Non-human primate iPSC-derived cardiomyocytes offer translational insight for early cardiac safety assessment

Jessica Koepke, Ilse Veldkamp-Baak, Pieter van Loenen, Silke Schwengberg
Ncardia Services BV, Leiden, The Netherlands, support@ncardia.com, www.ncardia.com

Abstract ID: 46
Poster: #20

Background and Purpose

Non-human primates (NHPs) are a key secondary species in preclinical cardiac safety testing yet no scalable in vitro NHP cardiomyocyte model exists to bridge in vivo NHP studies and human in vitro assays. To address this gap, we established a renewable NHP iPSC-derived ventricular cardiomyocyte (NHP CM) platform for translational in vitro safety assessment. Here we evaluate whether NHP CM recapitulate the expected acute and chronic electrophysiological responses to a mechanistically diverse panel of reference compounds, measured by multi-electrode array (MEA).

Methods

Cynomolgus macaque iPSCs[1] were differentiated into NHP-C vCM at large scale using stirred-tank bioreactors and cryopreserved for post-thaw functional analysis. Cardiomyocyte identity and ventricular specification were confirmed by flow cytometry and immunofluorescence for cTnT, α-actinin and MLC2V. For safety assessment, NHP CM were thawed, pre-cultured for 2 days and plated on 96-well Axion CytoView MEA plates. From day 4 post- thaw, cells were treated with reference compounds either acutely (recordings 15 min up to 1 h post-dose) or chronically (recordings at 6 h and every 24 h thereafter). Endpoints were field potential duration (FPD) and beat rate (BR) (n=3 replicates/condition; FPD not rate-corrected).

Ncyte® NHP-C vCardiomyocytes show high purity and stable beating

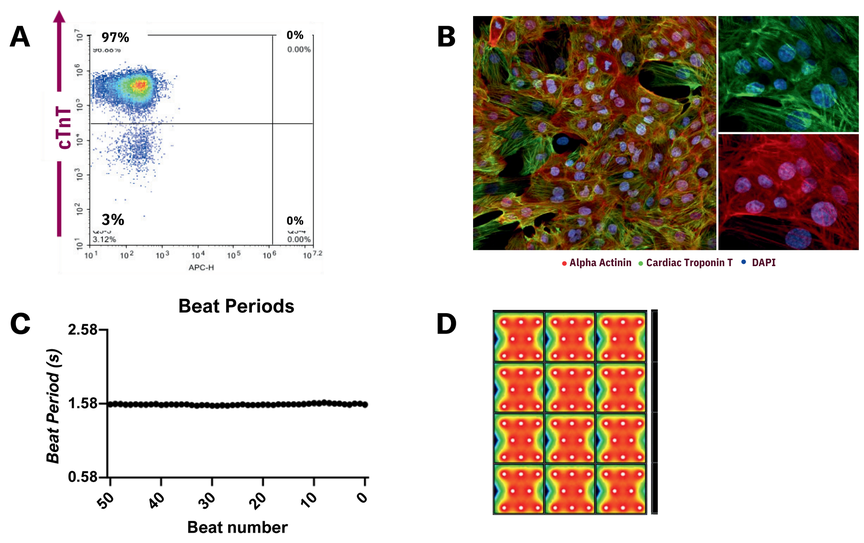

Figure 1. Characterization of NHP CM
(A) Flow cytometry analysis of cardiac Troponin T (cTnT) expression shows high purity with ≥97% cTnT-positive cells.
(B) Immunofluorescence staining of NHP CM demonstrating expression of α-Actinin (red), cardiac Troponin T (green), and nuclear counterstain DAPI (blue).
(C) Representative beat period recordings of NHP CM show stable beating over successive beats.
(D) Baseline electrical full activity across all electrodes (>300 µV).

