Development and Characterization of Non-Human Primate iPSC-Derived Ventricular Cardiomyocytes for High-Throughput Safety Pharmacology Screening

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Background

Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) are widely used in nonclinical cardiac safety studies; however, interspecies translation remains a limitation in early-stage pharmacology and toxicology. Non-human primates (NHPs) are physiologically closer to humans and often used as secondary species for *in vivo* studies and can provide translational insights. However, there are limited *in vitro* models using NHP-derived cardiomyocytes.

Here, we present Ncardia's scalable platform for generating ventricular cardiomyocytes from *Macaca fascicularis* (cynomolgus monkey) iPSCs[1], combined with our expertise in assay development and safety pharmacology testing. Our robust protocols and integrated assay platforms deliver high-quality, translational data, addressing key challenges in reproducibility, scalability, and predictive power for drug discovery and nonclinical safety assessment.

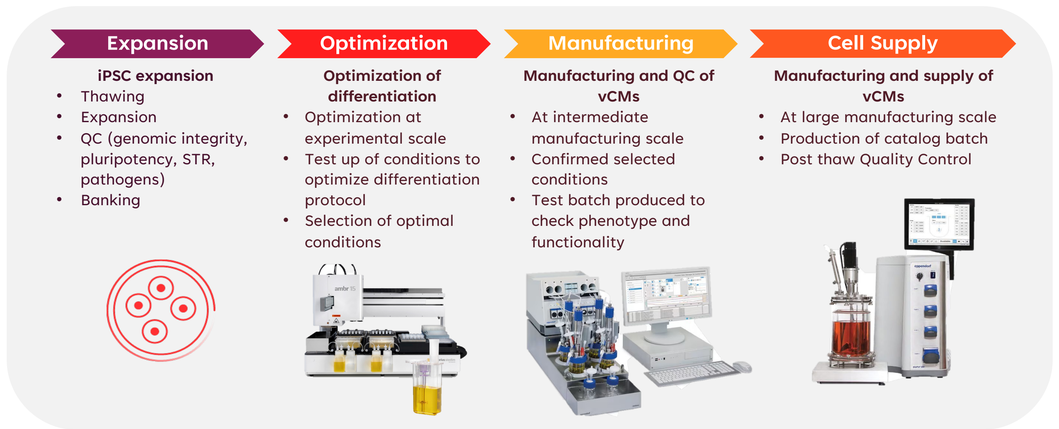

Figure 1. From concept to manufacturing, navigate therapeutic development smoothly by implementing an approach meticulously designed with the ultimate goal of achieving clinical success.
The process begins with iPSC expansion, banking, and quality control. Differentiation conditions are optimized at small experimental scale before transitioning to intermediate-scale manufacturing and QC of vCMs. Final large-scale manufacturing ensures production of clinically relevant batches, validated by extensive quality control. This iterative process identifies and monitors critical process parameters (CPPs), critical material attributes (CMAs), and critical quality attributes (CQAs), enabling predictive modeling and ensuring reproducibility and consistency in outcomes.

