

# HUMAN iPSC-DERIVED CARDIOMYOCYTES

## ADVANTAGES

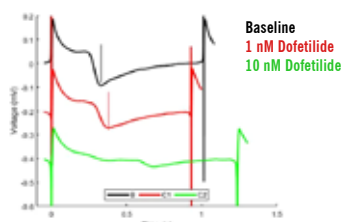
- ▶ Predictive and physiological cell model
- ▶ Applicable for drug development, preclinical research, and cardiac safety assessment
- ▶ Quantity, consistency and efficiency for HTS

A lack of physiologically relevant and translational *in vitro* test systems and disease models is a major constraint for the development of therapies for cardiovascular diseases. Concurrently, such test systems are essential to overcome cardiovascular safety and toxicity liabilities. Evotec's human iPSC-derived cardiomyocytes provide a well-characterized, highly standardized and cost-effective cellular model suitable to address these industry needs. It enables the assessment of cardiac safety and toxicity at the early preclinical stage, while using the same cell model in explorative research, disease modeling, and compound profiling.

### Predictive and physiological cell model

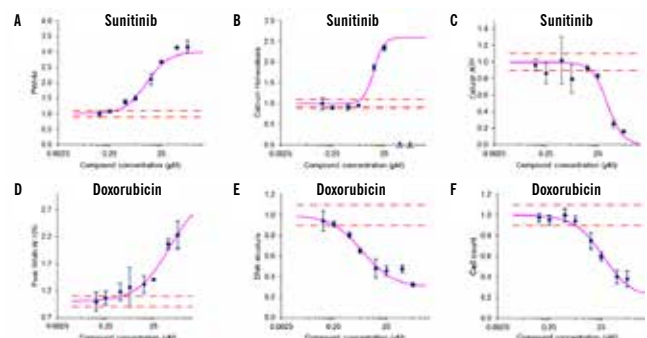
Evotec's human iPSC-derived cardiomyocytes are positive for TNTc (> 90%, flow cytometry) and each batch is tested for functional performance in Microelectrode Array (MEA) according to published CiPA protocols (Gintant G et al., Regul Toxicol Pharmacol. 2020).

**Figure A:** Field potential prolongation in human iPSC cardiomyocytes after treatment with Dofetilide. Cardiomyocytes were cultured for 7 days on 96w MEA plates and treated with Dofetilide for 30 min.



### Applicable for drug development, preclinical research, and cardiac safety assessment

Our human iPSC cardiomyocytes have been optimized for various functional and phenotypic assays, as well as high-content screening for structural cardiac toxicity.



**Figure B:** Detection of structural cardiotoxicity of kinase inhibitors using high-content imaging. Human iPSC cardiomyocytes were cultured in 384 well plates for 10 days. High content imaging of nuclei, calcium homeostasis and mitochondrial function was performed, and cellular ATP was measured. Images show representative dose response curves for FWHM (a), calcium homeostasis (b) & cellular ATP (c) for the dual cardiotoxin Sunitinib and representative dose response curves for peak width at 10% (d), DNA structure (e) and cell count (f) for the dual cardiotoxin Doxorubicin. (Data courtesy of Stephanie Ryder, Cyprotex)

### Quantity, consistency and efficiency for HTS

Evotec's human iPSC cardiomyocytes have been successfully applied in a RT-qPCR-based HTS screen within a myocyte disease project.

Pre-screen activities	<b>ASSAY DEVELOPMENT</b> <ul style="list-style-type: none"> <li>▶ Optimization of cell culture and treatment conditions</li> <li>▶ Establishment of robust and sensitive RT-qPCR assays</li> </ul>
	<b>CELL GENERATION</b> <ul style="list-style-type: none"> <li>▶ Targeted large-scale differentiation from iPSCs</li> <li>▶ General and assay-specific quality control</li> </ul>
	<b>HIGH-THROUGHPUT SCREEN SETUP</b> <ul style="list-style-type: none"> <li>▶ Definition of screening controls</li> <li>▶ Evaluation of assay parameters (DMSO tolerance, Z', variability etc.)</li> </ul>
High-throughput screen	<b>PILOT SCREEN</b> <ul style="list-style-type: none"> <li>▶ Screening of several hundred compounds at multiple concentrations</li> <li>▶ Evaluation of overall performance, expected number of hits, and toxicity</li> </ul>
	<b>PRIMARY SCREEN</b> <ul style="list-style-type: none"> <li>▶ Screening of 20K compound library at two concentrations</li> <li>▶ Selection of active compounds for hit confirmation and profiling</li> </ul>

**Figure C:** Set-up of an HTS screen using Evotec's human iPSC derived cardiomyocytes.

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## PRODUCT SPECIFICATIONS

**Cell type:** Evotec’s human iPSC-derived cardiomyocytes represent a highly translational, cost effective and validated *in vitro* model system suitable for various applications within the drug discovery and development process.

**Production technology:** Scalable; large lot sizes with minimal batch-to-batch variation. Thorough quality control, each batch is qualified for functional activity.

**Vial size:** 4M cryopreserved cells; alternative sizes on request

**Purity:** >95% cardiomyocytes

**Assay window:** Day 5 onwards, depending on read-out

## VALIDATED ASSAYS AND PROTOCOLS

Evotec’s iPSC cardiomyocytes are integrated into a variety of validated assays on dedicated platforms that can be implemented in drug discovery and development for safety and efficacy evaluation of novel compounds:

- ▶ Electrophysiology – Microelectrode Array (MEA)
- ▶ Ca<sup>++</sup> transient analysis
- ▶ Cell metabolism analysis
- ▶ High content imaging
- ▶ HTS (384w) screening

Evotec offers easy-to-follow protocols for most of these validated assays and their corresponding platforms. Reach out to [enquiries-cologne@evotec.com](mailto:enquiries-cologne@evotec.com) for more information on our application notes and manuals.

## EVOTEC *IN VITRO* iPSC RESEARCH SERVICES

Evotec further develops induced pluripotent stem cell (iPSC) based models and assays for efficacy and safety applications, in particular disease modeling and customized cell type development. We offer flexible entry and exit points for our clients and partners, who can choose only one or up to all of the following building blocks:

- ▶ Evotec or client iPSC lines
- ▶ Expansion & banking
- ▶ Genetic engineering
- ▶ Custom differentiation
- ▶ Disease modeling & exploratory research
- ▶ Compound screening & profiling

Do contact us to discuss how our iPSC technology can accelerate your drug development process.

