FUJIFILM
Cellular Dynamics

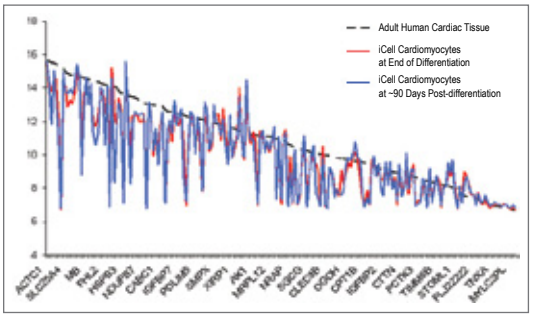
PRODUCT DATASHEET

iCell® Cardiomyocytes

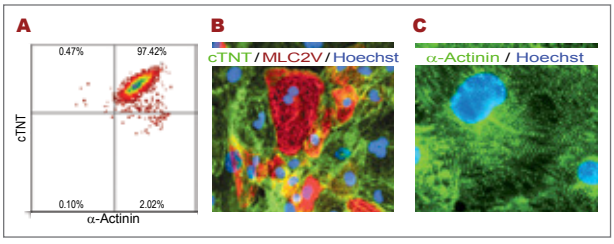
Basic cardiac research, drug discovery, and toxicity testing require an in vitro system that recapitulates native biology. FUJIFILM Cellular Dynamics, Inc. (FCDI), meets this need with iCell® Cardiomyocytes, human cardiomyocytes with proven, predictive, and published advantages over other cellular cardiac models for faithfully and robustly reflecting cardiovascular disease endpoints and for enabling early and accurate prediction of drug-induced cardiotoxicity. The human biology, ease of use, and far-reaching applicability of iCell Cardiomyocytes has had a profound impact on academic research and the search for new medicines and cures.

Genomic and Protein Characterization

iCell Cardiomyoctyes are differentiated from human induced pluripotent stem cells. Whole-genome transcript profiling and immunocytochemical characterization demonstrate that iCell Cardiomyocytes exhibit a stable human cardiac gene expression profile with proper protein expression and localization necessary for cardiac function.



▲ **Figure 1: Stable and Appropriate Gene Expression**
*Data for 203 cardiac genes demonstrate a stable genomic expression profile for iCell Cardiomyocytes that trends well with that of adult human cardiac tissue. (Data were provided by Hoffmann-La Roche and adapted from Babiarz et al. (2011) Stem Cells and Dev.)**



▲ **Figure 2: Pure Pan-cardiomyocyte Population**
*(A) Flow cytometry (cTNT, α-Actinin gating) demonstrates the >97% purity of iCell Cardiomyocytes. (B, C) Immunocytochemical labeling shows a pan-cardiac population with a sarcomeric myofibril organization. (Data were adapted from Kattman et al. (2011) J Cardiovasc Transl Res.)**

Advantages

- **Human cells:** iCell Cardiomyocytes are terminally differentiated from human iPS cells and exhibit functional characteristics similar to native human cardiomyocytes.
- **Homogenous and reproducible:** iCell Cardiomyocytes are highly pure, providing biologically relevant and reproducible results.
- **Acute and long-term testing:** iCell Cardiomyocytes remain viable and pure in culture for weeks, enabling assessment of both acute and sub-chronic responses.
- **Easy to implement:** iCell Cardiomyocytes are shipped cryopreserved with cell culture media specifically formulated for optimal cell performance. Simply thaw and use.

Electrophysiological Characterization

iCell Cardiomyocytes are electrically active with spontaneously occurring action potentials driving rhythmic contractions. High precision current- and voltage-clamp experiments demonstrate that the electrophysiological properties of iCell Cardiomyocytes are similar to native human cardiac myocytes.

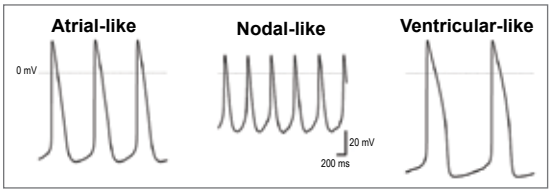


Figure 3: Action Potential Recording
*Spontaneous action potentials are classified as atrial-, nodal-, and ventricular-like, with ~50% of the iCell Cardiomyocytes showing a ventricular-like action potential phenotype. (Data were adapted from Ma et al. (2011) Am J Physiol Heart Circ Physiol.)**