1. Ncyte® NHP-C vCardiomyocytes show high purity and functionality

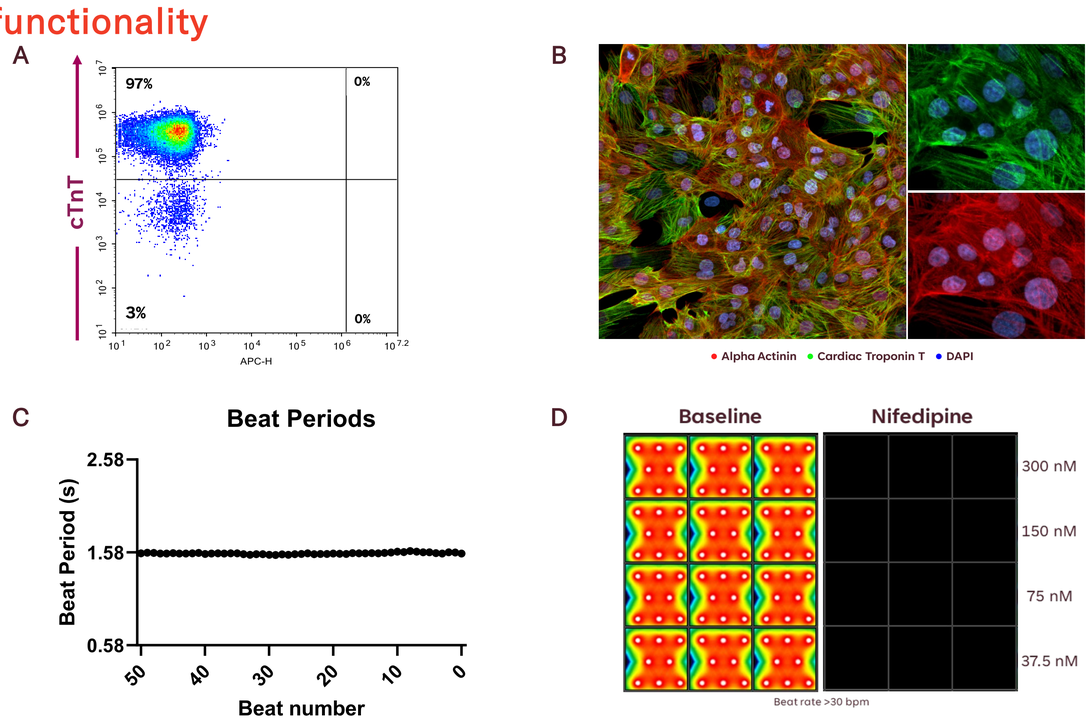

Figure 2. Characterization of Ncyte® NHP-C vCardiomyocytes
(A) Flow cytometry analysis of cardiac Troponin T (cTnT) expression shows high purity with ≥97% cTnT-positive cells.
(B) Immunofluorescence staining of NHP-C vCardiomyocytes demonstrating expression of α-Actinin (red), cardiac Troponin T (green), and nuclear counterstain DAPI (blue).
(C) Representative beat period recordings of NHP-C vCardiomyocytes show stable beating over successive beats.
(D) Functional response of NHP-C vCardiomyocytes to nifedipine (an L-type calcium channel blocker). Baseline electrical activity is suppressed at all doses (37.5–300 nM).

