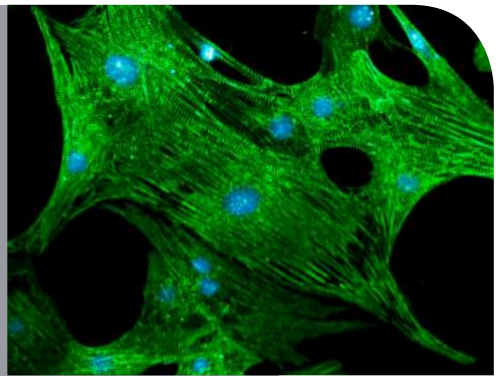
Cor.4U®

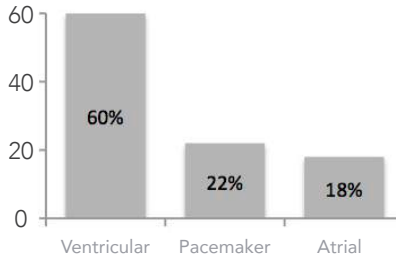
Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes

- Predictive and physiological cell model; applicable for drug development and preclinical research
- Established model system for cardiac preclinical safety assessment, currently validated by the CiPA initiative
- Quantity, consistency and efficiency for HTS – Get your results in 3 days or less



CHARACTERISTICS

A

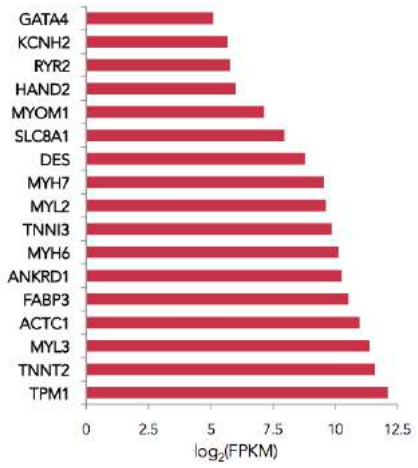


B

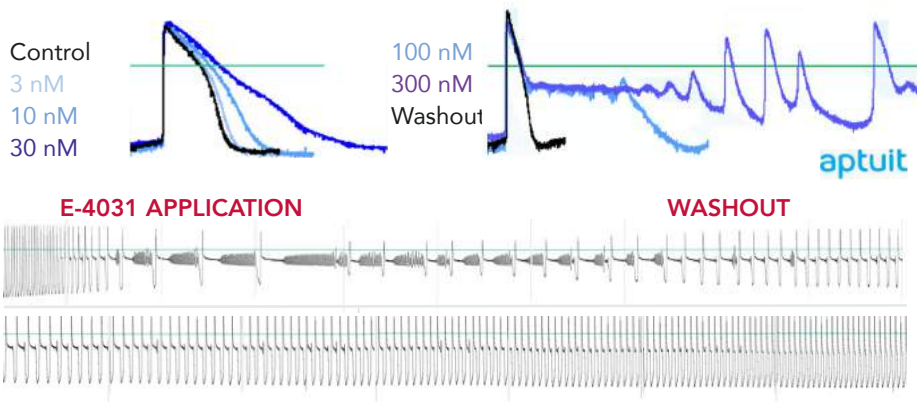
RMP	-79 mV
Amplitude	110 mV
Rate of Rise	75.9 V/s
APD90	429.9 ms

Ionic Transport Assays

Composition of Cor.4U® determined by manual patch clamp (n=50) (A). Electrophysiological characteristics of Cor.4U® reflect human levels (B).



Relative gene expression of Cor.4U®. Relevant cardiac genes, GPCRs, ion channels and cellular machinery are present.



Cor.4U® are a relevant arrhythmia model. Reaction to gold standard compound E-4031 as assessed by manual patch clamp, current clamp mode. Data courtesy of Caterina Virgino (Aptuit).

DESCRIPTION

Cor.4U® human cardiomyocytes are an essential tool both for general cardiovascular research and to address key unmet needs in drug development and pre-clinical research markets.

Cardiovascular safety liabilities are a major cause for compound failure in P2/3 clinical programs of drug development. New testing systems, such as human induced pluripotent stem cell (iPSC)-derived cardiomyocytes, enable the assessment of the safety pharmacology "core battery" at the preclinical stage.

The leading cause of morbidity in developed countries is cardiovascular disease. A major constraint for the development of adequate therapies has been the lack of suitable cell-based assays with physiological relevance.

Axiogenesis provides well - characterized, human iPSC-derived cardiomyocytes, named Cor.4U®, which represent a highly translational, cost effective and validated *in vitro* model system to address these industry needs.

