Hybrid Cell Analysis Screening

FLEXcyte 96 – CardioExcyte 96

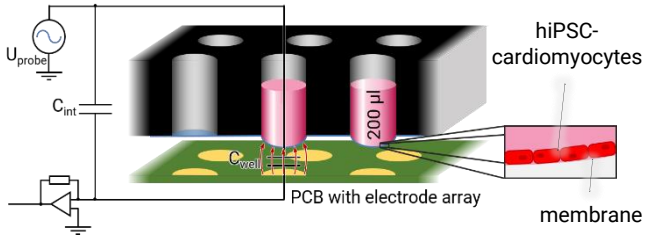
Simultaneous Assessment of Human iPSC-derived Cardiomyocyte Contractile, Electrophysiological and Cellular Properties

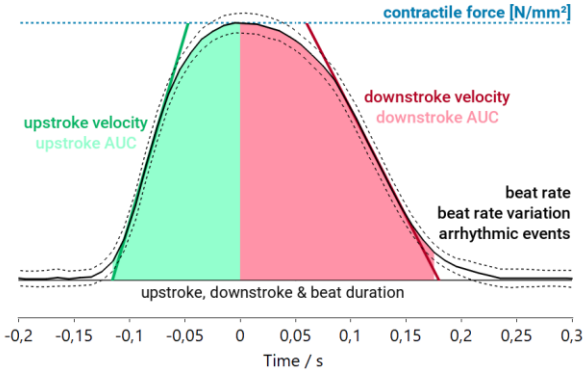
"We were very pleased with our choice to engage innoVitro's contractility service. The studies using human iPSC-derived cardiomyocytes were tailored to our needs to provide results comparable to already existing (in house) data and the fast execution followed by a comprehensive study report completed the service perfectly"

Nina Glaser
Head of Early Safety Electrophysiology
Merck Healthcare KGaA

- ✓ Both modules are CiPA applied instruments
- ✓ HiPS-cardiomyocytes for 100% human relevance
- ✓ Acute and chronic compound testing
- ✓ High throughput 96-well platform for time and cost efficiency
- ✓ Mechanical and optical pacing options
- ✓ Applicable for drug discovery up to preclinical safety and tox
- ✓ Mature functional cardiac phenotype for contractility analysis
- ✓ Real-time assessment of toxicity-related cellular changes

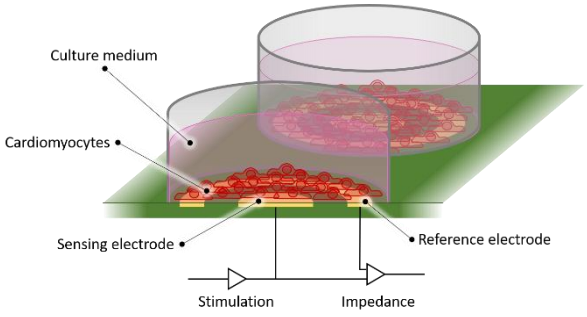
FLEXcyte Technology

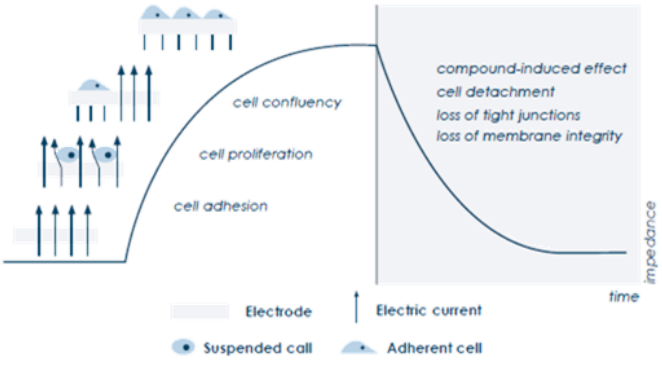




The FLEXcyte 96 module delivers a comprehensive set of parameters measured on the contractile behaviour of cardiomyocytes via label-free capacitive distance sensing. Human iPSC-cardiomyocytes are cultured on flexible membranes in a 96-well format to mimic *in vivo* conditions of the heart, resulting in a mature functional cardiac phenotype. Parameters measured are Beat Rate, Beat Duration, Upstroke and Downstroke Velocity, Upstroke and Downstroke Area Under Curve, Arrhythmic Events as well as **Contractile Force** (mN/mm^2).

