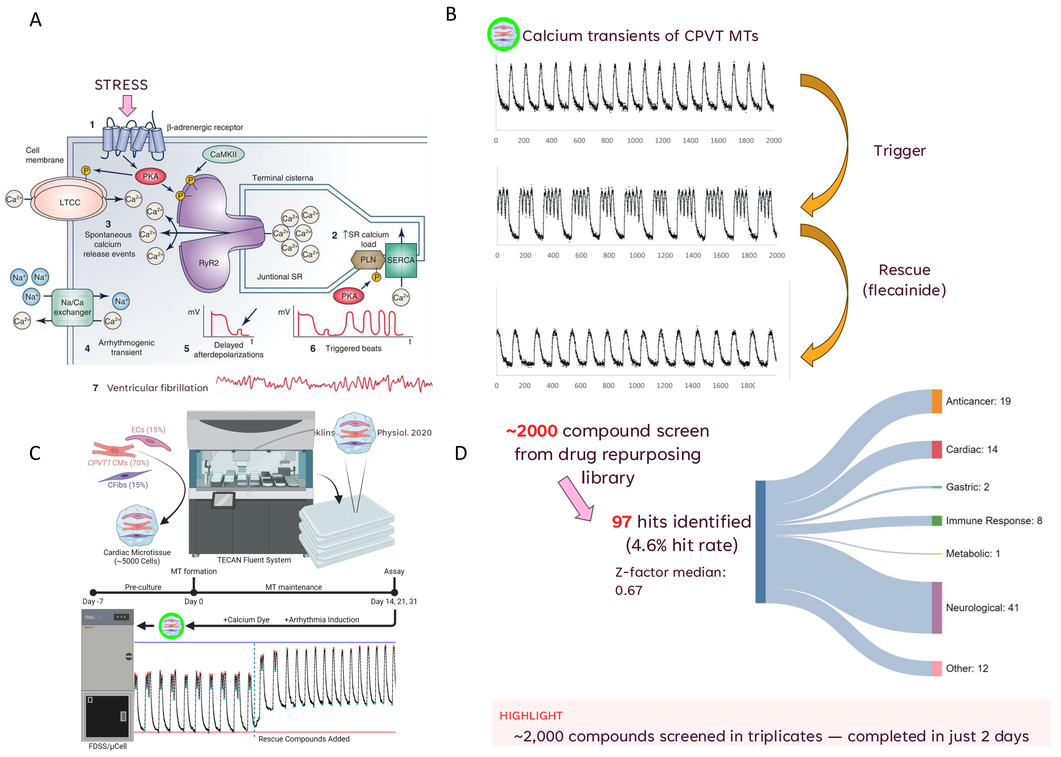

Figure 4. Disease modeling and High-throughput screen in CPVT1.
A. Schematic showing how β-adrenergic stimulation in CPVT1 leads to PKA-mediated phosphorylation of RYR2 on the sarcoplasmic reticulum, resulting in leaky channels, abnormal calcium release, and ventricular arrhythmias.
B. Representative calcium traces from CPVT MTs highlight arrhythmic activity and pharmacological correction.
C. Overview of the fully automated system for forming, maintaining, treating, recording, and analyzing calcium transients in CPVT microtissues.
D. Alluvial diagram summarizing results from ~2,000-compound screen. 97 hits identified (4.6% hit rate); median Z'-factor of 0.67 confirms assay robustness.

Leading the way in scalable production for disease modeling and therapeutic development.

- Advance the physiological relevance of *in vitro* models in a cost-effective and scalable solution
- Accelerate drug discovery with fully automated pipelines
- Supports precision medicine by modeling patient-specific responses
- Applicable for both cardiotoxicity assessment and drug discovery

Contact us at support@ncardia.com

Scan the QR code to download this poster