Cor.4U®

Human Induced Pluripotent
Stem Cell-Derived Cardiomyocytes

VALIDATED APPLICATIONS

- Manual and automated patch clamp
- Microelectrode array (MEA)
- Impedance assays
- Calcium transient analysis
- Voltage sensitive dyes
- Cell metabolism analysis
- High content analysis (e.g., hypertrophy disease modeling)
- Cell contraction force
- 3D organotypic cell culture / organ-on-a-chip

PRODUCT SPECIFICATIONS

Cell type	iPSC-derived cardiomyocytes
Source	iPSC of 26 y/o Caucasian female
Species	Human
Purity	100% (60% ventricular); fibroblast-free
Assay window	Stable beating after 72h. Refer to our protocols for assay-specific recommendations

EACH LOT IS TESTED QUALITY CONTROL PHARMACOLOGICALLY

DELIVERY OPTIONS

3 vials of 0.25 x 10^6
Ax-B-HC02-MPC

>1 x 10^6
Ax-B-HC02-1M

>4 x 10^6
Ax-B-HC02-4M

>0.5 x 10^6 T25 Flask
Ax-C-HC02-APC

>1 x 10^6 T25 Flask
Ax-C-HC02-FR1

>3 x 10^6 T75 Flask
Ax-C-HC02-FR3

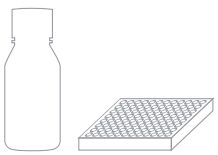
96w Plate
Ax-C-HC02-96

96w E-Plate
Ax-C-HC02-EPL

96w MEA Plate
Ax-C-HC02-APL

384w Plate
Ax-C-HC02-384

Cryopreserved Cor.4U®



Cultured Cor.4U®

AXIOGENESIS OVERVIEW

DIFFERENTIATED HUMAN CELLS

Axiogenesis is a leading expert in providing commercial-grade *in vitro* differentiated cell types derived from human induced pluripotent stem cells (iPSCs).
Core products include Cor.4U® cardiac myocytes and fibroblasts as well as Peri.4U™, Dopa.4U™, CNS.4U™ and Astro.4U™ neural cells.

VALIDATED ASSAYS & PROTOCOLS

Axiogenesis enables customer efficiency by providing ready to use cells along with validated protocols. Assays for each cell type have been developed for advanced drug discovery, safety pharmacology, *in vitro* toxicology applications, and disease and tissue modeling.
Based on its in-house assay capabilities, Axiogenesis can provide expert scientific support in order to facilitate selection and quick implementation of validated assays and technologies.

CONTRACT SERVICES

Axiogenesis provides compound testing services for HTS, electrophysiological and toxicology applications as well as disease modeling and customized cell type development for cardiac cells. Customized services are available upon request.

iPSC-derived neurons

iPSC-derived cardiac cells

FOR MORE INFORMATION VISIT WWW.AXIOGENESIS.COM OR CONTACT INFO@AXIOGENESIS.COM

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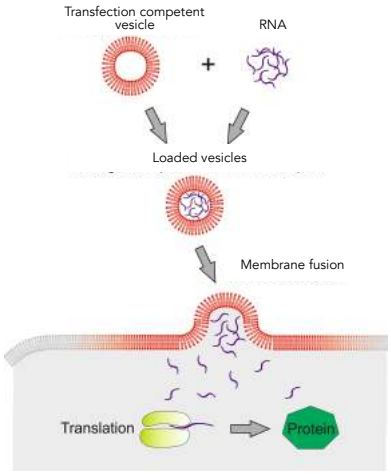
axioGENESIS

Xpress.4U™

Transient Transfection of Human iPSC-Derived Cells

OVERVIEW



- Transfection competent vesicles are formed around RNA cargo
- Loaded vesicles fuse with plasma membrane of target cells
- Cargo is directly released into cytosol, bypassing the endo- / lysosomal pathway
- Instant bioavailability of cargo molecules in cytosol
- Fluorescent tracer molecule in vesicles allows for verification of successful transfection or cell sorting in flow cytometry

Figure 1. Technology overview. The novel liposomal formulation of Xpress.4U™ facilitates single-step, rapid, and highly efficient transfection of iPSC-derived cells.

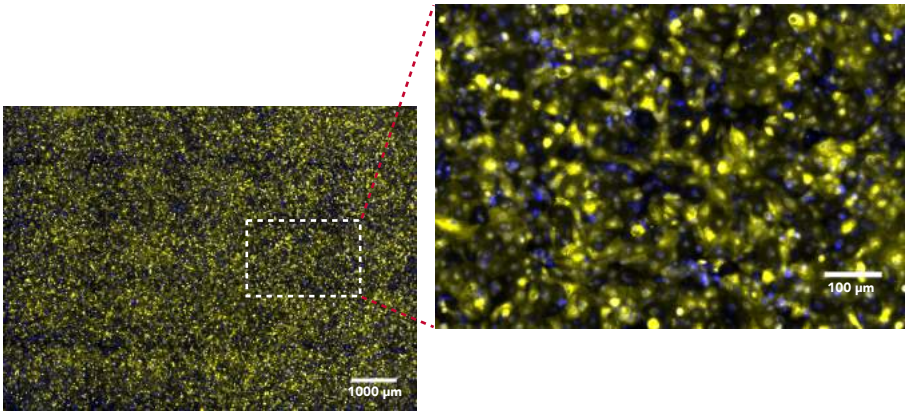


Figure 2. Highly efficient transfection. Overview images of Cor.4U® cells, transfected once for 10 minutes with ChR2-YFP mRNA using Xpress.4U™. Cells were fixed 24 hours post-transfection and stained for nuclei with DAPI (blue).