Ncyte® NHP-C vCardiomyocytes in safety assessment

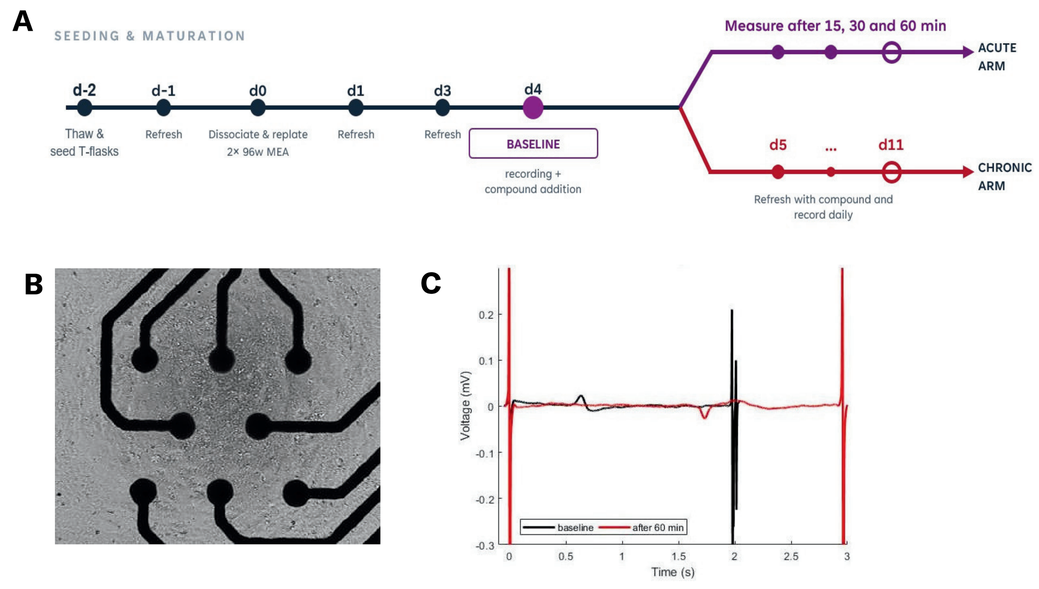

Figure 2. Experiment outline
(A) Experimental schedule showing both acute and chronic setup. Cryopreserved cells are thawed, plated into 96w Axion MEA plates and treated with a panel of test compounds for either up to 24 hours or 6 days.
(B) Example phase contrast image showing high-density seeded NHP CMs in a 96w MEA plate.
(C) Representative image showing Quinidine (red) at 3000 nM prolonged FPD (1 hour) compared to baseline (black). Clear field potential peaks allow fast and reliable FPD detection.

Ncyte® NHP-C vCardiomyocytes show expected responses to a panel of test compounds

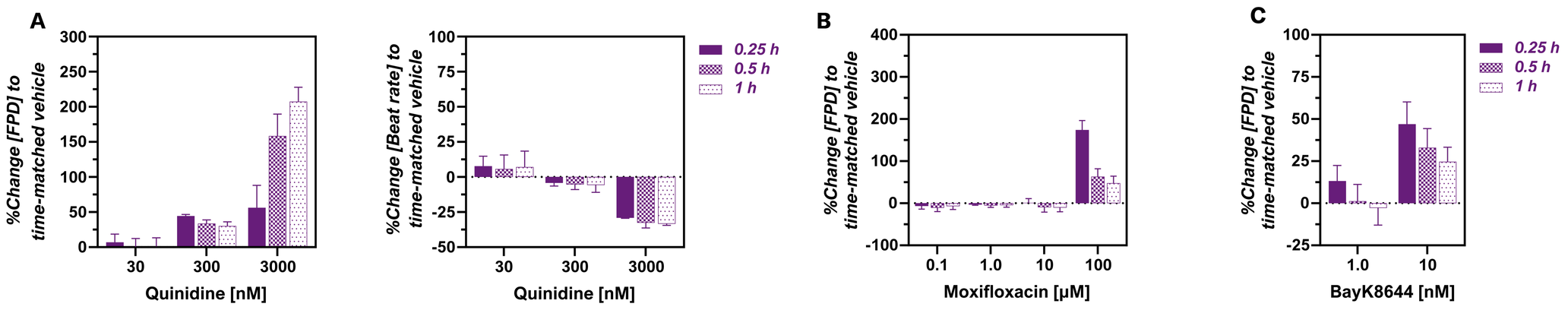

Figure 3. Cardiac safety assessment - acute
(A) Quinidine prolonged FPD concentration-dependently with no effect at 30 nM; ~30–45% at 300 nM and up to ~200% at 3000 nM consistent with IKr-mediated repolarization block. Spontaneous beat rate was concurrently reduced at 3000 nM (~30–35%) reflecting its multi-channel action.
(B) Moxifloxacin prolonged FPD at 100 µM time-dependently with no effect at 0.1–10 µM consistent with its known low-potency IKr block.
(C) BayK8644 produced a concentration- and time-dependent FPD prolongation, minimal at 1.0 nM and clear at 10 nM (~+47% vs. time-matched vehicle at 0.25 h) consistent with enhanced L-type Ca^{2+} influx prolonging the plateau.
(D) Dofetilide induced FPD prolongation >300% with arrhythmia at 0.01–0.1 µM, Nifedipine caused complete beating arrest above 0.1 µM, consistent with predicted calcium channel blockage (data presented at SPS2025). Terfenadine showed minimal effects, consistent with negative in vivo findings in absence of CYP blockers, and Aspirin did not exert any effect (data not shown).
- Overall, 5 of 6 compounds showed concordance with predicted in vivo effects and all 4 compounds with in vivo ECG findings induced aligned responses