CardioExcyte 96 Technology

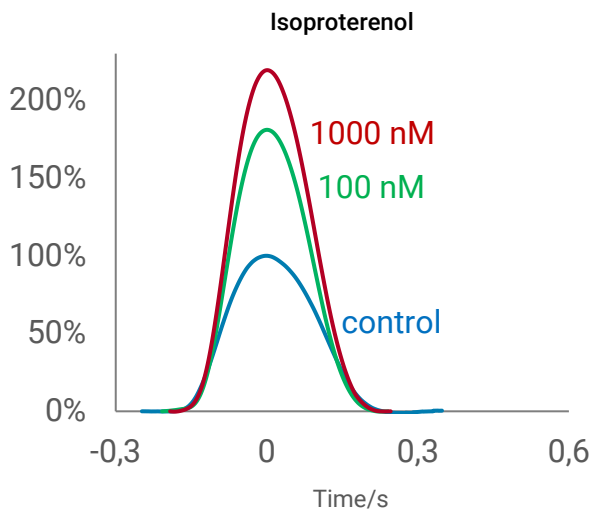


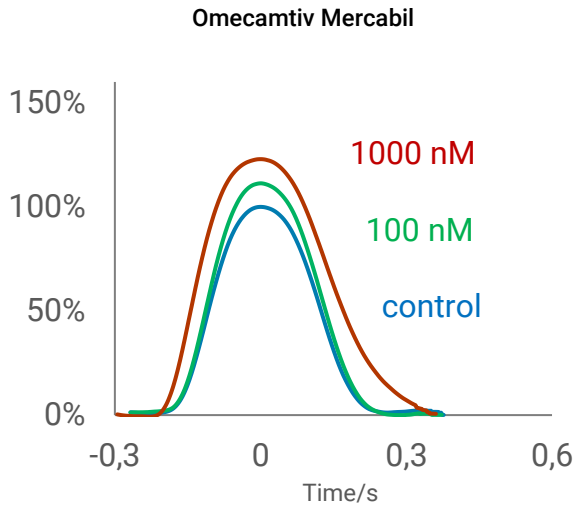


The CardioExcyte 96 module is an ideal tool for real-time assessment of compound-induced cellular and electrophysiological changes. Changes in morphology are analyzed with an electric current that is impeded by the cell monolayer. Changes of this monolayer, due to detachment, loss of tight junctions or membrane integrity causes a shift in base impedance that can be monitored for up to seven days. To analyze electrophysiological properties, electric field potential recordings can be recorded from the same wells.

Contractility assessment of human iPSC-cardiomyocytes with mature functional phenotype

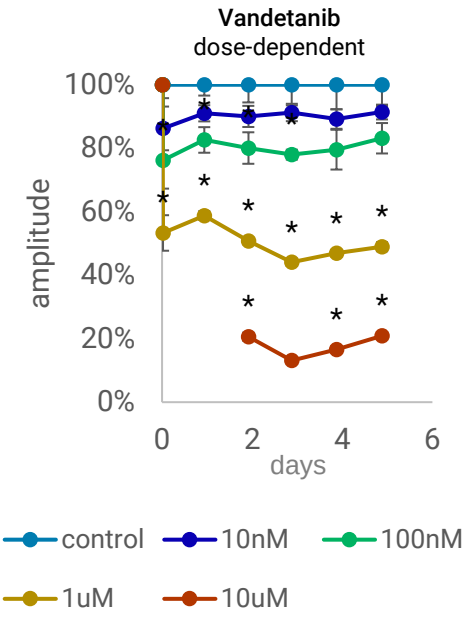
Drug-induced adult-like responses of human iPSC-cardiomyocytes usually fail due to the juvenile phenotype of the cells. The flexible membranes of the FLEXcyte 96 plates form a natural biohybrid layer with the cells and provide a physiological environment *in vitro* to promote cell maturation. Mature cardiomyocyte responses of commercially available human iPSC-cardiomyocytes can be detected with the FLEXcyte 96 module upon treatment with positive inotropic compounds, as shown with isoproterenol and omecamtiv mercabil.

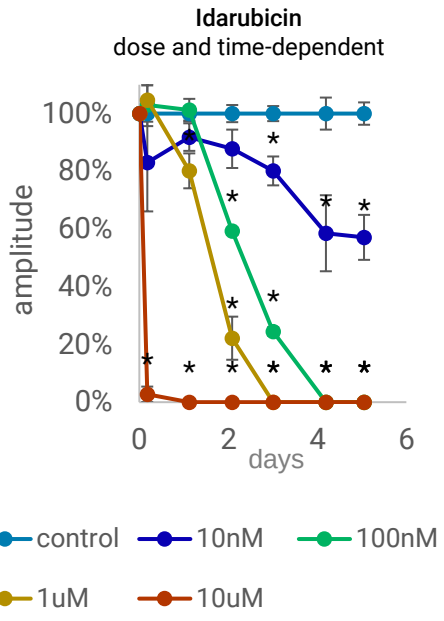




Long-term assessment of contractile properties to assess drug-induced dose- and time-dependent effects