DESCRIPTION

Axiogenesis exclusively offers a novel proprietary transfection technology for its human iPSC-derived cell portfolio. This opens up new opportunities for transient genetic modification of cells for drug development and disease modeling.

Protocols have been established for optogenetic pacing of Cor.4U® iPSC-derived cardiomyocytes transfected with channelrhodopsin-2 (ChR2; Figure 3) and for calcium transient analysis via transfection of Cor.4U® with GCaMP6f (Figure 4).

Transfection has been optimized for efficiency and long-term stability using modified RNAs.

We offer custom mRNA synthesis and transfection services yielding "ready-to-use" cells.

Inquire about our products and services related to Xpress.4U™!

BENEFITS

- Non-toxic, highly efficient transfection (>80 %)
- Integration-free, transient transfection of RNA
- High stability through modified RNA
- Compatible with entire Axiogenesis iPSC-derived cell portfolio

BROAD APPLICABILITY

- Highly customizable
- siRNA-mediated knock-down
- Dominant-negative overexpression of diseased genes
- Genetically encoded sensors (e.g.,ChR2)

Xpress.4U™

Transient Transfection of Human iPSC-Derived Cells

APPLICATION EXAMPLES

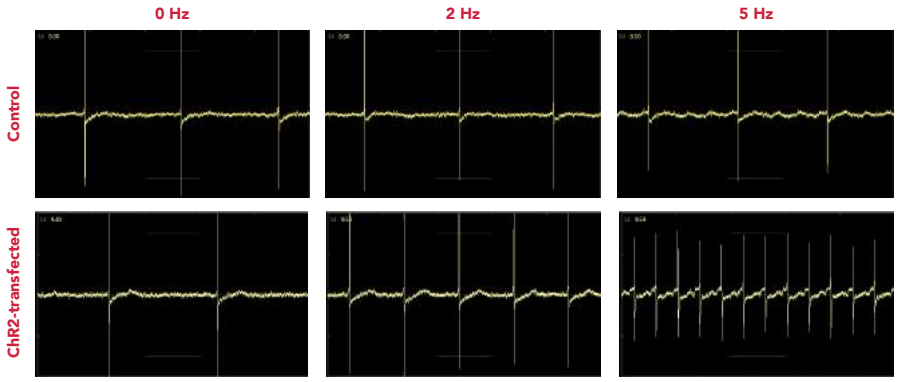


Figure 3. Optical pacing of ChR2-expressing Cor.4U®. Cor.4U® can be paced up to 5 Hz after Xpress.4U™-mediated transfection of ChR2 mRNA. Light stimulation of control (upper panel) and transfected Cor.4U®. Shown are representative MEA traces using Axion's Maestro™ system with the Lumos™ optical stimulation device. Optogenetic control of cardiomyocytes allows for investigation of beating rate-sensitive drug effects, avoids the need for frequency correction, and increases plate to plate reproducibility of drug effects.

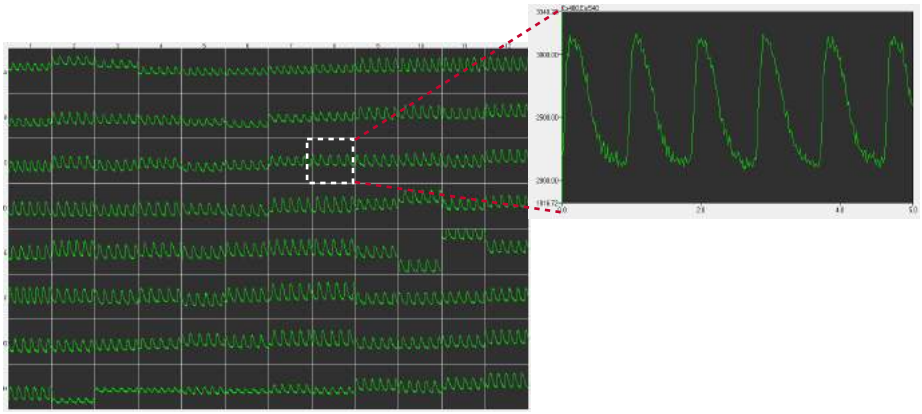


Figure 4. Calcium transients analysis using GCaMP6f-transfected Cor.4U®. Physiological beat rates of ~70 bpm at 37 °C were obtained in measurements with the Hamamatsu FDSS 7000EX system. Using transfected cells circumvents the need for (often toxic) chemical fluorescent dyes, which may affect cardiomyocyte function. The use of encoded sensors also shortens experimental time, reduces manual work, and facilitates quality control of cells prior to the start of the experiment.

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iPSC-derived cardiomyocytes

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