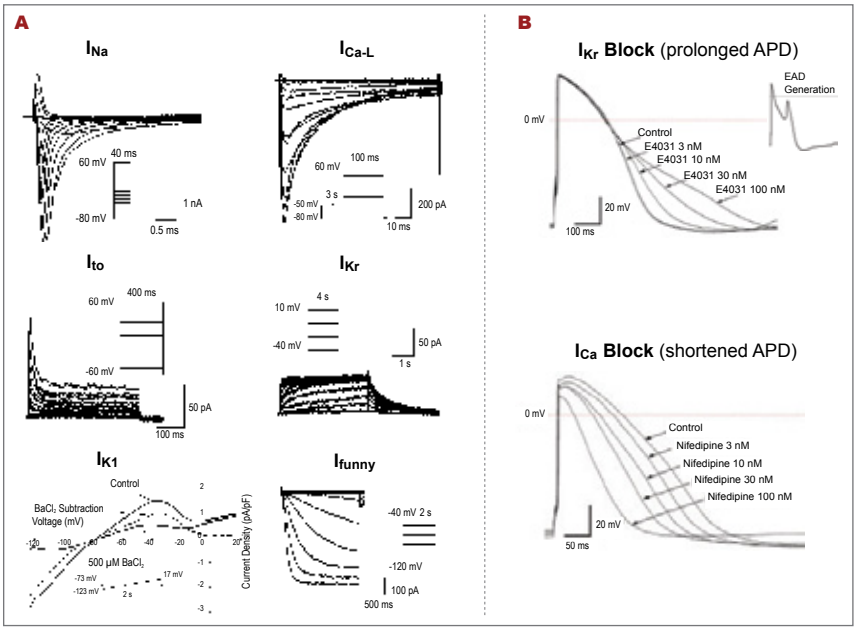


Figure 4: Ionic Currents
*iCell Cardiomyocytes contain the (A) expected human cardiac ionic currents and show the (B) expected effects when exposed to ion channel-blocking drugs. (Data were adapted from Ma et al. (2011) Am J Physiol Heart Circ Physiol.)**

Toxicity Testing

The adherent nature, ease of use, and recapitulation of human in vivo cardiac myocyte behavior make iCell Cardiomyocytes especially well suited for discriminating between generalized and cell-specific toxicities.

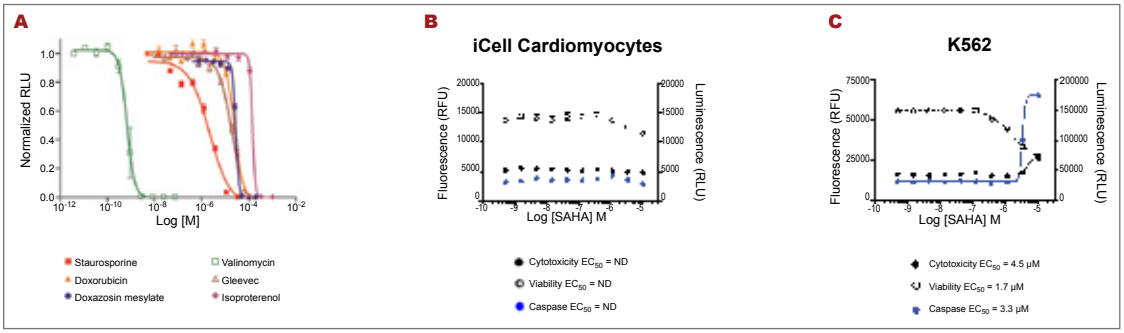


Figure 5: Cell-specific Effects
*(A) General toxicants demonstrate adverse effects on iCell Cardiomyocytes. (B, C) The HDAC inhibitor Vorinostat (SAHA) shows cell-type specific toxicity. iCell Cardiomyocytes were unaffected by compound application whereas the commonly used immortalized K562 cell line showed clear toxicity. Using only immortalized cell lines in such cell-based assays could result in false positive or negative assessments of terminally differentiated cell toxicity. (Data were provided by Promega Corp.)**

Higher Throughput Functional Testing

iCell Cardiomyocytes are suitable for examining functional endpoints across many higher throughput platforms, thus affording investigators the opportunity to examine compound effects in a relevant human cellular environment early in the discovery process.

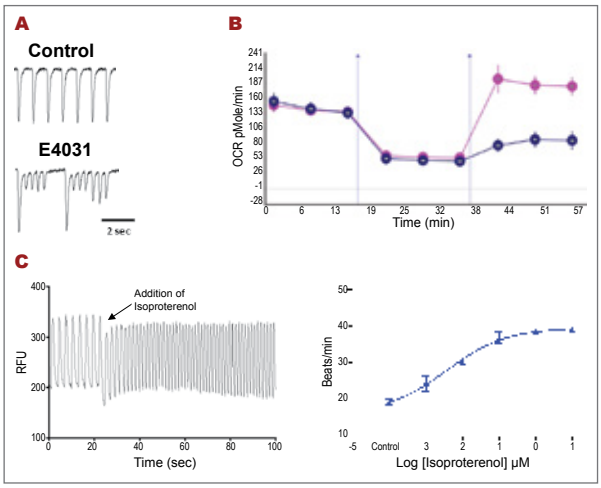


Figure 6: Higher Throughput Functional Analysis
*(A) Effects of ion channel and GPCR modulation on beating behavior were assayed using the xCELLigence RTCA Cardio System (Roche Applied Science). (B) Metabolic profiling with different energy substrates were assayed using the XF96 Extracellular Flux Analyzer (Seahorse Bioscience). (C) GPCR-mediated changes in Ca^{2+} cycling and contraction rate were assayed using the FLIPR® Tetra System (Molecular Devices, Inc.). (Data were provided by Molecular Devices, Inc.)**

Reporter Assays and Microscopy Applications

Their adherent nature and in vitro viability enable iCell Cardiomyocytes to be used for live or fixed reporter assays and microscopy applications uniquely tailored to an individual investigator's requirements.

