INTRODUCTION

The patch clamp assay has been the most valuable and reliable tool for assessing a potential drug-induced blockade of the hERG channel. However, any drug interaction on other ion channels important for the formation of the cardiac action potential could also lead to severe cardiac arrhythmias. Due to that, we expanded our cardiac portfolio and offer patch clamp assays for the following targets: hERG, Kv1.5, Kv1.3, Ca_{v}1.2, Na_{v}1.5 and K_{v}1.5. Furthermore, we offer efficacy screening on ion channels as: K_{v}, T_{v}, Na_{v}, P2RX or nAChR channels. All screens are carried out on the in-house developed CytoPatch™ Instruments. This automated technology mimics the manual patch procedure and generates the same high data quality, but is less cost-intensive. All assays are performed in the whole-cell configuration after gigaseal formation. An advanced rapid perfusion system avoids errors in the evaluation of drug effects and allows a constant perfusion of the compounds for up to 20 minutes. A professional compound handling of hydrophobic or light sensitive test substances prevents false negative measurements. All buffers and cells used are quality assured, all lab procedures are defined by the SOP documentation system. Study design and the final report are concise and approved by our CSO.

We offer scientific guidance and assay customization to meet the requirements of our customers for efficient and high quality ion channel screening.

BENEFIT OF THE CYTOPATCH™ TECHNOLOGY

The CytoPatch™ Instrument has a unique technique which is well suited for the investigation of ligand gated as well as voltage gated ion channels.

- **LONG CONTROL PHASE, LONG COMPOUND APPLICATION PHASE POSSIBLE (MAX. 20 MINUTES)**
- **NO STANDING SYSTEM, ONGOING PERFUSION**
- **NO CROSS-CONTAMINATION OR BACKFLOW OF COMPND**
- **CATCH OF ONE CELL, REMAINING CELLS ARE WASHED AWAY**
- **NO SEALING SOLUTIONS OR FLUORIDE IN INTRACELLULAR SOLUTION NEEDED FOR GIAGESEL FORMATION**
- **GIACHM SEAL THROUGH CYTOCENTERING CHANNEL TECHNOLOGY**
- **CURRENTS ARE COMPARABLE TO THOSE MEASURED WITH THE MANUAL PATCH CLAMP SETUP**
- **NO PROBLEMS WITH „STICKY COMPOUNDS“ DUE TO TELFON-COATED DISPENSER NEEDLE, GLASWARE „PRIMING“ OF TUBES WITH COMPOUND, GOOD AREA TO VOLUME RELATIONSHIP**
- **SERIAL RESISTANCE: 10 MOHM**
- **SERIAL RESISTANCE COMPENSATION POSSIBLE**
- **LOW SYSTEM CAPACITY (µ 10 PF)**
- **APPLICATION OF AGONISTS ACCOMPLISHED WITHIN 10 MS**
- **GLP CONFORM AUTOMATED ION CHANNEL SCREENING POSSIBLE**

Professional compound handling and flexible assay design in combination with the superior Cytocentrics automated patch clamp technology offers reliable and highest quality ion channel screening to the customer.

EXTENDED CELL LINE PORTFOLIO

Drug interaction on ion channels important for the formation of the cardiac action potential could lead to life-threatening arrhythmias. To compensate for this risk, we have expanded our cell line portfolio and offer different high quality patch clamp assays. Moreover, efficacy screening for a broad cell line portfolio can be performed.

CARDIAC SAFETY AND EFFICACY PORTFOLIO:
- hERG - HEK
- Kv_{1.5} - CHO
- Kv_{1.3} - CHO
- Na_{1.5} - CHO / HEK
- K_{73} / mink - HEK
- Ca_{1.2} - HEK

More ion channel cell lines and assays including Na_{v} and CABA cell lines as well as TRP channels and P2RX receptors are available for screening service.

www.cytocentrics.com

Outsourcing ion channel screening
For safety and efficacy with premium data quality

Olaf Scheel
Andrea van Bergen
Gesa Rascher-Eggstein
Thomas Knott

CytoCentrics AG, Germany
ADDRESS: Joachim-Jungius-Str. 9 | D-18059 Rostock
PHONE: +49 (0)381 44 0 388 40 | FAX: +49 (0)381 44 0 388 47
MAIL: info@cytocentrics.com | WEB: www.cytocentrics.com

H &G SCREENING in HEK293 Instant Cells

Concentration response relationship for the potent hERG inhibitors E-4031 (left) and terfenadine (right) determined with the CytoPatch™ Instrument (grey symbols and curves). In comparison to data obtained with manual patch clamp recordings are depicted in red.

K_{v}1.5 AND K_{v}1.3 SCREENING WITH THE CYTOPATCH™ INSTRUMENT

Whole-cell K_{v}1.3 currents stably expressed in CHO-K1 cells measured with the CytoPatch™ Instrument (right). Concentration-response relationship for the inhibition of K_{v}1.3 currents by the K channel blocker 4-AP (left).

FAST LIGAND GATED ION CHANNELS

Single channel currents of human α7 nicotinic acetylcholine receptor stably expressed in CHO-K1 cells measured with the CytoPatch™ Instrument (left) and concentration-response curves for the agonist acetylcholine measured with the CytoPatch™ Instrument (right).

CARDIAC SODIUM CHANNEL Na_{v}1.5

Current-voltage relationship for human Na_{v}1.5 stably expressed in HeK293 cells measured with the CytoPatch™ Instrument. Cells were ramped from holding potential of -100 mV to 0 mV in 10 mV steps to test voltage from -100 to +40 mV in 5 mV increments.