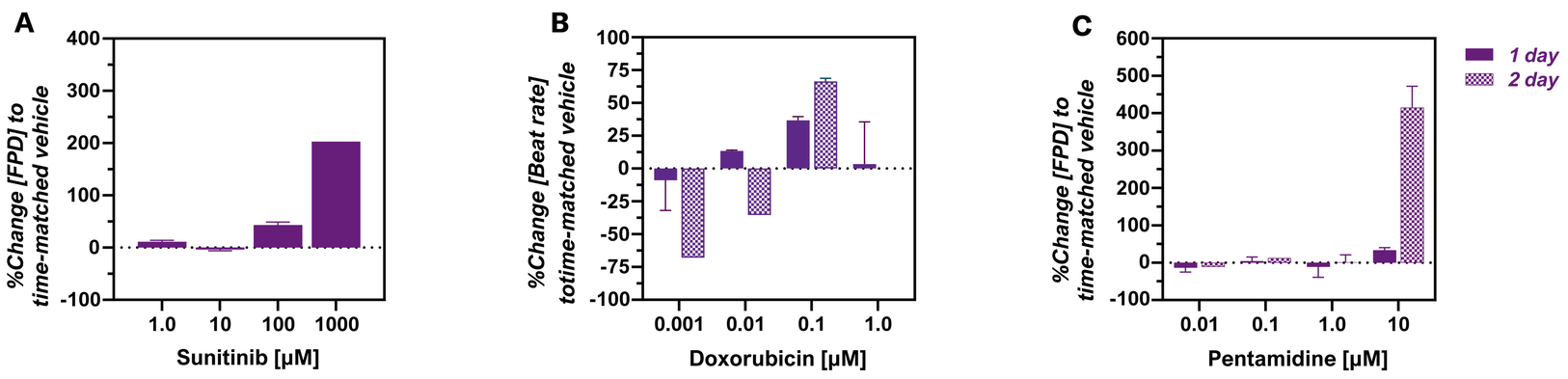

Figure 4. Cardiac safety assessment – sub-chronic
(A) Sunitinib caused a concentration-dependent increase in FPD, minimal at 1–10 µM, clear at 100 µM (~+45% vs. time-matched vehicle) and pronounced at 1000 µM (~+205%). Note that the highest concentration greatly exceeds therapeutic exposure where FPD changes may also reflect broader cardiotoxicity rather than ion-channel block alone.
(B) Doxurubicin induced up to 75% reduction in beat rate after 24 and 48 hours , and induced beat arrest at 1µM
(C) Pentamidine produced a clear time-dependent FPD prolongation at 10 µM — minimal after 1 day (~+25%) but pronounced after 2 days (~+415% vs. time-matched vehicle). This delayed onset is consistent with its mechanism of disrupted hERG channel trafficking and demonstrates the platform's sensitivity to chronic, trafficking-mediated proarrhythmic liability.

Conclusion

NHP CM can be differentiated at large scale, display high structural fidelity, stable function in MEA and impedance assays, and respond to cardioactive compounds.
NHP iPSC-derived vCardiomyocytes display reproducible electrophysiological behavior, and pharmacodynamic responses aligned with known cardiac safety profiles. These cells represent a translationally relevant model for integrated assessment of proarrhythmic risk and other cardiac liabilities, supporting their application in early nonclinical safety pharmacology workflows.

1. Tereshchenko, Y.; Esiyok, N.; Garea-Rodríguez, E.; Repetto, D.; Behr, R.; Rodríguez-Polo, I. Transgene-Free Cynomolgus Monkey iPSCs Generated under Chemically Defined Conditions. Cells 2024, 13, 558. https://doi.org/10.3390/cells13060558

Ncyte® NHP-C vCardiomyocytes open a new era in translational cardiac in vitro screening

Questions? Contact us at: support@ncardia.com, www.ncardia.com

Contact us at support@ncardia.com or scan the QR code to download the poster