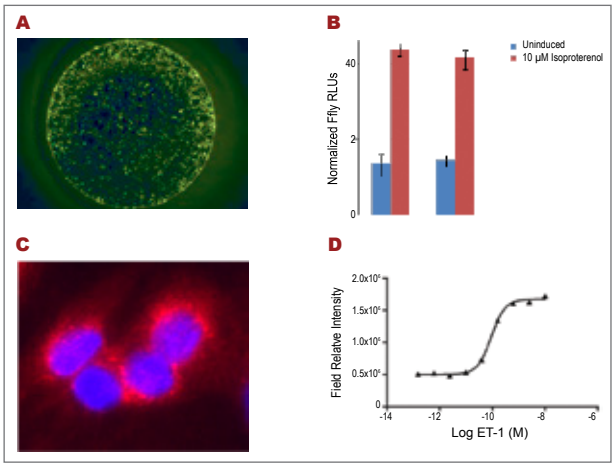


Figure 7: Reporter Assays and Microscopy Applications
*(A) GFP transiently transfected into iCell Cardiomyocytes verifies relatively high transfection efficiencies. (B) Isoproterenol induces a high level of transiently transfected CRE-luciferase activity (note log scale). (C) Fluorescent microscopy image illustrates the perinuclear localization of BNP staining. (D) Endothelin-induced increases in BNP expression were measured by fluorescent microscopy.**

Applications

iCell Cardiomyocytes are amenable to use on multiple platforms to study a variety of cellular functions and assay endpoints including:

- Proarrhythmia detection
- Biochemical and structural toxicity
- Bioenergetics
- Contractility
- Disease modeling
- Phenotypic screening
- Target identification
- Hit-to-lead validation and lead optimization

Specifications

Cell Type	Cardiomyocytes
Organism	Human
Source	Differentiated from an FCDI reprogrammed human iPS cell line
Purity	>95% cardiomyocytes
Quantity	≥1.0 x 10^6 or ≥4.0 x 10^6 viable cells per vial
Shipped	Frozen

Ordering Information

Kit	Component(s)[1]	Catalog Number
iCell Cardiomyocytes Kit, 01434	≥1.0 x 10^6 viable cells 30 ml Plating Medium 100 ml Maintenance Medium	R1057
	≥4.0 x 10^6 viable cells 30 ml Plating Medium 2 x 100 ml Maintenance Medium	R1007
iCell Cardiomyocytes Kit, 11713	≥1.0 x 10^6 viable cells 30 ml Plating Medium 100 ml Maintenance Medium	R1105
	3 x ≥1.0 x 10^6 viable cells 30 ml Plating Medium 2 x 100 ml Maintenance Medium	R1117
	≥4.0 x 10^6 viable cells 30 ml Plating Medium 2 x 100 ml Maintenance Medium	R1106
iCell Cardiomyocytes Maintenance Medium	100 ml Maintenance Medium	M1003

1 A User's Guide is provided in each kit.

For More Information

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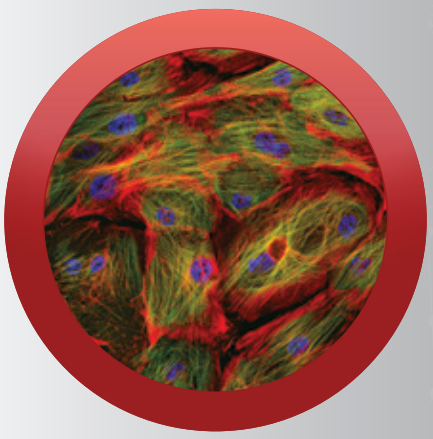
* Images and data are representative of iCell Cardiomyocytes derived from two different genetic backgrounds (donors 01434 and 11713).

iCell Products

Provide access to biologically relevant, human iPS cells for disease modeling, drug discovery, toxicity testing, and regenerative medicine. FCDI's rapidly growing portfolio of iCell products includes human cardiomyocytes, GABAergic, glutamatergic, dopaminergic and motor neurons, hepatocytes, endothelial cells, astrocytes, hematopoietic progenitor cells, skeletal myoblasts, macrophages, and others.

Visit the FCDI website for the most current list of supported cell types.



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