2. MEA Assay Confirms Stable Baseline and Expected Responses

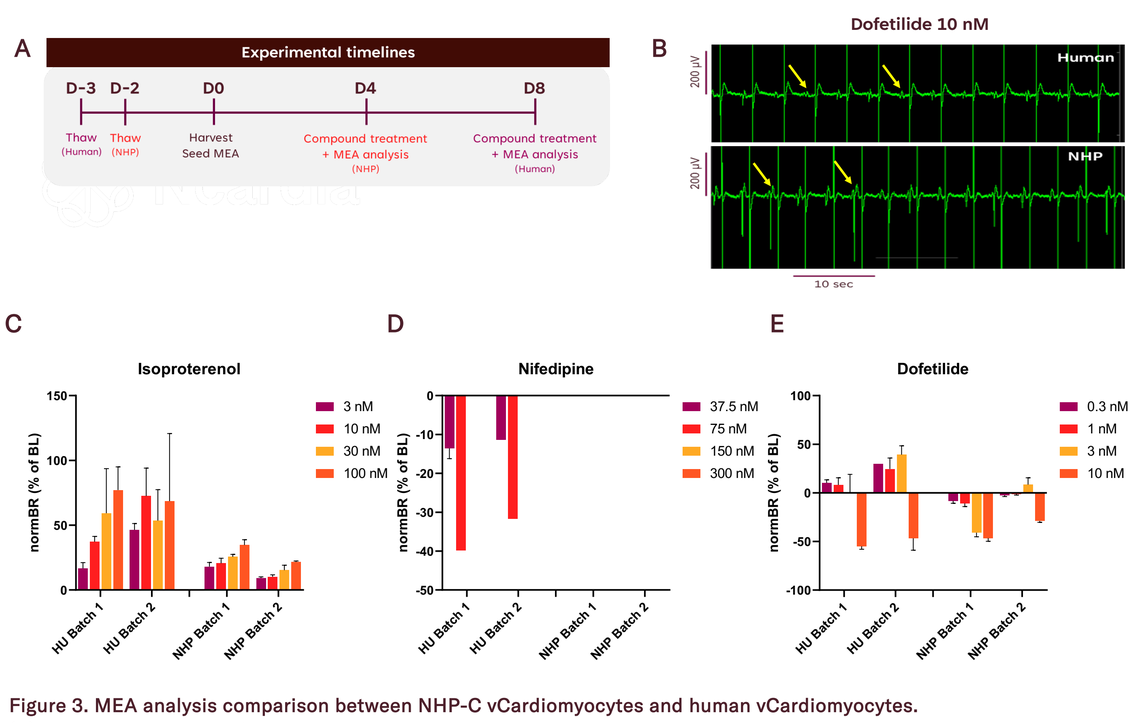

Figure 3. MEA analysis comparison between NHP-C vCardiomyocytes and human vCardiomyocytes.
(A) Experimental timeline for MEA analysis. Human vCardiomyocytes were thawed on day –3, NHP-C vCardiomyocytes on day –2, and both were harvested and seeded on day 0. Compound treatments and MEA recordings were performed on day 4 (NHP-C) and day 8 (human).
(B) Representative field potential recordings showing the arrhythmic effect of dofetilide (10 nM) on human and NHP-C vCardiomyocytes.
(C) Isoproterenol induced a concentration-dependent increase in beat rate across human and NHP-C vCardiomyocytes.
(D) Nifedipine suppressed electrical activity in a dose-dependent manner in human vCardiomyocytes and complete arrest in NHP-C.
(E) Dofetilide caused concentration-dependent changes in beat rate in human and NHP-C vCardiomyocytes.

3. Contractility Drug Response in Human and NHP-C vCardiomyocytes

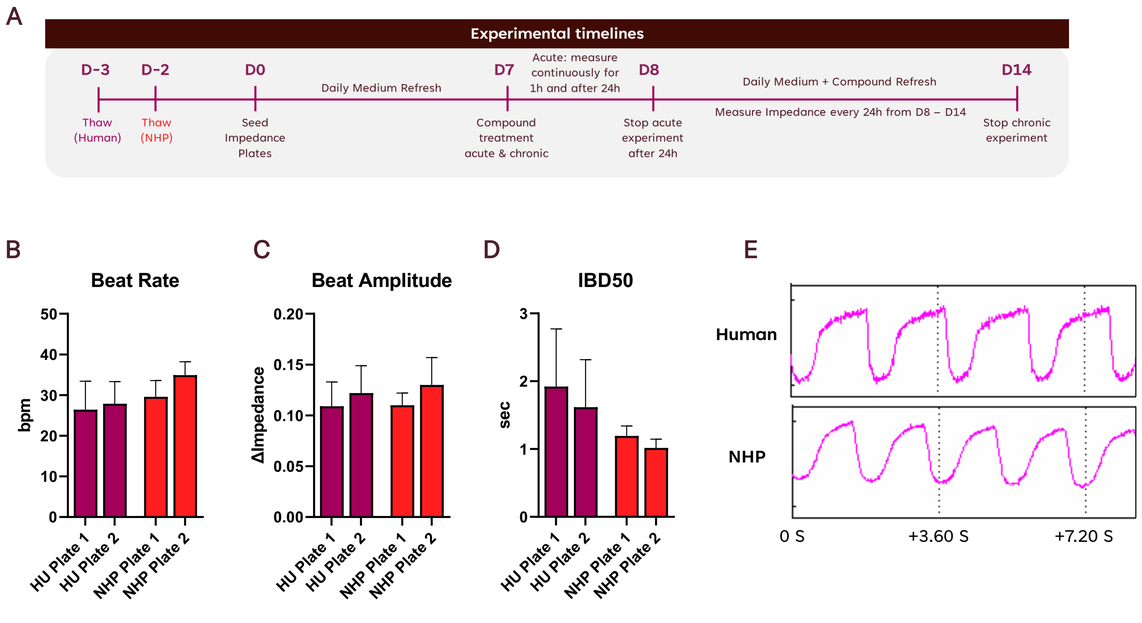

Figure 4. Impedance assay and drug response in NHP-C vs human ventricular vCardiomyocytes
(A) Experimental timeline for impedance assays. Human vCardiomyocytes were thawed on day –3 and NHP-C vCardiomyocytes on day –2. Both were seeded on impedance plates at day 0. Acute compound treatment was performed at day 7, followed by 24 h measurements (day 8). Chronic recordings were carried out daily until day 14.
(B) Baseline beat rate comparison between human and NHP-C vCardiomyocytes.
(C) Beat amplitude measured as changes in impedance (ΔImpedance).
(D) IBD50 values (inter-beat duration at 50%) showing consistency across replicates.
(E) Representative impedance traces of human and NHP-C vCardiomyocytes demonstrate stable and rhythmic beating patterns as well as marked differences in peak shape between species.
*n=96 for human and n=80 for NHP-C