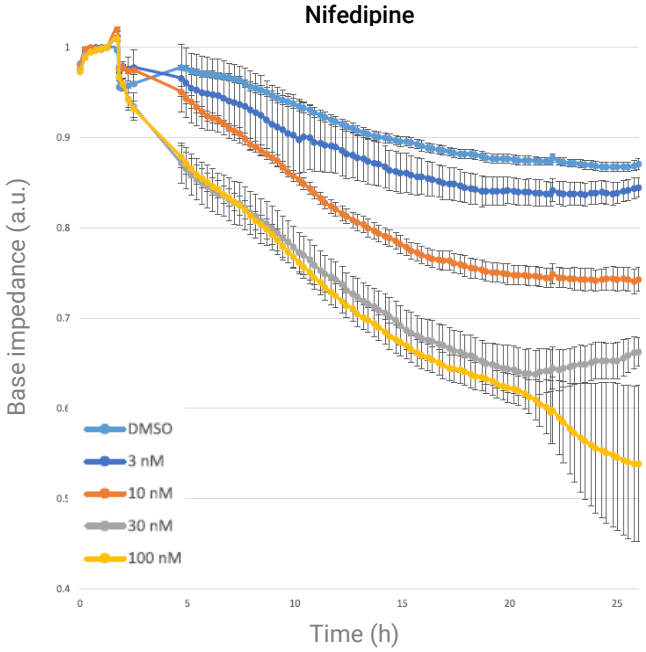
Acute and chronic measurements are feasible with the FLEXcyte 96 module and can be conducted from minutes up to five days after compound administration. Acute testing allows for fast data acquisition while long-term analysis offers valuable information regarding dose or time-dependent effects of drugs, as shown with vandetanib and idarubicin over a time span of five days.

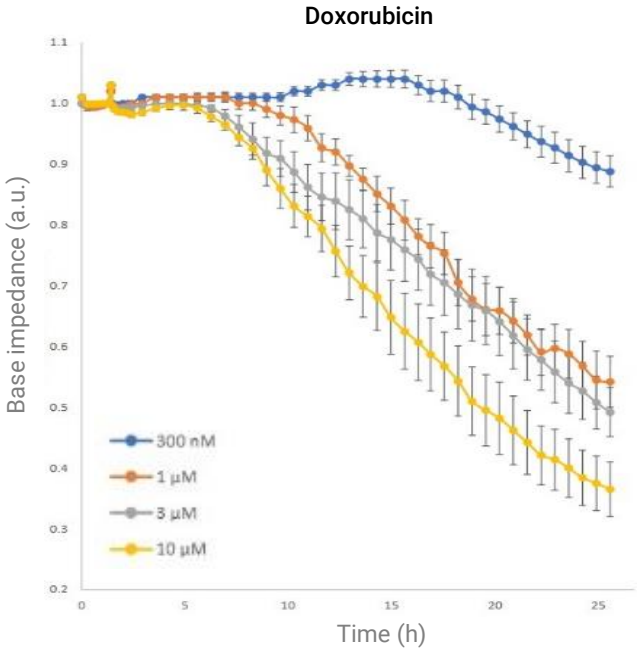




Real-time assessment of drug-induced human iPSC-cardiomyocyte structural changes

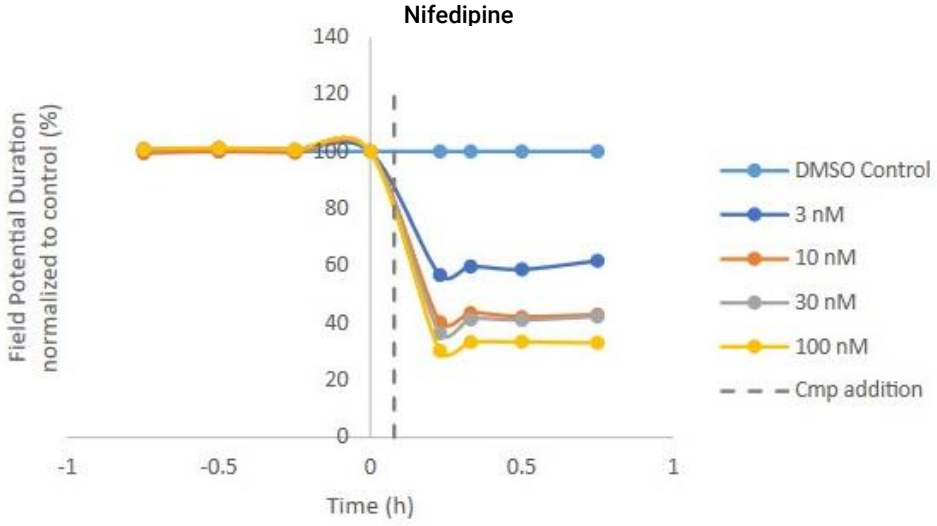
The electrical impedance spectroscopy of the CardioExcyte 96 module reveals cell and monolayer integrity changes in real-time for up to seven days as a measure of acute and chronic cell activity. Compound-induced structural toxicity of human iPSC-cardiomyocytes can be assessed with a decrease in base impedance, as shown after nifedipine and doxorubicin treatment over a time span of 24 hours.





Analysis of electrophysiological properties with the electric field potential (EFP) parameter

The EFP recording parameter of the CardioExcyte 96 module enables the analysis of human iPSC-cardiomyocyte electrophysiological properties after compound treatment, as shown with a dose-dependent decrease in field potential duration after treatment with nifedipine.



innoVitro GmbH
Artilleriestraße 2
52428 Jülich
Germany

FON +49 (0) 2461 3170561
FAX +49 (0) 2461 3173859
E-MAIL info@innovitro.de
Web www.innovitro.de