4. Impedance Assay Reveals Species-Specific Drug Effects

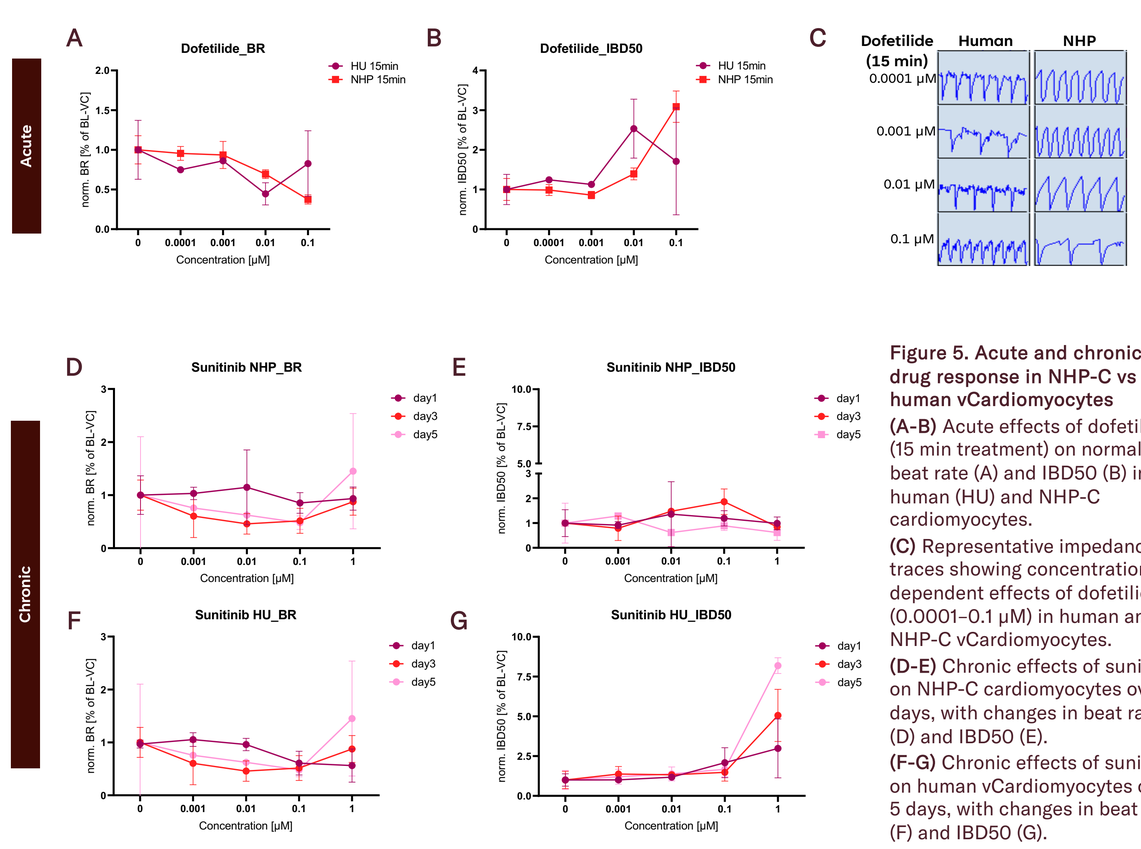

Figure 5. Acute and chronic drug response in NHP-C vs human vCardiomyocytes
(A-B) Acute effects of dofetilide (15 min treatment) on normalized beat rate (A) and IBD50 (B) in human (HU) and NHP-C cardiomyocytes.
(C) Representative impedance traces showing concentration-dependent effects of dofetilide (0.0001–0.1 µM) in human and NHP-C vCardiomyocytes.
(D-E) Chronic effects of sunitinib on NHP-C cardiomyocytes over 5 days, with changes in beat rate (D) and IBD50 (E).
(F-G) Chronic effects of sunitinib on human vCardiomyocytes over 5 days, with changes in beat rate (F) and IBD50 (G).

Conclusions

NHP-C iPSC-derived vCardiomyocytes differentiated at large scale display high structural fidelity, 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 nonclinical safety pharmacology workflows.

Driving the next generation of cardiac safety testing with robust and scalable iPSC platforms

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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